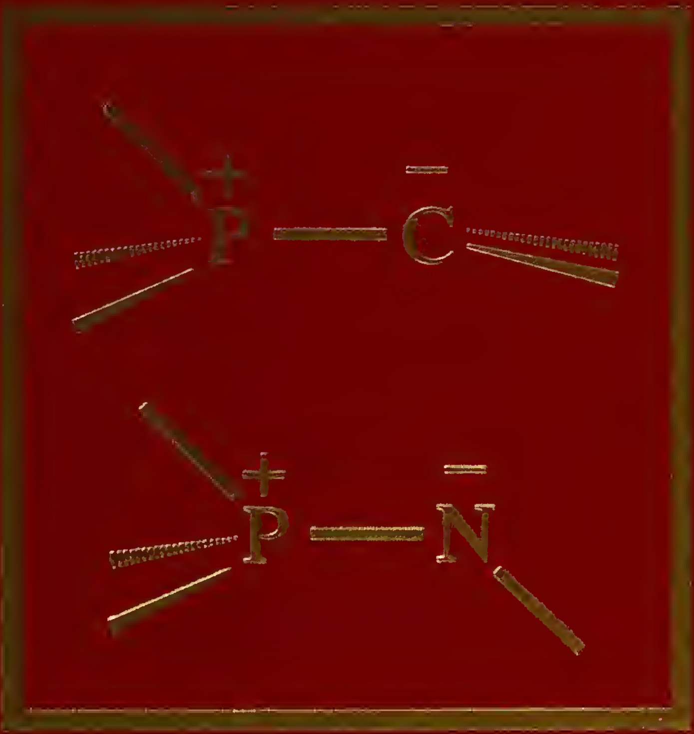
# YLIDES AND IMINES OF PHOSPHORUS



A. WILLIAM JOHNSON

# YLIDES AND IMINES OF PHOSPHORUS

# YLIDES AND IMINES OF PHOSPHORUS

**A. WILLIAM JOHNSON**
*The Chemistry Department*
*University of North Dakota*
*Grand Forks, North Dakota*

with special contributions by

**WILLIAM C. KASKA**
*Chemistry Department*
*University of California – Santa Barbara*
*Santa Barbara, California*

**K. ALEXANDER OSTOJA STARZEWSKI**
*Central Research Division*
*Bayer AG*
*Leverkusen, Germany*

and

**DAVID A. DIXON**
*Central Research and Development Department*
*E.I. DuPont de Nemours, Inc.*
*Wilmington, Delaware*

A Wiley-Interscience Publication
**JOHN WILEY & SONS, INC.**
New York • Chichester • Brisbane • Toronto • Singapore

This text is printed on acid-free paper.

***Library of Congress Cataloging in Publication Data:***

Johnson, A. William (Alyn William), 1933–
Ylides and imines of phosphorus/A. William Johnson, with special contributions by William C. Kaska, K. Alexander Ostoja Starzewski and David A. Dixon.
p. cm.
"A Wiley-Interscience publication."
Includes bibliographical references and index.
ISBN 0-471-52217-1 (alk. paper)
1. Organophosphorus compounds. 2. Ylides. 3. Imines.
4. Transition metal compounds. I. Title.
QD305.P46J64 1993
547′.07—dc20 92-39601

Printed in the United States of America

10 9 8 7 6 5 4 3 2 1

This monograph is dedicated to

***my parents***, Irene and Alyn Johnson, who provided the stimulus and opportunity for higher education

***my wife***, Joan, and my children, Pat, Nancy, Bob, and Kathy, who provided a wonderful and supportive family environment and the time for my scholarly pursuits

***my graduate students***, who provided the intellectual stimulation and the continuing motivation for me to exemplify scholarship for its own sake

***my university***, the University of North Dakota, which provided the opportunity and support for my resumption of scholarly pursuits after a hiatus in the halls of academic administration

# PREFACE

The first monograph on ylide chemistry, also written by this author, appeared in 1966 and included 840 references, including virtually every paper published on the topic, 544 of which dealt with the topics covered by this new monograph. Published 13 years after Georg Wittig discovered the reaction between phosphonium ylides and carbonyl compounds bearing his name, and six years after our discovery of the reaction between sulfonium ylides and carbonyl compounds to produce oxiranes, ylide chemistry was still a young field full of opportunity and with a great many unanswered questions. The intervening 27 years have seen a blossoming of research results in the field of ylide chemistry, including the filling of the gaps in knowledge revealed in that monograph, the discovery of new reactions, developing understandings of the mechanisms of many ylide reactions, application of ylides and imines to inorganic as well as organic chemistry, the discovery of considerable structural information, including that obtained from NMR spectroscopy, considerable attention by theoretical chemists, and elegant application of ylide chemistry to complex organic synthesis problems. So much knowledge has accumulated in these years that the time seemed appropriate to once again bring together the results of ylide chemistry research and produce a monograph which presents the field as it is today. This effort has two goals: to establish a new platform from which additional research can be launched and to make it easy for chemists to become familiar with the state of affairs in phosphorus ylide and imine chemistry.

The challenge of accomplishing these goals is immeasurably larger and more complex than it was 27 years ago! Accordingly, this monograph is devoted to the chemistry of the ylides and imines of phosphorus only, leaving the ylides of other heteroatoms to a later task. The magnitude of this task is indicated by the fact that this monograph alone contains over *3150* references, and those are only *selected* references!

It is the purpose of this monograph to present the current state of knowledge of the chemistry of phosphorus ylides and their nitrogen analogs, the imines. This purpose encompasses information on the preparation of such compounds, their molecular structure and physical properties, and their reactions with organic and inorganic substrates. Included are many examples of the application of ylides and imines in synthesis. Special features include chapters on theoretical descriptions of the bonding in ylides and the reactions of phosphorus ylides with transition metal compounds.

The authors have attempted to be encyclopedic with respect to the topics and chemistry covered, but not in citing all examples of every reaction. Neither is this book intended to be historic or chronologic. That information is available from the earlier (1966) monograph. Instead, this book is intended to be an up-to-date reference presenting the state of the art of ylide and imine chemistry of phosphorus, including the provision of references which will lead the interested reader into the pertinent literature for more details on any covered topic. The book is highly sectioned to assist the reader in locating topics and leading references.

It is hoped that this book will be of special use and interest to two different populations. The first are bench chemists and graduate students who need a reference to a particular application of ylide chemistry, or who need a simple means of obtaining an overview of ylides or imines of phosphorus. The second group are those who do research in ylide chemistry for its own sake and who wish to be brought up to date on some aspect of this chemistry. As was the case in the first monograph, it also is hoped that readers will be stimulated to conduct research that will "fill the gaps" in current knowledge laid bare by the presentations herein.

Attention is directed to two special items within this monograph. The first is a set of recommendations directed to both researchers who publish and primary journal editors to help systematize the nomenclature applied to the three named reactions – the *Wittig Reaction*, the *Wadsworth–Emmons Reaction*, and the *Horner Reaction*. These four names now are used in almost every possible combination to mean any one or several of the named reactions; there simply is no consistency of usage at present. Please refer to Page 314 for this author's recommendations and rationale, which have been sent to editors of major journals and to the editor of *Chemical Abstracts*. The second item is to advise readers that the Subject Index has been especially prepared to identify methods for synthesis of a wide variety of compounds using the reactions included within this monograph. Simply refer to the kind of compound desired, such as "Amines, allylic," for the application of ylides to its synthesis.

It is my fervent wish that this work will provide readers with a useful and stimulating book, easy access to helpful knowledge, and motivation for further research.

A. William Johnson

*Grand Forks, North Dakota*
*May 1993*

# ACKNOWLEDGMENTS

Many people and organizations have contributed directly or indirectly to the completion of this work, and their efforts are herewith gratefully acknowledged. Special thanks are due to Bill Kaska and David Dixon, who agreed to write special chapters on transition metal chemistry and theoretical treatments of ylide chemistry, respectively, and thereby contributed to the wholeness of the topical coverage. Thanks also are due to Alex Ostoja Starzewski for joining with Bill Kaska in preparing the transition metal chapter. The staff of the Chester Fritz Library of the University of North Dakota graciously provided office space and access to the collections during much of the writing and were immensely helpful in obtaining materials through interlibrary loan. The students and faculty of the Chemistry Department of the University of Massachusetts, Amherst, were gracious hosts for the spring semester of 1989 when the concept and broad outlines of this monograph took shape, in part through the opportunity to offer a special topics course on ylides. The University of North Dakota, and particularly the Chemistry Department, provided the intellectual environment and the time to concentrate on this large writing task. Finally, my wife put up with the major commitment of time and energy necessary for the completion of this task, time which could have been used in part for family activities. She understood that although this was a major task requiring long hours of hard work, I found the task enjoyable and intellectually rewarding.

Bill Kaska acknowledges the financial support of the Petroleum Research Fund of the American Chemical Society and the Army Research Office, Durham, for research on the transition metal chemistry of ylides. He also acknowledges the encouragement of his wife, Deborah, during the writing, as well as the assistance of his graduate and post-doctoral students, especially Dr.

Dennis Mitchell, in reading the entire manuscript. Professor Ekkehard Lindner and Dr. Hermann A. Mayer of the Anorganische Institut, University of Tubingen, are thanked for their hospitality, laboratory space, and facilities during the fall of 1991.

A. William Johnson

# CONTENTS

## 3 Introduction to Phosphonium Ylides 43

## 4 Preparation of Phosphonium Ylides 101

# LIST OF TABLES

# LIST OF FIGURES

# YLIDES AND IMINES OF PHOSPHORUS

# 1

# INTRODUCTION TO YLIDES AND IMINES

The chemistry of ylides, and of their nitrogen analogs the imines, is a phenomenon of the second half of the twentieth century. Although the first ylide appears to have been prepared almost a century ago,[1] and there were sporadic relevant experiments reported in the first half of this century, [2-4], ylide chemistry did not flower until the Nobel-Prize-winning work of George Wittig[5] and his students in 1953, resulting in the serendipitous discovery of the reaction bearing his name. The impact of the Wittig Reaction on synthetic organic chemistry has been monumental, being "of unmatched importance for specific introduction of carbon–carbon double bonds in a known location."[5] The discovery of that reaction led Wittig and many others to explore related chemistries and resulted in the field of knowledge presented in this monograph.

Why should ylide and related imine chemistry be of sufficient interest to warrant a monograph? The major reasons are that ylides have found use in a wide variety of reactions of interest to synthetic chemists, mainly organic but also inorganic in recent years, and the nature of ylide bonding and molecular structure have become fertile topics for study by those interested in unique molecules. The special and originally unexpected stabilization characteristic of many ylides and imines also has attracted attention and extrapolation. Bringing together and evaluating knowledge, perspectives, and questions from this diverse field, involving as it now does a variety of heteroatoms and of molecular fragments attached to the ylidic carbon or iminic nitrogen, should provide a new foundation from which further advances in the field may be expected. This was the experience following an earlier book by the author[6] and it is hoped that this history will repeat itself. Accordingly, this monograph is directed to two audiences, those who wish to use ylides to carry out synthetic chemistry and

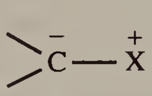
---

*Ylides and Imines of Phosphorus*, Edited by A. William Johnson.
ISBN 0-471-52217-1

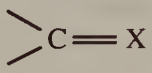
those who discover new ylides, explore their reactions and the mechanisms thereof, and shed light on the nature of ylide bonding.

This book does not present an historical and chronological development of the field of ylide and imine chemistry. Those interested in the chronological evolution of the field are referred to an earlier monograph by the author.[6] Instead, this book covers each topic as it exists today, regardless of when the knowledge became known, so that users of this chemistry might learn the "state of the art." However, many chapters include, in chronological order, a complete list of topical reviews at the beginning of the reference section. Each review reference is annotated briefly to assist readers in identifying sources of further information and in obtaining a perspective on the development of the field over time.

The general definition advanced for an ylide by this author[6] in 1966 seems to have withstood the test of time as evidenced by its continued use virtually unchanged.[7] A slight modification is suggested and shown below in italics as a result of the consideration of 1,3-dipolar compound chemistry. An ylide is hereby defined as **a substance in which a carbanion is attached directly to a heteroatom carrying a substantial degree of positive charge** ***and in which the positive charge is created by the sigma bonding of substituents to the heteroatom,*** as represented by **1**. The unique electronic and structural characteristic of ylides



**1**



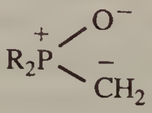
**2**

is the joining of two atoms to one another when they possess opposite charges and might be expected to show multiple bonding, as represented by **2**. The issue of the extent, if any, to which such multiple bonding exists has challenged ylide, theoretical, and structural chemists, and has provided the basis for numerous studies. **In this monograph the multiple bond drawing normally will be used in chemical formulae of ylides and imines for simplicity purposes only, and the use** ***does not*** **imply the specific nature of the C–X bond.**

Ylides and imines are known for a variety of heteroatoms, but the field now is so large that this book is restricted to those of phosphorus. The definition of ylides includes the most common kind, such as ordinary phosphonium ylides (**3**)

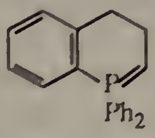
$$Ph_3\overset{+}{P} - \overset{-}{C}H_2$$

**3**

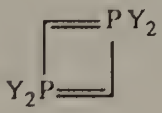


**4**

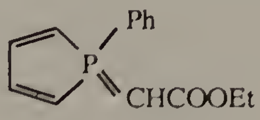
where the heteroatom formally carries a full unit positive charge. But the definition also includes substances in which the heteroatom carries less charge, such as those ylides based on the phosphinoxy group (**4**). Ylides resulting from the latter extrapolation are also discussed in this monograph. The phosphorus atom may be incorporated in a wide variety of structural environments (e.g., attached to alkyl, alkoxy, aryl, aza, and other groups), and even incorporated into ring systems such as **5**, **6**, and **7**. There is virtually no limit to the nature of the substituents that can be attached to the ylide carbon in **1**, and numerous examples are presented throughout this monograph.



**5**



**6**



**7**

This book also includes coverage of the chemistry of iminophosphoranes (e.g., **10**) which are isoelectronic with ylides and whose chemistry is very similar. For any molecular system in which it is possible to prepare an ylide, it is theoretically possible to prepare the corresponding imine, and in many instances the imines are easier to prepare and more stable. The same variety of heteroatom groups X are found in imines as in ylides.

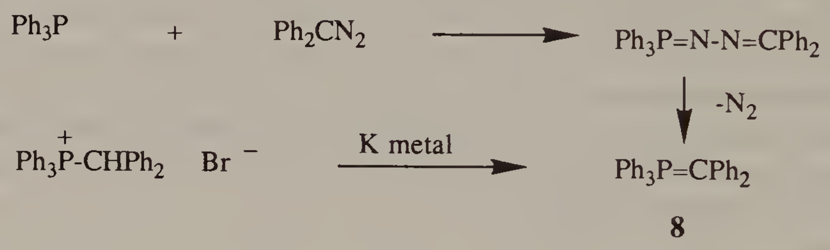
This book deals with ylide and imine chemistry of phosphorus and is organized into 14 chapters. It covers a theoretical description of the bonding in ylides (Chapter 2), the physical properties of phosphonium ylides (Chapter 3), the preparation of phosphonium ylides (chapter 4), the reactions of such ylides (Chapters 5–7), and a detailed treatment of the Wittig Reaction (Chapters 8 and 9). Chapters 10–12 deal with phosphonate, phosphinoxy, and other phosphorus carbanions, all of which exhibit chemistry similar to that of phosphonium ylides. Chapter 13 presents the chemistry of iminophosphoranes and related compounds. Chapter 14 discusses the emerging field of the reactions of ylides with transition metal compounds. Each chapter is highly sectioned to facilitate the location of detailed topics.

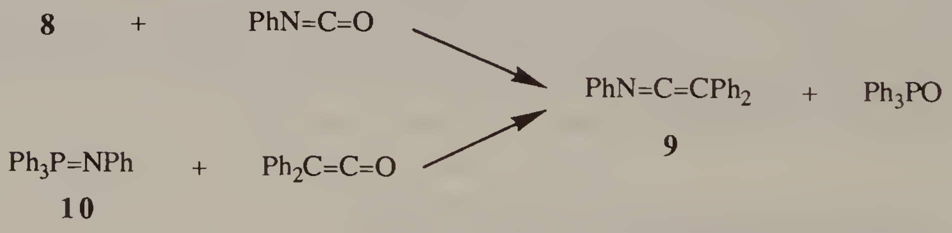
## 1.1 HISTORY OF YLIDES AND IMINES

Although the beginning of ylide chemistry must be traced to Michaelis and his students in 1894, they did not propose an ylide structure for the substances they prepared. Credit for the preparation and isolation of the first ylides and imines, and their recognition as such, must go to Staudinger and his students in 1919. It is for this reason that Wittig's elegant 1964 lecture illustrating the evolution of the Wittig Reaction was entitled "Variations on a Theme of Staudinger."[8] The historic era of ylide chemistry continued to 1953 when Wittig and his students discovered the Wittig Reaction. That year can be viewed as the beginning of modern ylide chemistry, and Wittig's publications ignited a flurry of research activity which has continued unabated to this day.

Michaelis and Gimborn[1] prepared the first phosphonium ylide, $(C_6H_5)_3P{=}CHCOOC_2H_5$, in 1894 by treating an aqueous solution of triphenyl-(carbethoxymethyl)phosphonium chloride with potassium hydroxide solution. They proposed a different structure for the substance, and it was left to Aksnes[9] in 1961 to demonstrate that it was an ylide. A similar scenario prevailed five years later when Michaelis and Kohler[10] prepared benzoyl ($R{=}C_6H_5CO{-}$) and acetyl ($R{=}CH_3CO{-}$) phosphonium ylides, $(C_6H_5)_3P{=}CH{-}R$, but this time it was left to Ramirez and Dershowitz,[11] 58 years later, to correctly identify the substances as ylides. Michaelis and his students did no significant ylide chemistry with these substances.

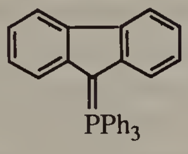
In 1919 Staudinger and Meyer[2] found that diazo compounds reacted with tertiary phosphines to form phosphinazines and that in one instance the azine would eliminate nitrogen to form the highly stabilized ylide (**8**), whose red crystals could be isolated and purified. Five years later another Staudinger student, Isler, reported in his dissertation that the same ylide could be obtained by reaction of the precursor phosphonium salt with metallic potassium.[12] The ylide (**8**) reacted with phenyl isocyanate to eliminate triphenylphosphine oxide and to form the ketenimine (**9**), the first example of a Wittig Reaction.[2] The same product was obtained by reaction of diphenylketene with the iminophosphorane (**10**),[13] obtained similarly by heating the product of the reaction of triphenylphosphine and phenyl azide, thereby eliminating nitrogen and affording the nitrogen analog (**10**) of an ylide (**8**). In 1922 another Staudinger student, Luscher, reported the successful "Wittig Reaction" of the ylide (**8**) with diphenylketene to produce tetraphenylallene.[14] Interestingly, the general nature of this reaction between ylides and carbonyl compounds to eliminate triphenylphosphine oxide



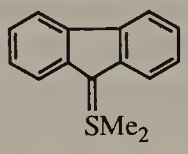


and form an olefin bond, the elaboration of which was to contribute to a Nobel prize, lay dormant for 30 years, until the 1950s, when modern ylide chemistry really began.

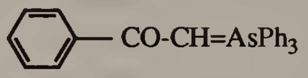
In those intervening years a number of isolated reports of ylides appeared in the literature. Coffmann and Marvel[4] repeated Isler's preparation of the stabilized ylide (**8**), but used butyllithium or trityl sodium as the base. They prepared, but did not isolate, ylides from alkyltriphenylphosphonium salts and found that the ylides hydrolyzed readily to form phosphine oxides. In 1930 Worrall,[15] unknowingly, probably prepared a phosphonium ylide by treating the precursor phosphonium salt with alcoholic KOH, as did Michaelis.[1] Schonberg and Ismail[16] claimed that a zwitterionic phosphonium salt was formed by reaction of triphenylphosphine with maleic anhydride, but Aksnes[17]showed in 1961 that it was a phosphonium ylide. Finally, Pinck and Hilbert[18] prepared and characterized triphenylphosphoniumfluorenylide (**11**), unsuccessfully sought by Staudinger and Meyer[19] using their phosphineazine pyrolysis method, by proton removal from the precursor salt using a base as weak as ammonium hydroxide, thereby providing an early indication of the unusual stability of some phosphonium ylides.



**11**



**12**



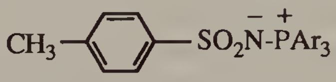
**13**

Ylides of other heteroatoms also made initial appearances in that 30-year span as well. Ingold and Jessop[20] prepared the first known sulfur ylide, dimethylsulfoniumfluorenylide (**12**), from the precursor sulfonium salt hoping, but failing, eventually to obtain difluorenylidene. No other sulfur ylide work was reported until the late 1950s. Only one instance of early work on arsenic ylides is known. Michaelis[21] reacted phenacyl bromide with triphenylarsine and obtained the arsonium salt, which he then treated with aqueous sodium hydroxide to afford a new substance which Krohnke[22] in 1950 showed to be the ylide (**13**).

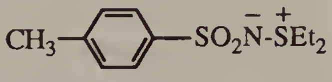
Nitrogen ylide chemistry began with Krohnke's 1935 report[3] that *N*-phenacylpyridinium bromide could be deprotonated readily with potassium carbonate to afford the pyridiniumphenacylide (**14**), which could be isolated, purified, and characterized. This was the first of a lengthy series of reports by Krohnke and his students elaborating much of the known pyridinium ylide chemistry. Pinck and Hilbert[23] prepared the pyridiniumfluorenylide in 1946.

The chemistry of the imines of various heteroatoms had its beginning in the 1920s. Staudinger and Meyer[2] were the first to prepare a phosphinimine, *N*-phenyliminotriphenylphosphine (**10**), by heating the adduct of phenyl azide and triphenylphosphine until it evolved nitrogen, which is still the method of choice for imine synthesis. Subsequently, Staudinger and Hauser[24] made a number of imines and elucidated a significant portion of their currently known chemistry, including numerous reactions with carbonyl compounds to form new C=N bonded substances, sometimes known as the aza-Wittig Reaction (e.g., conversion of **10** to **9**). Sixteen years later Mann and Chaplin[25] discovered that the reaction of chloramine-T with tertiary aryl phosphines produced *N*-tosyliminotriarylphosphines (**15**), a method still in limited use. Using the same method with triphenylarsine, they were able to obtain the first arsinimine, *N*-tosyliminotriphenylarsine.

**14**

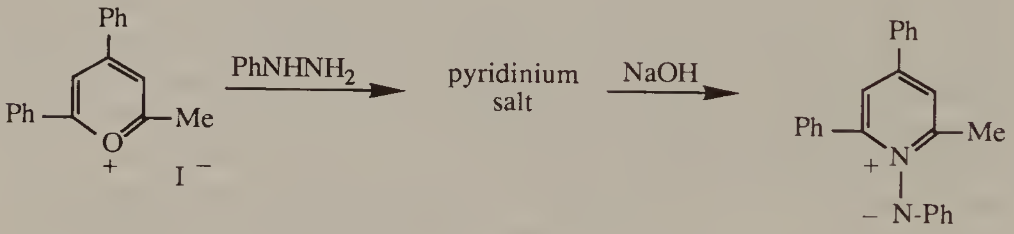


**15**



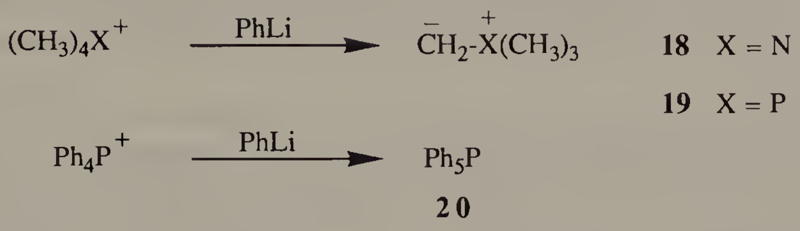
**16**

In 1922 Mann and Pope[26] prepared the first sulfimine (**16**) from the reaction of chloramine-T with diethylsulfide, and in 1927 Clarke et al.[27] explored the reaction and the imines further, realizing their similarity to sulfoxides and demonstrating their chirality. Tarbell and Weaver[28] were able to prepare the same kind of imines by dehydrating sulfoxides and *p*-toluenesulfonamides. Mann and Pope[26] failed in their attempt to prepare the first ammonium imines by reacting chloramine-T with amines, expecting reactions analogous to that found with sulfides, phosphines, and arsines. Instead, the first ammonium imines were prepared by Schneider from the reaction of pyryllium salts with phenylhydrazine, first in 1921[29] with an incorrect structural assignment, but corrected to the dark blue "anhydrobase," the imine (**17**), in 1924.[30]



**17**

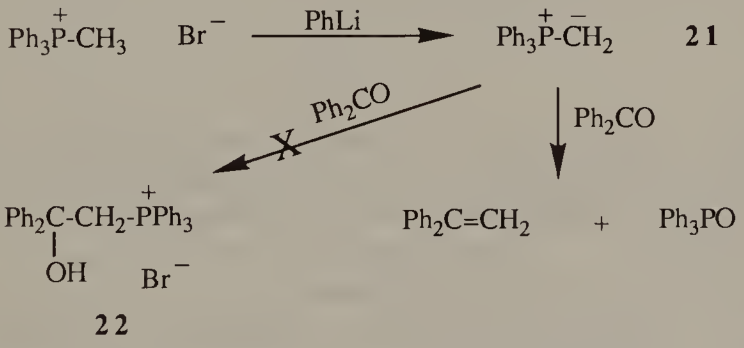
The modern era of ylide chemistry began with the resumption of the search for pentavalent group VA compounds. Schlenk[31] and Marvel[32] earlier had unsuccessfully attempted to prepare pentavalent nitrogen compounds by the reaction of strong carbanions with ammonium salts, hoping to form a new, and fifth, sigma bond about nitrogen in each case. Wittig and his students resumed this quest in the late 1940s and were able only to prepare, but not isolate, ammonium ylides such as **18**[33] from the reactions of ammonium salts with organolithium reagents. They were able to demonstrate the nucleophilicity of these "special carbanions," including their alkylation reactions with alkyl halides and their addition to carbonyl compounds to produce ammonium alcohols. Further, they coined the term “ylid” for these undesired “special carbanions.”



$$(CH_3)_4X^+ \xrightarrow{PhLi} \overset{-}{C}H_2\text{-}\overset{+}{X}(CH_3)_3 \qquad \mathbf{18}\ X = N \quad \mathbf{19}\ X = P$$

$$Ph_4P^+ \xrightarrow{PhLi} \underset{\mathbf{20}}{Ph_5P}$$

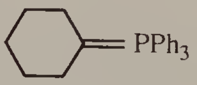
Continued lack of success in the pursuit of pentavalent nitrogen compounds led Wittig to shift his attention down the periodic table to phosphorus as a new target for pentavalency. Reaction of tetramethylphosphonium bromide with phenyllithium[34] afforded the phosphonium ylide (**19**) which demonstrated carbanionic behavior essentially identical to that of **18**. In an attempt to possibly stabilize the desired pentavalent phosphorus target compound (**20**), Wittig and Reiber[35] reacted phenyllithium with tetraphenylphosphonium chloride and thereby recorded the first synthesis of a phosphorus compound containing five organic substituents, pentaphenylphosphorus (**20**). Since they were able to obtain the desired pentavalent compound for a fully phenylated system, but not for a fully methylated system, they chose to explore the reaction of a mixed substituent system. Treatment of triphenylmethylphosphonium iodide with phenyllithium[36] did not afford methyltetraphenylphosphorus as desired, but instead afforded the yellow ylide (**21**) in solution. They proceeded as before to prove the existence of the ylide by various trapping reactions, including that with benzophenone, which regularly had afforded addition products (**22**). In this instance, however, no product corresponding to **22** could be found, and instead triphenylphosphine oxide (78%) and 1,1-diphenylethene (84%) were obtained.



These unsought products were the first obtained by the modern Wittig Reaction, and its discovery surely classifies as a serendipitous discovery, fitting elegantly the Horace Walpole definition of “a discovery, by accident, of things not sought for.”[37] Wittig and his students[38,39] proceeded in the next two years to elaborate this new reaction and demonstrate its exciting usefulness in preparing olefins devoid of contamination by positional isomers. The significance is well illustrated by the fact that a patent[40] was issued to BASF in 1954 covering the application of the Wittig Reaction to the total and commercial synthesis of Vitamin A, this reaction being used in the final olefin-forming step of the synthesis. The awarding of the Nobel Prize to Wittig in 1979, mainly for the research relating to the Wittig Reaction, is ultimate testimony to the significance of his work.[5]

This introductory chapter concludes with a brief discussion of the nomenclature of ylides and imines. The original term "ylid" was coined in the German language by Wittig[41] in 1944 by using the suffix "yl" to indicate an open valence, as with methyl, and the ending "id" to indicate anionicity , as with methanid or acetylid. Wittig later used the term "ylen" to represent the double bonded form of the ylide structure (**2**). *Chemical Abstracts* has determined that the anglicized form "ylide" should be used in the American literature, and the term "ylene" has virtually disappeared from use because its implication is too arbitrary for use in formal nomenclature. It is occasionally used generically when discussing the nature of ylide bonding.

Phosphonium ylides are named by at least three distinct systems: as derivatives of phosphoniumalkylides, phosphine-methylenes, or phosphorane ($PH_5$). For example, **23** could be named triphenylphosphoniumcyclohexylide, cyclohexylidenetriphenylphosphine, cyclohexyltriphenylphosphorane, or triphenylphosphoranylcyclohexane. Specific examples of ylide and imine nomenclature will be used throughout this monograph.



**23**

## REVIEWS

**1966** Johnson, A. Wm., *Ylid Chemistry*, Academic Press, New York. The first monograph to cover the entire field of ylide chemistry (all heteroatoms), including the Wittig Reaction, complete with historical developments.

**1967** Nesmeyanov, N. A., *Mendeleev Chem. J. 12*, 35–44. A review of phosphorus, arsenic, nitrogen, and sulfur ylide chemistry.

**1970** Lowe, P. A., *Chem. Ind.*, 1070–1079. Review of ylides of phosphorus, arsenic, antimony, nitrogen, and sulfur.

**1975** Wittig, G., *J. Organomet. Chem.*, *100*, 279–287. Broad review of the chemistry of nitrogen, phosphorus, and sulfur ylides.

**1983** Morris, D. G., *Recent Advances in the Chemistry of Ylides in Survey of Progress in Chemistry*, G. G. Wubbels, Ed.; Butterworths: London. Vol. 10, pp. 189–257. Review of ylide chemistry by kind of chemistry (e.g., preparations) rather than by element.

**1984** Lloyd, D., *Non-Benzenoid Conjugated Carbocyclic Compounds*, Elsevier Press, Amsterdam. pp. 32–46. A review of the chemistry of various 'onium cyclopentadienylides.

## REFERENCES

[1] Michaelis, A.; Gimborn, H. V. *Chem. Ber.* **1894**, *27*, 272.
[2] Staudinger, H.; Meyer, J. *Helv. Chim. Acta.* **1919**, *2*, 635.
[3] Krohnke, F. *Chem. Ber.* **1935**, *68*, 1177.
[4] Coffmann, D. D.; Marvel, C. S. *J. Am. Chem. Soc.* **1929**, *51*, 3496.
[5] See Vedejs, E. *Science* **1980**, *207*, 42–44 for a review of Wittig's prize-winning work. Wittig's own Nobel lecture was reprinted in *Science*, **1980**, *210*, 600–604.
[6] Johnson, A. Wm., *Ylid Chemistry*; Academic: New York, 1966.
[7] Morris, D. G. *In Survey of Progress in Chemistry*; Wubbels, G. G., Ed.; Academic: New York, 1983; p. 189.
[8] Wittig, G. *Pure Appl. Chem.* **1964**, *9*, 245.
[9] Aksnes, G. *Acta Chem. Scand.* **1961**, *15*, 438.
[10] Michaelis, A.; Kohler, E. *Chem. Ber.* **1899**, *32*, 1566.
[11] Ramirez, F.; Dershowitz, S. *J. Org. Chem.* **1957**, *22*, 41.
[12] Isler, H. Dissertation at ETH, Zurich, **1924**.
[13] Staudinger, H.; Meyer, J. *Chem. Ber.* **1920,** *53*, 72.
[14] Luscher, G. Dissertation at ETH, Zurich, **1922.**
[15] Worrall, D. E. *J. Am. Chem. Soc.* **1930,** *52*, 2933.
[16] Schonberg, A.; Ismail, A. F. A. *J. Chem. Soc.* **1940**, 1347.
[17] Aksnes, G. *Acta Chem. Scand.* **1961**, *15*, 692.
[18] Pinck, L. A.; Hilbert, G. E. *J. Am. Chem. Soc.* **1947**, *69*, 723.
[19] Staudinger, H.; Meyer, J. *Helv. Chim. Acta* **1919**, *2*, 619.
[20] Ingold, C. K.; Jessop, J. A. *J. Chem. Soc.* **1930**, 713.
[21] Michaelis, A. *Liebigs Ann. Chem.* **1902,** *321*, 174.
[22] Krohnke, F. *Chem. Ber.* **1950**, *83*, 291.
[23] Pinck, L. A.; Hilbert, G. E. *J. Am. Chem. Soc.* **1946**, *68*, 2011.
[24] Staudinger, A.; Hauser, E. *Helv. Chim. Acta* **1921**, *4*, 861.
[25] Mann, F.; Chaplin, E. J. *J. Chem. Soc.* **1937**, 527.
[26] Mann, F.; Pope, W. J. *J. Chem. Soc.* **1922**, *121*, 1052.
[27] Clarke, S. G.; Kenyon, J.; Phillips, H. *J. Chem. Soc.* **1927**, 188.
[28] Tarbell, D. S.; Weaver, C. *J. Am. Chem. Soc.* **1941**, *63*, 2939.
[29] Schneider, W.; Seebach, F. *Chem. Ber.* **1921**, *54*, 2285.
[30] Schneider, W. *Liebigs Ann. Chem.* **1924**, *438*, 115.
[31] Schlenk, W.; Holtz, J. *Chem. Ber.* **1916**, *49*, 603.
[32] Marvel, C. S.; Hager, F. D. *J. Am. Chem. Soc.* **1926**, *48*, 2689.
[33] Wittig, G.; Wetterling, M. H. *Liebigs Ann. Chem.* **1947**, *557*, 193.

[34] Wittig G.; Rieber, M. *Liebigs Ann. Chem.* **1949**, *562*, 177.

[35] Wittig G.; Rieber, M. *Liebigs Ann. Chem.* **1949**, *562*, 187.

[36] Wittig, G.; Geissler, G. *Liebigs Ann. Chem.* **1953**, *580*, 44.

[37] Roberts, R. M., *Serendipity: Accidental Discoveries in Science*; Wiley: New York, 1989.

[38] Wittig, G.; Schollkopf, U. *Chem. Ber.* **1954**, *87*, 1318.

[39] Wittig, G.; Haag, W. *Chem. Ber.* **1955**, *88*, 1654.

[40] Wittig, G.; Pommer, H. Ger. Patent 32741 IVB/120, 1954.

[41] Wittig, G.; Felletschin, G. *Liebigs Ann. Chem.* **1944**, *555*, 133.

# 2

# THEORETICAL DESCRIPTION OF THE BONDING IN YLIDES

DAVID A. DIXON

The electronic structure of simple ylides has been of great interest not only because of the importance of these compounds as synthetic reagents but also because of their unique electronic structure. An ylide can be considered as an isomer of a stable species where a "zwitterionic" structure is generated by $H^+$ transfer from one group to another, as reflected in the simplest phosphorus case (Eq. 2.1). The molecule on the left is the simple methyl phosphine, whereas its

$$CH_3\text{-}PH_2 \longrightarrow \overset{-}{C}H_2\text{-}\overset{+}{P}H_3 \qquad (2.1)$$

isomer is a phosphonium ylide containing a carbon whose normal valence can only be satisfied by placing a negative charge at this center, and containing a phosphorus which has more than the usual number of bond pairs, necessitating a positive charge in a Lewis structure. However, through this process a zwitterion has been created with the two charged centers adjacent to one another, and this may lead to changes in the normal Lewis picture of the bonding. Because the phosphorus group is now formally cationic, it will have very stable unoccupied molecular orbitals (UMOs), including the 3*d* and the P–H $\sigma^*$ orbitals. The carbon as an anion will have a very high energy highest occupied molecular orbital (HOMO) with low ionization potential, and this orbital can donate into the available UMOs on phosphorus, which is referred to as back-bonding. This back-bonding could potentially lead to a shortening of the P–C bond. The mixing of the lone pair on carbon with the P–H $\sigma^*$ orbitals has been called negative hyperconjugation[1] and is a general manifestation of the anionic hyperconjugation found in fluorinated carbanions.[2-4] The ability of the carbon group to transfer electron density will depend on the substituents on the

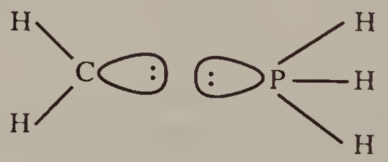
---

*Ylides and Imines of Phosphorus*, Edited by A. William Johnson.
ISBN 0-471-52217-1

carbon and on the ability of phosphorus to accept the density, the latter affected also by its substituents.

Because it is possible to view the ylide as resulting from an internal proton transfer, estimates can be made of the heat of formation by examining the relative energies of the isomers (i.e., the energy of reaction, Eq. 2.1). The energy of the reaction involves components from breaking a C–H bond in a heterolytic fashion to form $H_2C^-$ and $H^+$ and the $-PH_2$ group accepting a proton. The first process is the gas-phase acidity and the second is the gas-phase proton affinity. This process always should be endothermic as the gas-phase acidity is always larger than the proton affinity. The acidity of $CH_4$ (proton affinity of $CH_3^-$) is greater than 400 kcal/mol and the proton affinities of neutral bases are 170–220 kcal/mol.[5]

At this point it is appropriate to consider further the nature of the simple ylide $CH_2{=}PH_3$ and consider the bonding if there were no charge on the carbon and phosphorus atoms. In this case the molecule now resembles a lowest-energy singlet carbene bonded to a neutral phosphine (**1**). (As we have not considered geometry at this point, we cannot know which singlet state of the carbene is actually present.) Such a molecule would certainly dissociate as the two lone pairs directly interacting will lead to a strong repulsion and the energy of this dissociation also must be considered when examining the stability of the gas-phase free ylide. The proton transfer channel (Eq. 2.1) must be lower in energy than the channel which leads to formation of the singlet carbene and phosphine (Eq. 2.2).



**1**

$$\overset{-}{C}H_2\text{-}\overset{+}{P}H_3 \longrightarrow CH_2{:} \; + \; {:}PH_3 \qquad (2.2)$$

Another alternative is to place the lone pair on the carbon in an out-of-plane orbital so that the lone pair on phosphorus can donate into an empty orbital on carbon. However this would lead to a very high-energy carbene. For $CH_2$ this state is the second $^1A_1$ state and is ~ 90 kcal/mol higher in energy[6] and would not lead to a stable structure for the ylide. This was noted by Trinquier and Malrieu,[7] who studied the dissociation of $CH_2PH_3$ to $PH_3$ and $CH_2{:}^1A_1$. A state correlation diagram can be drawn which shows how the various orbitals correlate on dissociation (Fig. 2.1).

Analysis of the basic properties of these potentially unstable systems, most of which have not been characterized or determined experimentally, necessitates the application of theoretical methods. Ab initio molecular orbital (MO) theory can be used to describe the electronic structure of novel structures such as the

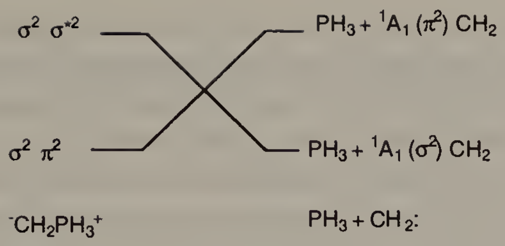


**Figure 2.1** State correlation diagram for dissociation of $CH_2PH_3$ to $PH_3 + CH_2$. The σ-orbital for the ylide is the P–C bond which correlates with the lone pair on $PH_3$. The π-orbital of the ylide is the lone pair on the carbanion center which delocalizes into the phosphorus and correlates with the out-of-plane *p*-orbital of $CH_2$. The σ* orbital is the P–C antibonding orbital which correlates with the in-plane $sp^2$ lone pair orbital of $CH_2$. Reprinted with permission from *J. Am. Chem. Soc.* **1979**, *101*, 7169. Copyright 1979 American Chemical Society.

simplest ylides. Although empirical–semiempirical MO methods such as extended Hückel[8,9] can be used to make qualitative analyses, the use of more rigorous methods is desirable to account for the geometry and the energetics of ylide systems.

## 2.1 THEORETICAL METHODS

Although there are many excellent texts and reviews on ab initio molecular orbital theory,[10,11] it is useful to review a few of the basic concepts of the theoretical methodology to show how they can be applied to ylides. The technique employed is the solution of the Schrödinger equation (Eq. 2.3) for

$$H\Psi = E\Psi \tag{2.3}$$

$$H = -\sum_i \frac{\nabla_i^2}{2} - \sum_i \sum_A \frac{Z_A}{R_{iA}} + \sum_i \sum_{j>i} \frac{1}{r_{ij}} \tag{2.4}$$

electronic motion in the Born–Oppenheimer (fixed nuclei) approximation, using the Hamiltonian (Eq. 2.4). For this expression capital letters correspond to nuclei and lowercase letters correspond to electrons, with $R_{iA}$ being the electron-nuclear distance and $r_{ij}$ the distance between two electrons. The first term corresponds to the kinetic energy of the electrons, which is repulsive, and the second term corresponds to the nuclear attraction energy, which is the only stabilizing energy term. The last term corresponds to the electron repulsion. A final term needs to be added to the energy, the nuclear repulsion energy, but this can be evaluated by classical electrostatics because it does not involve the electronic motion. To perform the calculations the wave function is expanded in a set of atomic orbitals (AOs) called basis functions.[12] These basis functions are formed from Gaussian-type orbitals (GTOs) or sums of such orbitals. The largest part of the computation of the energy is the calculation of the two electron integrals which determine the mutual repulsion energy of the electrons. This part of the calculation scales as $N^4$ where $N$ is the number of basis functions, and this contributes significantly to the computer requirements of the computation. The Hamiltonian matrix is constructed following the pioneering work of Roothaan,[13] and a variational approach is used to find the minimum energy. An $N \times N$ matrix is constructed and diagonalized a number of times until the wave function does not vary between cycles by more than a prescribed amount. This yields an electronic energy for a given nuclear configuration (the only inputs are the atomic coordinates and the sets of atomic orbitals for each atom). This approach to determining the energy is the Hartree–Fock Self-Consistent Field (HF–SCF) method.

The basis sets employed in the calculations are constructed from Gaussian-type functions. Although the basis sets should have an exponential in $r$ (from the exact solution of the Schrödinger equation for the hydrogen atom) as opposed to $r^2$, as used for GTOs, the integrals over GTOs are much easier to calculate and are usually employed in molecular calculations. However, a significant number of GTOs are used in order to properly treat the region near the nuclei. These basis functions are usually grouped together (contracted) to reduce the size of the matrix that needs to be diagonalized. The number of contracted basis functions (AOs) for a given atom is based on the electron configuration of the atom. The minimum number of functions needed to describe an atom is the number of atomic functions given by the Periodic Table. For carbon with electron configuration $1s^2$, $2s^2$, $2p^2$, such a minimum basis set has $1s$, $2s$, $2p_x$, $2p_y$, and $2p_z$ orbitals. For the calculations needed to describe the ylides, the number of basis functions on all atoms are doubled, leading to a double zeta basis set. This basis set then is augmented by additional functions with a different angular component. These polarization functions typically have an orbital angular momentum number one higher than the highest in a minimum basis set. For hydrogen, a set of $p$ functions is employed, whereas for carbon or phosphorus a set of $d$ functions is employed. In some cases, because of the partial negative ion character of the carbon, diffuse $s$ and $p$ functions have been added to the carbon. For calculating the electronic properties of ylides, the minimum basis set that can be used to provide at least semiquantitative information is a double zeta basis augmented by polarization functions on the two zwitterionic atoms. The expansion of the basis set in terms of orbitals is called the one-particle expansion and, of course, truncations are made in this space as a finite basis set is used.

Although the HF–SCF wave function provides a very good description of the behavior of the electrons in a molecule, especially with a large enough basis set, it does suffer from one inherent approximation. The form of the Hamiltonian (Eq. 2.4) shows that it is solved for the potential of a given electron in the average field of the other $n - 1$ electrons. Thus any pair of electrons can get too close, leading to the correlation energy problem. This becomes clear by studying the behavior of two electrons in a given orbital. According to the Pauli Principle, the two electrons can have the same quantum numbers as long as the spin quantum numbers are opposite, which allows the electrons to occupy the same spatial area if interaction forces are ignored. Of course the interaction forces cannot be ignored, because classical physics shows that the electrons repel each other and, in fact, two electrons at the same spatial position would have an infinite repulsion. Thus the motion of the two electrons is correlated since the two electrons are avoiding each other, leading to the term *correlation energy.* Correcting the interactions of the electrons with each other is known as the *n*-particle problem. Thus the size of the basis set (one-particle problem) and the correlation energy (*n*-particle problem) treatment must be considered when performing an ab initio MO calculation of the electronic structure of a molecule.

There are a number of ways to account for the correlation energy, the two most prominent ones being configuration interaction (CI) and many-body perturbation methods. These methods can be extremely expensive computationally. For example, CI calculations including all single and double excitations scale as $N^6$ and also scale with the number of electron pairs. The cheapest computational method for treating the correlation energy is the second-order Møller–Plesset (MP2) method[14] which scales as $N^5$. The MP2 correction can provide a good estimate of the correlation energy corrections for many systems and is size consistent,[15] which is important when dealing with a large number of electron pairs. Higher-order terms can be included in the perturbation energy expansion and these lead to the quantities MP3, MP4, and so on.

One other way to consider the electronic wave function is to use methods based on multiconfiguration self-consistent field (MCSCF) techniques. In the Hartree–Fock approach, a single wave function (a Slater determinant) is used and coefficients are optimized in the sum of atomic orbitals that make up a molecular orbital. In the simplest CI calculation, the wave function is represented as a sum of Slater determinants (Eq. 2.5) formed by excitation from

$$\Psi = \sum_i c_i \Phi_i \tag{2.5}$$

the Hartree–Fock determinant. The coefficients $c_i$ are optimized in the sum, but the coefficients in each $\Phi_i$ are not varied. An even better solution optimizes both sets of coefficients simultaneously, leading to MCSCF methods, but this is extremely expensive computationally. A more restricted form of the MCSCF wave function is the general valence bond (GVB)[16,17] wave function, which incorporates some of the features of the MCSCF wave function, including proper dissociation of the electron pair in a bond, but is not so computationally expensive. Furthermore, it allows more chemical insight into the bonding. As a simple example consider the $\sigma$ bonding orbital for $H_2$. The MO is $\sigma^2\alpha\beta$ where there are two electrons with opposite spin in a single MO. The simplest GVB wave function for this system is $\sigma_\alpha\sigma_\beta(\alpha\beta-\beta\alpha)$, which incorporates the best features of both MO and valence bond methods. As shown here, a GVB orbital will have one electron in $\sigma_\alpha$ and one in $\sigma_\beta$ with both electrons spin coupled to form a singlet. A GVB wave function accounts for only part of the correlation energy and the wave function can be improved by performing a CI calculation.[18] Both MP*n* and GVB/CI results will be discussed.

At this point the energy at a single nuclear configuration can be evaluated. However, more than the energy of a given nuclear configuration is of interest as the initial nuclear configuration may be simply a guessed structure if an experimental structure is not available. Also, to calculate relative energies, an internally consistent set of calculations is needed, requiring the optimum theoretical structure to be determined, normally by using analytic gradient methods. The set of first derivatives of the energy with respect to the $3n$ nuclear coordinates is required. One of the great triumphs of modern quantum chemistry has been the development of analytic derivative methods.[10,19,20] When coupled with modern computers, the ability to study the electronic structure of novel molecular systems has been revolutionized.

The determination of a zero gradient for a structure does not guarantee that the structure is a minimum. For example, symmetry constraints can force the structure to have a zero gradient but not be a minimum. Thus, it is also important to evaluate the matrix of second derivatives[21,22] to determine the curvature of the potential energy surface in this region. If all of the directions of curvature are positive, the structure is a minimum on the potential energy surface. (This does not guarantee that the structure is at the global minimum, but that point is not important for this discussion.) A transition state is defined as a structure with a zero gradient and one negative direction of curvature which corresponds to an imaginary frequency. The second derivative matrix can be converted into a force constant matrix, which can then be transformed into a set of harmonic vibrational frequencies. The set of vibrational frequencies describes the motions of the molecule due to its interaction with infrared radiation and also can be used to calculate the zero-point energy of the molecule.

The calculation of a relative energy is done today with the following prescription. The atomic coordinates are generated, usually with some sort of graphics interface. A basis set for each atom is chosen and an initial energy is obtained. The geometry of the molecule is then optimized using analytical gradient methods. At the conclusion of the optimization, a second derivative calculation is done to ensure that the structure is at a minimum or is a transition state, if that is what is required. If not, the structure is distorted in the appropriate direction and is reoptimized.

## 2.2 ENERGETICS

The energetics associated with the ylides, beginning with the model phosphonium ylide, are considered first. The results for a variety of basis sets and levels of correlation correction are shown in Table 2.1.[23] These results do not depend strongly on whether there are polarization functions on H or on the correlation energy method for the energy of the ylide relative to methyl phosphine. The best calculation is at the MP4 level with the largest basis set [6-311G (df, p)]. The authors also calculated the dissociation energy channel to $PH_3 + CH_2$: (Eq. 2.2) and it is clear that the ylide is much lower in energy than the dissociation

**TABLE 2.1** Energies Relative to $PH_2CH_3$[23a]

| | $PH_3CH_2$ | TS[b] | $CH_2{:} + PH_3$[c] | $CH_2PH_2\cdot + H\cdot$ |
|---|---|---|---|---|
| HF/6-31G* | 59.0 | 109.9 | 104.2 | 82.2 |
| MP2/6-31G* | 56.9 | 92.7 | 125.2 | 98.7 |
| MP3/6-31G* | 59.0 | 95.3 | 120.0 | 98.7 |
| HF/6-31G** | 58.3 | 108.0 | 103.5 | 82.9 |
| MP2/6-31G** | 55.6 | 124.3 | | |
| MP3/6-31G** | 58.3 | 93.7 | 119.3 | 99.4 |
| MP4/6-31G** | 56.9 | 118.8 | | |
| MP2/6-311G (df, p) | 53.3 | 127.9 | | |
| MP4/6-311G (df, p) | 54.5 | 122.4 | | |

[a] Energies are in kilocalories per mol.

[b] TS = transition state for $H^+$ transfer for Eq. 2.1.

[c] $^1A_1$ state of $CH_2{:}$.

channel. It is interesting to note that breaking the P–H bond is a lower-energy process than breaking the P–C bond for the ylide. The transition state for proton transfer from methyl phosphine to form the ylide was also calculated and it is clearly higher in energy than the ylide. Thus the ylide is a stable species. The energetics are summarized in Figure 2.2.[23,24] Trinquier and Malrieu[7] have

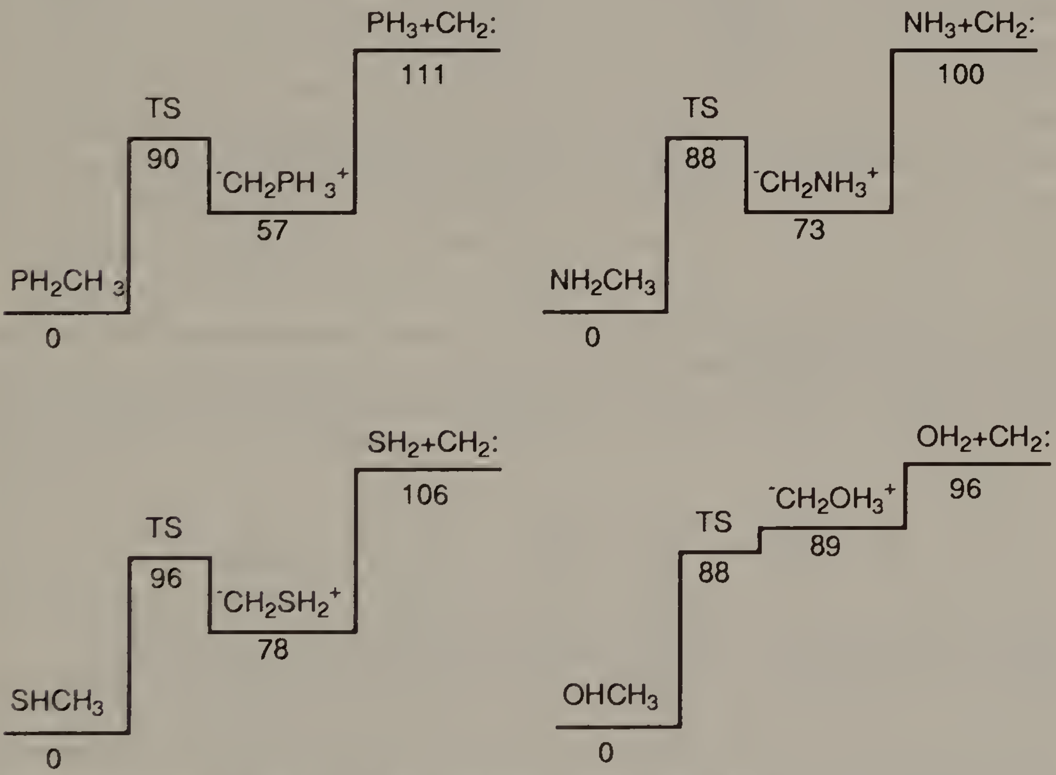


**Figure 2.2** Energy diagrams for ylide formation from MP3/6-31G** calculations. Energies in kilocalories per mole. Reprinted with permission from *J. Am. Chem. Soc.* 1987, 109, 2250. Copyright 1987 American Chemical Society.

shown that the $CH_2$: will add directly to $PH_3$ to form an ylide via a path where the $CH_2$: initially approaches perpendicular to the $C_{3v}$ axis and then, as it starts to back-bond, the $CH_2$ group rotates up so that it achieves a near planar structure. Nguyen and Hegarty[25] also studied the path for internal proton transfer in the phosphonium ylide at the MP4SDQ/6-31G** level and obtained results similar to those of Yates et al.[23] Nguyen and Hegarty showed a correlation between the magnitude of the imaginary transition state frequency and the free energy of activation.

The energetics for the internal proton transfer for a set of simple model ylide compounds involving phosphorus, nitrogen, sulfur, and oxygen, and represented by reactions 2.1, 2.2 and 2.6 through 2.8, respectively, are shown in Table 2.2.[26,27] The energies of the stable isomers were calculated from ab initio

$$CH_3\text{-}NH_2 \longrightarrow \overset{-}{C}H_2\text{-}\overset{+}{N}H_3 \longrightarrow CH_2: + :NH_3 \qquad (2.6)$$

$$CH_3\text{-}SH \longrightarrow \overset{-}{C}H_2\text{-}\overset{+}{S}H_2 \longrightarrow CH_2: + :SH_2 \qquad (2.7)$$

$$CH_3\text{-}OH \longrightarrow \overset{-}{C}H_2\text{-}\overset{+}{O}H_2 \longrightarrow CH_2: + :OH_2 \qquad (2.8)$$

molecular orbital theory[26,27] and the dissociation energies were calculated from experimental data.[28] The geometries used in the earlier work[26,27] were optimized numerically by calculating energies on a selected grid as analytic gradient methods were not widely available at this time. The energetics of the internal proton transfer reaction are quite positive and the correlation energy corrections are not large. The least amount of energy is required for the formation of the model phosphonium ylide and the most energy is required to form the oxonium ylide. How do these energies compare with the dissociation energies for the second part of the reaction, the formation of the singlet carbene? As

**TABLE 2.2 Energies of the Ylide ($CH_2XH$) and the Dissociation Channel for Formation of the Carbene Relative to the Nonzwitterionic Isomer ($CH_3X$)[a]**

| | SCF[26,27] | GVB[27] | POL-CI[27] | SCF[27,b] | MP2[b] | ZPE[b,c] | POL-CI + ZPE[d] | MP4[23] | MP4[23] + ZPE[e] | Dissociation[b,f] |
|---|---|---|---|---|---|---|---|---|---|---|
| P | 57.5 | 57.1 | 52.5 | 55.9 | 53.5 | – 1.9 | 50.6 | 54.5 | 52.6 | 114.0 |
| N | 68.7 | 67.7 | 66.3 | 68.5 | 68.3 | – 0.5 | 65.8 | 66.9 | 66.2 | 95.9 |
| S | 81.7 | 83.8 | 82.9 | 79.6 | 74.2 | – 2.1 | 80.8 | 75.5 | 73.9 | 101.9 |
| O | 86.5 | 88.5 | 92.8 | 82.1 | 92.7 | – 4.1 | 88.7 | 86.3 | 83.9 | 91.7 |

[a] Energies are given in kilocalories per mole. References are cited with the column headings.

[b] Calculations done expressly for this chapter with a polarized double zeta basis set. Basis sets from reference 6.

[c] Zero-point energy in kilocalories per mole scaled by 0.9 to account for correlation energy and anharmonicity corrections.

[d] ZPE correction from previous column.

[e] ZPE correction from reference 23.

[f] Dissociation channel to form $PH_3 + {}^1A_1CH_2$:; $\Delta H_f^0$ (products) from experimental data.

noted in Table 2.2, these calculations show that it is easiest to form the carbene in the case of oxygen ylide decomposition, followed by nitrogen, and then the ylides from the second-row atoms sulfur and phosphorus. The most stable ylide in terms of the internal proton transfer process, $PH_3CH_2$, is least able to form a carbene.

As discussed above, the ability of the group to capture the proton should be related to its stability. The experimental proton affinities[28] of the parent hydrides and the corresponding methyl derivatives are shown in Table 2.3. Based on these data, it would be expected that the most stable ylide would be the ammonium and the least stable the oxonium. This, of course, ignores any electron density transfer. It is known that the phosphonium ylide is more stable than the ammonium ylide, and both of these ylides are more stable than the sulfonium or the oxonium ylides. The proton affinity model is just one aspect of the more general case of nucleophilicity. Phosphorus is more nucleophilic than sulfur, so it is not surprising that it forms a more stable species with a $CH_2^-$ group.

**TABLE 2.3 Proton Affinities in Kilocalories per Mole**[a]

| X | $XH_n$ | $XMe_n$ |
|---|---|---|
| P | 188.6 | 204.1 |
| N | 204.0 | 214.1 |
| S | 170.2 | 187.4 |
| O | 166.5 | 181.9 |

[a] Data taken from reference 28. Although there are more recent values in reference 5, the data in reference 28 are more accessible and suffice for this purpose.

As shown in Figure 2.2, there are significant barriers to rearrangement of the phosphorus, nitrogen, and sulfur ylides back to their nonzwitterionic counterparts. The largest barrier to transfer the $H^+$ from the ylide heteroatom back to the carbanion is for the phosphonium ylide (33 kcal/mol relative to the ylide), followed by the sulfonium (18 kcal/mol) and the ammonium (15 kcal/mol) ylides.

The oxonium ylide has no barrier to reversion to methanol and the stability of the ylide is interesting to consider. At the Hartree–Fock level the ylide is a minimum, but at the correlated MP3 level and including zero point energy corrections the minimum disappears and there is no barrier to rearrangement.[23, 29, 30]. At the MP4 level with a large basis set, the oxonium ylide is stable by about 1 kcal/mol with respect to the transition state.[23] The technique of neutralization–reionization mass spectrometry (NRMS) has been used to infer the existence of the oxonium ylide with a lifetime of about $10^{-6}$ s.[31–33] However, there is really no direct, unequivocal evidence for the existence of the isolated oxonium ylide. Oxonium ylides have been inferred as intermediates if the carbanion is stabilized and if the substituents are not good leaving groups.[34] The instability of the naked oxonium ylide is not surprising as there are two energetic features working against it: (1) a low ability of the oxygen to accept a proton, and (2) a low energy channel for formation of a singlet carbene.

The possibility of forming ylides derived from the simplest halogens has been addressed both theoretically[23,35] and experimentally[31,34] for the fluoronium and chloronium ylides. The highest level theoretical results[23] show that the chloronium ylide $CH_2ClH$ is a stable structure with a long C–Cl bond (2.373 Å at the MP4/6-31G* level) as compared to that for $CH_3Cl$ (1.778 Å calculated at the MP2 level). The calculations suggest that the chloronium ylide is stable by 4.3 kcal/mol with respect to dissociation to HCl and $CH_2$: and is 12 kcal/mol below the transition state for rearrangement to $CH_3Cl$. The stability of this structure is in accord with NMRS results[31] which show that a significant fraction of the chloronium ylide lives for $10^{-6}$ s. Stabilized chloronium ylides have been isolated[34].

The fluoronium ylide is predicted not to form.[23,35] No minimum was found at the Hartree–Fock or correlated levels for the ylide $CH_2FH$. The only possible structure is the one formed by hydrogen bonding of HF to methylene. This structure is only stable by 1.5 kcal/mol with respect to the barrier to rearrangement to $CH_3F$. As in the case of the oxonium ylide, NRMS experiments[31] suggest that the ylide can be formed in the gas phase.

Stabilized iodonium ylides are well known[36] and bromonium ylides also have been prepared and isolated.[34,37]

## 2.3 MOLECULAR GEOMETRIES

Before proceeding to a more detailed discussion of the electronic structure, it is necessary to examine the geometries of the simplest ylides. Geometry parameters of the simple model ylides ($CH_2XH \leftrightarrow {}^{-}CH_2XH^{+}$) of phosphorus ($X = PH_2$), nitrogen ($X = NH_2$), sulfur ($X = SH$), and oxygen ($X = OH$), as calculated with a polarized double zeta basis set, are given in Table 2.4 and correspond to the structures in Figure 2.3. The structure of the phosphonium

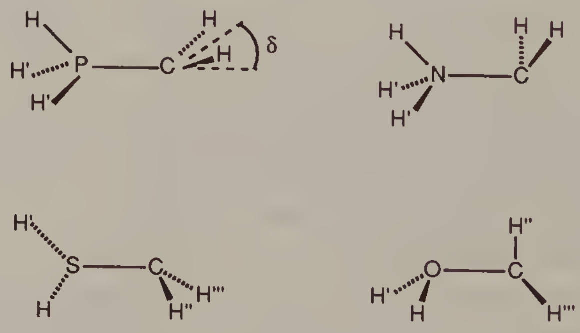


Figure 2.3 Molecular conformations of optimized ylide structures.

**TABLE 2.4 Molecular Geometries of $CH_3X$ and $CH_2XH$[a]**

| Molecule | $r$(X–C) | $q$(HCH) | $q$(CXH) | $q$(CXH′) | $q$(XCH) |
|---|---|---|---|---|---|
| $CH_3PH_2$ | 1.859 | | 99.0 | | 108.9, 113.1 |
| $CH_2PH_3$ | 1.672 | 117.8 | 127.3 | 112.3 | 118.6 |
| $CH_3NH_2$ | 1.457 | | 111.0 | | 109.4, 114.5 |
| $CH_2NH_3$ | 1.588 | 106.4 | 118.5 | 107.0 | 102.0 |
| $CH_3SH$ | 1.820 | | 98.1 | | 106.2, 111.3 |
| $CH_2SH_2$ | 1.689 | 117.0 | 117.7 | 106.8 | 110.3, 117.6[c] |
| $CH_3OH$ | 1.403 | | 109.7 | | 107.2, 111.9 |
| $CH_2OH_2$ | 2.177 | 104.4 | 115.2 | 93.5 | 88.2, 90.7[c] |
| $CH_2OH_2$[b] | 1.805 | 102.2 | 101.4 | 96.0 | |

[a] Bond distances are in Angstroms. Bond angles are in degrees. Results of calculations done with a polarized double zeta basis set[12] expressly for this chapter.
[b] MP2/6-31G* geometry optimization.
[c] First angle is to H″. Second angle is to H‴.

**Table 2.5 Optimized Geometric Parameters[a] of $CH_2{=}PH_3$ at Various Computational Levels[38]**

| Level | P=C | P–H | P–H′ | C–H | H–P–C | H′–P–C | H–C–P | $\delta$ |
|---|---|---|---|---|---|---|---|---|
| HF/6-31G* | 1.666 | 1.416 | 1.390 | 1.075 | 128.4 | 112.2 | 118.2 | 25.0 |
| HF/6-31 + G* | 1.672 | 1.414 | 1.389 | 1.075 | 127.5 | 112.3 | 118.4 | 23.3 |
| HF/6-31G** | 1.666 | 1.419 | 1.392 | 1.075 | 128.1 | 112.3 | 118.0 | 24.7 |
| HF/6-31 + G** | 1.672 | 1.416 | 1.392 | 1.075 | 127.2 | 112.3 | 118.4 | 22.9 |
| HF/G-311 + G** | 1.669 | 1.421 | 1.395 | 1.075 | 127.1 | 112.3 | 118.0 | 25.2 |
| MP2/6-31G*[b] | 1.674 | 1.440 | 1.404 | 1.084 | 130.6 | 111.5 | 116.8 | 30.7 |
| MP2/6-31 + G* | 1.680 | 1.436 | 1.403 | 1.085 | 129.6 | 111.5 | 117.1 | 29.6 |
| MP2/6-31G** | 1.672 | 1.429 | 1.395 | 1.078 | 130.6 | 111.5 | 116.5 | 31.4 |
| MP2/6-31 + G** | 1.679 | 1.425 | 1.394 | 1.080 | 129.5 | 111.5 | 116.8 | 30.3 |
| MP2/6-311 + G** | 1.677 | 1.430 | 1.398 | 1.084 | 129.2 | 111.7 | 116.4 | 32.0 |
| CISD/6-31G* | 1.671 | 1.438 | 1.404 | 1.082 | 130.1 | 111.7 | 117.3 | 28.9 |

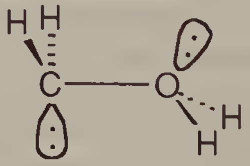
[a] Bond distances are in Angstroms. Bond angles are in degrees. See Figure 2.3 for labelling conventions.
[b] See reference 23.

ylide recently has been calculated at several levels[38] and the results, shown in Table 2.5, indicate that there is not a strong dependence of the geometry on the basis set or the level of correlation[23] once polarization functions are included on the phosphorus and carbon. The basic structure of the phosphonium ylide is that of a $PH_3$ group bonded to a $CH_2$ group. The P–C bond is almost 0.2 Å shorter than the P–C bond in $CH_3PH_2$. The bonding at P is not tetrahedral with the unique HPC angle near 130° and the HPH bond angles near 100°. The $CH_2$ group is not planar. The structure compares favorably with that of the recently redetermined crystal structure of the triphenyl derivative ($Ph_3PCH_2$).[39] The P–C distance was 1.692 Å and the $CH_2$ group was clearly nonplanar with a deviation from the plane of about 30°. These higher-order results differ from the earlier X-ray crystallographic[40] and electron diffraction results[41,42] which were interpreted in terms of a nearly planar carbon.

The S–C bond of the model sulfonium ylide ($CH_2SH_2$) is shorter than the value in $CH_3SH$, this time by 0.13 Å. The value of the S–C bond in this ylide is comparable to that determined in $(CH_3)_2SC(CN)_2$, although the difference in the carbon substituents is significant.[43,44] The optimum structure of the ylide has $C_1$ symmetry with the orbital of the $CH_2$ group essentially orthogonal to the $SH_2$ lone pair. The $CH_2$ group is clearly nonplanar, as is the $SH_2$ group, and the hydrogens on both S and C are not equivalent. This calculation produced a geometry different from that described by Yates et al.,[23] who reported a structure with $C_s$ symmetry (i.e., a planar $CH_2$ group).

The structure of the ammonium ylide ($CH_2NH_3$) is clearly different from that of the phosphonium ylide. The C–N bond is now longer by 0.13 Å as compared to the value in $CH_3NH_2$. The $CH_2$ group is nonplanar with an HCN angle near 100° and therefore the $CH_2$ is bent strongly away from the C–N axis. The ammonium moiety is again asymmetric with a much larger HNC bond angle. Although it is possible to describe this ylide as a complex between methylene and ammonia, the electronic structure analysis (see discussion below) shows that it is more appropriate to describe it as an ylide.

The structure of the oxonium ylide ($CH_2OH_2$) is quite different from that of all the other ylides. The C–O bond length is greater than 2.10 Å at the Hartree–Fock level and the $CH_2$ group is essentially perpendicular to the C–O bond. Thus the structure is essentially that of methylene solvated by water. Whereas correlation corrections are small for the other ylides (the largest effect is a shortening of the C–N bond by about 0.05 Å in the ammonium ylide), correlation corrections are large for the oxonium ylide. The results of an optimization at the MP2 level with the 6-31G* basis set[30] are given in Table 2.4. The C–O bond shortens significantly to 1.80 Å, but this is still 0.4 Å longer than that in $CH_3OH$. This is consistent with the energetic results. There is not complete agreement on the lowest energy conformation for the oxonium ylide. With the 6-31G* basis set at both the SCF and MP2 levels, Yates et al.[23] found that the $C_1$ structure is not a minimum but has the conformation shown in **2**. With a DZ + P basis set this structure was found to be a transition state and the $C_1$ structure was of lower energy.



2

Strich[45] reported a geometry optimization of the model arsonium ylide $CH_2AsH_3$, using a double zeta basis set augmented by a *d*-orbital on As. This basis set will lead to a geometry at carbon that is too planar as it is well-established that *d*-orbitals on carbon are required to obtain the correct geometry in simple carbanions. An As–C bond distance of 1.782 Å was obtained, which is probably somewhat short as the same level of calculation yields a bond distance of 1.640 for $CH_2PH_3$.

### 2.3.1 Rotation Barriers

The barriers to internal rotation about the C–X ylide bond have been calculated.[26, 27] The barrier to rotation about the P–C bond has been found to be very low (0.24 kcal/mol)[26, 27] in essentially all of the calculations on this ylide[31, 38, 46–49] so there is essentially free rotation about the P–C bond. The barrier to rotation is surprisingly low considering the short bond length and the apparent presence of two $\tau$ orbitals (see discussion below). For $CH_2AsH_3$ Strich[45] also obtained a near zero rotation barrier about the As–C bond. The barrier in the ammonium ylide also is small (2.3 kcal/mol)[26, 27] and is comparable to that in $CH_3NH_2$ (2.0 kcal/mol).[50] A much higher barrier to rotation (21.2 kcal/mol)[26, 27] was found for the sulfonium ylide. Here the preferred conformation has the lone pair on the S essentially orthogonal to the lone pair on the C (see below for a discussion) to alleviate lone-pair repulsions. The large barrier occurs when the two lone pairs can directly interact. A significant rotation barrier has also been predicted for $(CH_3)_2SCH_2$.[51] The barrier to rotation at the Hartree–Fock level in the oxonium ylide is surprisingly high (5.6 kcal/mol)[26, 27] considering the long C–O distance but can be attributed to electronic repulsions between the lone pairs on the methylene and the water groups. The preferred conformation has the lone pair on the methylene group approximately orthogonal to the lone pair not solvating the methylene on the water molecule in one optimization[27] (see Figure 2.3) and anti in another optimization, the same conformation as shown in **2** for the oxonium ylide.[23]

## 2.4 ELECTRONIC PROPERTIES

### 2.4.1 Orbitals

Before considering the various electronic properties it is essential to consider the bonding orbitals in ylides. One advantage of the GVB method is that it can be used to obtain chemical insight into various bonding processes.[26] In considering the prototypical model for $CH_2PH_3$ the orbitals in $CH_3PH_2$ must be considered, beginning with the P–C bond. As shown in Figure 2.4, the P–C bond is made up of two orbitals, each with one electron. One orbital is predominantly localized on the phosphorus and one is predominantly localized on the carbon. The former orbital is more diffuse than the latter, which is consistent with

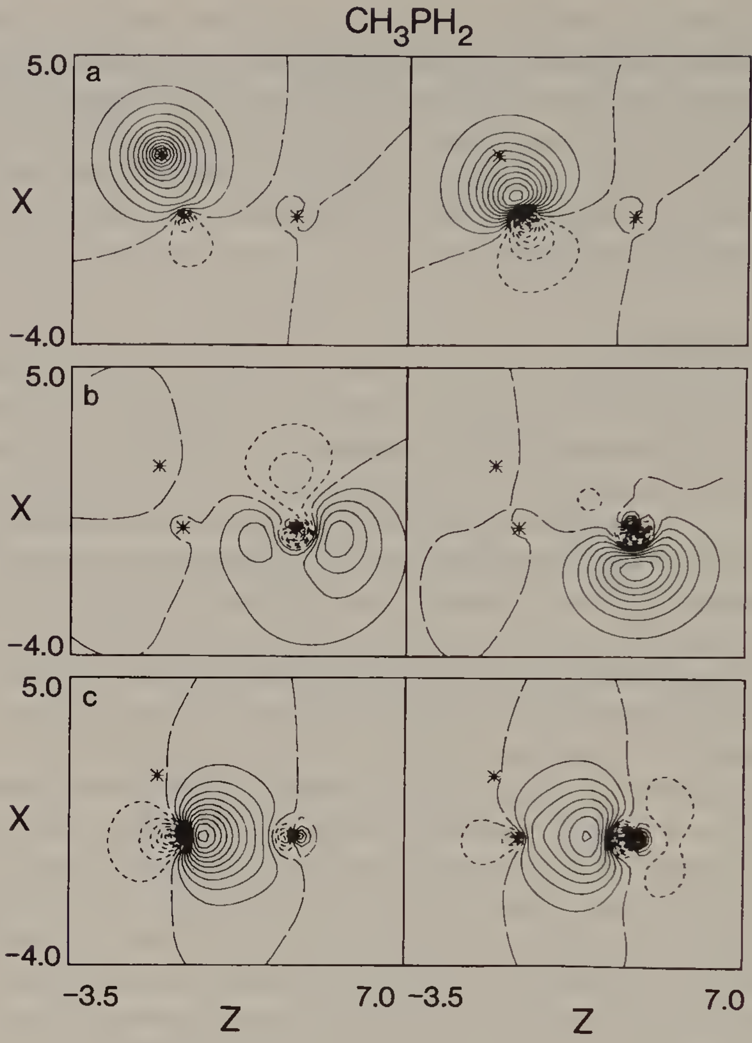


**Figure 2.4** GVB orbitals for $CH_3PH_2$. Contour intervals are in units of 0.05. Asterisks mark atoms in the plane. The carbon is always the atom to the left of center and the heteroatom is always to the right of center. Any remaining atoms are hydrogens. The units for the axes are in atomic units. Solid lines indicate positive amplitude and short dashed lines indicate negative amplitude. Long dashed lines indicate the nodal surface where there is zero amplitude for the wave function. There are two orbitals for each bond or lone pair. (*a*) C–H bond pair showing left–right correlation. (*b*) Lone pair on P showing in–out correlation. (*c*) P–C bond pair showing left–right correlation. Reprinted with permission from *J. Am. Chem. Soc.* **1983**, *105*, 7011. Copyright 1983 American Chemical Society.

phosphorus having a lower electronegativity. This kind of splitting of the bond pair is called left–right correlation and is typical of normal chemical bonds. The lone pair on phosphorus has a different type of correlation. Since there is not a second center to give left–right correlation, the lone pair has what is called in–out correlation, which gives a tight inner electron and a more diffuse outer electron. The inner part of the lone pair resembles that in many other systems, but the more diffuse part shows some broadening into the region of the P–C $\sigma$

bond. This arises because *p* and *d* character are incorporated into the lone pair, which has a large 3*s* character on phosphorus.

The orbitals for the ylide $CH_2PH_3$ have a different kind of bonding scheme (Fig. 2.5) which can be described as two strongly polarized $\tau$ (banana) bonds between the phosphorus and the carbon. Each pair has a tight component on the carbon and a more diffuse component on the phosphorus. The two bond pairs are not equivalent as the $CH_2$ group is not planar. The pair with the most diffuse character on phosphorus lies on the side where the two hydrogens are bent below the P–C axis. The orbital on carbon for this orbital also has more lone-pair-type character. These bonds are similar to those reported by Lischka,[46] who obtained localized molecular orbitals with the Boys technique.[52] He obtained two bonds that were slightly different from each other with most of the density on the carbon. However, these were two electron bonds

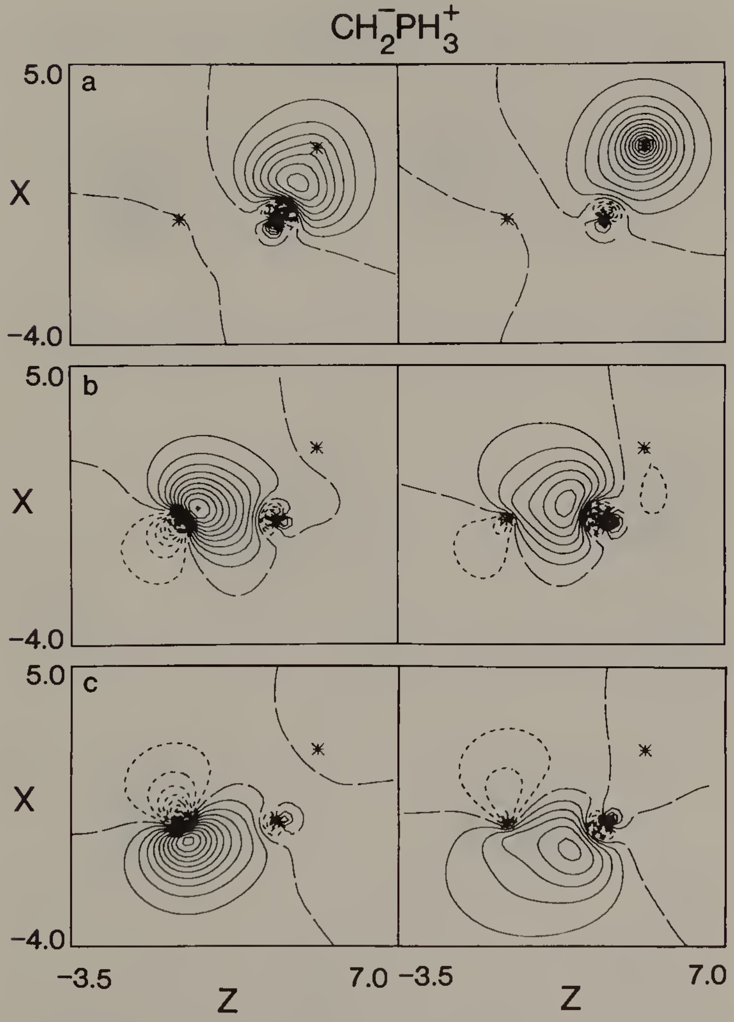


**Figure 2.5** GVB orbitals for $CH_2PH_3$ (see Fig. 2.4). (*a*) P–H bond pair (*b*). P–C $\tau$ (bent) bond pair. (*c*) P–C $\tau$ bent bond pair. Reprinted with permission from *J. Am. Chem. Soc.* **1983**, *105*, 7011. Copyright 1983 American Chemical Society.

as opposed to the GVB orbitals (which are determined by energy optimization) shown in the figures. The presence of the back bonding can also account for the large C–P–H bond angle to the unique hydrogen on phosphorus in the phosphonium ylide. The electrons in the P–H bond move away from the P–C $\tau$ bonds to decrease electron repulsion between these bonds and the P–H bond pair.

The orbitals for the analogous ammonium ylide ($CH_2NH_3$) show that the best description of the structure is that of an ylide (Fig. 2.6). The C–N bond clearly is a $\sigma$ orbital with left–right correlation. The tighter density is on the nitrogen, as expected from electronegativity differences. The C–N bond in the ylide is very similar to that in $CH_3NH_2$. A lone pair with in–out correlation is found on the carbon. The diffuse electron is significantly more diffuse in the ylide as compared

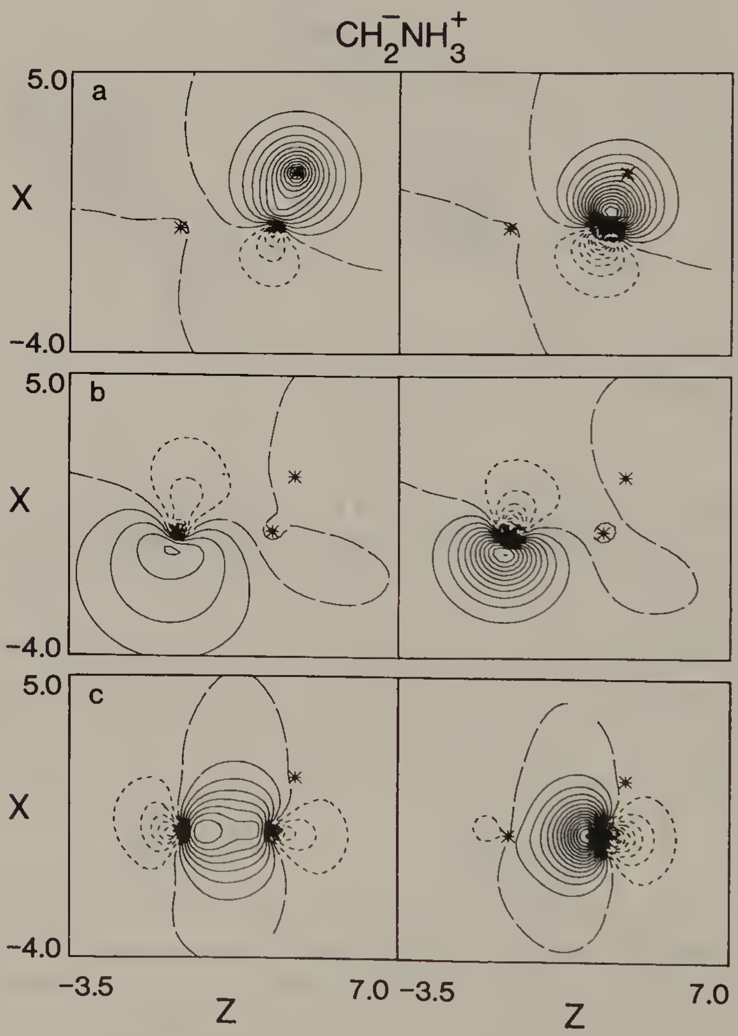


**Figure 2.6** GVB orbitals for $CH_2NH_3$ (see Fig. 2.4). (*a*) N–H bond pair. (*b*) Lone pair on C. (*c*) C–N bond pair. Reprinted with permission from *J. Am. Chem. Soc.* **1983**, *105*, 7011. Copyright 1983 American Chemical Society.

to $CH_3NH_2$, which is consistent with the carbanionic nature of the carbon in the ylide. There is really no back bonding of the lone pair to the nitrogen. The presence of the lone pair on nitrogen does lead to an increase in the C–N–H bond angle, but it is smaller than in the phosphonium ylide, which is consistent with the fact that there is essentially no back bonding in the ammonium ylide.

The orbitals for the analogous oxonium ylide (Fig. 2.7) do not resemble those of the ammonium ylide. There is no C–O bond pair with left–right correlation. Rather there is a perturbed oxygen lone pair that exhibits in–out correlation and is strongly polarized along the C–O axis. The lone pair on the carbon is now almost perpendicular to the C–O axis and is not as diffuse as the lone pair in the ammonium ylide. The lone pair on carbon does not back bond to the oxygen. These results support the conclusions given above that the oxonium ylide is best described as a solvated carbene.

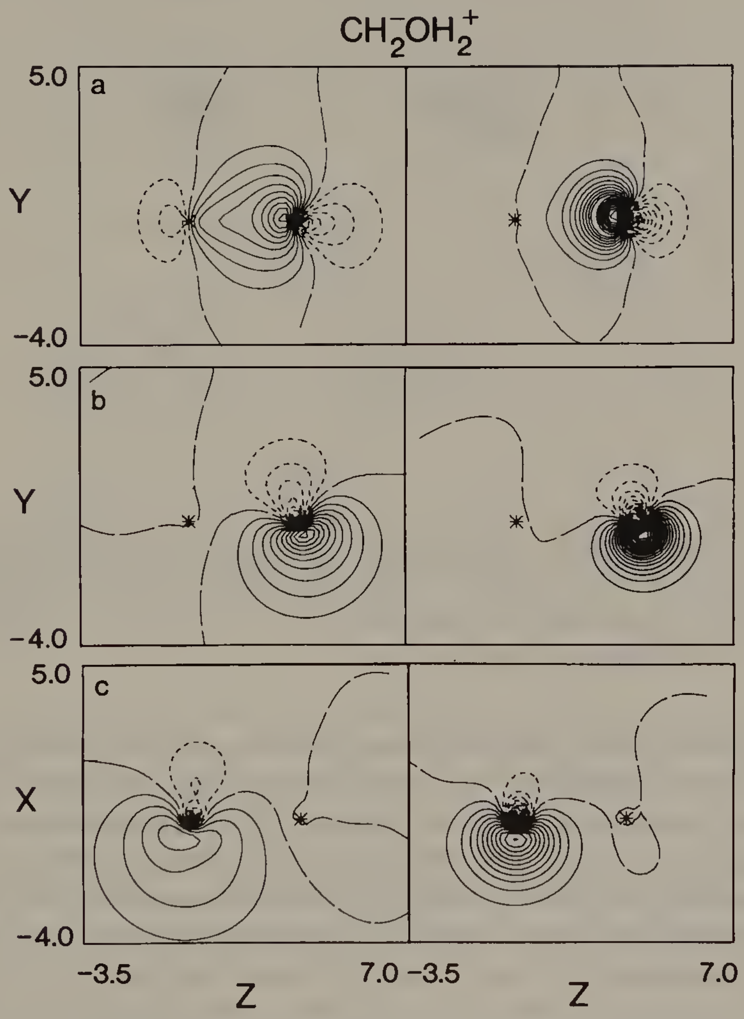


**Figure 2.7** GVB orbitals for $CH_2OH_2$ (see Fig. 2.4). (*a*) Lone pair on O donating toward C. (*b*) Lone pair on O. (*c*) Lone pair on C. Calculated at a C–O bond distance of 1. 870 Å. Reprinted with permission from *J. Am. Chem. Soc.* **1983**, *105*, 7011. Copyright 1983 American Chemical Society.

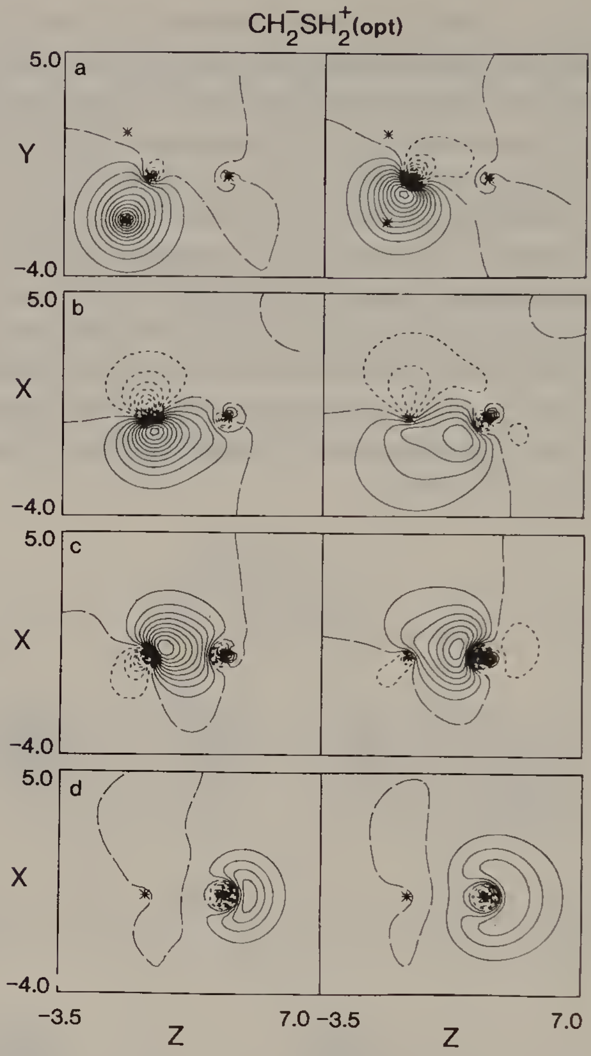


**Figure 2.8** GVB orbitals for $CH_2SH_2$ minimum energy structure with a planar carbon (see Fig. 2.4). (*a*) C–H bond pair. (*b*) C–S bond pair, mostly $\sigma$. (*c*) C–S bond pair, mostly $\pi$. (*d*) Lone pair on S. Reprinted with permission from *J. Am. Chem. Soc.* **1983**, *105*, 7011. Copyright 1983 American Chemical Society.

The sulfonium ylide ($CH_2SH_2$) (Fig. 2.8) has a different electronic structure with the optimum configuration having two very different bent orbitals. One orbital is very much like a $\sigma$ bond showing left–right correlation and is best described as a bent $\sigma$ bond. The other bond pair is derived from the lone pair on the carbon and has $\pi$ character with a tight orbital on carbon and a more diffuse orbital on sulfur. Thus the bonding is intermediate between that of the ammonium and phosphonium ylides. There also is a lone pair on sulfur which has significant 3*s* character and is very similar to the lone pair in $CH_3SH$. The presence of the additional lone pair with significant 3*s* character helps to explain why the C–S bond does not have much $\pi$ character. The lone pair on carbon cannot delocalize onto the sulfur because of increased electron repulsions from the 3*s* lone pair which is closely held by the sulfur.

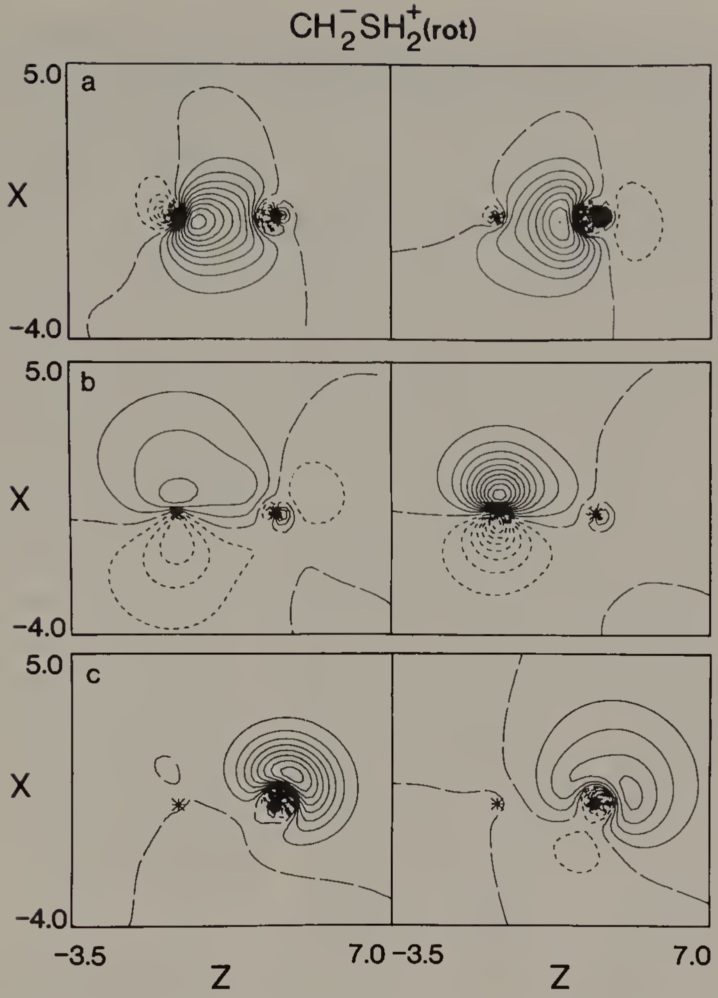


**Figure 2.9** GVB orbitals for $CH_2SH_2$ rotational transition state structure (see Fig. 2.4). (*a*) C–S bond pair, mostly $\sigma$. (*b*) Delocalizing lone pair on C. (*c*) Lone pair on S. Reprinted with permission from *J. Am. Chem. Soc.* **1983**, *105*, 7011. Copyright 1983 American Chemical Society.

The orbitals for the structure corresponding to the top of the barrier of the sulfonium ylide (Fig. 2.9) are quite different from those shown in Figure 2.8. The C–S $\sigma$ bond now is oriented almost along the C–S axis. The $\pi$-type bond now more closely resembles a lone pair on carbon that is strongly delocalized onto the sulfur. The 3*s* lone pair moves toward the C–S axis as it tries to minimize the repulsion of the delocalizing lone pair on the carbon. Clearly the presence of two electron pairs in the same region of space leads to the high barrier to rotation.

### 2.4.2 Charge Distributions

The charge distributions of ylides also can provide insight into their bonding. To compare the charges a base point must be defined, especially when comparing *d* orbital populations, and the nonzwitterionic isomer can be used. Group charges are used, rather than atomic charges, to minimize the effect of the substituents. Group charges are obtained by adding in the charges of the substituents to the atomic charge on the central atom of the group. For example, for a $PH_2$ group the charges on the two H's are added to that on the P. Charges for the model ylides ($CH_2XH$) and their nonzwitterionic isomers ($CH_3X$) are given in Table 2.6. The phosphonium ylide shows a significant amount of charge transfer as compared to methyl phosphine. The phosphorus gains 0.41 e of positive charge as compared to the nonzwitterionic structure. As a consequence the dipole moment more than doubles in the ylide as compared to the phosphine. There is also a significant gain in the *d* orbital population on the phosphorus (0.15 e) on formation of the ylide. For the ammonium ylide, there is even a greater amount of charge transfer with the N gaining 0.5 e of positive charge. The dipole is higher in the ammonium ylide as compared to the phosphonium ylide, showing the greater amount of charge transfer. The dipole moment has increased by a factor of almost 4 compared to the amine. As would be expected, there is no change in the amount of *d* orbital participation between the ammonium ylide and the amine. The sulfonium ylide also shows a significant amount of charge transfer with the sulfur gaining 0.45 e of positive charge. The dipole moment undergoes a significant increase. The change in *d* orbital character on the sulfur also is significant (0.14 e) and is comparable to that for the phosphonium ylide. For the oxonium ylide, the system shows very little charge transfer with the oxygen being slightly positive, as would be expected, because it is donating electron density into the vacant orbital. For this case the population in the *d* orbitals decreases on formation of the oxonium ylide.

One other feature worth investigating is the change in the energy of the HOMO upon ylide formation by internal proton transfer within the non-

**TABLE 2.6 Electronic Properties of Ylides and Nonzwitterionic Isomers**[a]

| | $q(X)$[b] | $d(X)$[c] | $d(C)$[c] | $\mu$[d] | HOMO[e] |
|---|---|---|---|---|---|
| $CH_3PH_2$ | 0.10 | 0.16 | 0.08 | 1.24 | 9.71 |
| $CH_2PH_3$ | 0.51 | 0.31 | 0.07 | 2.90 | 7.62 |
| $CH_3NH_2$ | −0.09 | 0.06 | 0.09 | 1.49 | 10.47 |
| $CH_2NH_3$ | 0.41 | 0.07 | 0.07 | 5.76 | 7.21 |
| $CH_3SH$ | −0.02 | 0.06 | 0.09 | 1.78 | 9.67 |
| $CH_2SH_2$ | 0.43 | 0.20 | 0.08 | 3.33 | 7.84 |
| $CH_3OH$ | −0.20 | 0.05 | 0.11 | 1.88 | 12.14 |
| $CH_2OH_2$ | 0.07 | 0.03 | 0.05 | 2.56 | 9.59 |

[a] Calculations performed with a polarized double zeta basis set expressly for this chapter. Basis set from reference 12. Geometries are those in Table 2.4.

[b] Group charge in electrons.

[c] The *d* orbital population in electrons.

[d] Dipole moment in debye.

[e] Negative of energy of highest occupied molecular orbital (HOMO) in electronvolts. This is the ionization potential from Koopmanns' theorem.

zwitterionic isomer. The HOMO of the nonzwitterionic isomer would be expected to be the lone pair on the heteroatom. Upon ylide formation, the HOMO is expected to be the carbanion lone pair and the ionization potential should become lower, leading to a more reactive orbital. The difference in the HOMO energies will depend on the stability of the ylide and on the nature of the heteroatom. This makes comparisons somewhat more difficult for different heteroatoms, but within a series of substituents with one heteroatom, the comparison is easier. All of the ylides show a decrease in the HOMO energy from that of the precursor nonzwitterionic isomer. The ammonium ylide shows a larger destabilization of the HOMO than does the phosphonium ylide, consistent with the result that there is more back bonding in the phosphonium than in the ammonium ylide. The sulfonium ylide shows the smallest difference in the HOMO energies.

Musher[53] described two types of hypervalent (HV) binding environments which he labeled $HV_I$ and $HV_{II}$. The term hypervalent should be given to a bond with a specific arrangement of atoms. An atom is not hypervalent, but a group of electrons can participate in a hypervalent bond involving different atomic centers. The ylides are not of class $HV_I$ (3-center, 4-electron bonds which require a minimum of three centers, whereas in the ylide cases under consideration only two centers are present), but are of class $HV_{II}$. The $HV_{II}$ class of molecules were defined as those in which the heteroatom attains its highest possible valence by utilizing the *s* orbital lone-pair electrons to form additional bonds. This necessitates "complete electronic and geometric reorganization"[53] and the molecule attempts to generate the most symmetrical geometry available to the complex as it attains its maximum valence. Simple examples are the phosphine oxide $F_3PO$ and the amine oxide $(CH_3)_3NO$ if one divalent ligand is added. In neither case did Musher invoke the use of *d* orbitals to expand the coordination number or the valency about the central atom. In the case of ylides it is not really necessary to invoke the $HV_{II}$ definition, but it is presented here as it has previously been discussed in the literature. The $HV_{II}$ definition was developed as Musher apparently did not want to write charge separated structures nor account for hybridization between *s* and *p* orbitals. Thus, as he noted, $CH_4$ can be considered as an $HV_{II}$ molecule.

### 2.4.3 The Role of *d*-Orbitals

For decades many unique physical and chemical properties of ylides have been attributed to the role of *d* orbitals, including the invoking of $dsp^3$ hybridization. Modern quantum mechanical calculations permit determination of the role of *d* orbitals for these species. The calculations clearly show that *d* orbitals are required to correctly predict the P–C bond length in $PH_3CH_2$. At the 3-21G level (no polarization functions), $r(\text{P–C}) = 1.728$ Å as compared to a value of 1.666 Å at the 3-21G* level with polarization functions on carbon and phosphorus.[54] There is clearly a difference in the *d*-orbital participation in the ylides as compared to their nonzwitterionic isomers, but it is $\leq 0.15$ e. This does not support $dsp^3$ hybridization at phosphorus. There are a number of models for the actual role of *d* orbitals, but precisely how important each role is has not been quantified for the ylides.

As discussed above, the increase in *d*-orbital character occurs because the positive ion character of the phosphorus or sulfur ylide lowers the energy of the empty 3*d* orbitals so that the lone pair can back bond into them. If there is enough back bonding the lone pair orbital can mix with the $\sigma$ C–X bond and this will lead to the formation of $\tau$ bonds. However, the *d*'s can be incorporated only for $n \geq 3$, not for $n = 2$, so there is no role for the *d*'s for nitrogen or oxygen ylides other than as polarization functions. This use of *d* orbitals on the heteroatom is consistent with the molecular orbital plots shown in this chapter, those given by Lischka,[46] and with the discussions of Kutzelnigg.[55]

Francl et al.[56] showed orbital plots that suggest the dominance of the zwitterionic component in the phosphonium ylide but did not discuss the role of *d* orbitals quantitatively. Streitwieser et al.[54] noted that the primary role of the *d* orbitals on phosphorus is to polarize the electron density at the phosphorus away from the negatively charged carbon and to polarize the excess density at the carbanion center toward the positive phosphorus. This second polarization term arises to increase the Coulombic attraction between the positive and negative centers. They[54] suggested that *d* orbitals are needed in the basis set in order to include higher-order electrostatic terms and they argued against charge transfer. However, the higher-level GVB calculations discussed earlier show that some charge transfer has occurred.

Reed and Schleyer[1] recently investigated the chemical bonding in a variety of hypervalent molecules and also emphasized the role of ionic bonding in the $\sigma$ system. They noted that the role of *d* orbitals is for back bonding from the ligands to the central main group atom and to improve the overlap of the central atom *sp* hybrid orbitals with the appropriate ligand orbitals. They also emphasized the importance of negative hyperconjugation and have attempted to quantify how much back bonding occurs into the *d* orbital as compared to the amount that mixes with the main group element–ligand $\sigma^*$ orbitals. Based on a natural bond orbital (NBO) analysis[57] they suggested that mixing into the $\sigma^*$ orbitals is usually more important than mixing into the *d* orbitals. Although these authors did not explicitly treat ylides, they did study some hypervalent phosphorus compounds. It is useful to note that the compound most like a phosphonium ylide, $H_3PO$, showed the weakest negative hyperconjugation. Thus there will probably be a balance between back bonding to the *d* orbitals and to the P–R $\sigma^*$ orbitals in the ylides. The ratio between the two types of back bonding will depend strongly on the nature of the substituents on phosphorus and, to a lesser extent, the substituents on carbon.

Why do the C–X bond distances shorten so much from the nonzwitterionic isomers to the sulfonium and phosphonium ylides? A number of reasons can account for the shortening of the bonds. There is clearly more ionic character, which will lead to some shortening. The hybridization at carbon has changed from $sp^3$ to $sp^2$ and this too will lead to a shortening of the bond. Finally, the back bonding also can account for some of the bond shortening. Clearly "hypervalent" atoms do not have to be invoked to arrive at reasonable explanations for C–P and C–S bond shortening.

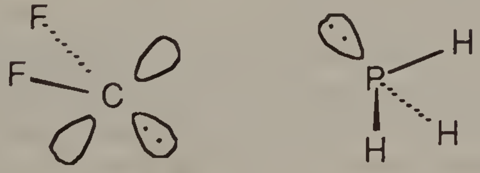
Why is the rotation barrier so low in phosphonium ylides? First the barrier is sixfold and these barriers are known to be low.[58] In the zwitterionic valence bond structure, the P–C bond is a single bond and there should be a low barrier to rotation. Why does the back bonding not lock in a conformation? Because of the presence of low-lying 3*d* and P–H σ*-orbitals on the phosphorus, there is a vacant orbital available at all rotational orientations of the $CH_2$ group with respect to the $PH_3$ group into which the diffuse carbanion lone pair may be donated.

It is well known that sulfonium ylides can be generated much more readily than ammonium ylides. Based on the internal proton transfer energies, it would appear that the ammonium ylide should be more stable, in a thermodynamic sense, than its nonzwitterionic isomer, methyl amine. However, this calculation was for an isolated molecule in the gas phase and did not consider kinetic stability. A number of factors could lead to the larger kinetic stability of the sulfonium ylides compared to ammonium ylides. The HOMO of the sulfonium ylide is not as accessible as that of the ammonium ylide, suggesting that it is less susceptible to certain kinds of attack. Furthermore the sulfonium ylide has a higher activation energy than the ammonium ylide to back transfer of the proton and regeneration of the nonzwitterionic isomer. Solvation effects also have not been considered and these could lead to changes in the stabilization energies.[25]

## 2.5 SUBSTITUTED PHOSPHONIUM YLIDES

### 2.5.1 Fluorine Substitution

The geometries of a number of substituted phosphonium ylides have been calculated at reasonable theoretical levels. The geometries of fluorinated ylides of the form $H_3PCRR'$ have been calculated[59] and are shown in Table 2.7. Fluorinated (at carbon) ylides generally showed a slight lengthening of the P–C bond (except for R = R′ = F) but fluorination (at carbon) of the phosphine isomer caused a similar lengthening. Fluorination of phosphorus ($PF_3CH_2$) leads to a much shorter P–C bond length [$r$(P–C) = 1.590 Å].[56] For R = R′ = F, the calculated structure showed that the ylide dissociates to the carbene $CF_2$: ($^1A_1$) and $:PH_3$ (**3**). The lone pairs for $CF_2$: and $:PH_3$ line up essentially parallel to each other (**3**) in contrast to the result found for the oxonium ylide (**2**).



3

**TABLE 2.7 Molecular Geometries of Fluorinated Derivatives[a–c]**

| Molecule | $r$(P–C) | $\theta$(ACA) | $\theta$(CPH) | $\theta$(CPH′) | $\theta$(PCA) |
|---|---|---|---|---|---|
| $PH_2CH_3$ | 1.856 | 108.6 | 97.8 | 112.7 | |
| $PH_3CH_2$ | 1.675 | 117.4 | 127.7 | 112.1 | 118.4 |
| $PH_2CH_2F$ | 1.854 | 108.8 | 97.6 | | 113.3<br>(110.0H) |
| $PH_3CHF$ | 1.723 | 109.7 | 131.7 | 109.6<br>(106.4) | 113.0<br>(115.8H) |
| $PH_2CHF_2$ | 1.873 | 106.9 | 95.1 | | 109.5<br>(115.4H) |
| $PH_3CF_2$ | 3.54 | 104.8 | 165.1 | 94.1 | 104.2 |
| $PH_2CH(CF_3)_2$ | 1.917 | 112.7 | 95.0 | | 110.2 |
| $PH_3C(CF_3)_2$ | 1.707 | 118.2 | 118.9 | 112.4 | 120.8 |

[a] Data from reference 59.

[b] DZ basis set augmented with $d$ orbitals on $^{+}P$ and $C^{-}$.

[c] Bond distances are in Angstroms. Bond angles are in degrees.

**TABLE 2.8 Reaction Energies for Fluorinated Derivatives[a,b]**

| Compound | $H^+$ Transfer[c] | Dissociation[d] |
|---|---|---|
| $PH_2CH_3$ | 56.0 | 109.2 |
| $PH_2CH_2F$ | 67.3 | 83.9 |
| $PH_2CHF_2$ | 50.1 | 51.3 |
| $PH_2CH(CF_3)_2$ | 34.0 | 93.5 |

[a] Data from reference 59.

[b] Energy given in kilocalories per mole.

[c] Energy required to form ylide.

[d] Dissociation channel to form $PH_3 + {}^1A_1\text{: } CRR'$.

As shown in Table 2.8, the energetics for the proton transfer reaction as compared to the dissociation reaction to form the carbenes follow the geometric trends. If the dissociation process is of low energy, then the ylide is unlikely to form. The prototypical carbene ($CH_2$:) has a ground state triplet with an excited state singlet about 10 kcal/mol higher in energy.[6] For $CF_2$: the singlet is the ground state and is much lower in energy ($\sim$ 45 kcal/mol) as compared to the triplet.[60] This leads to an extremely low energy dissociation channel and consequently the ylide cannot form.

One feature we have not considered yet is the stabilization of the carbanion center in fluorinated phosphonium ylides. The carbon atom can best donate electron density into the low-lying empty orbitals on the phosphonium center if it is planar. It is known that methyl carbanion has a very low inversion barrier ($< 2$ kcal/mol)[61] and that α-fluorination leads to increased inversion barriers (inversion barriers in $CH_2F^-$, $CF_2H^-$, and $CF_3^-$ are 14.0, 45.6, and 106.0 kcal/mol, respectively).[62] These large values have pronounced effects on the structures of the various ylide carbanions. Thus in $H_3PCF_2$ there is a strong driving force for the $CF_2$: group to be nonplanar and, therefore, a good back bond cannot be formed. This, coupled with the low energy for the dissociation channel, leads to the dissociated structure. For $H_3PCHF$ the CHF group wants to be nonplanar, leading to a relatively longer P–C bond and a larger proton transfer energy. The isodesmic reaction (Eq. 2.9) shows that the fluorine

$$H_3PCH_2 + CH_3F \longrightarrow H_3PCHF + CH_4 \tag{2.9}$$

destabilizes the ylide by 10.8 kcal/mol relative to hydrogen as a substituent. If two $CF_3$ groups are substituted for the two hydrogens, a very stable ylide is formed. In this case the carbene is a ground state triplet and the inversion barrier is expected to be low. The $CF_3$ groups also can stabilize the carbanion center by fluorine hyperconjugation.[4] As a consequence of these factors the dissociation channel is of high energy and the proton transfer process is of low energy. Reaction 2.10 has a negative value for $\Delta E$ of $-16.7$ kcal/mol, showing the stabilizing effect of the $CF_3$ group relative to H.

$$H_3PCH_2 + CH_2(CF_3)_2 \longrightarrow H_3PC(CF_3)_2 + CH_4 \tag{2.10}$$

The charge distributions for the fluorinated phosphonium ylides show trends similar to those discussed above for the simple model ylides, as shown in Table 2.9. If an ylide is formed, there is a significant increase in the positive charge on the $PH_3$. This leads to a significant increase in the dipole moment. There is also an increase in the 3*d* orbital population on the phosphorus and the HOMO of

**TABLE 2.9 Electronic Properties of Fluorine-Substituted Phosphines and Phosphonium Ylides**[59]

| | $q(P)^a$ | $d(P)^b$ | $\mu^c$ | HOMO$^d$ |
|---|---|---|---|---|
| $PH_2CH_3$ | 0.14 | 0.19 | 1.19 | 9.80 |
| $PH_3CH_2$ | 0.50 | 0.37 | 2.86 | 7.71 |
| $PH_2CH_2F$ | 0.17 | 0.29 | 1.34 | 10.51 |
| $PH_3CHF$ | 0.52 | 0.36 | 4.73 | 8.12 |
| $PH_2CHF_2$ | 0.19 | 0.20 | 3.03 | 11.00 |
| $PH_3CF_2$ | 0.01 | 0.20 | 0.88 | 10.52 |
| $PH_2CH(CF_3)_2$ | 0.34 | 0.19 | 3.99 | 11.56 |
| $PH_3C(CF_3)_2$ | 0.77 | 0.36 | 8.30 | 10.62 |

[a] Group charge in electrons.
[b] The *d* orbital population in electrons.
[c] Dipole moment in debye.
[d] Homo energy in electronvolts.

**TABLE 2.10 Heats of Formation for Ylides**[a]

| Ylide | $\Delta H_f$[b] |
|---|---|
| $CH_2PH_3$[c] | 45.7 (47.7) |
| $CH_2NH_3$ | 60.3 (60.7) |
| $CH_2SH_2$ | 75.3 (68.4) |
| $CH_2OH_2$ | 40.5 (35.7) |
| $PH_3CHF$ | − 43.6 |
| $PH_3CF_2$ | − 43.9 |
| $PH_3C(CF_3)_2$ | − 288.2 |

[a] Heats are given in kilocalories per mole. Based on $\Delta H_f^0$'s for the nonzwitterionic isomers from references 5, 28, and 59. The value for $\Delta H_f^0$ ($PH_2CH_3$) is from reference 59.

[b] Values in parentheses are MP4 values.

[c] For $CH_2PH_3$ the value of $\Delta H_f$ corresponding to the same level as those for the fluorine-substituted systems is 51.1 kcal/mol.

the ylide is destabilized. As discussed above, the derivative with $R = R' = CF_3$ is the most stable. It has the largest charge separation, the largest dipole moment, and the smallest change in energy of the HOMO as compared to its isomer. The compound with $R = R' = F$ does not exhibit any of these features and, as expected, does not form an ylide. The charge separation is essentially zero, and the dipole moment is small. The HOMO is only slightly destabilized and there is essentially no change in the *d*-orbital character on phosphorus.

The heat of formation of the model ylides can be calculated from the energy difference between the ylide and its nonzwitterionic isomer and the heat of formation of the isomer (Table 2.10). The zero point corrected energies in Table 2.2 from the POL-CI and MP4 calculations for the simple model ylides and the SCF values in Table 2.8 for the fluoro-substituted ylides were used to produce the heats of formation.

### 2.5.2 Alkyl Substituents

The geometries of a number of alkyl derivatives have been optimized at the HF/6-31G* level, as shown in Table 2.11.[38] The P–C bond lengths do not show much variation for the C-alkyl derivatives (1.66–1.70 Å). Alkylation of the phosphine also has only a small effect on the bond length. An important result of this work is that all of the ylides with a $CH_3$ substituent on carbon have pyramidal geometry at carbon. If the group on carbon does not stabilize the ylide, the carbon is not planar.[38] The inversion barriers for alkylated phosphonium ylides are very small (Table 2.12), less than 1 kcal/mol, if the carbanion is not in a strained ring. Even if the carbanion is in a cyclopropyl ring, the barrier to inversion is on the order of 4 kcal/mol. The rotation barriers also are small, on the order of 1 kcal/mol or less, as was found for $H_3PCH_2$. The calculated

**TABLE 2.11 Geometric Parameters of Alkyl Derivatives of Phosphonium Ylides**[a,b]

| Compound | P=C | P–C–X | X–C–X′ | $\delta^c$ |
|---|---|---|---|---|
| $H_3P{=}CH_2$ | 1.666 | 118.2 | 117.3 | 25.0 |
| $H_3P{=}CHMe$ | 1.666 | 123.1 (C)<br>114.8 (H) | 118.1 | |
| $H_3P{=}CMe_2$ | 1.669 | 120.0 | 116.5 | 18.2 |
| $MeH_2P{=}CH_2$ | 1.664 | 118.9 | 117.7 | 20.8 |
| $Me_3P{=}CH_2$ | 1.671 | 118.5 | 116.8 | 24.6 |
| $Me_3P{=}CMe_2$ | 1.676 | 121.1 | 114.2 | 18.0 |
| $H_3P{=}C(CH_2)_2$ | 1.672 | 130.1 | 60.5 | 41.8 |
| $Me_3P{=}C(CH_2)_2$ | 1.683 | 127.6 | 60.3 | 45.1 |
| $H_3P{=}C(CH_2)_3$ | 1.663 | 131.6 | 92.3 | 16.6 |
| $H_3P{=}C(CH_2)_4$ | 1.693 | 125.6 | 107.4 | 10.8 |
| $H_3P{=}CHCHO$ | 1.684 | 121.0 (C)<br>119.5 (H) | 119.5 | 0.0 |
| $Me_3P{=}CHCHO$ | 1.698 | 124.8 (C)<br>117.0 (H) | 118.2 | 0.0 |

[a] SCF/6-31G* from reference 38.
[b] Bond distances are in Angstroms. Bond angles are in degrees.
[c] Out-of-plane bending angle at $C^-$ in degrees (see Fig. 2.3).

**TABLE 2.12 Inversion and Rotation Barriers for Alkyl-Substituted Phosphonium Ylides**[38]

| Compound | Inversion Barrier (kcal/mole) | Rotation Barrier (kcal/mole) |
|---|---|---|
| $PH_3CH_2$ | 0.87 | 0.13 |
| $H_3PC(CH_3)_2$ | 0.99 | 1.00 |
| $(CH_3)_3PCH_2$ | 0.70 | 0.22 |
| $(CH_3)_3PC(CH_3)_2$ | 0.85 | − 0.02 |
| $H_3PC(CH_2)_2$ | 3.97 | 0.32 |
| $(CH_3)_3PC(CH_2)_2$ | 4.15 | |

structure for the phosphonium cyclopropylide [$H_3PC(CH_2)_2$] is in good agreement with that calculated by Vincent et al.[63] with a similar basis set. Bachrach[38] emphasized the importance of the ionic resonance structure in phosphonium ylides.

### 2.5.3 Other Heteroatom Substituents

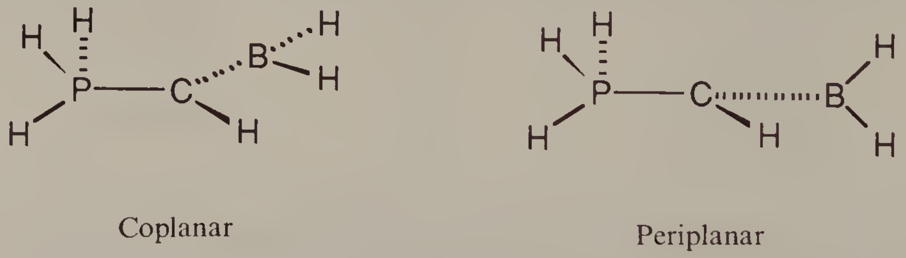
Bestmann and co-workers[64] have investigated the effect of a variety of heteroatom substituents (X) on the structure of the phosphonium ylides ($H_3PCHX$) at

**TABLE 2.13 Substituent Effects in $H_3PCHX$[64]**

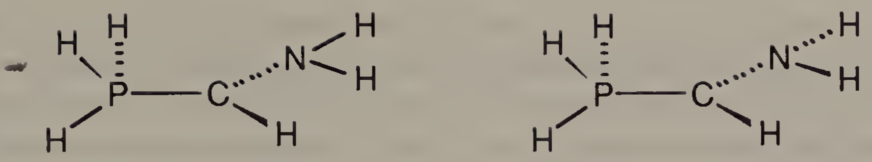
| X | $r$(P–C)[a] | –CHX Geometry[b] | $\Delta E$ of Reaction 2.11[c] | $\Delta E$ Dissociation[d] |
|---|---|---|---|---|
| H | 1.658 | pyr | | |
| Li | 1.658 | pl | – 15.6 | 74.8 |
| BeH | 1.671 | pl | – 19.5 | 89.6 |
| $BH_2$ | 1.695 | pl | – 31.4 | 63.1 |
| $CH_3$ | 1.658 | pyr | 3.3 | 53.2 |
| $NH_2$ | 1.660 | pl | – 1.1 | 8.1 |
| OH | 1.678 | pyr | 4.3 | 13.0 |
| F | 1.678 | pyr | 9.8 | 23.7 |
| CN | 1.678 | pl | – 12.8 | |

[a] P–C bond distance given in Angstroms.
[b] pyr = pyramidal; pl = planar.
[c] $\Delta E$ given in kilocalories per mole.
[d] Dissociation energy from ylide to $PH_3$ + :CHX ($^1A_1$).

the HF/3-21G* level. The results of their theoretical studies are summarized in Table 2.13. A surprising result of this work is that the P–C bond length is again essentially independent of the substituent even though the energetic effects are quite different. The groups that are σ donors and π acceptors (Li, BeH, and $BH_2$) all have planar carbanion centers, as would be expected from the earlier discussion. For X = $BH_2$, the coplanar orientation was found to be 28.6 kcal/mol lower in energy than the periplanar orientation of the $BH_2$ group with respect to the carbanion center (**4**). The cyano group also has a planar carbanion and this π acceptor is known to stabilize planar carbanions. The OH group lead to a pyramidal carbanion, just as found for the $CH_3$ and F substituents. These authors calculated the inversion barrier at carbon for $H_3PCHF$ to be 2.8 kcal/mol. For the $NH_2$ substituent, the lowest energy structure studied had a planar $NH_2$ group which was periplanar to the carbanion center (**5**). The structure with a coplanar $NH_2$ was 21.0 kcal/mol higher in energy.



**4**



Periplanar

Coplanar

5

Bestmann et al.[64] used reaction 2.11, which is like Eqs. 2.9 and 2.10, to study the energetic effects of substituents (X) in the phosphonium ylide relative to hydrogen. The energy of reaction 2.11 is given in Table 2.13 for the various

$$H_3\overset{+}{P}\overset{-}{C}H_2 + CH_3X \longrightarrow H_3\overset{+}{P}\overset{-}{C}HX + CH_4 \qquad (2.11)$$

$$^{-}CH_3 + CH_3X \longrightarrow {}^{-}CH_2X + CH_4 \qquad (2.12)$$

$$CH_2CH_2 + CH_3X \longrightarrow CH_2CHX + CH_4 \qquad (2.13)$$

substituents. A negative value of the energy shows that the substituent stabilizes the ylide relative to hydrogen, whereas a positive value represents a destabilizing effect. The sigma donors/pi acceptors that have a planar carbanion center have a negative value for $\Delta E$, whereas the substituents that tend to be pi donors have positive values and a nonplanar carbanion center. The dissociation energy channel to form the singlet carbene was also given in this work and all of the ylides are bound with respect to dissociation.

Based on reactions 2.12 and 2.13 these authors[64] concluded that the anionic character (the $\pi$ density) of an ylide carbanion lies between that of an olefin and a carbanion. They reached this conclusion because the magnitude of the energies calculated for reaction 2.12 tended to be larger than those for reaction 2.11 and those for reaction 2.13 tended to be smaller. This conclusion is qualitative at best since the same trends were not always found in the three reactions. For example, this analysis did not work well for either F or Li.

## 2.6 SUMMARY

Based on the results of high-quality ab initio molecular orbital calculations, one can conclude that the dominant resonance structure in the phosphonium ylide is the ionic one. There is clearly not a full separation of charge with a $+1.0$ on phosphorus and a $-1.0$ on carbon, but there is a cationic phosphorus and an anionic carbon. The results also show that there is delocalization of the lone pair on the carbanion toward the phosphorus. The extent of this delocalization depends on the quality of the basis set and the level of the calculation. The most extensive calculation in terms of the *n*-particle treatment shows a significant amount of delocalization which leads to mixing of the delocalized lone pair with the P–C $\sigma$ bond and the formation of two highly polarized $\tau$ bonds.

The other question that arises is with which vacant orbitals on the phosphorus does the carbanion lone pair mix? There is clearly some back bonding into the *d* orbitals, but this is probably less than 0.2 e. There is also the possibility of the lone pair mixing with the P–R $\sigma^*$ orbitals, but again this amount has not been quantified, although it easily could be of the same magnitude as mixing with the *d* orbitals. It is clear from the results that the most important role for *d* orbitals on phosphorus is to polarize the charge density in the molecule, especially that of the carbanion lone pair and the density around the phosphorus. The phosphonium ylide clearly should not be classified as a hypervalent molecule as its bonding can easily be described by simple chemical principles. The bonding in the optimum geometry of the sulfonium ylide shows less delocalization of the carbanion lone pair to the heteroatom. In the transition state for rotation about the S–C bond there is even less, so that there is no evidence of left–right correlation. In the ammonium ylide, the carbanion lone pair cannot delocalize strongly onto the nitrogen and only in–out correlation is predicted. Again these ylides are consistent with simple models for the bonding and should not be considered as hypervalent. The simplest oxonium ylide is not expected to form a stable structure other than that of a solvated methylene.

## REFERENCES

[1] Reed, A. E.; Schleyer, P. von R. *J. Am. Chem. Soc.* **1990**, *112*, 1434.

[2] Schleyer, P. von R.; Kos, A. J. *Tetrahedron* **1983**, *39*, 1141.

[3] Farnham, W. B.; Smart, B. E.; Middleton, W. J.; Calabrese, J. C.; Dixon, J. A. *J. Am. Chem. Soc.* **1985**, *107*, 4565.

[4] Dixon, D. A.; Fukunaga, T.; Smart, B. E. *J. Am. Chem. Soc.* **1986**, *108*, 4027.

[5] Lias, S. G.; Bartmess, J. E.; Liebman, J. F.; Holmes, J. L.; Levin, R. D.; Mallard, W. G. *J. Phys. Chem. Ref. Data*, **1988**, *17*, Supplement 1.

[6] Herzberg, G. *Electronic Structure and Electronic Spectra of Polyatomic Molecules*; Van Nostrand Reinhold: New York, **1966**.

[7] Trinquier, G.; Malrieu, J. P. *J. Am. Chem. Soc.* **1979**, *101*, 7169.

[8] Hoffmann, R.; Boyd, D. B.; Goldberg, S. Z. *J. Am. Chem. Soc.* **1970**, *92*, 3929.

[9] Boyd, D. B.; Hoffmann, R. *J. Am. Chem. Soc.* **1971**, *93*, 1064.

[10] Hehre, W. J.; Radom, L.; Schleyer, P. von R.; Pople, J. A. *Ab Initio Molecular Orbital Theory*; Wiley: New York, 1986.

[11] Hirst, D. M. *A Computational Approach to Chemistry*; Blackwell Scientific: Oxford, Great Britain, 1990.

[12] Dunning, T. H., Jr.; Hay, P. J. In *Methods of Electronic Structure Theory*; Schaefer, H. F., III, Ed.; Plenum: New York, 1977; Chapter 1.

[13] Roothaan, C. C. J. *Rev. Mod. Phys.* **1951**, *23*, 69.

[14] (a) Moller, C.; Plesset, M. S. *Phys. Rev.* **1934**, *46*, 618. (b) Pople, J. A.; Binkley, J. S.; Seeger, R. *Int. J. Quantum Chem. Symp.* **1976**, *10*, 1.

[15] Bartlett, R. J. *J. Phys. Chem.* **1989**, *93*, 1697.

[16] Goddard, W. A., III; Dunning, T. H., Jr.; Hunt, W. J.; Hay, P. J. *Acc. Chem. Res.* **1973**, *6*, 368.

[17] Goddard, W. A., III; Harding, L. B. *Ann. Rev. Phys. Chem.* **1978**, *29*, 363.

[18] Hay, P. J.; Dunning, T. H., Jr. *J. Chem. Phys.* **1976**, *64*, 5077.

[19] Pulay, P. In *Applications of Electronic Structure Theory*; Schaefer, H. F. III, Ed.; Plenum: New York, 1977; p. 153.

[20] Komornicki, A.; Ishida, K.; Morokuma, K.; Ditchfield, R.; Conrad, M. *Chem. Phys. Lett.* **1977**, *45*, 595.

[21] King, H. F.; Komornicki, A. *J. Chem. Phys.* **1986**, *84*, 5465.

[22] King, H. F.; Komornicki, A. In *Geometrical Derivatives of Energy Surfaces and Molecular Properties*; Jorgenson, P.; Simons, J. Eds.; NATO ASI Series C., Vol. 166; Reidel: Dordrecht, 1986; p. 207.

[23] Yates, B. F.; Bouma, W. J.; Radom, L. *J. Am. Chem. Soc.* **1987**, *109*, 2250.

[24] Yates, B. F.; Bouma, W. J.; Radom, L. *J. Am. Chem. Soc.* **1984**, *106*, 5805.

[25] Nguyen, M. T.; Hegarty, A. F. *J. Chem. Soc. Perkin Trans. (2)* **1987**, 47.

[26] Dixon, D. A.; Dunning, T. H.; Eades, R. A.; Gassman, P. G. *J. Am. Chem. Soc.* **1983**, *105*, 7011.

[27] Eades, R. A.; Gassman, P. G.; Dixon, D. A. *J. Am. Chem. Soc.* **1981**, *103*, 1066.

[28] Lias, S. G.; Liebman, J. F.; Levein, R. D., *J. Phys. Chem. Ref. Data* **1984**, *13*, 695.

[29] Pople, J. A.; Raghavachari, K.; Frisch, M. J.; Binkley, J. S.; Schleyer, P. von R. *J. Am. Chem. Soc.* **1983**, *105*, 6389.

[30] Harding, L. B.; Schlegel, H. B.; Krishnan, T.; Pople, J. A. *J. Phys. Chem.* **1980**, *84*, 3394.

[31] Wesdemiotis, C.; Feng, R.; Danis, P. O.; Williams, E. R.; McLafferty, F. W. *J. Am. Chem. Soc.* **1986**, *108*, 5847.

[32] McLafferty, F. W. *Science* **1990**, *247*, 925.

[33] Lorquet, J. C.; Leyh-Nihant, B.; McLafferty, F. W. *Int. J. Mass Spectrom.* **1990**, *100*, 465.

[34] Janulis, E. P.; Arduengo, A. J., III *J. Am. Chem. Soc.* **1983**, *105*, 3563.

[35] Pople, J. A. *Chem. Phys. Lett.* **1986**, *132*, 144.

[36] Moriarty, R. M.; Vaid, R. K. *Synthesis* **1990**, 431.

[37] Atwood, J. L.; Sheppard, W. A. *Acta Cryst.* **1975**, *31B*, 2638.

[38] Bachrach, S. M. *J. Org. Chem.* **1992**, *57*, 4367.

[39] Schmidbaur, H.; Jeong, J.; Schier, A.; Graf, W.; Wilkinson, D. L.; Muller, G. *New. J. Chem.* **1989**, *13*, 341.

[40] Bart, J. C. J. *J. Chem. Soc.* **1969**, 350.

[41] Ebsworth, E. A. V.; Fraser, T. E.; Rankin, D. W. H. *Chem. Ber.* **1977**, *110*, 3494.

[42] Ebsworth, E. A. V.; Fraser, T. E.; Rankin, D. W. H.; Gasser, O.; Schmidbaur, H. *Chem. Ber.* **1977**, *110*, 3508.

[43] Christensen, T.; Witmore, W. G. *Acta. Cryst.* **1969**, *25B*, 73.

[44] Cook, A. F.; Moffat, J. G. *J. Am. Chem. Soc.* **1968**, *90*, 740.

[45] Strich, A. *Nouv. J. Chem.* **1979**, *3*, 105.

[46] Lischka, H. *J. Am. Chem. Soc.* **1977**, *99*, 353.

[47] Mitchell, D. J.; Wolfe, S.; Schlegel, H. B. *Can. J. Chem.* **1981**, *59*, 3280.

[48] Bernardi, F.; Shlegel, H. B.; Whangbo, M. H.; Wolfe, S. *J. Am. Chem. Soc.* **1977**, *99*, 5633.

[49] Absar, I.; Van Wazer, J. R. *J. Am. Chem. Soc.* **1972**, *94*, 2382.

[50] Lide, D. R. Jr. *J. Chem. Phys.* **1954**, *27*, 343.

[51] Graham, S. L.; Heathcock, C. L. *J. Am. Chem. Soc.* **1980**, *102*, 3714.

[52] Boys, S. F. In *Quantum Theory of Atoms, Molecules, and the Solid State*; Lowdin, P.O., Ed.; Interscience: New York, 1967; p. 253.

[53] Musher, J. I. *Angew. Chem.* **1969**, *8*, 54; *Tetrahedron* **1974**, *30*, 1747.

[54] Streitweiser, A.; Rajca, A.; McDowell, R. S.; Glaser, R. *J. Am. Chem. Soc.* **1987**, *109*, 4184.

[55] Kutzelnigg, W. *Angew. Chem.* **1984**, *23*, 272.

[56] Francl, M. M.; Pellow, R. C.; Allen, L. C. *J. Am. Chem. Soc.* **1988**, *110*, 3723.

[57] Reed, A. E.; Weinhold, F.; Curtiss, L. A. *Chem. Revs.* **1988**, *88*, 899.

[58] Payne, P. W.; Allen, L. C. In *Applications of Electronic Structure Theory*; Schaefer, H. F., III, Ed.; Plenum: New York, 1977; Chapter 2, p. 79.

[59] Dixon, D. A.; Smart, B. E. *J. Am. Chem. Soc.* **1986**, *108*, 7172.

[60] Dixon, D. A. *J. Phys. Chem.* **1986**, *90*, 54.

[61] Marynick, D. S.; Dixon, D. A. *Proc. Natl. Acad. Sci. USA* **1977**, *74*, 410.

[62] Dixon, D. A.; Fukunaga, T.; Smart, B. E. *J. Phys. Org. Chem.* **1988**, *1*, 153.

[63] Vincent, M. A.; Schaefer, H. F., III; Schier, A.; Schmidbaur, H, *J. Am. Chem. Soc.* **1983**, *105*, 3806.

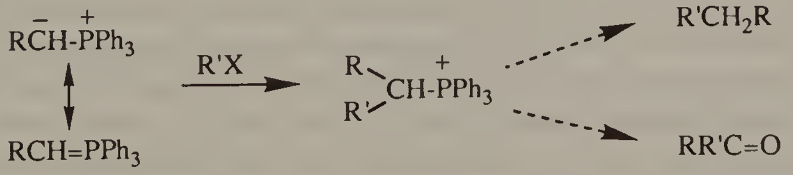
[64] Bestmann, H. J.; Kos. A. J.; Witsgall, K.; Schleyer, P. von R. *Chem. Ber.* **1986**, *119*, 1331.

# 3

# INTRODUCTION TO PHOSPHONIUM YLIDES

The first phosphonium ylide, $Ph_3P{=}CHCOOC_2H_5$, was prepared and isolated by Michaelis and Gimborn in 1894[1], but its structure was not proven until 1961[2]. Staudinger and Meyer[3] must be credited with the first phosphonium ylide whose structure was identified as such, $Ph_3P{=}CPh_2$, although they did not call it an ylide and they went to no special lengths to prove its structure. They seemed comfortable with the concept of a pentavalent phosphorus as written in the "ylene" structure, making no special comment thereon nor on an "ylide" structure. Ramirez and Dershowitz[4] were the first to prove an ylide structure beyond reasonable doubt when they repeated the 1899 work of Michaelis and Kohler[5] to show that phenacyltriphenylphosphonium bromide was converted into the ylide $Ph_3P{=}CHCOPh$ upon treatment with aqueous sodium hydroxide. Wittig and Reiber[6] earlier had deduced the structure of $Me_3P{=}CH_2$ from its addition reaction with benzophenone, mainly by analogy with the behavior of the corresponding nitrogen ylide. At present ylides can be identified by cleavage reactions (see Chapter 5), by their reactions with carbonyl or nitroso compounds (see Chapter 8), and by the spectroscopic techniques discussed in this chapter.

Phosphonium ylides function chemically as carbanions, effecting both substitution and addition reactions. Thus, new carbon–carbon *single* bonds can be formed using phosphonium ylides as nucleophiles, and the ability to later remove the phosphonium group (see Chapter 5) makes ylides useful synthetic reagents for that purpose (Eq. 3.1). The more dominant synthetic use of ylides,

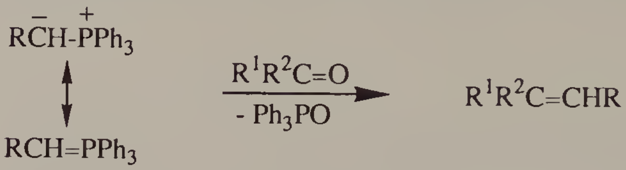


(3.1)

---

*Ylides and Imines of Phosphorus*, Edited by A. William Johnson.
ISBN 0-471-52217-1

however, is the reaction with carbonyl compounds (see Chapter 8) which regioselectively affords new carbon–carbon *double* bonds (Eq. 3.2). The discovery of this reaction in 1953[7] produced a major revolution in alkene synthesis, and resulted in the award of the 1979 Nobel Prize to Georg Wittig and the naming of the reaction for him. The reactions of ylides to form new carbon–carbon single bonds does not normally depend on the active participation of the phosphonium group, other than to facilitate and direct the regiospecific formation of the carbanion. On the other hand, the reaction of ylides to form alkenes depends on the phosphonium group for active participation in the reaction mechanism, but the nature of the phosphonium group also has an important effect on the reactivity of the ylides. Therefore, the "special" carbanionic nature of phosphonium ylides has been a matter of considerable study and importance.

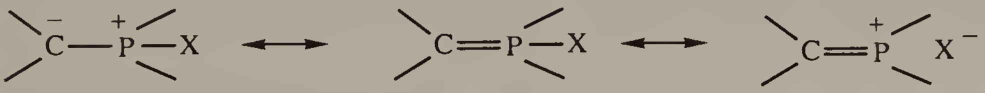


$$\begin{array}{c}R\overset{-}{C}H\text{-}\overset{+}{P}Ph_3\\ \updownarrow \\ RCH{=}PPh_3\end{array} \xrightarrow[-\,Ph_3PO]{R^1R^2C{=}O} R^1R^2C{=}CHR \qquad (3.2)$$

It has been clear from the earliest days of ylide chemistry that phosphonium ylides are especially stable carbanions, with the "extra" stabilization coming from the phosphonium group. This stability is reflected in the case of formation of various ylides by proton abstraction from the phosphonium salt, a topic discussed later in this chapter and also in Chapter 4 but also in the case of isolation of those same ylides. The latter is really a reflection of the same property, the basicity of ylides. For example, whereas it is not practical to try to isolate the fluorenyl carbanion, the corresponding ylide, triphenylphosphoniumfluorenylide, is readily isolable and storable in the presence of oxygen and moisture.[8] Similarly, the cyclopentadienylide,[9] the phenacylide,[4] and the methoxycarbonylide[2] and related ylides all are stable enough to be isolated as crystalline substances. In all of these instances the ylide is too weak a base to react with water. More reactive ylides, such as the liquid trimethylphosphoniummethylide[10] ($Me_3P{=}CH_2$), may be isolated, but only in the strict absence of moisture. Thus, the terms "stabilized," "semistabilized," and "nonstabilized (or reactive)" ylides have come to imply the isolability *and* the carbanionic stability of phosphonium ylides, both terms reflecting a single property. Stabilized ylides usually are isolable and have strong electron withdrawing groups on the carbanion, groups such as cyclopentadienyl, carbalkoxy, and acyl which can provide significant delocalization for the carbanion. Semistabilized ylides are those such as the benzylide and allylide, but these usually are not isolable. Nonstabilized ylides include the alkylides ($RCH{=}PPh_3$, R = alkyl), which usually are not isolated but are instead prepared and used in solution. These ylides generally are yellow in color; some of the stabilized ylides are orange and even reddish purple. The progress of reactions involving the formation or the disappearance of ylides often can be monitored by color changes.

That the phosphonium group can provide significant stabilization for a carbanion has been known for some time. The fact that vinylammonium salts did not undergo anionic addition[11] whereas vinylphosphonium salts did[12] (see Chapter 4) has been rationalized by the ability of the phosphonium group to provide stabilization for the carbanion adduct. Similarly, tetramethylphosphonium iodide more rapidly exchanged protons for deuterium in deuteroxide solution than did tetramethylammonium iodide,[13] ylides being the proposed intermediates. Finally, triphenylfluorenylphosphonium bromide has a p$K_a$ of about 10, whereas the trimethylfluorenylammonium salt is about 19, and fluorene itself is about 22.[14]

The special stabilization of phosphonium ylides relative to other carbanions historically has been attributed to the ability of the positively charged phosphorus atom, perhaps through the use of low-energy 3*d* orbitals, to provide delocalization of the negative charge on the carbanion (see Chapter 2 for a full discussion). Phosphonium ylides usually have been represented as hybrids of the canonical forms **1** and **2a**. Although there has been debate over whether (1) there is *pπ–dπ* bonding between the carbon and phosphorus atoms to the extent represented by structure **2a** (the *ylene* form), (2) There is major polarization even though the negative charge is concentrated in a carbon *p* orbital as represented by structure **1** (the *ylide* form),[15] or (3) the major bonding results from negative hyperconjugation (*π–σ** bonding) facilitated by 3*d* orbitals as represented by **2b**,[16] it is clear from physical evidence and from theoretical work (see Chapter 2) that special stabilization of the ylide carbanion is provided by the adjacent phosphonium group.



**1** **2a** **2b**

That phosphonium ylides are very polar molecules is clear from an examination of their dipole moments. Experimental dipole moments ranging from 3.2 to 9.3 D have been reported (Table 3.1). Several groups have estimated the bond character of the P–C ylide bond from dipole moment data. The cyclopentadienylide was estimated to have 50% double bond character[9] and Lumbroso et al.,[20] calculating that a $^+$P–C$^-$ ionic bond would have a dipole of 8.15 D and estimating that the P–C bond moment in $Ph_3P{=}CH_2$ was 4.5 ± 0.5 D, claimed that the P–C bond had about 55% ionic character.

It is interesting to note that electron donating groups on phosphorus resulted in an *increase* in the dipole moments of comparable ylides, implying a larger charge separation in the P–C bond, whereas electron withdrawing groups on phosphorus resulted in lower charge separation. The latter instances may imply more contribution from an “ylene” form (i.e., more *pπ–dπ* overlap) or more polarization or negative hyperconjugation as the phosphorus is made more

TABLE 3.1 **Dipole Moments of Phosphonium Ylides ($X_3P{=}CR'R''$)**

| X | R′ | R″ | Dipole Moment (D)[a] | Reference |
|---|---|---|---|---|
| Ph | H | H | 3.2 | 17 |
| $p$-$MeOC_6H_4$ | H | H | 4.1 | 17 |
| Ph | H | Cl | 4.2 | 20 |
| Ph | Cl | Cl | 5.1 | 20 |
| Ph | H | $C_6H_5$ | 4.9 | 17 |
| Ph | H | $C_6F_5$ | 6.8 | 17 |
| Ph | H | $p$-$CH_3C_6H_4$ | 5.5 | 20 |
| Ph | H | $p$-$ClC_6H_4$ | 6.8 | 20 |
| Ph | H | $p$-$NO_2C_6H_4$ | 9.3 | 20 |
| Ph | H | CHO | 6.5 | 20 |
| Ph | H | $COCH_3$ | 5.6 | 20 |
| Ph | H | $COC_6H_5$ | 5.5 | 4 |
| $p$-$ClC_6H_4$ | H | $COC_6H_5$ | 4.3 | 20 |
| $p$-$ClC_6H_4$ | H | $COC_6H_4Cl$ (p) | 5.2 | 20 |
| Ph | H | COOEt | 5.0 | 20 |
| Ph | $CH_3$ | COOEt | 5.4 | 20 |
| Ph | Fluorenylide | | 7.1 | 8 |
| Ph | 2.7-Dibromofluorenylide | | 7.2 | 18 |
| $p$-$ClC_6H_4$ | 2,7-Dibromofluorenylide | | 5.0 | 18 |
| $p$-$Me_2NC_6H_4$ | 2,7-Dibromofluorenylide | | 9.1 | 18 |
| $n$-$C_4H_9$ | Fluorenylide | | 7.4 | 19 |
| Ph | Cyclopentadienylide | | 7.0 | 9 |

[a] Rounded off to one decimal point for comparison.

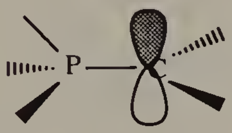
electron deficient. The placement of more electron withdrawing groups on the carbon end of the ylide bond resulted in an *increase* in the charge separation, perhaps from the ylide obtaining more stabilization from C–to–C delocalization and less from C–to–P delocalization.

Although they are polar molecules, ylides are soluble in organic solvents and do not behave therein as zwitterions. Their polarity is further demonstrated by the fact that they formed 1:1 charge transfer complexes with tetracyanoquinodimethane.[21] In a series of phenacylides, $Ph_3P{=}CHCOC_6H_4$-X($p$), the binding energy of the complex increased with electron donating substituents (X) and the rate of complex formation increased in the same direction, leading to a Hammett $\rho$ value of $-1.06$. The ylide clearly was serving as the donor molecule, and the phenyl substituents clearly were affecting the electron density on the carbanion.

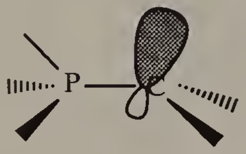
Much of this chapter focuses on the application of various spectroscopic and structural techniques to the study of ylides, and especially to studies of the nature of the "ylide bond." In Section 3.4 several unique classes of phosphonium ylides are discussed, including allylic ylides, several kinds of bis-ylides, cyclic ylides, and ylides with unusual substituents on carbon or phosphorus.

## 3.1 MOLECULAR STRUCTURE OF PHOSPHONIUM YLIDES

The actual molecular structure of phosphonium ylides, particularly the spatial arrangements around the P–C ylide bond, continues to be a subject of experimental and theoretical study. The phosphorus atom is expected to be $sp^3$ hybridized with tetrahedral geometry among its four substituents, the same as for its precursor phosphonium salt. The carbanion usually has been expected to be $sp^2$ hybridized with trigonal geometry (**3**), the lone pair of electrons residing in a *p* orbital. However, there has been evidence for pyramidalization of the carbanion of some ylides, with the lone pair perhaps residing in an $sp^3$ hybrid orbital (**4**). Overlap of the carbon orbital carrying the lone pair of electrons has been presumed to occur with the $3d_{xy}$ or $3d_{xz}$ phosphorus orbitals. With both sets being available and providing essentially cylindrical symmetry, there is no electronic reason for not observing free rotation about the P–C bond. Little consideration seems to have been given to the possibility that the phosphorus atom in ylides is $sp^3d$ hybridized with either a basal or axial vacant orbital providing overlap with the carbanion *p* or $sp^3$ orbital. The overriding evidence seems to be that *most* ylides have approximately tetrahedral phosphorus bonding and that stabilized ylides have trigonal planar carbanions, whereas many nonstabilized ylides now appear to have slightly pyramidalized carbon atoms (see Section 2.3).[15]



**3**



**4**

### 3.1.1 Bond Lengths and Bond Angles

Most interest has focused about the P–C bond length in ylides, as determined by X-ray crystallographic analysis or electron diffraction analysis. The theoretical P–C single bond distance is 1.872 Å, the double bond distance is 1.667 Å,[22] and the measured distances in various ylides often has been used as an indication of the contribution of the ylene canonical form (**2a**)—the shortness of the bond presumably reflecting increasing ylene-like character. The bond angles about phosphorus and carbon also are key to understanding the molecular structure and the hybridization about phosphorus and carbon. Tables 3.2 and 3.3 list the P–C bond distance for most ylides whose structure has been determined to date.

Inspection of the data in Tables 3.2 and 3.3 reveals P–C bond lengths ranging from 1.640 to 1.78 Å, with the majority of the lengths near 1.71 Å. Those ylides with only hydrogen on the ylide carbon exhibit the shortest lengths, virtually the

**TABLE 3.2 Structural Data on Triphenylphosphonium Ylides ($Ph_3P{=}CR'R''$)**

| R′ | R″ | P–C Distance (Å) | Reference |
|---|---|---|---|
| H | H | 1.661, 1.697 | 23, 24 |
| | CHO | 1.709 | 25 |
| | COPh | 1.71 | 26 |
| | Tosyl | 1.709 | 27 |
| | $^+PPh_3\ Br^-$ | 1.695/1.710 | 28 |
| CR′R″ = Cyclopropylidene | | 1.696 | 29 |
| Cyclobutylidene | | 1.668 | 30 |
| Hexafluorocyclobutylidene | | 1.713 | 31 |
| Complex cyclobutylidene | | 1.769 | 32 |
| Complex cyclohexylidene | | 1.71/1.77 | 33 |
| | | 1.77 | 34 |
| Cyclopentadienylide | | 1.718 | 35 |
| Substituted cyclopentadienylide | | 1.756 | 36 |
| CN | CN | 1.753 | 37 |
| | Complex phosphino group | 1.703/1.717 | 38 |
| COPh | Cl | 1.736 | 39 |
| | I | 1.71 | 40 |
| | SePh | 1.746 | 41 |
| $COC_6H_4Ph$ (p) | $^+I\text{-}C_6H_4CH_3$ (o) | 1.710 | 42 |
| $COCH_3$ | COOEt | 1.753 | 43 |
| | H | 1.69 | 44 |
| COOMe | $CH_2COOH$ | 1.732 | 45 |
| | Indazolinone ring system | 1.71 | 46 |
| | $C(COOMe){=}N^+R_2$ | 1.753 | 47 |
| | $C(COOMe){=}NC_6H_4Br$ (p) | 1.70 | 48 |
| | $C(COOMe){=}CHPh$ (cis) | 1.718 | 49 |
| | $C(COOMe){=}CHPh$ (trans) | 1.752 | 48 |
| COOEt | 2-(Cycloheptatrienylone) | 1.76 | 50 |
| $PPh_2$ | $PPh_2$ | 1.720 | 51 |
| $SbPh_2$ | $SbPh_2$ | 1.692 | 52 |
| $AsPh_2$ | $AsPh_2$ | 1.698 | 53 |
| SPh | SePh | 1.707 | 54 |
| $^+PPh_3$ | $C(NPh)_2$ | 1.726 | 55 |
| $PPh_2$ | $C(NPh_2){=}NPh$ | 1.748 | 56 |

same as the theoretical P–C double bond length of 1.667 Å.[22] Those with strongly conjugating or very bulky groups on the carbanion generally show longer P–C bonds, perhaps reflecting less overlap with phosphorus orbitals and more with the carbanion substituents. None of the ylides show P–C lengths near the single bond length of 1.872 Å.[22] In those few instances where the P–C distance has been determined for the corresponding conjugate acid of the ylide (i.e., the phosphonium salt),[59,63,65] the P–C bond has lengthened to near

**TABLE 3.3 Structural Data on Other Phosphonium Ylides (XP=CR′R″)**

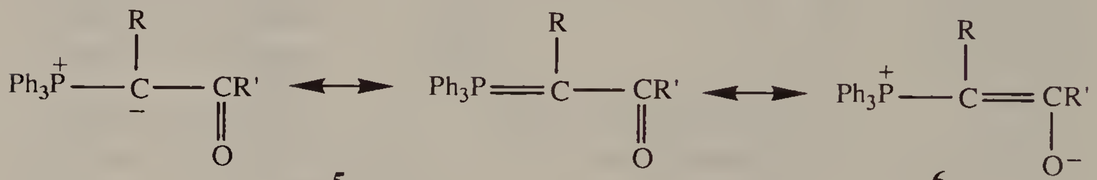
| X | R′ | R″ | P–C Distance (Å) | Reference |
|---|---|---|---|---|
| $Me_3$ | H | H | 1.640 | 57 |
| | | $SiH_3$ | 1.653 | 58 |
| | $^+PMe_3$ | $^+PMe_3$ | 1.75 | 59 |
| | $SiCl_3$ | $SiCl_3$ | 1.733 | 60 |
| $Me_2Br$ | $SiMe_2CH_2SiMe_2CH_2$ | $SiMe_2$ | 1.646 | 61 |
| $^tBu_2Cl$ | Ph | Ph | 1.67 | 62 |
| $[(CH_3)_2CH]_3$ | Me | Me | 1.731 | 63 |
| $(n\text{-}C_3H_7)_2Ph$ | CN | CN | 1.743 | 64 |
| $(\text{Morpholino})_3$ | H | COPh | 1.717 | 65 |
| Ferrocenyl | H | H | 1.629 | 24 |
| $(n\text{-}C_4H_9)_3$ | Diselenacyclopentadienylide | | 1.78 | 66 |
| $(p\text{-}CH_3\text{–}C_6H_4)_3$ | A cyclopentylidenone | | 1.728 | 67 |

1.80 Å. Thus, the P–C bond of ylides clearly is one of unique shortness, whether described as ylide (**1**) or ylene (**2**).

The substituents on phosphorus, usually three phenyl groups as in Table 3.2, but occasionally others as in Table 3.3, generally are close to tetrahedrally oriented about phosphorus, and usually with the phenyl groups oriented in a propeller-like manner with respect to the P–C bond.[23, 27, 35, 37, 45] The P-phenyl lengths generally are near 1.82 Å, close to the P-phenyl distance in triphenylphosphine. The change of P-substituent from phenyl to alkyl has little effect on ylide geometry, except for a steric effect when the alkyl group is large,[63] resulting in lengthening of the P–C ylide bond.

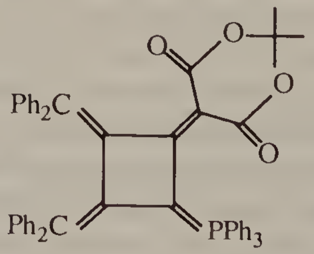
The bond angles at the ylide carbon generally reveal that the P–CXY group (X = atom attaching group R′; Y = atom attaching group R″, both in Tables 3.2 and 3.3) is close to planar when the groups X and Y are electron withdrawing, consistent with $sp^2$ hybridization and a trigonal planar configuration of the ylide carbanion. Some deviation from planarity occurred when the R′ and R″ groups were bulky[53] and often when the groups X and Y were alkyl.[15] Considerable deviation occurred with the cyclopropylidene (59°)[29] and cyclobutylidene (19°)[30] ylides, the former being essentially pyramidal at the ylide carbanion. This angle of a triphenylphosphonio substituent with the ring plane is typical for cyclopropanes. Interestingly, these two ylides also had shorter than average P–C bond lengths (1.696 and 1.668 Å, respectively), but no explanation is obvious. Vincent et al.,[68] using calculations on a model compound, claimed that (1) a relatively low energy of inversion at the cyclopropylide carbanion and (2) the hybridization, falling between $sp^2$ and $sp^3$, nonetheless produced an ylide bond not very different from planar examples. More recently, Schmidbaur et al.[24] reinvestigated the structure of $Ph_3P{=}CH_2$ and obtained higher-order data which indicated that the two methylenic protons were out of the P=C plane, leading them to describe the ylidic carbon as “an easily pyramidizeable carbanion stabilized by the adjacent tetrahedral phosphonium center” by an unspecified mechanism.

When the ylide carbanion was conjugated with carbonyl groups evidence of delocalization was available from the structural data. Many β-keto ylides (5)[25, 26, 34, 39, 40–43, 65, 67] have C=O lengths ranging from 1.22 to 1.30 Å, with most being near 1.25 Å, compared to the normal C=O of 1.215 Å[69] and to a determined length of 1.217 Å in a corresponding phosphonium salt.[65] Likewise, the C–CO lengths ranged from 1.35 to 1.48 Å, with most being near 1.40 Å, compared to an expected length of 1.506 Å[70] and to a determined length of 1.51 Å in a phosphonium salt.[65] The lengthening of the C=O bond and the shortening of the C–CO bond both are attributed to significant delocalization of the carbanion electrons through the carbonyl group, as represented by contributing structure **6**. This conclusion is consistent with the infrared data discussed later in this chapter. It is often noted that the carbonyl substituent (e.g., R′ = phenyl) is twisted out of the plane of the carbonyl group.[65] Similar structural evidence is available for the conjugation of an ylide carbanion with the carbonyl group of an ester function, but the magnitude of the effect is smaller.

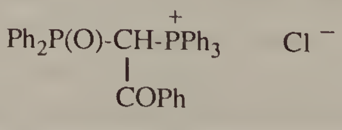


**5** **6**

Brown et al.[32] recently reported an interesting example of an extended conjugated ylide system (7) in which the P–C bond was unusually long (1.769 Å), the C1–C2 ring bond was unusually short (1.389 Å), and the exocyclic bond to the six-membered ring was unusually long (1.459 Å), again indicating extensive delocalization to the carbanion substituent. Three groups have reported on the structure of ylide complexes with $BH_3$,[71] $B_3H_7$,[72] and $Me_3SnCl$,[73] and found that the P–C “ylide” bond was 1.76 ± 0.01 Å long, longer than an ylide bond but shorter than a nonylide P–C bond. Antipin et al.[74] recently reported

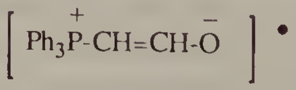


**7**



$Ph_2P(O)\text{-}\underset{COPh}{CH}\text{-}\overset{+}{P}Ph_3 \quad Cl^-$

**8**



$\left[ Ph_3\overset{+}{P}\text{-}CH\text{=}CH\text{-}\overset{-}{O} \right]^{\bullet}$

**9**

evidence for a hydroxyphosphonium ylide as one of three crystalline tautomers of the phosphonium salt (**8**), the $Ph_2P(O)–C$ bond being 0.05 Å shorter in the ylide form than in **8** or the enol form. Finally, Geoffrey et al.[25] were the first to propose a trigonal bipyramid structure for phosphorus in an ylidic molecule—a radical (**9**) produced by electron capture by the precursor triphenylphosphoranylideneacetaldehyde.

A number of phosphacumulenes ($Ph_3P{=}C{=}X$) have been studied by X-ray crystallography and their structures are discussed in Section 3.4.3.1. The P–C ylide bonds in such compounds ranged from 1.58 to 1.65 Å and these are even shorter than the typical isolated ylide bond.

### 3.1.2 Other Structural Features

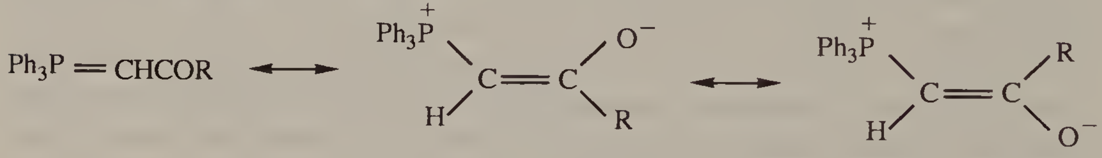
*3.1.2.1* ***Optical Activity in Phosphonium Ylides.*** Tertiary phosphines are enantiomerically stable, in contrast to amines, and can be alkylated to chiral phosphonium salts.[75] The chiral phosphonium salts have been converted to ylides using aqueous base[75] or phenyllithium in ether,[76] and the ylides were configurationally stable at phosphorus. This configurational stability at phosphorus persisted through alkylation,[75] hydrolysis,[75] reduction,[75] and Wittig reactions,[76] as well as reactions with epoxides.[77]

There are no known optically active phosphonium ylides wherein the chirality is due to the carbon end of the ylide bond, suggesting the absence of stable pyramidal geometry at the carbanion.

*3.1.2.2* ***P=C Bond Rotation.*** Ab initio molecular orbital theory has predicted that there should be no significant barrier to rotation about the P–C ylide bond, regardless of the relative contributions of the ylide (**1**) and ylene (**2**) forms.[78,79] If *d* orbitals are involved, overlap of the carbon 2*p* orbital with the phosphorus 3*d* orbitals is possible using the $3d_{xy}$ or $3d_{xz}$ orbitals. If polarization of the carbanion or negative hyperconjugation are involved, these effects should not vary with rotation about the P–C bond. Most experiments have failed to detect any significant barrier to such rotation. For example, Liu and Schlosser[80] found that for triphenylphosphoniummethylide, a series of mono- and dialkylides, and for the benzylide, no evidence for restricted rotation about the P–C bond could be detected by $^{13}C$ NMR spectroscopy down to − 105°. However, Lucken and Mazeline[81] earlier claimed some evidence for restricted rotation based on the ESR spectrum of the radical cation from methylenetriphenylphosphorane. Recently, Grutzmacher and Pritzkow reported the detection of three independent molecules of $(^tBu)_2ClP{=}CPh_2$ in a unit cell, corresponding to three rotamers of the ylide.[62]

Restriction of rotation has been detected for some substituents on the ylide carbanion. The $^1H$ and $^{13}C$ NMR spectra of triphenyl- and trimethylphosphoniumbenzylide were temperature dependent, indicating a torsional barrier of about 8.5 kcal/mol for rotation of the benzylide ring.[80] Earlier Schmidbaur et al.,[51] using $^{31}P$ NMR spectra and X-ray crystallography, detected restricted rotation with a 12-kcal/mol barrier, about the C–P single bonds in bis(diphenylphosphino)methylenetriphenylphosphorane. A lower barrier was detected for the bis(diphenylarsino) analog[53] and no barrier was detected with the similar 1,1-bis-(diphenylphosphino)-ethylene,[82] leading to the proposal that the rotational barrier was due to repulsion between the carbanion lone pair electrons [perpendicular to the P–C(P)$_2$ plane] and the phosphine lone pairs which seemed oriented in that plane.[83] Diastereotopic methyl groups were detected for $Ph_3P{=}CH{-}P(CH(CH_3)_2)_2$ from − 80 to + 200°, leading to an estimated 40 kcal/mol energy barrier for inversion at phosphorus for the same reason.[84]

*3.1.2.3* ***Isomerism in β-Carbonyl Ylides.*** To the extent that β-carbonyl groups stabilize an ylide by delocalization through the carbonyl group, the possibility exists for two isomeric forms of the enolate (**10** and **11**). Randall and Johnson,[85] and then others,[86–90] showed by monitoring the methine proton doublet using $^1$H NMR that scrupulously dry β-ketoylides (**10** and **11**, R = alkyl or aryl) existed only in the cis form (**10**) over the temperature range − 60 to + 150°. However, for the formylide[87,88] both the cis (**10**, R = H) and the trans (**11**, R = H) forms could be detected, and the P–H coupling for the cis was almost exactly the same as for the single observed form of the phenacylide (**10**, R = Ph).[85] The P–C couplings also differed for the cis (5–10 Hz) and trans (15–20 Hz) forms.[91] The presence of any proton source confused the analyses by causing NMR spectral changes due to rapid ylide–phosphonium salt equilibria[85] (see Section 3.2.1.1). These conclusions have been verified by recent additional studies.[92]



**10**
(*Z*, cis)

**11**
(*E*, trans)

After initial erroneous reports regarding the temperature-dependent collapse of the methine quartet in the $^1$H NMR spectrum of the ester ylide (**10**, **11**, R = $OCH_3$), it was demonstrated [85,86,93] that the ylide existed in two geometric forms, **10** and **11**, with a coalescence temperature of about 35–43°C. When the α-proton was replaced with substituents[87,94,95] the coalescence temperature increased and the former cis:trans ratio of 2–3:1 changed to as little as 1:3. When the methoxy group of the ester was replaced with larger alkoxy groups,[96] the cis:trans ratio also decreased. Both of these changes were attributed to steric effects. Rotation barriers have been determined to be from 10 to 15 kcal/mol.[91, 93–95, 97] Recently, $^1$H, $^{31}$P and $^{13}$C NMR studies have confirmed these earlier conclusions.[91,92,98] The similar but conjugated ylide $Ph_3P{=}CH{-}C(CH_3){=}CHCOOEt$[99] also showed cis–trans isomerism. Ylides with thione ester groups also exhibited cis–trans isomerism and a higher coalescence temperature than for the corresponding oxygen analog, and both isomers could be trapped by methylation.[100]

## 3.2 SPECTROSCOPIC STUDIES OF PHOSPHONIUM YLIDES

### 3.2.1 NMR Spectroscopy

***3.2.1.1 Proton NMR Spectroscopy.*** [All chemical shifts are $\delta$ values relative to TMS with positive values indicating deshielding, and all coupling constants ($J$) are in hertz (Hz)]. As a reference the proton NMR spectra of phosphonium salts will be mentioned. The triphenylphosphonium group deshields protons on adjacent carbons, $Ph_3P^+{-}CH_3$ showing a doublet from geminal P–H coupling centered at 3.17 with $J_{PH}$ of 13.1.[101] The chemical shift is sensitive to the nature of both P and C substituents, but the $J_{PH}$ values are not. Thus, tri-*n*-butylmethylphosphonium salts have a methyl chemical shift of 2.07 and $J_{PH}$ of 13.2, while triphenylethylphosphonium salts have a methylene chemical shift of 3.79 and a $J_{PH}$ of 12.4.

Phosphonium ylides show increased shielding of protons on the ylidic carbon relative to the phosphonium salts, $PH_3P{=}CH_2$ showing a chemical shift of 0.61 and $J_{PH}$ of 7.0,[102] undoubtedly due to the increased electron density on carbon. Electron withdrawing groups on the carbanion deshield the methine proton further, $Ph_3P{=}CHCN$ being shifted to 3.71,[102] $Ph_3P{=}CHCOCH_3$ to 3.19,[102] and $Ph_3P{=}CHCOC_6H_5$ to 4.43.[85] The PH coupling is larger in the substituted ylides, usually about 25 Hz.[85, 102]

Methylenetrimethylphosphorane ($Me_3P{=}CH_2$) showed a methyl doublet ($J_{PH} = 6.9$) and a methylene doublet ($J_{PH} = 12.6$) at room temperature. Either heating the solution to 100°C or adding a small amount of methanol collapsed the spectrum to a sharp singlet. The collapse was attributed to rapid proton exchange in both instances, between methyl and methylene in the first instance, and with the methanol proton in the second.[103] The temperature-dependent proton exchange phenomenon also was observed with $\beta$-carbonyl ylides,[85, 86, 91, 93, 102] a phenomenon separate from but superimposable on the cis–trans isomerism discussed in Section 3.1.2.3.

***3.2.1.2 $^{31}P$ NMR Spectroscopy*** (All spectra are with reference to 85% $H_3PO_4$, with positive values indicating deshielding). The $^{31}P$ NMR study of phosphonium ylides is only about 20 years old, and readers are referred to an excellent 1987 review by Grim for a detailed discussion.[104] Phosphonium salts are deshielded by about 15–65 ppm from 85% $H_3PO_4$, whereas phosphonium ylides are deshielded by a lesser amount, usually about 7–30 ppm, making the salt-minus-ylide value usually positive (~ 5–30 ppm). Caution must be exercised, however, for the preparation of ylides using lithiated bases often leads to lithium–ylide complexes in solution whose chemical shifts are almost indistinguishable from those of phosphonium salts[105] and those of ylide–$BF_3$[106]

**TABLE 3.4** $^{31}$P NMR Spectra of Phosphonium Ylides

| Ylide | δ (ppm) | $J_{P=C}$ (Hz) | Reference |
|---|---|---|---|
| $Me_3P{=}CH_2$ | – 2.1 | 90.5 | 110 |
| $Et_3P{=}CH_2$ | 23.6 | 86.8 | 111 |
| $Ph_3P{=}CH_2$ | 20.3 | 98.6 | 112 |
| $Ph_3P{=}CHCH_3$ | 13.8 | 110.7 | 110 |
| $Ph_3P{=}C(CH_2)_2$ | 15.6 | 3.9 | 29 |
| $Ph_3P{=}C(CH_2)_3$ | 16.5 | 83.0 | 30 |
| $Ph_3P{=}CMe_2$ | 9.8 | | 29 |
| $Ph_3P{=}CHCN$ | 22.6 | | 113 |
| $Ph_3P{=}CHPh$ | 7.1 | | 110 |
| $Ph_3P{=}CHCOOEt$ | 19.1 | | 111 |
| $Ph_3P{=}CHCOPh$ | 21.6 | | 111 |
| $Ph_3P{=}CHSiMe_3$ | – 1.2 | | 114 |
| $Ph_3P{=}CHCl$ | 25.1 | | 115 |
| $Ph_3P{=}C(COPh)CH_2COPh$ | 16.9 | | 116 |
| $Bu_3P{=}C(COPh)CH_2COPh$ | 21.3 | | 114 |
| $Ph_3P{=}C(PPh_2)_2$ | 27.8 | | 51 |

and ylide–$BH_3$[107] complexes. Table 3.4 lists the $^{31}$P NMR spectra of a few representative ylides.

Inspection of the data and that quoted by Grim[104] reveals that in phosphorus substitution downfield shifts are in the order *t*-Bu > *i*-Pr > Et > Me, but the differences are not large. Upon replacement of alkyl groups on phosphorus by aryl groups the shielding usually decreases, implying electron withdrawal by the aryl group. On the ylide carbanion placement of electron-withdrawing groups leads to small downfield shifts and electron-donating groups provide small upfield shifts, both being the expected direction in terms of the electron density experienced by phosphorus. The triphenylphosphoniumcyclopropylide (15.6) and cyclobutylide (16.5) are both slightly less shielded than the isopropylide (9.8)[29] but the five- (4.8) and six-membered (6.4) ring ylides are more shielded.[108]

Albright et al.[109] reported that phosphorus bonded to an $sp^2$ hybridized carbon is more shielded than when bonded to an $sp^3$ hybridized carbon. This pattern prevailed with vinyl- (19.3) and ethyl- (25.5) triphenylphosphonium bromide and with vinyl- (27.4) and ethyl- (36.6) tri-*n*-butylphosphonium bromide. It was argued that $^{31}$P peak positions could reflect the relative hybridization of different phosphonium ylides, with smaller values indicating more $sp^2$ character for the ylide carbanion.

The $^{31}$P chemical shifts of ylides have not been especially useful in discerning the fine points of ylide structure. The P–C coupling constants have been much more useful, revealing the nature of the hybridization of the ylide carbon and are discussed in detail in Section 3.2.1.3.

*3.2.1.3* ***$^{13}$C NMR Spectroscopy*** (All values are relative to the TMS reference, with positive values reflecting deshielding). It seems difficult to make broad generalizations from the $^{13}$C chemical shift data that is available, in part because of considerable conflicting data. The method of preparing the ylide is crucial because lithium complexes of ylides give quite different results than do the uncomplexed ylides.[105] Comparisons seem valid within closely related substances, and some comparative examples are listed in Table 3.5.

Replacement of alkyl groups on phosphorus with phenyl groups leads to deshielding of the ylide carbon and a more positive chemical shift, testifying further to the overriding inductive withdrawal effect of phenyl. Likewise, placement of electron withdrawing groups on the ylide carbon leads to deshielding. In most instances the ylide carbanion is more shielded than is the corresponding carbon in the conjugate acid, although that is not the case in the phenacylides. Perhaps the strong delocalization effect of the acyl group more than offsets the carbanion effect.

The coupling constants available from $^{13}$C NMR spectra are more revealing. The larger values for $J_{C-H}$ in the ylides ($\sim$150 Hz) than in the phosphonium salts ($\sim$130 Hz) are a reflection of the increase in the percentage of *s* character in the CH bond, and thus an increase in the extent of trigonal hybridization of the carbanion.[125] The lithium complex of triphenylphosphoniummethylide (133 ppm)[105] shows about the same coupling as the phosphonium salt (135 ppm)[117] and benzyllithium (116–135 ppm),[125] all of which are larger than methyllithium (98 ppm).[125] The rather low coupling for $Me_3P{=}CHSiMe_3$ (135 ppm)[111] may indicate some pyramidalization of the carbanion, which is unexpected as an electronic effect but perhaps explainable as a steric effect.

The $^{13}C{-}^{31}P$ coupling constants also are helpful in understanding ylide structure. In phosphonium salts, with $sp^3$ carbon attached to a triphenylphosphonio group, such values usually range from 47 to 63 ppm (see Table 3.5); the

**TABLE 3.5 $^{13}$C NMR Spectra of Phosphonium Ylides and Salts**

| Ylide | $^{13}$C Shift (ppm) | | $J_{PC\alpha}$ (Hz) | | $J_{CH}$ (Hz) | | Reference |
|---|---|---|---|---|---|---|---|
| | Y[a] | S[a] | Y | S | Y | S | |
| $Me_3P{=}CH_2$ | −2.3 | 11.3 | 91 | 56 | 149 | 134 | 111, 117 |
| $Ph_3P{=}CH_2$ | −4.1 | 11.4 | 100 | 57 | 153 | 135 | 105, 117 |
| $Ph_3P{=}CMe_2$ | 9.0 | 21.5 | 122 | 47 | | | 105 |
| $Ph_3P{=}(CH_2)_2$ | 15.6 | 0.4 | 3.9 | 87 | | | 29, 118 |
| $Ph_3P{=}(CH_2)_3$ | 14.7 | 25.4 | 83 | 45 | | | 30, 119 |
| $Ph_3P{=}CHCOPh$ | 50.4 | 38.8 | 112 | 63 | 164 | 130 | 65, 120, 121 |
| $Ph_3P{=}CHCOOR$ | 28.9 | 32.6 | 131 | 57 | | | 122, 123 |
| $(i\text{-Pr})_3P{=}CMe_2$ | −2.6 | | 133 | | | | 124 |

[a] Y = Ylide; S = corresponding phosphonium salt.

cyclopropyl salt is unusually large (87 ppm), but the cyclobutyl and higher homologs return to normal (42–49 ppm).[118] When the carbon atom adjacent to phosphorus is $sp^2$ hybridized, however, the $J_{PC}$ values increase, such as in vinylic phosphonium salts which have values near 90 ppm.[109,126] Table 3.5 reveals $J_{P=C}$ values for ylides ranging from 83 to 133 ppm, with the cyclopropylide being a stark exception. It has been suggested that the larger the coupling constant, the more trigonal is the hybridization of the ylide carbanion (i.e., the more *s* character there is in the P–C sigma bond), and that strong electron withdrawing groups ensure such a geometry over and above the normal tendency of ylides. The cyclopropylide would appear to be pyramidal by virtue of its extremely low $J_{P=C}$ value (3.9 ppm), an argument substantiated by the X-ray crystallographic analysis.[29]

Schlosser et al.[91] recently reexamined the $^1H$, $^{31}P$, and $^{13}C$ NMR spectra of several ylides and argued, on the basis of qualitative comparisons only of chemical shift data, that phosphonium alkylides have, at best, a 20% contribution of the ylene form (**2a**), and that $\beta$-ketoylides are about 50:50 enolate and ylide, with no contribution of the ylene form! They claim, without providing new evidence, that ylides are mainly "pyramidal at carbon, although flat."

## 3.2.2 Other Spectroscopies

*3.2.2.1 **Infrared Spectroscopy.*** Luttke and Wilhelm[127] determined that the P–C stretching frequency in triphenylphosphonium ylides was at 887–899 $cm^{-1}$, and calculated a force constant of 4.6 mdynes/Å for the methylide. They estimated a bond order for the P–C bond of 1.3. Later, Sawodny[128] studied the liquid ylide $Me_3P{=}CH_2$ by infrared and raman spectroscopy and determined a force constant of 5.59 mdynes/Å, leading to a bond order of 1.65.

Stabilization of phosphonium ylides by delocalization through substituents, such as carbonyl groups [e.g., $Ph_3P{=}CH{-}C(R){=}O \leftrightarrow Ph_3P^+{-}CH{=}C(R){-}O^-$], ascribes considerable single bond character to the carbonyl group, which has been demonstrated by infrared spectroscopy and by previously cited X-ray studies.[25,44] In the proof of structure for triphenylphosphoniumphenacylide the carbonyl absorption was at 1529 $cm^{-1}$, whereas in the conjugate acid precursor it was at 1667 $cm^{-1}$, and in the acetylide the absorptions were at 1542 and 1719 $cm^{-1}$, respectively.[4,129] Similarly, the alkoxycarbonyl ylides[121,129] absorbed at 1620 $cm^{-1}$ while their conjugate acids absorbed at 1720–1740 $cm^{-1}$. It can be concluded that the keto ylides are more enolic than ester ylides and provide more stabilization for the ylide carbanion. Further substantiation has been provided by the observed *O*-alkylation of $\beta$-carbonyl ylides to enol ethers (see Section 6.4). Others have accumulated considerable data on frequency changes in various substituted ylides.[89,130,131]

*3.2.2.2 **Miscellaneous Spectroscopies.*** Ultraviolet spectra have been reported for only a few phosphonium ylides with little unique structural information being obtainable. Grim and Ambrus[132] noted an absorption at 341–391 nm which seemed characteristic of alkylides. *p*-Nitrobenzylides absorbed near 520 nm[133] and phenacylides absorbed slightly over 300 nm.[134] The spectra of conjugated fluorenylidene ylides have also been reported.[135].

ESR spectroscopy of the radical produced by extended X irradiation of phosphonium salts led to the conclusion that there was little delocalization of the unpaired electron on the α-carbon to the phosphonium atom, although the phosphorus atom was thought to lie in the same plane as the $CH_2$ group in the methylide.[80,136] X irradiation of $Ph_3P{=}CH\text{–}CHO$ led to electron capture and production of a radical anion whose structure has been explained on the basis of an allylic phosphoranyl radical with a trigonal bipyramidal phosphorus atom $(Ph_3P'\text{–}CH{=}CH\text{–}O^-)$.[25]

Photoelectron spectra have been reported for a few phosphonium ylides. The excitation energies remained about the same when trimethylsilyl groups were placed on the ylide carbanion.[137,138] Compared to styrene, $Me_3P{=}CHPh$ showed a much lower ionization energy, leading to the conclusion that the ylide carbon[139] has considerable benzyl anionic character. Seno et al.[123] concluded that the phosphorus 2*p* binding energy was a function of the positive character of the phosphorus atom, which was influenced by the extent to which carbanion substituents provided delocalization.

$^{35}Cl$ NQR spectra of a series of dichloromethylenephosphoranes ($XYZP{=}CCl_2$) revealed similarity with that of $CH_2{=}CCl_2$, arguing for a trigonal ylidic carbon with considerable ylene character.

## 3.3 BASICITY OF PHOSPHONIUM YLIDES

It became evident very early in ylide chemistry that phosphonium ylides varied considerably in their basicity, and this property was used to study electronic effects in ylides, to further address the question of the bonding in ylides, and to predict the reactivity of ylides. Early clues regarding basicity evolved from observation of the process called *transylidation.* Bestmann[141] found that reaction of methylenetriphenylphosphorane with phenacyltriphenylphosphonium bromide afforded a high yield of the phenacylide (Eq. 3.3), and was able to

$$Ph_3P{=}CH_2 \ + \ Ph_3\overset{+}{P}\text{-}CH_2COPh \ \rightleftharpoons \ Ph_3\overset{+}{P}\text{-}CH_3 \ + \ Ph_3P{=}CHCOPh \qquad (3.3)$$

construct a hierarchy of "acidifying groups" (PhCO > COOR > Ph > Alkyl) for phosphonium salts. The converse is of course the ability of the group to stabilize the ylide through electron delocalization. This conversion of one ylide to another was but an acid–base reaction, but it turned out to be useful, even permitting the use of the methylide as a base to generate other ylides for subsequent reaction.[141–144]

The basicity of ylides, as measured by their p$K_a$'s, has been used particularly to determine the influence of substituents on ylide stability. The next two sections discuss the effect of carbon and phosphorus substituents on the basic properties of phosphonium ylides.

### 3.3.1 Effect of Carbanion Substituents

Measurement of the $pK_a$ of an ylide conjugate acid has been a favorite technique to determine the influence of substituents, but solvent variability has limited comparison of data. For a series of acylides ($Ph_3P{=}CH{-}COR$) Speziale and Ratts[113] found $pK_a$'s of 9.7 ($R = Ph_2N$), 9.2 ($R = OEt$), 6.0 ($R = Ph$), and 7.5 (CN replaces COR). For another series of acylides Fliszar et al.[145] found $pK_a$'s of 11.0 ($R = NH_2$), 8.8 ($R = OMe$), 6.6 ($R = CH_3$), 4.5 ($R = ClCH_2$), 6.7 [$R = C_6H_4OMe(p)$], 6.0 ($R = Ph$), and 4.2 [$R = C_6H_4NO_2(p)$]. For the phenacylides the rho value was + 2.25. Bordwell, in his magnificent compendium of equilibrium acidities measured in DMSO solvent,[146] reported the following $pK_a$'s for ylide conjugate acids ($Ph_3P^+{-}CH_2R$): 6.1 ($R = COPh$), 7.05 ($R = CN$), and 22.5 ($R = H$). Issleib and Linder[147] measured the $pK_a$'s of a similar series and found the acidifying effects of the substituents R to be in the order $Ph_3P^+ > COPh > COMe > CN > COOR > Ph_2P(O) > Ph_2P > Ph > H >$ Me. Johnson et al. [14] determined a rho value of + 5.0 for the $pK_a$'s for an extensive series of (2-substituted)-fluorenyltriphenylphosphonium salts. In all of these instances, therefore, the substituents appear to stabilize the ylide being formed by electron withdrawal from the ylide carbanion. Mastryukova et al.[148] recently reported the $pK_a$'s of large series of substituted phosphonium salts.

Placement of more electron withdrawing groups on the ylide carbanion is also reflected by increased $^{13}C$ deshielding, as discussed in Section 3.2.1.3. The $^{31}P$ NMR spectra also reveal small deshielding effects by similar placement of electron withdrawing groups on the carbanion, as discussed in Section 3.2.1.2. Froyen[121] reported this effect with a series of *p*-substituted phenacylides [$Ph_3P{=}CHCOC_6H_4\text{-}X(p)$], and also observed a steady decrease in $J_{PC}$ values as the substituents (X) became more electron withdrawing. The kinetic acidities of a series of triphenylalkylphosphonium salts recently have been determined to decrease in the following order: $PhCH_2{-} > HCCCH_2{-} > CH_2CHCH_2{-} > CH_3(CH_2)_3{-}$.[149] Alunni[150] recently reported a rho value of + 3.33 for the exchange of proton for deuterium in a series of phosphonium salts $RCH_2P^+(t\text{-}C_4H_9)_3$, probably involving ylide intermediates.

Variation in the nature of the ylide carbanion substituents can have a significant effect on the basicity of phosphonium ylides, and also can affect their ability to participate in many reactions discussed in later chapters.

### 3.3.2 Effect of Phosphorus Substituents

With but few exceptions the substituents placed on phosphorus in phosphonium ylides have been phenyl or simple alkyl, mainly because of the ready availability of triphenylphosphine and a few trialkylphosphines. The early observation that $Me_3P{=}CH_2$ would not[6] undergo the Witting reaction with benzophenone, but that $Ph_3P{=}CH_2$ would do so,[7] provided the first clue that phosphorus substituents could have major effects on ylides.

Determination of the basicity of ylides, through measurement of the $pK_a$ values for their conjugate acids, has revealed that aryl groups on phosphorus are acidifying with respect to alkyl groups. In the fluorenylide series, the tri-*n*-butylphosphonium ylide (8.0) was more basic than the triphenylphosphonium ylide (7.5),[19] and in several other series the trialkylphosphonium ylides were determined to be more basic than the triphenylphosphonium ylides.[147] Aksnes and Songstad[151] found that in a series of phenacylphosphonium salts, gradual replacement of methyl with phenyl on phosphorus led to an increase in the acidity of the salts, a stabilization of the formed ylide. Using a series of tri(substituted-phenyl)phosphoniumfluorenylides, the rho value for the $pK_a$'s was determined to be $+4.8$, indicating that electron withdrawal was stabilizing the ylide being formed.[14] Recently[152] a series of $\sigma$ constants have been developed for various phosphonium groups with exemplary values as follows: $Me_3P = 0.94$; $Me_2PhP = 1.02$; $MePh_2P = 1.12$; $Ph_3P = 1.22$; $(p\text{-}MeOC_6H_4)_3P = 1.11$; $(p\text{-}CH_3C_6H_4)_3P = 1.15$; $(p\text{-}ClC_6H_4)_3P = 1.31$. All of these examples demonstrate that the dominant effect of the phenyl groups on the phosphonium cation is the inductive withdrawal effect, and not a conjugative effect.[153] In contrast, McEwen et al.[154] reported that replacement of phenyl groups by ferrocenyl groups resulted in an increase in ylide basicity, probably a small conjugative effect between ferrocene and phosphorus.

A study of the same effect using NMR spectroscopy completes the picture. The $^1H$ NMR spectra of the methyl group in $MeP^+(C_6H_4X)_3$ salts indicated that the influence of the phenyl groups was mainly via an inductive effect.[155] Similarly, analysis of the $^{19}F$ NMR spectra of a series of fluorophenylphosphonium salts revealed that the inductive interaction between the fluorine atom and the phosphonium group was even larger than that between fluorine and a comparable carbocation, and the resonance effect was less than a third of the size.[156] Thus, the overriding influence of a phenyl substituent on positively charged phosphorus was transmitted by an inductive mechanism.

Variation in the nature of the phosphorus substituents has a significant influence on the basicity of ylides, and also can influence the ease with which the phosphorus atom itself is attacked by other reagents.

## 3.4 UNUSUAL PHOSPHONIUM YLIDES

Phosphonium ylides ($Ph_3P{=}CR'R''$) are known with a virtually limitless variety of substituents (R′ and R″) on the ylide carbon. They include alkyl, cycloalkyl, aryl, carbonyl, ester, carboxyl, sulfonyl, phosphoryl, phosphinyl, phosphonyl, nitrile, alkoxy, thioalkoxy, seleno, and amido groups. This section presents the chemistry of several classes of phosphonium ylides with unique structures and/or properties.

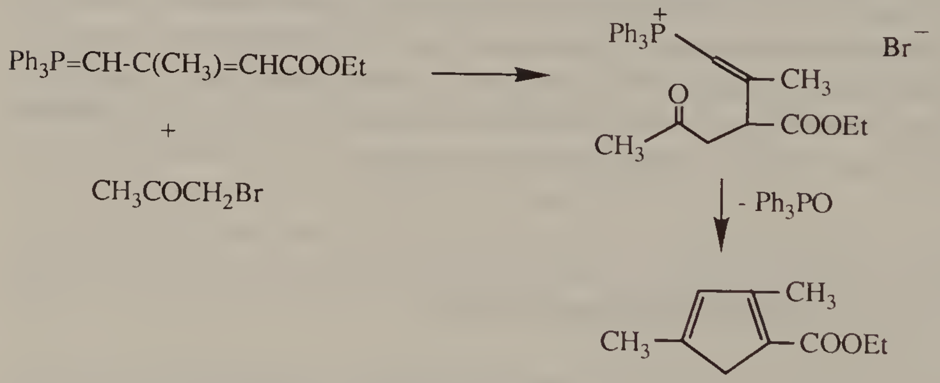
### 3.4.1 Allylic Phosphonium Ylides

Allylic phosphonium ylides (i.e., vinylic methylides) are those carrying an allylic group on the phosphorus atom, such as allylidenetriphenylphosphorane ($Ph_3P{=}CH{-}CH{=}CH_2$). Through a wide variety of reactions of the kind to be discussed in detail in Chapters 5–8, it has been demonstrated that in many instances the negative charge of the carbanion can be detected at both the α- and the γ-carbon. Bestmann et al.[157] and Schweizer et al.[158] demonstrated this fact by tritium and deuterium labelling in the course of normal Wittig reactions (see Chapter 8) between such ylides and aldehydes. In most instances allylic ylides have reacted with carbonyls using the α-carbon to afford the expected alkene,[159–164] but in some instances[165,166] attack occurred using both the α- and γ-carbons (Eq. 3.4), while in others it occurred using either the α- or the γ-carbon (Eq. 3.5).[167] The addition of a proton source such as methanol or the use of a weaker base to form the ylide increased the proportion of reaction at the γ-carbon, perhaps by facilitating proton transfer.

$$Ph_3P{=}CH{-}CH{=}CH_2 \xrightarrow{PhCHO} \begin{array}{c} PhCH{=}CH{-}CH{=}CH_2 \\ + \\ PhCH{=}CH{-}CH{=}CH{-}CH(OH)Ph \end{array} \qquad (3.4)$$

$$\begin{array}{c} Ph_3P{=}CH{-}C(CH_3){=}CHCOOMe \\ + \\ n\text{-}C_5H_{11}CHO \end{array} \longrightarrow \begin{array}{c} n\text{-}C_5H_{11}CH{=}CH{-}C(CH_3){=}CHCOOMe \\ + \\ n\text{-}C_5H_{11}CH{=}C(COOMe){-}C(CH_3){=}CH_2 \end{array} \qquad (3.5)$$

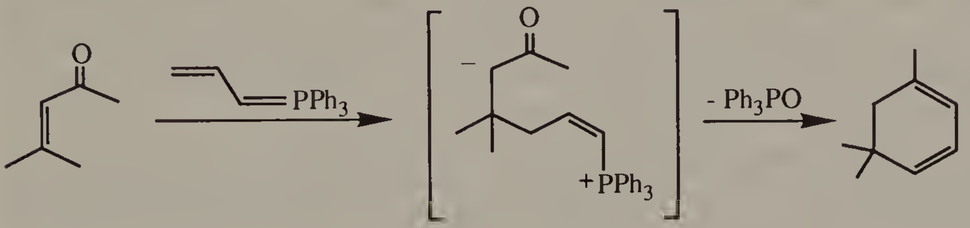
$$Ph_3\overset{+}{P}{-}CH_2CH{=}CH_2 \xrightarrow[2.\ CF_3COOEt]{1.\ BuLi} Ph_3P{=}CH{-}CH{=}CHCOCF_3 \qquad (3.6)$$



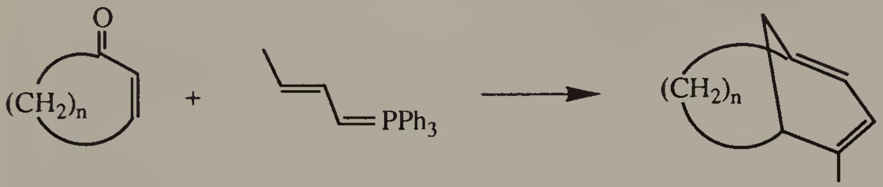
(3.7)

Acylations[168,169] of allylic ylides often occur at the γ-carbon, such as that shown in Eq. 3.6.[170] Many alkylations also occur at the γ-carbon, such as that (Eq. 3.7) recently reported by Hatanaka et al.[171] and similar reactions using heteroatom halides such as phosphorus,[172] sulfur,[173] silicon,[174] and selenium.[175] Normal alkylation occurred, however, using the farnesyl halides, perhaps because of substitution at the γ-carbon.[176] Reaction with benzyne occurred only at the γ-carbon[177] of the allyl group, but reaction with alkynes occurred at the α-carbon.[178]

Allylic ylides have effected Michael additions to conjugated esters[179] and to conjugated aldehydes[180] or ketones.[181–183] For example, allylidenetriphenylphosphorane reacted with mesityl oxide to afford 1,5,5-trimethylcyclohexadiene (Eq. 3.8) via an initial Michael addition by the γ-carbanion, followed by proton transfer to form the new ylide and then an intramolecular Wittig reaction.[182]



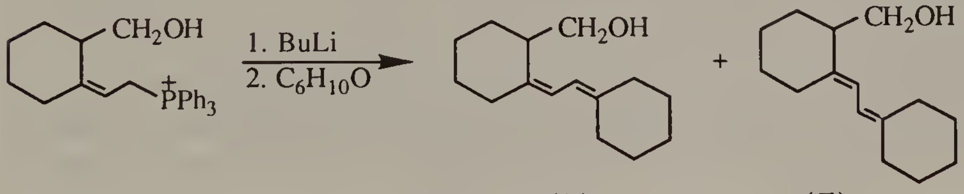
(3.8)



(3.9)

The same reaction has been employed with cycloalkenones to afford bicyclic *bridgehead* dienes (Eq. 3.9)[183] and to fuse a six-membered ring to the cephalosporin framework.[181]

Additional evidence for the mesomeric nature of allylic phosphonium ylides accrues from the fact that stereoisomerization often is observed in a γ-substituted ylide. A mixture of *Z*- and *E*-crotyltriphenylphosphonium salts afforded Wittig reaction products in which the initial double bond was totally isomerized to the trans isomer in one report,[158] but in another report[162] the pure *E*-salt produced a 70:30 mixture of the *E*:*Z* isomers. Harrison and Lythgoe[160] found about 20% isomerism of the original double bond of an allylic ylide at 40°C but only a small amount occurred at 5°C (Eq. 3.10). Howe,[161] and later Corey and



(3.10)

**(Z)** **(Z)** **(*E*)**

Erickson,[167] found that either *E*- or *Z*-β-methyl-γ-carbethoxy allylide reacted with benzaldehyde to produce the same mixture of dienes, with the newly formed double bond (at C-4) being 56:46 *E*:*Z* as expected for semistabilized ylides, but the preexisting C-2 double bond had isomerized to a 40:60 *E*:*Z* mixture (Eq. 3.11). Removal of the β-methyl group resulted in less isomerization,

$$\underset{(E \text{ or } Z)}{Ph_3P{=}CH\text{-}C(CH_3){=}CHCOOEt} \xrightarrow{PhCHO} PhCH{=}CH\text{-}C(CH_3){=}CHCOOEt$$

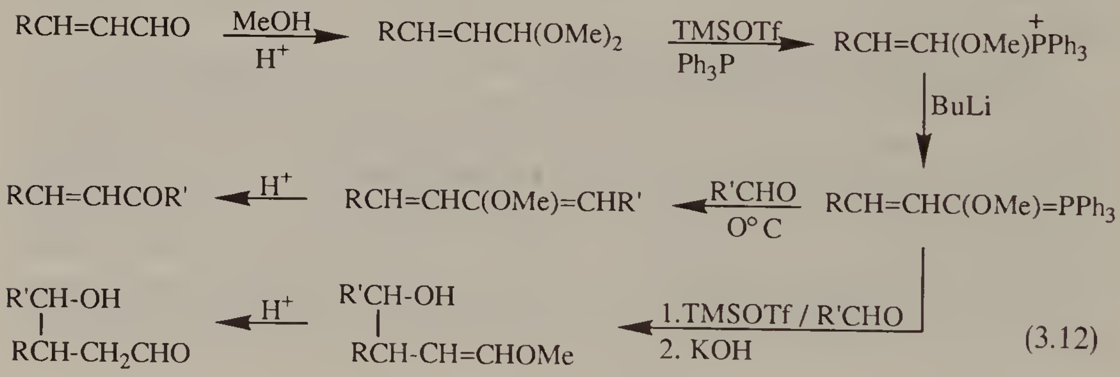
| $\Delta^4$ | $\Delta^2$ | Yield (%) |
|---|---|---|
| trans | trans | 21 |
| cis | trans | 19 |
| trans | cis | 23 |
| cis | cis | 37 |

(3.11)

with pure trans ylide affording 94% trans product. On the other hand, Naf et al.[163] reported several instances in which the allylic double bond retained its stereochemical integrity, and Shen and Wang[174] reported only an *E* configuration to result from the preexisting double bond.

Isomerism about the allylic double bond also has been demonstrated by NMR studies in which *E*- and *Z*-isomers about the enolate double bond in the ester ylide shown in Eq. 3.11 have been detected[161,167] in a ratio close to that found in the Wittig reaction isomerization.

Finally, Kim and Kim[164] discovered that reaction at the α- or γ-carbon of an allylide can be controlled by reaction conditions. Reaction of α-methoxyallylides with aldehydes occurred at the α-carbon at 0° to afford the expected enol ether, but in the presence of trimethylsilyl triflate the product from reaction at the γ-carbon could be obtained (Eq. 3.12). They also demonstrated the allylic rearrangement of some phosphonium salts.



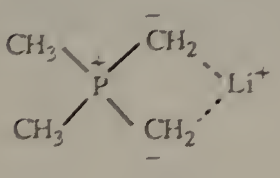
(3.12)

From the above evidence it is clear that allylic ylides can react with a variety of electrophilic reagents at both or either of the α- and γ-positions as a result of delocalization of the negative charge of the ylide carbanion over the allylic framework. It is not always possible to predict which will be the most reactive site.

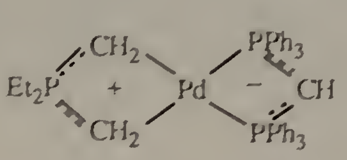
### 3.4.2 Phosphonium Ylide Anions

Phosphonium ylide anions are phosphonium ylides from which an additional proton has been removed leaving a species carrying a net negative charge. There are two known forms of such anions, the first exemplified by $(CH_3)_2P^+(CH_2^-)_2$

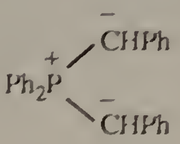
$Li^+$ having been proposed by Wittig and Reiber[6] on the basis of obtaining diethyldimethylphosphonium iodide from the reaction of tetramethylphosphonium iodide with excess phenyllithium and then methyl iodide. This conclusion was confirmed later[184] with a symmetrical lithium complex structure (**12**) being



**12**



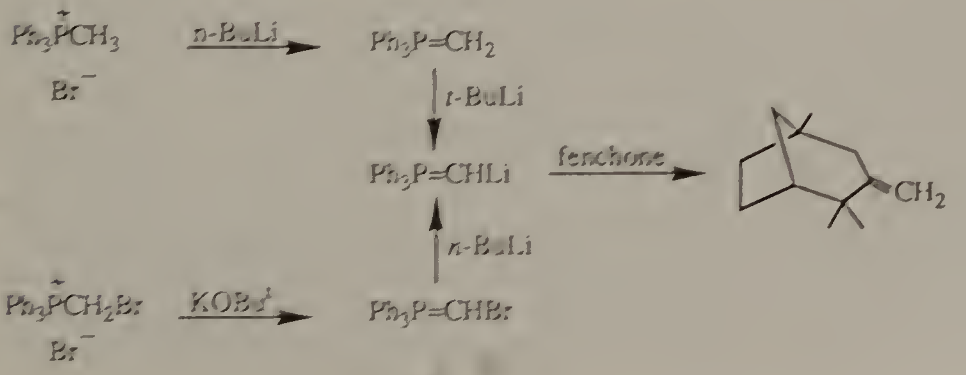
**13**



**14**

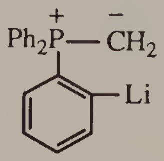
proposed, and such ylide anions were used extensively in forming complexes such as **13** with metals. The structure of $[Ph_2P(CH_2)_2]^- Li^+$ has been shown to be that of an eight-membered ring dimer with four carbon–lithium bonds of 2.17 Å average length and P–C distances of 1.69–1.71 Å.[185] Cristau et al. showed that ylide anions would react as ylides, but were more reactive, in Wittig reactions,[186,187] in acylations,[188] and in conjugate addition reactions.[189] More recently it has been shown that ylide anions such as **14** are more reactive than the corresponding simple ylide $[Ph_2P(CH_2Ph){=}CHPh]$ and that Wittig reaction with benzaldehyde occasionally resulted in increased *E*:*Z* ratios of alkenes.[190]

The other kind of ylide anion is formulated as $Ph_3P{=}CRLi$, the first (R = *n*-$C_3H_7$) having been so proposed by Schlosser et al.[191] based on the reaction of pentaphenylphosphorus with excess *n*-butyllithium followed by deuteration of the solution. Ab initio SCF–MO calculations indicated that the parent molecule $H_3P{=}CHLi$ was best described as a contact ion pair whose chemistry would be that attributable to the free anion, and that the geometry of the anionic center would be more favorable for execution of a nucleophilic attack at a carbonyl group than would the free ylide.[192] Corey et al.[193] did find that the orange ylide anion $Ph_3P{=}CHLi$, prepared by treatment of the yellow methylide with *t*-butyllithium, would react with hindered ketones such as fenchone, whereas the methylide itself would not (Eq. 3.13). They also prepared the ylide anion from

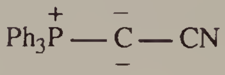


(3.13)

bromomethyltriphenylphosphonium bromide using, sequentially, potassium *t*-butoxide for proton removal then *n*-butyllithium for bromine removal. However, Schaub et al.[194,195] report being unable to repeat the Corey experiments and claimed, on the basis of NMR and methyl iodide trapping experiments, that the bulk of the substance formed by treatment of the methylide with organolithium reagents was the ortho-metallated species (**15**), although they acknowledged the presence of small amounts of $Ph_3P{=}CHLi$.



**15**



$Ph_3\overset{+}{P}-\overset{-}{\underset{-}{C}}-CN$

**16**

Bestmann and Schmidt[196] reported the preparation of the cyanoylide anion (**16**) from the precursor cyanoylide by treatment with sodium (bis-trimethylsilyl)amide and its alkylation, acylation, halogenation, and ring-opening reaction with epoxides.[197] Most of the products are the same as would be expected from the parent ylide, but the ylide anion was much more reactive.

### 3.4.3 Carbodiphosphoranes and Phosphacumulenes

Carbodiphosphoranes are bis-phosphonium ylides with the two ylide functions cumulated to each other. Other unique bis-ylides, both conjugated and isolated, are discussed in Section 3.4.4. Phosphacumulenes include phosphonium ylides with one or more double bonds cumulatively attached to the ylide carbon. Those with a methylene group on the carbanion are called phosphaallenes (Section 3.4.3.2), and those with vinylidene groups on the carbanion are called phosphacumulenes (Section 3.4.3.3).

***3.4.3.1 Carbodiphosphoranes.*** First prepared and characterized by Ramirez et al.[198] in 1961, these unique and relatively stable substances contain the molecular grouping $R_3P{=}C{=}PR_3$ (R groups may be mixed in almost any combination) which of course may be written in the ylene, double ylide, or phosphonioylide form. They generally have been prepared by variations of one of five methods: (1) reaction of a dihalomethane with two equivalents of phosphine, followed by removal of the two protons using a strong base;[199] (2) reaction of a diphosphinomethane with two equivalents of alkyl halide, followed by removal of the two protons with a strong base;[142] (3) reaction of a phosphine with carbon tetrachloride;[200] (4) reaction of an ylide with a dihalophosphine, followed by transylidation and removal of the final proton with a strong base;[201] and (5) fluorination of a diphosphinomethane, followed by dehydrofluorination to afford a *P,P′*-difluorocarbodiphosphorane[202] (Eq. 3.14).

1. $Ph_3P + CH_2Br_2 \longrightarrow (Ph_3P)_2CH_2 \longrightarrow Ph_3P{=}C{=}PPh_3$

2. $Ph_2PCH_2PPh_2 + CH_3Br \longrightarrow (MePh_2P)_2CH_2 \longrightarrow Ph_2MeP{=}C{=}PPh_2Me$

3. $3\,Ph_3P + CCl_4 \longrightarrow (Ph_3P)_2CCl \longrightarrow Ph_3P{=}C{=}PPh_3$ (3.14)

4. $Ph_3P{=}CH_2 + Ph_3PCl_2 \longrightarrow (Ph_3P)_2CH \longrightarrow Ph_3P{=}C{=}PPh_3$

5. $Ph_2PF_2CH_2PF_2Ph_2 \longrightarrow Ph_2FP{=}C{=}PFPh_2$

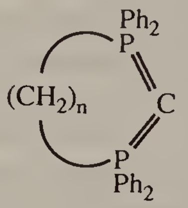
Hexaphenylcarbodiphosphorane ($Ph_3P{=}C{=}PPh_3$), the first discovered,[198] was a strongly basic, high-melting crystalline yellow material that exhibited triboluminescence (TL)—the emission of light caused by mechanical stress to the crystals,[203] but with no chemical change resulting.[204] Its dipole moment was 4.69 D[20] and it was stable in oxygen but reactive in moisture. Initial X-ray crystallography[205] revealed two distinct molecules with different P=C distances (1.629 and 1.633 Å), but with both P=C distances identical within each form. Later work[206] revealed that these forms lost their TL properties upon standing and the non-TL form had a bond length of 1.610 Å at room temperature and 1.635 Å at − 160 °C. In general the P=C bond lengths were considerably shorter than normal ylides (see Tables 3.2 and 3.6). The P=C=P framework usually was bent, with P=C=P bond angles ranging from 116.7°[207,208] to 180°[209] (see Table 3.6). Different forms had different angles (TL forms showed

**TABLE 3.6 Structural Data for Carbodiphosphoranes**

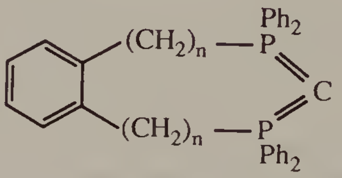
| Ylide | < P–C–P° | $d$(P=C) (Å) | $\delta^{31}P$ | $\delta^{13}C$ | $^1J_{(P=C)}$ | References |
|---|---|---|---|---|---|---|
| $Ph_3P{=}C{=}PPh_3$ | 130.1<br>143.6 | 1.633<br>1.629 | − 3.5 | | | 199, 205 |
| $MePh_2P{=}C{=}PPh_2Me$ | 121.8 | 1.645 | − 6.70 | 12.6 | 92.8 | 208, 222 |
| $Me_3P{=}C{=}PMe_3$ | 116.7 | 1.594 | + 29.6 | 10.8 | 32 | 200, 207, 219 |
| $(Me_2N)_3P{=}C{=}P(Me_2N)_3$ | 180 | 1.584 | + 27.72 | − 6.78 | 305 | 209 |
| $Ph_3P{=}C{=}PPh_2Me$ | | | − 13.27<br>− 5.56 | | | 216 |
| $Ph_3P{=}C{=}PPMe_2$ | | | − 18.27<br>− 7.54 | | | 216 |
| $Ph_3P{=}C{=}PMe_3$ | | | − 21.31<br>− 10.10 | | | 216 |
| $Ph_3P{=}C{=}PBu_3$ | | | − 2.7<br>+ 14.2 | 7.8 | 127.7 | 218 |
| $MePh_2P{=}C{=}PPh_2CH(CH_2)_2$ | | | − 13.4<br>+ 1.0 | 3.6 | 109.4<br>112.3 | 217 |
| $-(CH_2)_3{-}PPh_2{=}C{=}PPh_2{-}$ | 116.7 | 1.645<br>1.653 | − 9.63 | | | 208, 212, 213 |
| $-(o)C_6H_4{-}PPh_2{=}C{=}PPh_2{-}$ | | | + 29.5 | | | 215 |

angles of 143.6 and 130.1°; the non-TL form showed 134.4° at room temperature and 131.7° at − 160°C).[205,206]. Calculations by Glidewell[210] and by Albright et al.[211] predicted that the more electron donating were the P substituents, the more nearly linear should be the P=C=P bond.

Cyclic carbodiphosphoranes also are known. The hexacyclic example (**17**, n = 3) has been isolated[212,213] and shown to contain the smallest known P=C=P bond angle of 116.7°.[207,208] The pentacycle (n = 2) and the heptacycle (n = 4) were isolated but were poorly characterized.[212] The heptacycle **18** (n = 1) could not be obtained, the usual reaction instead producing a conjugated bis-ylide.[214] However, the pentacycle **18** (n = 0) was isolated and showed very deshielded $^{31}P$ atoms ( + 29.5).[215]

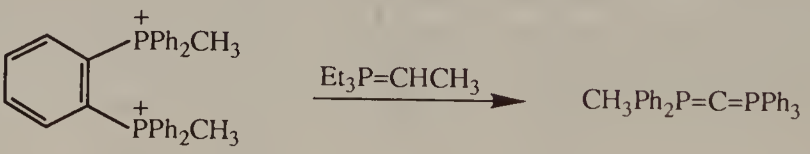


**17**



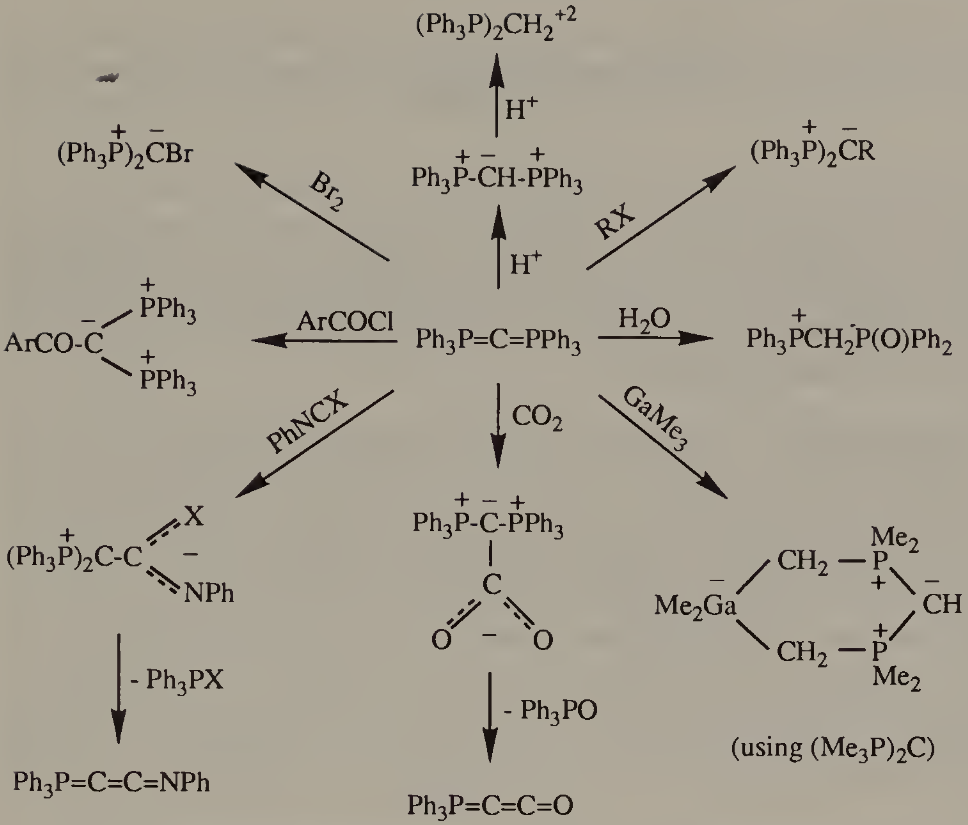
**18**

The stability of carbodiphosphoranes has been illustrated by the fact that they were formed in the rearrangement of some other ylides.[142] In addition, reaction of some bis-phosphonium salts with strong base, expected to form normal bis-ylides, afforded instead carbodiphosphoranes (Eq. 3.15).[216,217] However, thermal rearrangement of a carbodiphosphorane into a mono-ylide also has been reported.[218]



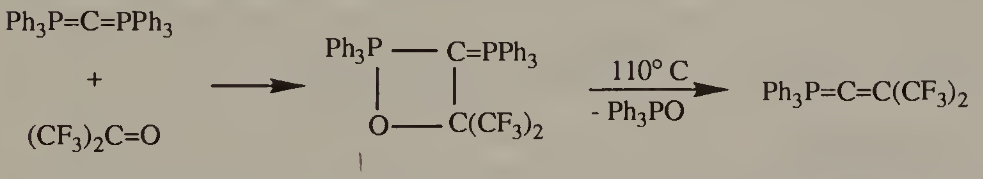
(3.15)

Carbodiphosphoranes reacted with a variety of electrophiles, as shown in Eq. 3.16. These include (1) protonation to the starting bis-phosphonium salt;[198,199,219] (2) alkylation on the ylidic carbon;[208,212,220] (3) reaction with halophosphines;[221] (4) reaction with trimethylsilyl chloride;[200,222] (5) hydrolysis in water to an ylide–phosphine oxide with cleavage of a P substituent, usually benzene[198,214,222] (but an explosive reaction with the hexamethyl derivative formed methane and trimethylphosphine oxide[200]); (6) bromination;[198] (7) formation of complexes with a variety of metals;[214,223] (8) addition reactions with carbodiimides,[199] isocyanates,[199] and isothiocyanates;[224] (9) acylation with acyl halides[220] and cyclic anhydrides;[220] and (10) formation of an adduct with carbon dioxides.[225] The latter, upon heating, eliminated triphenylphosphine oxide in the manner of a Wittig reaction to afford a phosphacumulene.



(3.16)

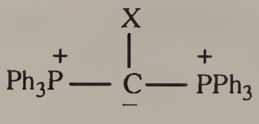
Normal Wittig reactions using carbodiphosphoranes are virtually unknown, although Bestmann and Kloeters[226] reported an example. A most significant reaction was that between hexaphenylcarbodiphosphorane and hexafluoroacetone which resulted in the isolation of the first oxaphosphetane, considered by many as the intermediate in a Wittig reaction (Eq. 3.17).[227] Heating the latter to 110 °C resulted in the expulsion of triphenylphosphine oxide and the formation of the phosphoranylideneallene, as would be expected for a Wittig reaction.



(3.17)

Table 3.6 lists many of the known carbodiphosphoranes together with some of their physical properties. The $^{31}P$ NMR spectra cover a considerable range, but in general show more shielding than for other ylides. The $^{1}J$ (P=C) values are generally lower than other ylides, and those with the smallest P=C=P angles have the lowest coupling constants. In other words, the more linear examples probably have the highest contribution of *sp* hybridization at the ylide carbon.

Finally, mention must be made of mesomeric phosphonium ylides such as **19**, whose chemistry often is overlooked because of their intermediate position on the way to carbodiphosphoranes. First prepared by Ramirez et al;[198] they were stable to moisture and exhibited a photochromic effect.[228] Examples are known



$$Ph_3\overset{+}{P}—\overset{X}{\underset{-}{C}}—\overset{+}{P}Ph_3$$

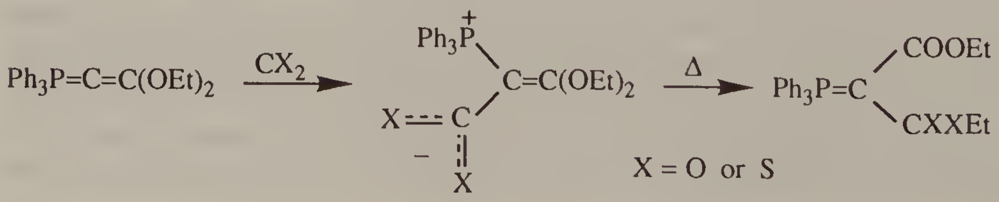
**19**

where X = H,[199] Br,[198] $BH_3$,[213] $BPh_3$,[228,229] and F.[230] The parent ylide (X = H) has unequal P–C lengths of 1.710 and 1.695 Å, longer than most ylides, and a P–C–P angle of 128.2°.[31] This same ylide does not effect Wittig reactions, serving as a reductant instead.[231]

***3.4.3.2 Phosphaallenes.*** The chemistry of phosphaallene ylides ($Ph_3P{=}C{=}CR_2$) has been reviewed by Bestmann.[232] The diethoxy ylide (R = OEt) was isolated by O-ethylation of the ester ylide ($Ph_3P{=}CHCOOEt$) followed by deprotonation with sodium amide,[233] and the di-trifluoromethyl ylide (R = $CF_3$) was obtained from a carbodiphosphorane (Eq. 3.16).[227] The P=C length of the diethoxy ylide was normal for ylides (1.682 Å), the C=C length was normal for an allene, and the P=C=C chain was bent at an angle of 125.6°, indicating trigonal geometry at the ylide carbon.[234] Because of the relatively poor acceptor quality of the =C($OEt_2$) group, a sharp angle was expected at the ylide carbon.[210, 211] The ylide dipole moment was small (3.23 D)[20] compared to other ylides.

The ylides hydrolyzed normally[227, 233] with loss of benzene, they were protonated to the vinylphosphonium salts,[227] and they were alkylated on the ylide carbon to afford vinylphosphonium salts.[235] Both ylides reacted normally with carbonyl compounds which did not possess α-hydrogen to afford Wittig reaction products[227, 235–237] (Eq. 3.18). If the ketone had an α-hydrogen it was removed by the ylide and a Michael addition to the salt followed, producing a new cumulated ylide. Reaction of the latter ylide with aldehydes provided access to γ,δ-unsaturated β-diketones (Eq. 3.18).[237] Reaction of the phosphaallenes

$$\begin{tikzcd}
Ph_3P{=}C{=}CR_2 \;+\; R'_2C{=}O \arrow[r, "- Ph_3PO"] \arrow[d, "\begin{array}{l}(R = OEt)\\ R^1CH_2COR^2\end{array}"] & R'_2C{=}C{=}CR_2 \\
Ph_3P{=}C{=}C(OEt)\text{-}CHR_1COR_2 \arrow[r, "1.\ R^3CHO", "2.\ H^+"'] & R^3CH{=}CHCOCHR^1COR^2
\end{tikzcd} \tag{3.18}$$



(3.19)

with isocyanates produced heterocyles[232] and reaction with carbon dioxide or carbon disulfide afforded initial adducts which could be thermally rearranged to stabilized diester ylides (Eq. 3.19).[232]

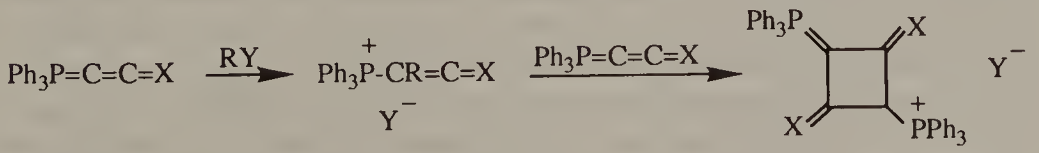
*3.4.3.3* ***Phosphacumulene Ylides.*** Five phosphacumulene ylides ($Ph_3P{=}C{=}C{=}X$) have been synthesized as follows: (1) X = O by eliminating triphenylphosphine oxide from the carbon dioxide adduct of hexaphenylcarbodiphosphorane[238] or by eliminating methanol from the carbomethoxymethylide;[239] (2) X = S by the same routes and from triphenylphosphoniummethylide and thiophosgene;[240] (3) X = NPh from the thiocyanate adduct of the carbodiphosphorane[224] and from phenylisocyanide dichloride and the methylide;[240] (4) X = fluorenylidene from reaction of 9-dibromomethylenefluorene with the methylide;[241] and (5) X = $CPh_2$ from double dehydrohalogenation of $\beta$-bromo-$\gamma,\gamma$-diphenylallyltriphenylphosphonium bromide.[242]

The structures of the first four phosphacumulenes have been determined with the P=C bond lengths and P=C=C bond angles as follows: X = O (1.648 Å, 145.5°);[243] X = S (1.677 Å, 168.0°);[244] X = NPh (1.677 Å, 134.0°);[245] X = fluorenylidene (1.703 Å, 136.5°).[246] The P=C ylide bonds are in the normal range, but the adjacent C=C bonds are very short (1.209–1.248 Å), being closer to alkyne length (1.21 Å) than to allene length (1.31 Å), perhaps indicating considerable contribution from the triple-bonded resonance form (**20**). The dipole moments of the first three phosphacumulenes also are quite large (6.77, 8.51, and 6.66 D, respectively),[20] much larger than for the phosphaallenes and comparable to simple ylides. The more linear the phosphacumulene, the larger is the dipole moment[20] and the larger are the $^1J_{P=C}$ values,[211] perhaps indicating an increasing contribution of the linear *sp* hybrid form of the ylide carbanion. The $^{31}P$ NMR spectra of phosphacumulenes revealed a higher level of phosphorus shielding than for simple ylides.[224, 239, 240]

$$Ph_3P{=}C{=}C{=}X \longleftrightarrow Ph_3\overset{+}{P}\text{-}C{\equiv}C\text{-}\overset{-}{X}$$

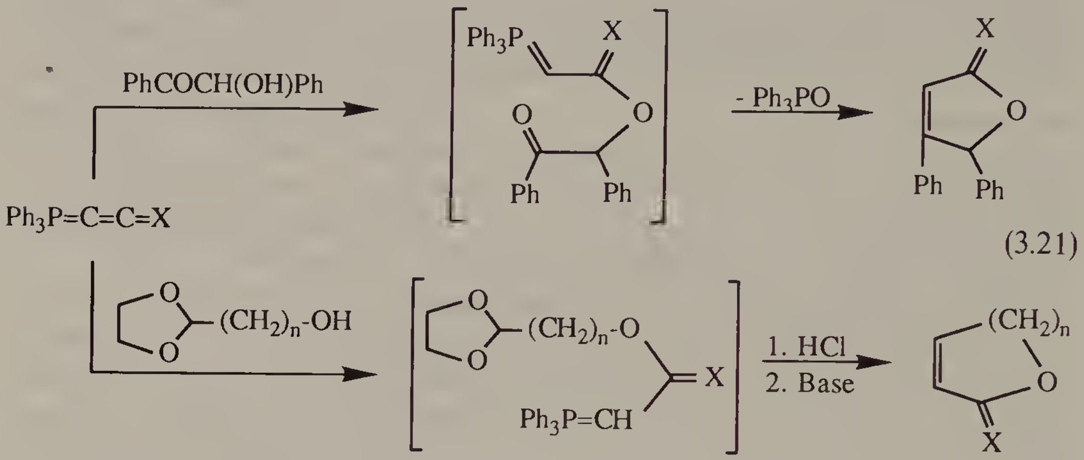
**20**

The reactions of phosphacumulenes were reviewed by Bestmann in 1977.[232] Although ketene-like in their structure, phosphacumulenes do not dimerize. However, protonation with HCl[247] and alkylation with methyl iodide[244, 247] both lead to dimers, their formation being rationalized by initial alkylation or protonation of the ylidic carbon, thereby creating a true ketene, which then underwent a (2 + 2) cyclization with the phosphacumulene (Eq. 3.20). Reaction



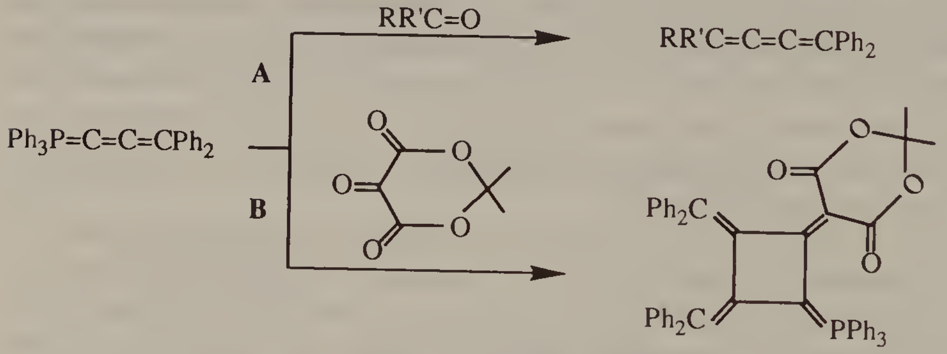
(3.20)

with alcohols also involved protonation of the ylidic carbon, but the nucleophilicity of the anion caused overall 1,2-addition at the C=C bond to afford an ester- or amide-ylide.[248] This reaction, when applied to substances with carbonyl groups elsewhere in the molecule, has been used for the synthesis of fused heterocyclic rings[249] and macrocyclic lactone natural products[250] (Eq. 3.21).



(3.21)

The most common reaction of phosphacumulenes is addition across the C=C bond, but reaction with carbonyls occurs across the P=C bond in a normal Wittig reaction. Reactive ketones with $Ph_3P{=}C{=}C{=}O$ apparently afforded vinylidene ketenes which cyclized to four-membered rings in reaction with unreacted phosphacumulene.[251] 1,2,3-Butatrienes[241, 242, 252] have been obtained from aldehydes and ketones (Eq. 3.22, path A), but in one recent instance[251] cyclization with an unreacted ylide was reported (Eq. 3.22, path B).



(3.22)

Ketenes have been reported to undergo Wittig reactions with phosphacumulenes to afford tetraenes (as their dimers),[242] and also to simply undergo a (2 + 2) cyclization with the phosphacumulene to afford a 2-phosphoranylidene-cyclobutane-1,3-dione,[251] the same product obtained by reaction of a simple ylide with carbon suboxide.[253]

A wide variety of addition reactions occurred with phosphacumulenes at the C=C bond. Five-membered rings resulted from (2 + 3) addition reactions with 1,3-dipolar compounds,[254] including azides, diazo compounds, nitrile oxides, and nitrones,[232] with the positive end of the dipoles coupling with the ylidic carbon of the phosphacumulene in each instance. Isocyanates and isothiocyanates effected a (2 + 2) addition with phosphacumulenes to afford four-membered adducts, with the ylide carbon apparently attacking the carbonyl or thiocarbonyl group,[232, 255] although one instance of a normal Wittig-type reaction has been reported with $Ph_3P{=}C{=}C{=}CPh_2$.[242] Use of a conjugated isocyanate resulted in a (4 + 2) addition.[256] Addition reactions (2 + 2) occurred between alkenes or imines and phosphacumulenes,[232] while conjugated alkenes appeared to undergo (4 + 2) additions.[257] Alkynes reacted with phosphacumulenes in an initial (2 + 2) addition followed by ring opening[241] in a manner analogous to the reaction of simple ylides with alkynes (see Section 7.1.2).

### 3.4.4 Bis-Ylides

Double deprotonation of a molecular system $C\text{–}P^+\text{–}C\text{–}P^+\text{–}C$ could produce three different species. If both protons were removed from the central carbon, carbodiphosphoranes would result (Section 3.4.3.1). If one proton was removed from each of the terminal carbons, an "isolated" bis-ylide would result. If one was removed from the central carbon and one from a terminal carbon, a "conjugated" bis-ylide would result. Both these groups of ylides are discussed in this section.

Bis-ylides have been of interest since the earliest days of ylide chemistry. Wittig et al.[258] found that 1,2-bis(triphenylphosphonio)ethane eliminated triphenylphosphine when treated with a strong base, and no ylide (**21**, n = 0) could be obtained.[222] However, both the 1,3-disubstituted propane and the 1,4-disubstituted butane afforded bis-ylides (**21**, n = 1 or 2)[258] which underwent normal reactions, especially with carbonyl compounds. Bestmann et al.[259] reported bis-ylides (**21**) where n = 2–5. There is no reason for even higher homologs not to be stable enough to produce. Such ylides complexed with nickel, displacing cyclopentadiene from nickelocene, but only when n = 2 or 3[260] and five- or six-membered rings resulted. A unique and stable 1,2-bis-ylide incorporated the benzocyclobutene structure, in which case elimination of triphenylphosphine would have, but did not, afford benzocyclobutadiene.[261] The recently reported reaction of 1,2-bis-triphenylphosphonioethene with butyllithium and a substituted benzaldehyde to afford 1,4-diarylbutatriene indicates that the unusual bis-ylide $Ph_3P{=}C{=}C{=}PPh_3$ may have been involved.[262]

$$Ph_3P{=}CH\text{-}(CH_2)_n\text{-}CH{=}PPh_3$$

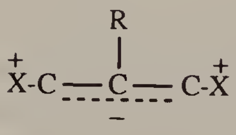
**21**

$$Ph_3P{=}CH\text{-}A\text{-}CH{=}PPh_3$$

**22**

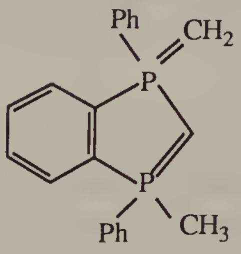
Bis-ylides are known with other structural components between the two ylide groups. The bis-ylide (**22**, A = $-CH{=}CH-$) from 1,4-bis(triphenylphosphonio)-2-butadiene could not be prepared because of competing elimination,[263] but the ylides (**22**, A = $-C_6H_4-$) from α,α′-bis(triphenylphosphonio)-*p*-xylene[264] and the ortho isomer[265] could be prepared and used in reactions. The ylide (**22**, A = –CO–) from 1,3-bis-(triphenylphosphonio) acetone eventually was obtained after an initial failure,[263, 266, 267] and the stabilized bis-ylide [**22**, A = –CO–O–$(CH_2)_2$–O–CO–] was readily prepared from the corresponding bis-phosphonium salt.[263] Bestmann et al.[268] reported numerous bis-ylides (**22**) where A was a variety of aromatic nuclei.

Recently two examples of related mono-ylides (**23**) have been described, although Nesmeyanov and Reutov[269] reported the poorly characterized parent compound (X = $Ph_3P$, R = H) in 1966. Schmidbaur et al.[270] isolated their ylide (**23**, X = $MePPh_2$, R = $CH_3$) and demonstrated magnetic equivalence of the phosphorous atoms above 96°C. Below that temperature rotational isomerism of the allylic anion system resulted in two peaks in the $^{31}$P NMR spectra. A similar result was reported by Bestmann and Kisielowski[271] for **23** when X = $Ph_3P$ and R = Ph. The first ionic phosphenium chloride ($Ph_3P{=}CPh{-}P^+{-}CPh{=}PPh_3Cl^-$), an analog of **23**, recently was reported to exhibit ylidic characterisitics.[272]

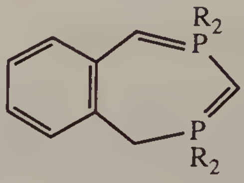


$\overset{+}{X}\text{-C}-\overset{\overset{R}{|}}{\underset{-}{C}}-\text{C-}\overset{+}{X}$

**23**



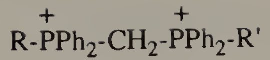
**24**



**25**

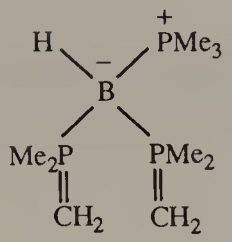
The conjugated bis-ylides clearly are energetically favored over isolated bis-ylides, and often over carbodiphosphoranes. For example, the carbodiphosphorane **17** (n = 3) was obtained to the exclusion of the alternate isolated bis-ylide.[213] The conjugated ylide (**24**) was obtained to the exclusion of the isolated bis-ylide *or* the carbodiphosphorane, even though a similar structure existed as the carbodiphosphorane.[215] Likewise, two examples of the ylide (**25**) are known to be formed from the precursor diphosphonium methanide, as indicated by distinguishing $^{31}$P and $^{13}$C NMR spectra.[214]

Attempts to prepare bis-methylides by double proton abstraction from bis-methylphosphonium salts resulted in the probable formation of such species, followed by rapid rearrangement to the more stable carbodiphosphoranes (Eq. 3.14).[216, 217] Two groups have attempted to increase the stability of the bis-methylide structure by adding special stabilization to the methyl groups. Starting with bis-phosphonium salts (**26**) Schmidbaur et al.[273, 274] found that in three combinations (R = benzyl, R′ = methyl; R = R′ = benzyl; R = R′ = fluorenyl), each of which should produce a somewhat stabilized isolated bis-ylide, only the conjugated ylides were obtained. The only instances in which other isomers were obtained were when R = $CH_2$-mesityl and R′ = $CH_3$ or $CH_2$-mesityl, the former producing a 1:3 ratio of conjugated ylide and carbodiphosphorane, and the latter producing a 2:3 ratio.[274] At about the same



$R\text{-}\overset{+}{P}Ph_2\text{-}CH_2\text{-}\overset{+}{P}Ph_2\text{-}R'$

**26**



**29**

**27** **28**

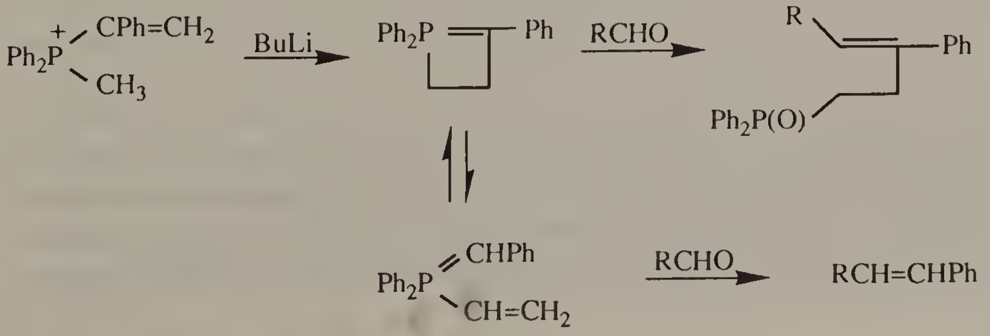
time Appel et al.[275] prepared the only known example of a bis-ylide of the type C=P–C–P=C (**27**), which existed only at less than 10°C. Above that temperature the conjugated form (**28**) existed as shown by X-ray crystallographic analysis and the NMR spectra. Wimmer et al.[276] recently reported the X-ray crystallographic analysis of a bis-ylide structure (**29**) in the boron series.

It may be concluded that conjugated bis-ylides usually are more stable than the isomeric carbodiphosphoranes, and both are far more stable than the isomeric "isolated" bis-ylides, of which only two examples are known.

### 3.4.5 Cyclic Phosphonium Ylides

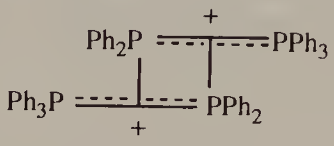
Most of the ylides mentioned to this point have included the ylide group (P=C) in an acyclic environment, but it is possible to envision the ylide group as part of a cyclic environment (i.e., as part of a phosphacycle), and such ylides are briefly described in this section. Davies and Hughes[277] reviewed the field as of 1972. Three-membered cyclic ylides are not known, but four-, five-, and six-membered cyclic ylides are well known.

*3.4.5.1* ***Four-membered Ylides.*** The first such ylide was detected by Savage and Trippett[278] when, from the reaction of a vinylphosphonium salt with butyllithium, followed by addition of an aldehyde, an alkene containing the phosphinoxy group was obtained in the product mixture, indicating that some

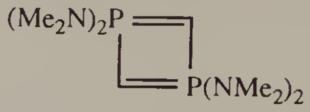


(3.23)

phosphete ylide had been present (Eq. 3.23). The interesting bis-ylide (**30**), a 1λ⁵,3λ⁵-diphosphete, is almost square, with nearly identical ring P–C bond lengths (1.765 and 1.760 Å), but slightly shorter exocyclic P–C bond lengths (1.714 Å), indicating there is more "ylidic" character to the exo bonds.[279] Keller et al.[280] recently reported an analog with exocyclic phosphinoxy groups. Svara et al.[281] prepared a C-unsubstituted analog (**31**) by treating methyldifluorobis(dimethylamino)phosphorane with two equivalents of butyllithium, perhaps forming the phosphaalkyne which dimerized. This molecule was virtually square with identical P–C bond lengths (1.725 Å) and the $^{31}P$ and $^{13}C$ NMR spectra, as well as the photoelectron spectra,[282] were consistent with an ylide structure. The substance also reacted as an ylide, effecting a single Wittig reaction with benzaldehyde, thereby opening the ring to an alkene–ylide–phosphonamide.[283] A more highly substituted 1λ⁵,3λ⁵-diphosphete was isolated recently and its similar structure determined.[284]

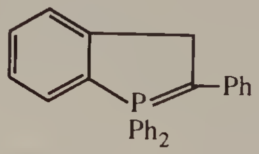


**30**

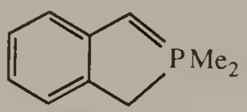


**31**

*3.4.5.2 Five-Membered Ylides.* Markl[285] prepared the first five-membered cyclic ylide (a λ⁵-phosphole) when he converted an *o*-disubstituted benzene to a 1,1,2-triphenyl-1-phosphaindane and then removed the α-proton with phenyllithium, trapping the resulting ylide (**32**) in a Wittig reaction with benzaldehyde. Savage and Trippett[278] also trapped a transient five-membered ylide. Schmidbaur et al.[286] found that 1,1-dimethyl-1-phosphacyclopentane, when treated with sodium amide, did not afford the pentacyclic ylide from removal of a ring proton, but instead afforded the exocyclic methylide. However, fusing a benzene ring to the 3,4 position of the pentacycle resulted in the ability to isolate the corresponding pentacyclic ylide (**33**), which showed the expected $^{31}P$ and $^{13}C$ NMR spectra.[287]

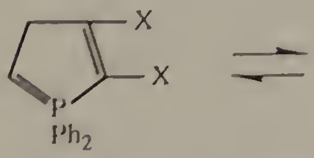


**32**



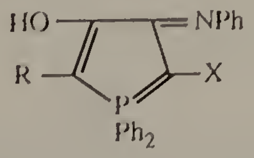
**33**

Diphenylvinylphosphine added to dimethyl acetylene dicarboxylate (DMAD) to produce the unisolable phosphacyclopentadiene (**34**), which appeared to exist in an equilibrium mixture of two isomers, hydrolysis indicating one and Wittig reaction with *p*-nitrobenzaldehyde indicating the other.[288] Addition of bisdiphenylphosphinomethane to DMAD produced a 1,3-diphosphacyclopentadiene bis-ylide which was isolated.[289] More recently a phosphinimine was added to DMAD in a familiar reaction, but further treatment with strong base led to cyclization and isolation of the phosphacyclopentadiene (**35**).[290]



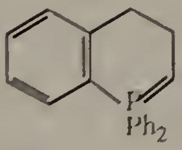
34

X = COOMe

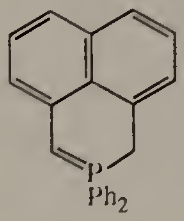


35

3.4.5.3 *Six-Membered Ylides.* Simple such ylides almost have been ignored because most interest has focused on phosphabenzene derivatives. Using standard techniques Markl[291] prepared 1,1-diphenyl-3,4-dihydro-1-phosphanaphthalene (**36**) and detected its presence by a Wittig reaction, indicating normal ylidic character. The phosphanaphthalene counterpart, however, was a much more stable ylide, not undergoing a Wittig reaction, but being normally hydrolyzeable and reversibly convertible to the phosphonium salt. The question of aromatic stabilization was raised at this time. Much later others[287] isolated a dibenzostabilized ylide (**37**) whose chemistry was not explored but whose spectra clearly indicated its ylidic character. Recently, Karsch reported a novel hexacycle containing aluminium, silicon, two carbons, and two phosphorus atoms, one of which was pentavalent and exhibited a typical ylide P=C bond of 1.732 Å.[292]

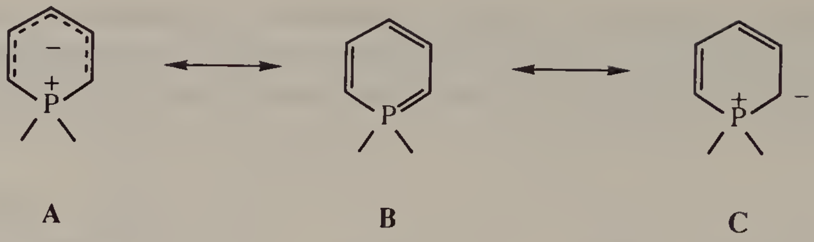


36



37

Most of the interest in six-membered ylides has focused on $\lambda^5$-phosphorins ($\lambda^5$-phosphinines, $\lambda^5$-phosphabenzenes) and the question of their aromaticity and their ylidicity. Reviews of this subject have appeared periodically,[293] and readers are referred there for details of this chemistry. In contrast to the aromaticity documented for $\lambda^3$-phosphorins ($\lambda^3$-phosphinines), the phosphorus analog of pyridine, $\lambda^5$-phosphorins are not aromatic, but they clearly are highly stable substances exhibiting very little ylide character. They have been described as a superimposition of structures A (an internal salt with a pentadienyl unit and a phosphonium group) and B (a cyclic conjugated system utilizing the $3d_{yz}$

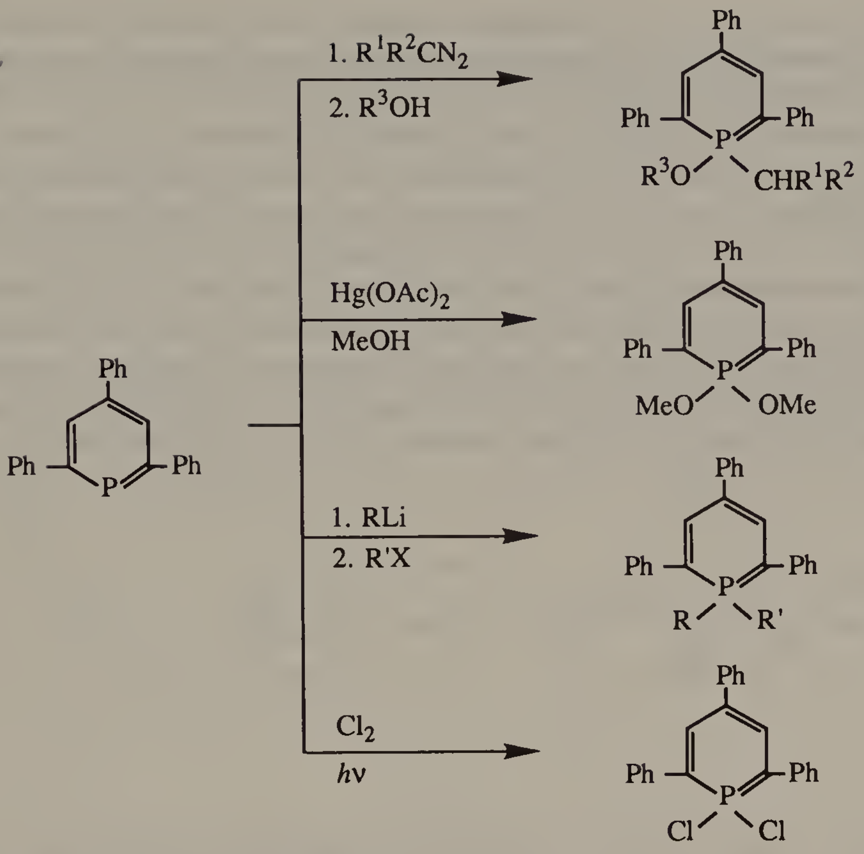


**38**

orbital on phosphorus) (**38**),[294] with no significant contribution of structure **C** (a normal conjugated ylide). This description implies considerable positive charge on phosphorus and negative charge at carbons 2,4, and 6.[295]

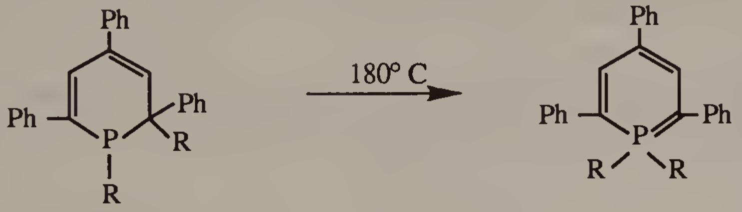
Considerable physical evidence exists on the structure of $\lambda^5$-phosphorins, with most of it from the 2,4,6-triphenyl substituted derivatives. The $^{13}C$ NMR spectra clearly indicated both chemical shifts and large P–C coupling constants typical of ylides for carbons 2 and 6, and quite different than for $\lambda^3$-phosphorins.[296, 297] The $^{31}P$ NMR spectra also exhibited clear differences from those of $\lambda^3$-phosphorins and similarities to the higher field absorptions known for phosphonium ylides.[298] ESCA spectroscopy[299] and photoelectron spectroscopy[294] also confirmed the highly stabilized ylide character for $\lambda^5$-phosphorins. Bird's recent aromaticity calculations also agree.[300] Four X-ray crystallographic analyses have been reported,[301] all cases using 2,4,6-trisubstituted derivatives, and involving the 1,1-dimethyl, 1,1-dimethoxy, and 1,1-bisdimethylamino derivatives. The P-C2 and P-C6 distances all fell within the range 1.72–1.751 Å, only slightly longer than the usual P=C ylide bond length (see Section 3.1.1). The ring C–C distances were within the range 1.38–1.42 Å, and the C–P–C angles were from 105 to 107°. The ring was essentially planar in all instances, and the plane of the 1,1-substituents and the P atom was approximately perpendicular to the ring plane.

Dimroth[293e] has reviewed the methods of synthesis for $\lambda^5$-phosphorins. The original synthesis of the 1,1-diphenyl derivative by Markl[302] was lengthy and involved ring closure to a phosphacyclohexane followed by laborious sequential introduction of the double bonds. Ashe and Smith[297] shortened the process considerably in their synthesis of the 1,1-dimethyl derivative. In both instances the final step was removal of a proton from the $\alpha$-carbon of a 1,1-disubstituted-1-phosphoniocyclohexadiene, and as with most ylides this step was reversible. Several methods are available for conversion of the more readily available $\lambda^3$-phosphorins to $\lambda^5$-phosphorins, as illustrated for the triphenyl derivative (Eq. 3.24). The phosphorus substituents have been attached by attack of diazo compounds,[303] carbanions,[304] mercuric diacetate and then alcohols,[305] and radicals.[306] Further, the 1,1-dichloro derivative served as a starting material for exchange of a wide variety of substituents.[307] Conversion of pyryllium salts to $\lambda^5$-phosphorins has been accomplished, but is of little use as a practical method.[308] More recently, Markl et al. reported an effective means of creating the phosphahexacycle ring by converting 1,4-pentadiynes to $\lambda^3$-phosphorins[309] and dialkynyl phosphines to $\lambda^5$-phosphorins.[310]



(3.24)

The chemistry of $\lambda^5$-phosphorins demonstrates vividly the special stability of the ylidic ring system, even though it is not aromatic, and its integrity through a variety of substitution reactions. Initially it should be noted that a 1,2-dihydrophosphorin rearranged at 180° to produce the *more stable* $\lambda^5$-phosphorin (Eq. 3.25).[311] Dimroth et al.[312] converted the 4-formyl group of 1,1-dimethoxy-2,6-diphenyl-4-formyl-1$\lambda^5$-phosphorin to a variety of other substituents without



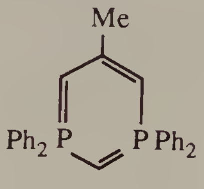
(3.25)

affecting the integrity of the ring system. Markl and Hock were able to halogenate the ring with $PCl_5$[313] and to acylate it with phosgene or acyl halides.[314] The phosphorins complexed readily with metal carbonyls of Cr, Mo, and W.[315] In contrast to the comparable $Cr(CO)_3$ complex with a $\lambda^3$-phosphorin, which was a $\eta^6\pi^6$ complex, that with the $\lambda^5$-phosphorin was a $\eta^5\pi^6$ complex, the Cr being bonded to the pentadienyl portion of the ring. The ring was boat-shaped with the P-1 and C-4 atoms being about 0.4 and 0.2 Å, respectively, above the plane of carbons 2,3,5, and 6, and the P–C distances being slightly elongated compared to the uncomplexed compound.[316, 317]

Methyl substituents on phosphorus exhibited acidity toward strong bases to form intermediate carbanions (ylides) which effected nucleophilic reactions but not typical ylide reactions, such as the Wittig reaction.[318]

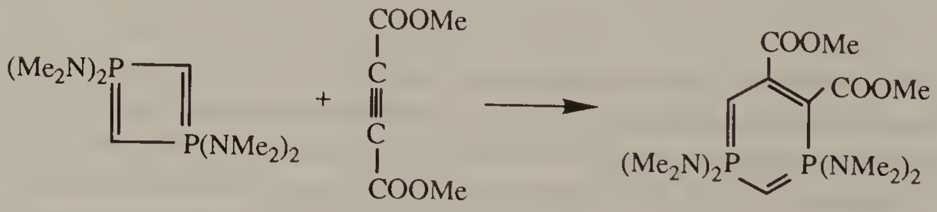
A number of related $\lambda^5$-phosphorins are known. 1,1-Diphenyl-1-phosphanapthalene behaved as a stable ylide, not undergoing the Wittig reaction with carbonyl compounds but capable of protonation to phosphonium salts and hydrolysis with ring cleavage.[291] 9-Phenyl-9-benzyl-9-phosphaanthracene also is known, but appeared to be an equilibrium mixture of the endocyclic and exocyclic ylides (**39**), and also exhibited nucleophilicity at C-10.[319] A 3,4-diaza-$1\lambda^5$-phosphorin also has been well characterized by NMR spectra and X-ray crystallographic analysis, existing in a distorted boat conformation with a P=C distance of 1.744 Å and a very compressed C–P–C angle of 99.3°.[320]

**39**



**40**

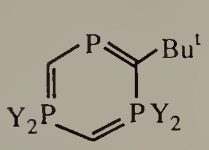
Several examples exist of phosphorins containing more than one $\lambda^5$-phosphorus atom. Markl[321] first prepared but poorly characterized 1,1,3,3,-tetraphenyl-$1\lambda^5$,$3\lambda^5$-diphosphabenzene, but Schmidbaur et al.[322] recently reported a complete structural analysis of the 5-methyl derivative (**40**), indicating a planar ring, short P–C distances (1.699 and 1.695 Å), and C–P–C angles of 110°. They characterized this diphosphabenzene bis-ylide as having two separate regions of conjugation, a $P^+–C^-–P^+$ region and a $^-C–C(CH_3)–C^-$ region (C–C lengths of 1.393 and 1.387 Å), with the P atoms acting as conjugation barriers as earlier proposed by Dewar et al.[323] Using a totally different synthetic approach, two different ring expansions of a 1,3-diphosphacyclobutadiene to a $1\lambda^5$, $3\lambda^5$-diphosphabenzene (Eq. 3.26), Fluck et al.[281, 324] found that the carbodiphosphorane-like P–C distance was short (1.682 Å), but that the other P–C distance was longer (1.736 Å), and the molecule was only slightly nonplanar.



(3.26)

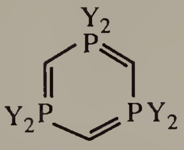
The $1\lambda^5$,$4\lambda^5$-diphosphabenzenes were first prepared by Shaw[289] and then by Davies[288] via the addition of cis-1,2-bis(diphenylphosphino)ethene to DMAD, but have not been well characterized.

The $\lambda^5$-triphosphabenzenes have been prepared by the Fluck group. Similar to the reaction shown in Eq. 3.26, addition of the recently available *t*-butylphosphaacetylene to a diphosphacyclobutadiene afforded **41**, which contained two ylidic phosphorus atoms.[325] The $^{31}P$ and $^{13}C$ NMR spectra indicated clearly the difference between ylidic and nonylidic P–C bonds, although the lengths of the bonds were very similar (mean 1.702 ± 0.012 Å) except for the longer $\lambda^5P–C(Bu^t)$ bond. The first known example of a tri-$\lambda^5$-1,3,5-phosphabenzene (**42**) has been reported by the same group as a byproduct from the reaction of methyldifluorobis(dimethylamino)phosphorane with two equivalents of butyllithium,[326] perhaps by formation first of a phosphaalkyne which then trimerized. This symmetrical tris-ylide, which was sufficiently stable to resist the usual hydrolysis conditions, was almost planar with P–C bonds of 1.687–1.697 Å, C–P–C angles of 113–113.4°, and P–C–P angles of 126.6–127°.



**41**

$Y = NMe_2$



**42**

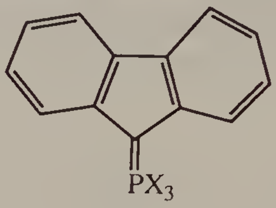
### 3.4.6 Uniquely Substituted Phosphonium Ylides

Throughout this chapter a wide variety of different ylides have been described, sufficient to provide the reader with a sense of the tremendous variety of phosphonium ylides that have been synthesized. At this mature stage of the development of phosphorus ylide chemistry the literature simply is too vast to attempt a complete listing of all known phosphonium ylides. Instead, on pages 80–83 are three tables (Tables 3.7–3.9) providing *examples* of the variety of ylides known. The text of this section is devoted to a few special examples of ylides with unique properties.

*3.4.6.1 Unique Carbon Substituents.* One of the interesting early ylides was triphenylphosphoniumcyclopentadienylide (**43**), first prepared by Ramirez and Levy.[9] It proved to be very stable, melting at 229–231°C and resistant to hydrolysis, reduction, and reaction with carbonyl compounds. Its crystal structure has been determined,[35] as has its NMR spectra.[121] Plass et al.[327] recently isolated and spectrally characterized the methylbis(dimethylamino)phosphonium analog. Both showed typical ylidic $^{13}C$ NMR spectra with large $^1J_{P-C}$ values of 113.1 and 141.1, respectively. The aromatic character of the cyclopentadienylide was demonstrated when it would not undergo Diels–Alder addition with DMAD[328] or tetracyanoethylene,[329] but reacted with these reagents and a variety of other electrophiles to undergo electrophilic substitution at C-2.[9,330–332] The ylide also formed complexes with metal carbonyls[333] and served as a nucleophile using C-3 in a substitution reaction with chloranil.[334] Lloyd[335] reviewed the chemistry of phosphonium (and other) cyclopentadienylides, including extensive reference to the work of he and his colleagues, especially on the chemistry and spectroscopy of the 2,3,4-triphenyl- and 2,3,4,5-tetraphenyl-derivatives. Grutzmacher and Pritzkow,[35] Smolii,[336] Moore and Bryce,[337] and Brovarets et al.[338] all recently reported heterocyclic analogs of the cyclopentadienylides.

The benzologs of **43** also are known. The indenylide was prepared from 1-bromoindene, but little of its chemistry has been reported.[339] The fluorenylides (**44**) have been extensively studied by Johnson et al.[8, 14, 19, 340] and ring-substituted derivatives also have been studied.[18, 341] The fluorenylides also are very stable ylides, but are of intermediate nucleophilicity such that they will effect a Wittig reaction with aldehydes, but usually not with ketones. Acidity constant correlations and dipole moments have been determined, both demonstrating that electron-withdrawing groups on the fluorenyl ring or on the phosphorus atom decrease the basicity of the ylide.


**43**


**44**

Although cyclopropenylphosphonium salts are known,[342, 343] the ylide only has been prepared in solution and has not been characterized.[344]

Finally, a series of phosphonium ylides ($Ph_3P{=}CRR'$) are known in which the R substituent is another onium-type group which can complement the initial $PPh_3$ group or compete with it in reactions. The carbodiphosphoranes (see Section 3.4.3), in which $R = {}^+PPh_3$, are well known. Other examples are $R = P(O)(OPh)_2$,[345, 346] where the phosphonio group was the most reactive

**TABLE 3.7 Exemplary Monosubstituted Triphenylphosphonium Ylides ($RCH{=}PPh_3$)**

| R | Reference |
|---|---|
| $-H$ | 375 |
| $-CH_3$ | 81, 375 |
| $-C_2H_5$ | 375 |
| $-C_3H_7$-*n* | 375 |
| $-C_4H_9$-*t* | 81, 143 |
| $-(CH_2)_3Br$ | 376 |
| $-(CH_2)_nOH$ | 377, 378 |

**TABLE 3.7** Continued

| R | Reference |
|---|---|
| $-(CH_2)_n\ NMe_2$ | 377 |
| $-(CH_2)_n\ NHMe$ | 377 |
| $-(CH_2)_nNH_2$ | 377 |
| –Cyclopropyl | 379 |
| –Cyclobutyl | 380 |
| –Cyclopentyl | 380 |
| –Cyclohexyl | 380 |
| $-CH{=}CH_2$ | 172, 174, 181 |
| $-CH{=}CH{-}CH_3$ | 162, 183 |
| $-CH{=}CHC_6H_5$ | 157, 381 |
| –Cyclohexenyl | 175 |
| $-CH_2COC_6H_5$ | 382 |
| $-COOC_2H_5$ | 383 |
| $-COOC_4H_9$-*t* | 384 |
| $-CSSCH_3$ | 239 |
| $-(CH_2)_nCOOC_2H_5$ | 385 |
| $-(CH_2)_nCOOH$ | 377, 386, 387 |
| $-CH{=}CH{-}COOCH_3$ | 388 |
| $-CHO$ | 28 |
| $-COCH_3$ | 4 |
| $-COC_6H_5$ | 4 |
| $-COCH{=}CHC_6H_5$ | 145 |
| –CON (Me) (OMe) | 389 |
| $-C_6H_5$ | 381 |
| –Ferrocenyl | 390 |
| –CN | 196 |
| $-CH_2CN$ | 391 |
| –NC | 392 |
| $-CH{=}NNMe_2$ | 393 |
| –Cl | 394 |
| –Br | 395 |
| –I | 395, 396 |
| –F | 397, 398 |
| $-OCH_3$ | 399 |
| $-SCH_3$ | 399 |
| $-SC_6H_5$ | 350 |
| $-{}^+S\ (CH_3)_2$ | 350 |
| $-SO_2CH_3$ | 400 |
| $-PMe_3$ | 24 |
| $-P\ (Pr^i)_2$ | 84 |
| $-PPh_2$ | 24 |
| $-P\ (O)\ (C_6H_5)_2$ | 349 |
| $-P\ (O)\ (OC_6H_5)_2$ | 345, 346 |
| $-Si\ (CH_3)_3$ | 81, 143 |

**TABLE 3.8 Exemplary Disubstituted Triphenylphosphonium Ylides ($RR'C{=}PPh_3$)**

| R | R′ | Reference |
|---|---|---|
| $-CH_3$ | $-CH_3$ | 81 |
|  | $-C_6H_5$ | 178 |
|  | $-CHO$ | 401 |
|  | $-COOC_2H_5$ | 402 |
| RR′C = Cyclopropylidene |  | 29 |
| Cyclobutylidene |  | 30 |
| Cyclopentylidene |  | 403 |
| Cyclohexylidene |  | 403 |
| Cyclopentadienylidene |  | 9 |
| Fluorenylidene |  | 8 |
| $-C_6H_5$ | $-T$ | 157 |
|  | $-C_6H_5$ | 404 |
| $-COOC_2H_5$ | $-COOC_2H_5$ | 405 |
|  | $-D$ | 406 |
|  | $-Cl$ | 407 |
| $-COOC_2H_5$ | $-COCH_3$ | 43, 405 |
| $-COOCH_3$ | –cyclopropyl | 408 |
|  | $-CH_2C_6H_5$ | 409 |
| $-CHO$ | $-C_6H_5$ | 410 |
| $-COCH_3$ | $-COCH_3$ | 411 |
|  | $-C_6H_5$ | 412 |
| $-COCF_3$ | $-C_6H_5$ | 413 |
| $-COC_6H_5$ | $-COC_6H_5$ | 411 |
|  | $-Cl$ | 414 |
|  | $-I$ | 111 |
|  | $-CN$ | 415 |
|  | $-OCH_3$ | 416 |
| $-CONHC_6H_5$ | $-CONHC_6H_5$ | 417 |
| $-OC_6H_5$ | $-OC_6H_5$ | 418 |
| $-SC_6H_5$ | $-SC_6H_5$ | 419 |
|  | $-SeC_6H_5$ | 54 |
| $-SO_2C_6H_5$ | $-SO_2C_6H_5$ | 405 |
| $-SeC_6H_5$ | $-SeC_6H_5$ | 420 |
| $-Si\ (CH_3)_3$ | $-Si\ (CH_3)_3$ | 109 |
| $-N{=}NC_6H_5$ | $-N{=}NC_6H_5$ | 421 |
| $-P(C_6H_5)_2$ | $-P(C_6H_5)_2$ | 51 |
| $-As\ (C_6H_5)_2$ | $-As\ (C_6H_5)_2$ | 53 |
| $-Sb\ (C_6H_5)_2$ | $-Sb\ (C_6H_5)_2$ | 52 |
| $-CN$ | $-CN$ | 37 |
|  | $-COCF_3$ | 422 |
|  | $-COOC_2H_5$ | 407 |
| $-Cl$ | $-Cl$ | 423–425 |
| $-Br$ | $-Br$ | 426 |
| $-F$ | $-F$ | 427 |
|  | $-Cl$ | 428 |
| RR′C = Diazo |  | 429 |

group; R = P(O or S)$Ph_2$,[347–349] in which the PO group was more acidifying than the PS group; R = P(O)MePh;[222] R = $^+SMe_2$;[350] R = $^+IAr$.[42]

Readers are referred to Tables 3.7 and 3.8 for examples of various carbon substituents on phosphonium ylides.

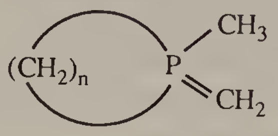
***3.4.6.2 Unique Phosphorus Substituents.*** Most phosphonium ylides designed to be used in syntheses contain the triphenylphosphonium group because of the availability, stability, and nice reactivity of triphenylphosphine usually used in the preparation of the ylide. When a more nucleophilic ylide is desired, or when it is desired to reduce the likelihood of anionic attack on phosphorus in the course of a reaction, tri-*n*-butylphosphine usually is the choice for the same reasons. Most other phosphorus substituents, including ring-substituted triphenylphosphines, have been utilized for single special purposes, usually for the study of ylide characteristics, and therefore there often is little comparative information available. A few such ylides are mentioned in this section to demonstrate some unique properties, and examples are listed in Table 3.9.

**TABLE 3.9 Exemplary *P,P,P*-Trisubstituted Phosphonium Ylides ($RR'C{=}PX_3$)**

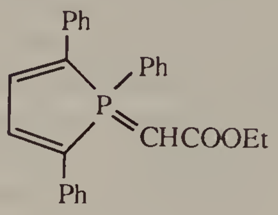
| X | R | R′ | Reference |
|---|---|---|---|
| N-Piperidyl | –H | –H | 430 |
| *p*-Anisyl | –H | –H | 430 |
| N-Dimethylamino | $-COOCH_3$ | –H | 358 |
|  | $-C_6H_5$ | –H | 358 |
| N-Diethylamino | –H | –H | 359 |
| Methyl | –H | –H | 10,375 |
|  | $-SiMe_3$ | –H | 64, 109 |
|  |  | $-SiMe_3$ | 109 |
|  | $-PbMe_3$ | $-PbMe_3$ | 112 |
| Ethyl | $-SiMe_3$ | –H | 144 |
| *i*-Propyl | –H | –H | 356 |
|  | $-CH_3$ | $-CH_3$ | 123 |
| *n*-Butyl | $-COOC_2H_5$ | –H | 431 |
|  | $-CH{=}CH_2$ | –H | 176 |
|  | RR′C = –fluorenylidene |  | 19 |
| *t*-Butyl | –H | –H | 150, 355 |
|  | –H | $-C_6H_5$ | 150 |
| *n*-Hexyl | $-COOC_2H_5$ | –H | 383 |
| Cyclopropyl | $-COC_6H_5$ | –H | 351 |
|  | RR′C = –cyclopropylidene |  | 124 |
| Cyclohexyl | $-COOC_2H_5$ | –H | 383 |
| $(CH_3)_n(C_6H_5)_{3-n}$ | $-COC_6H_5$ | –H | 412 |
| Mesityl | –H | –H | 432 |
| Ferrocenyl | $-CH_2C_6H_5$ | –H | 154 |
|  | –H | –H | 24 |

Alicyclic phosphines have been used in ylide formation. Denney and Gross[351] prepared tricyclopropylphosphine and converted it to an ylide which was more basic and nucleophilic than the triphenyl analog. Bestmann used tricyclohexylphosphonium ylides in his early work,[352] but not to any obvious advantage.

Schmidbaur et al. incorporated the phosphorus atom in a five-membered (phospholane) ring (**45**, n = 4)[286] and in a six-membered (phosphorinane) ring (**45**, n = 5),[353] and the ylide formed by proton removal was exocyclic in both cases. Campbell et al.[354] found that the ester ylide **46**, easily prepared from 1,2,5-triphenyl-1-phosphacyclopentadiene, was more stable than the triphenylphosphonium analog.



**45**

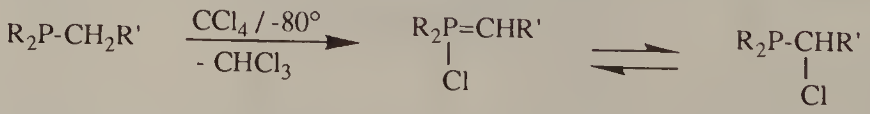


**46**

Schmidbaur et al.[355] prepared bulky ylides by using bulky phosphines, especially tri-*t*-butylphosphine. Although the methylide was crystallized, it readily decomposed to isobutylene and methylbis(*t*-butyl)phosphine, probably as the result of an intramolecular Hoffman-type elimination. The tris(isopropyl)-phosphonium ylides were more stable.[356]

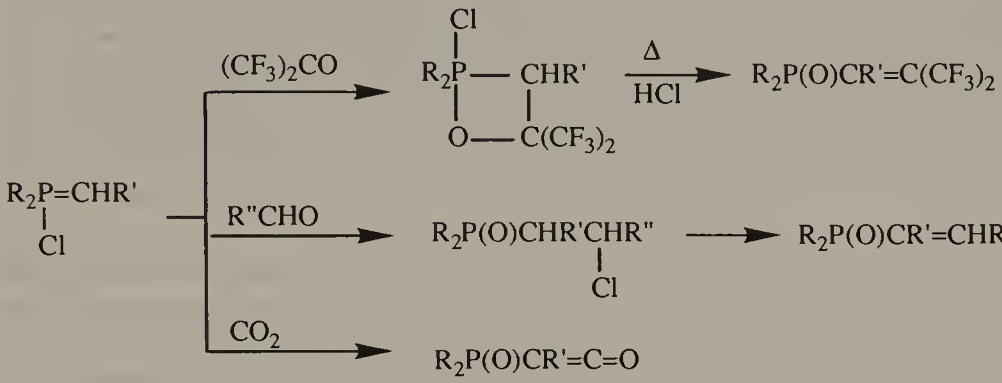
Phosphonium ylides derived from tris-(substituted amino)phosphines have been known for some time. Wittig et al.[357] found that tris-(piperidino)phosphonium ylides were more nucleophilic than the triphenyl analogs, but the phosphorus atom was less susceptible to oxyanion attack in the Wittig reaction. Oediger and Eiter[358] were early investigators of tris-(dimethylamino)phosphonium ylides and found them easy to prepare and effective in the Wittig reaction. More recently, Schmidbaur et al.[359] used the diethylamino substituent in preparation of a series of silyl-substituted phosphonium ylides. Fluck et al.[327] isolated methylbis(dimethylamino)phosphoniumcyclopentadienylide and have used the dimethylamino group as the P-substituent in a series of P-fluoro ylides (see below) and in a series of cyclic ylides (see Section 3.4.5).[326]

Kolodiazhnyi[360] recently reviewed the preparation and reactions of P-chloro ylides, work done almost exclusively by his group at Kiev. Most readily prepared from phosphines and carbon tetrachloride under mild conditions,[361] the ylides have been isolated and spectroscopically characterized (Eq. 3.27). The



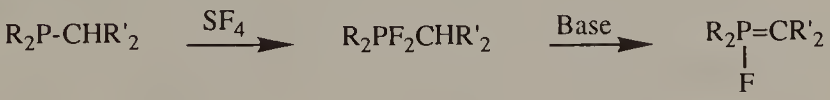
$$R_2P\text{-}CH_2R' \xrightarrow[-\,CHCl_3]{CCl_4\,/\,-80^\circ} \underset{\displaystyle Cl}{R_2\overset{}{P}}{=}CHR' \rightleftharpoons \underset{\displaystyle Cl}{R_2P}\text{-}CHR' \qquad (3.27)$$

other two P-substituents usually have been *t*-butyl, phenoxy, dimethylamino, or diethylamino groups. Carbon substituents have varied widely from alkyl to aryl to carboalkoxy. In solution the P-chloro ylides are in equilibrium with the C-chlorophosphines, with nonpolar solvents and with electron-withdrawing groups (R′) favoring the ylide form.[362, 363] Treatment of a P-chloro ylide ($^t\text{Bu}_2\text{ClP{=}CPh}_2$) with aluminum chloride produced a crystalline methylene phosphonium ion with a P=C length of 1.68 Å, only 0.02 Å longer than the P=C length in the ylide precursor.[62] The P-chloro ylides were susceptible to reaction with nucleophiles in a protic environment (i.e., phenols, secondary amines) which resulted in proton addition to the carbon and displacement of the halogen. Reaction with hexafluoroacetone resulted in isolation of diastereoisomeric oxaphosphetanes, which were converted to vinylphosphine oxides, rather than Wittig reaction products, upon heating (Eq. 3.28).[364] Reaction of P-chloro ylides with aldehydes at low temperatures also produced oxaphosphetanes, as detected in solution by NMR spectroscopy, but warming led to production of $\beta$-chlorophosphine oxides.[365] The latter could be converted to vinylphosphine oxides by heating or by carrying out the reaction with two equivalents of ylide to serve as base. Use of carbon dioxide, carbon disulfide,[366] or isocyanates as the carbonyl reagent afforded heterocumulenes (Eq. 3.28).



(3.28)

Fluck et al. prepared several P-fluoro ylides, usually by treatment of a phosphine with $SF_4$ to form a difluorophosphorane from which a proton was removed with butyllithium or lithium bis(trimethylsilyl)amide (Eq. 3.29).[367] The ylides have been characterized spectroscopically, and appeared to be more stable, and less reactive, than the P-chloro ylides.[368] Further treatment of the P-fluoro methylide with butyllithium resulted in apparent dehydrofluorination to a phosphonioalkyne which dimerized to a cyclic bis- (**31**) or tris- (**42**) ylide[326] (see Section 3.4.5). Kolodiazhnyi and Ustenko[369] used the same dehydrofluorination method to prepare P,P-difluoro ylides from triflurophosphoranes and found them to add alcohols and react with aldehydes. The Bertrand group formed P-fluoro ylides by adding dimesitylboron trifluoride to a phosphinocarbene.[370]

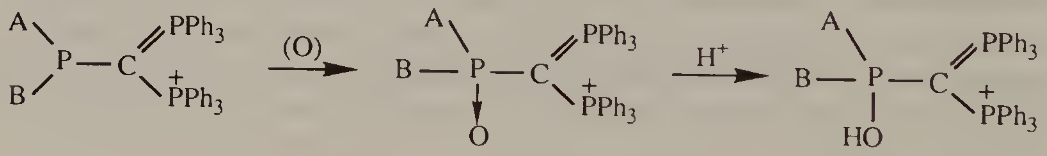


$$\text{R}_2\text{P-CHR'}_2 \xrightarrow{\text{SF}_4} \text{R}_2\text{PF}_2\text{CHR'}_2 \xrightarrow{\text{Base}} \underset{\text{F}}{\underset{|}{\text{R}_2\text{P}}}\text{=CR'}_2 \qquad (3.29)$$

Mastryukova et al.[371] reviewed the evidence for the existence, at least in solution and in especially favorable cases, of certain P-hydrogen ylides, those prone to “dyadic phosphorus–carbon tautomerism” (Eq. 3.30). X-Ray crystallographic analysis of one example (A = B = *n*-Bu; R = R′ = $^+PPh_3$) indicated, by the fact that the central carbon atom appeared trigonal, that the proton must be on the phosphorus atom carrying the butyl groups, even though the proton could not be located directly. That phosphorus atom was slightly distorted from the tetrahedral shape. The same starting material underwent methylation on the dibutylphosphorus group, so it was argued that a proton would be expected to be located similarly. The equilibrium (Eq. 3.30) could be detected in solution for the compounds (A = B = Ph, R = $^+PPH_3$, R′ = COOEt)[371] and (A = B = alkyl, R = R′ = COOMe)[372] by NMR spectroscopy, with the proportions being solvent- and temperature-dependent.

(3.30)

Oxidation of a phosphine-ylide afforded a phosphinoxy ylide, which could be protonated to a P-hydroxy ylide whose structure has been determined (Eq. 3.31).[373] Alternatively, in solution certain phosphine oxides were shown to be prototropic (Eq. 3.32),[348, 374] and one (A = B = Ph, R = Ts, R′ = $^+PPh_3$) was characterized by X-ray crystallography.[348] Methylation of $Ph_2P(O)\text{–}CH{=}PPh_3$ with methyl sulfate resulted in O-methylation and formation of a P-methoxy ylide.[349] Methylation of $Ph_2P(O)CH(SO_2Ph)_2$ with diazomethane also afforded a P-methoxy ylide.[374] Although the P-hydrogen, P-hydroxy, and P-methoxy ylides are interesting, they have found no special use in synthesis.



(3.31)

$$\text{ABP(O)CHRR'} \rightleftharpoons \text{ABP(OH)=CRR'} \qquad (3.32)$$

## REVIEWS

**1969** Matthews, C. N.; Birum, G. H. *Acc. Chem. Res. 2*, 373–379. A review of the chemistry of carbodiphosphoranes and phosphacumulenes.

**1972** Bestmann, H. J.; Zimmermann, R. In *Organic Phosphorus Compounds*, Kosolapoff, G. M.; and Maier, L., Eds.; Wiley-Interscience, New York; Vol. 3, Chapter 5, pp. 1–184. A review of the preparation, reactions, and properties of phosphonium ylides.

**1972** Davies, M.; Hughes, A. N. *J. Heterocycl. Chem. 9*, 1–19. A review of cyclic phosphonium ylides.

**1977** Markl, G. *Phosphorus and Sulfur 3*, 77–108. A review of aromatic phosphorus heterocycles.

**1977** Bestmann, H. J. *Angew. Chem. 16*, 349–364. A review of phosphacumulene and phosphaallene ylides.

**1980** Mastryukova, T. A.; Aladzheva, I. M.; Leonteva, I. V.; Petrovski, P. V.; Fedin, E. I.; Kabachnik, M. I. *Pure Appl. Chem. 52*, 945–957. A review of dyadic phosphorus–carbon tautomerism.

**1982** Dimroth, K., *Acc. Chem. Res. 15*, 58–64. A review of $\lambda^5$-phosphorins (1,1-disubstituted phosphabenzenes).

**1983** Kolodiazhnyi, O. I.; Kukhar, V. P. *Russ. Chem. Revs. 52*, 1096–1112. A review of P-heterosubstituted phosphorus ylides.

**1989** Kolodiazhnyi, O. I. *Z. Chem. 29*, 396–405. A review of the preparation, reactions, and properties, of P-halo (mainly chloro) ylides.

**1991** Kolodiazhnyi, O. I. *Russ. Chem. Revs. 60*, 391–409. A review of P-halogen substituted ylides.

## REFERENCES

[1] Michaelis, A; Gimborn, H. V. *Chem. Ber.* **1894**, *27*, 272.

[2] Aksnes, G. *Acta Chem. Scand.* **1961**, *15*, 438.

[3] Staudinger, H.; Meyer, J. *Helv. Chim. Acta* **1919**, *2*, 619.

[4] Ramirez, F.; Dershowitz, S. J. *Org. Chem.* **1957**, *41*, 22.

[5] Michaelis, A.; Kohler, E. *Chem. Ber.* **1989**, *32*, 1566.

[6] Wittig, G.; Reiber, M. *Liebigs Ann. Chem.* **1949**, *562*, 177.

[7] Wittig, G.; Geissler, G. *Liebigs Ann. Chem.* **1953**, *580*, 44.

[8] Johnson, A. Wm. *J. Org. Chem.* **1959**, *24*, 282.

[9] Ramirez, F.; Levy, S. *J. Am. Chem. Soc.* **1957**, *79*, 67.

[10] Schmidbaur, H.; Tronich, W. *Angew. Chem.* **1967**, *6*, 448.

[11] Doering, W. von E.; Schreiber, K. C. *J. Am. Chem. Soc.* **1955**, *77*, 514.

[12] Keough, P. T.; Grayson, M. *J. Org. Chem.* **1964**, *29*, 631.

[13] Doering, W. von E.; Hoffmann, A. K.; *J. Am. Chem. Soc.* **1955**, *77*, 521.

[14] Johnson, A. Wm.; Lee, S. Y.; Swor, R. A.; Royer, L. D. *J. Am. Chem. Soc.* **1966**, *88*, 1953.

[15] Bachrach, S. M. *J. Org. Chem.* **1992**, *57*, 4367.

[16] Reed, A. L.; Schleyer, P. von R. *J. Am. Chem. Soc.* **1990**, *112*, 1434.

[17] Adlaf, P. C. *Diss. Abstr. Int.* **1970**, *30B*, 5417.

[18] Goetz, H.; Klabuhn, B. *Liebigs Ann. Chem.* **1969**, *724*, 1.

[19] Johnson, A. Wm.; LaCount, R. B. *Tetrahedron* **1960**, *9*, 130.

[20] Lumbroso, H.; Cure, J.; Bestmann, H. J. *J. Organomet. Chem.* **1978**, *161*, 347.

[21] Tsuchiya, S., Mitomo, S. I.; Kise, H.; Seno, M. *J. Chem. Soc. Perkin Trans. (2)* **1986**, 245.

[22] Pauling, L. *Nature of the Chemical Bond,* 3rd Ed.; Cornell University Press: Ithaca, NY, 1960; p. 224.

[23] Bart, J. C. J. *J. Chem. Soc. (B)* **1969**, 350.

[24] Schmidbaur, H.; Jeong, J.; Schier, A.; Graf, W.; Wilkinson, D. L.; Muller, G. *New. J. Chem.* **1989**, *13*, 341.

[25] Geoffrey, M.; Rao, G.; Tancic, Z.; Bernardinelli, G. *J. Am. Chem. Soc.* **1990**, *112*, 2826.

[26] Shao, M.; Jin, X.; Tang, Y.; Huang, Q.; Huang, Y. *Tetrahedron Lett.* **1982**, 5343.

[27] Wheatley, P. J. *J. Chem. Soc.* **1965**, 5785.

[28] Carroll, P. J.; Titus, D. D. *J. Chem. Soc. Dalton Trans.* **1977**, 824.

[29] Schmidbaur, H.; Schier, A.; Milewski-Mahrla, B.; Schubert, U. *Chem. Ber.* **1982**, *115*, 722.

[30] Schmidbaur, H.; Schier, A.; Neugebauer, D. *Chem. Ber.* **1983**, *116*, 2173.

[31] Howells, M. A.; Howells, R. D.; Baenziger, N. C.; Burton, D. J. *J. Am. Chem. Soc.* **1973**, *95*, 5366.

[32] Brown, R. F. C.; Eastwood, F. W.; Fallon, G. D.; LaVecchia, L.; Schank, K. *Aust. J. Chem.* **1989**, *42*, 451.

[33] Cameron, T. S.; Prout, C. K. *J. Chem. Soc. (C)* **1969**, 2292.

[34] Bailey, A. S.; Peach, J. M.; Cameron, T. S.; Prout, C. K. *J. Chem. Soc. (C)* **1969**, 2295.

[35] Ammon, H. L.; Wheeler, G. L.; Watts, P. H. *J. Am. Chem. Soc.* **1973**, *95*, 6158.

[36] Rendle, D. F. *Diss. Abstr. Int.* **1973**, *33B*, 5178.

[37] Richter, R.; Hartung, H.; Deresch, S.; Kaiser, J. *Z. Anorg. Allg. Chem.* **1980**, *469*, 179.

[38] Grutzmacher, H.; Pritzkow, H. *Chem. Ber.* **1989**, *122*, 1411.

[39] Stephens, F. S. *J. Chem. Soc.* **1965**, 5658.

[40] Stephens, F. S. *J. Chem. Soc.* **1965**, 5640.

[41] Husebye, S. *Acta Crystallogr. (C)* **1986**, *42*, 90.

[42] Moriarty, R. M.; Prakash, I.; Prakash, O.; Freeman, W. A. *J. Am. Chem. Soc.* **1984**, *106*, 6082.

[43] Abell, A. D.; Clark, B. M.; Robinson, W. T.; *Aust. J. Chem.* **1989**, *42*, 1161.

[44] Cherepinskii-Malov, V. D.; Alexandrov, G. G; Guser, A. I.; Struchkov, Y. T. *Zh. Strukt. Chem.* **1972**, *29*, 298; *Chem. Abstr.* **1972**, *77*, 40213.

[45] Cameron, A. F.; Duncanson, F. G.; Freer, A.; Armstrong, V. W.; Ramage, R. *J. Chem. Soc. Perkin Trans. (2)* **1975**, 1030.

[46] Alemagna, A.; Buttero, P. D.; Licandro, E.; Maiorana, S.; Gaustini, G. *J. Chem. Soc. Chem. Commun.* **1983**, 337.

[47] Gilardi, R. D.; Karle, I. *Acta Crystallogr. (B)* **1972**, *28*, 3420.

[48] Mak, T. C. W.; Trotter, J. *Acta Crystallogr.* **1965**, *18*, 81.

[49] Lingner, V. U.; Burzlaff, H. *Acta Crystallogr. (B)* **1974**, *30*, 1715.

[50] Kawamoto, I.; Hata, T.; Kishida, Y.; Tamura, C. *Tetrahedron Lett.* **1972**, 1611.

[51] Schmidbaur, H.; Deschler, U.; Milewski-Mahrla, B. *Chem. Ber.* **1983**, *116*, 1393.

[52] Schmidbaur, H.; Milewski-Mahrla, B.; Muller, G.; Kruger, C. *Organometallics* **1984**, *3*, 38.

[53] Schmidbaur, H.; Nußstein, P., Muller, G. *Z. Naturforsch.* **1984**, *39B*, 1456.

[54] Schmidbaur, H.; Zybill, C.; Krueger, C.; Kraus, H. J.; *Chem. Ber.* **1983**, *116*, 1955.

[55] Ross, F. K.; Hamilton, W. C.; Ramirez, F. *Acta Crystallogr. (B)* **1971**, *27*, 2331.

[56] Ross, F. K.; Muir, L. M.; Hamilton, W. C.; Ramirez, F.; Pilot, J. F. *J. Am. Chem. Soc.* **1972**, *94*, 8738.

[57] Ebsworth, E. A. V.; Fraser, T. E.; Rankin, D. W. H. *Chem. Ber.* **1977**, *110*, 3495.

[58] Ebsworth, E. A. V.; Rankin, D. W. H.; Gasser, B. Z.; Schmidbaur, H. *Chem. Ber.* **1980**, *113*, 1637.

[59] Gasser, B. Z.; Neugebauer, D.; Schubert, U.; Karsch, H. H. *Z. Naturforsch.* **1979**, *34B*, 1267.

[60] Fritz, G.; Braun, U.; Schick, W.; Honle, W.; Schnering, H. G. *Z. Anorg. Allg. Chem.* **1981**, *472*, 45.

[61] Fritz, G.; Schick, W.; Honle, W.; Schnering, H. G. *Z. Anorg. Allg. Chem.* **1984**, *511*, 95.

[62] Grutzmacher, H.; Pritzkow, H. *Angew. Chem.* **1992**, *31*, 99.

[63] Schmidbaur, H.; Schier, A.; Frazao, C. M.; Muller, G. *J. Am. Chem. Soc.* **1986**, *108*, 976.

[64] Dreissig, W.; Hecht, H. J.; Plieth, K. *Z. Krystallogr.* **1973**, *137*, 132.

[65] Nevstad, G. O.; Moe, K. M.; Ramming, C.; Songstad, J. *Acta Chem. Scand.* **1985**, *39A*, 523.

[66] Fritz, H. P.; Muller, G.; Reber, G.; Weis, M. *Angew. Chem.* **1985**, *24*, 1058.

[67] Kennard, O.; Motherwell, W. D. S. *J. Chem. Soc. (C)* **1971**, 2461.

[68] Vincent, M. A.; Schaefer, H. F.; Schier, A.; Schmidbaur, H. *J. Am. Chem. Soc.* **1983**, *105*, 3806.

[69] Sutton, L. E. *Tables of Interatomic Distances and Configuration in Molecules and Ions*; Special Publication No. 18; The Chemical Society: London, 1965; p. S21s.

[70] Sutton, L. E. *Tables of Interatomic Distances and Configuration in Molecules and Ions*; Special Publication No. 18; The Chemical Society: London, 1965; p. S15s.

[71] Schmidbaur, H.; Muller, G.; Milewski-Mahrla, B.; Schubert, U. *Chem. Ber.* **1980**, *113*, 2575.

[72] Andrews, S. J.; Welch, A. J. *Acta Crystallogr. (C)* **1985**, *41*, 1496.

[73] Buckle, J.; Harrison, P. G.; King, T. J.; Richards, J. A. *J. Chem. Soc. Chem. Commun.* **1972**, 1104.

[74] Antipin, M. Y.; Struchkov, Y. T.; Hadzheva, I. M.; Leonteva, I. V.; Mastryukova, T. A.; Kabachnik, M. I. *J. Gen. Chem.* **1990**, *60*, 21.

[75] Horner, L.; Winkler, H. *Liebigs Ann. Chem.* **1965**, *685*, 1.

[76] McEwen, W. E.; Kumli, K. F.; Blade-Font, A.; Zanger, M.; Vanderwerf, C. A. *J. Am. Chem. Soc.* **1964**, *86*, 2378.

[77] McEwen, W. E.; Blade-Font, A.; Vanderwerf, C. A. *J. Am. Chem. Soc.* **1962**, *84*, 677.

[78] Eades, R. A.; Gassman, P. G.; Dixon, D. A. *J. Am. Chem. Soc.* **1981**, *103*, 1066.

[79] Francl, M. M.; Pellow, R. C.; Allen, L. C. *J. Am. Chem. Soc.* **1988**, *110*, 3723.

[80] Liu, Z. P.; Schlosser, M. *Tetrahedron Lett.* **1990**, *31*, 5753.

[81] Lucken, E. A. C.; Mazeline, C. *J. Chem. Soc. (A)* **1967**, 437.

[82] Schmidbaur, H.; Herr, R.; Riede, J. *Chem. Ber.* **1984**, *117*, 2322.

[83] Schmidbaur, H.; Bowmaker, G. A.; Deschler, U.; Dorzbach, C.; Herr, R.; Milewski-Mahrla, B.; Schier, A.; Zybill, C. E. *Phosphorus and Sulfur* **1983**, *18*, 167.

[84] Schmidbaur, H.; Schier, A; Lauteschlager, S.; Riede, J.; Muller, G. *Organometallics* **1984**, *3*, 1906.

[85] Randall, F. J.; Johnson, A. W. *Tetrahedron Lett.* **1968**, 2841.

[86] Bestmann, H. J.; Liberda, H. G.; Snyder, J. P. *J. Am. Chem. Soc.* **1968**, *90*, 2963.

[87] Wilson, I. F.; Tebby, J. C. *Tetrahedron Lett.* **1970**, 3769.

[88] Filleux-Blanchard, M. L.; Martin, G. J., *C. R. Seances Acad. Sci.* **1970**, *270C*, 1747.

[89] Dale, A. J.; Froyen, P. *Acta Chem. Scand.* **1970**, *24*, 3772.

[90] Le Corre, M., *Bull. Soc. Chim. Fr.* **1974**, 1951.

[91] Schlosser, M.; Jenny, T.; Schaub, B. *Heteroatom Chem.* **1990**, *1*, 151.

[92] Kayser, M. M.; Hatt, K. L.; Hooper, D. L. *Can. J. Chem.* **1991**, *69*, 1929.

[93] Crews, P. *J. Am. Chem. Soc.* **1968**, *90*, 2961.

[94] Bestmann, H. J.; Joachim, G.; Lengyel, I.; Oth, J. F. M.; Merenyi, R.; Weitkamp, H. *Tetrahedron Lett.* **1966**, 3355.

[95] Zeliger, H. I.; Snyder, J. P.; Bestmann, H. J. *Tetrahedron Lett.* **1969**, 2199.

[96] Snyder, J. P. *Tetrahedron Lett.* **1971**, 215.

[97] Barluenga, J. *J. Chem. Soc. Perkin Trans. 2* **1988**, 903.

[98] Kayser, M. H.; Hooper, D. L. *Can. J. Chem.* **1990**, *68*, 2123.

[99] Howe, R. K. *Abstracts of Papers,* 161st Annual Meeting of the American Chemical Society, Los Angeles; American Chemical Society: Washington, DC, 1971; ORGN 176.

[100] Yoshida, H.; Matsuura, H.; Ogata, T.; Inokawa, S.; *Bull. Soc. Chem. Jpn.* **1975**, *48*, 2907.

[101] Griffin, C. E.; Gordon, M. *J. Organomet. Chem.* **1965**, *3*, 414.

[102] Bestmann, H. J.; Snyder, J. P. *J. Am. Chem. Soc.* **1967**, *89*, 3936.

[103] Schmidbaur, H.; Tronich, W. *Chem. Ber.* **1968**, *101*, 604.

[104] Grim, S. O. In *Phosphorus-31 NMR Specctroscopy in Stereochemical Analysis;* Verkade, J. G.; Quin, L. D., Eds.; Volume 8 of the series Methods in Stereochemical Analysis, Marchand, A. P., Ed.; VCH Publishers, Deerfield Beach, FL, 1987; Chapter 18, pp. 645–664.

[105] Albright, T. A.; Schweizer, E. E. *J. Org. Chem.* **1976**, *41*, 1168.

[106] Fluck, E.; Bayha, H.; Heckmann, G. *Z. Anorg. Allg. Chem.* **1976**, *421*, 1.

[107] Schmidbaur, H.; Muller, G.; Blaschke, G. *Chem. Ber.* **1980**, *113*, 1480.

[108] Grim, S. O.; McFarlane, W.; Marks, T. J. *J. Chem. Soc. Chem. Commun.* **1967**, 1191.

[109] Albright, T. A.; Freeman, W. J.; Schweizer, E. E. *J. Am. Chem. Soc.* **1975**, *97*, 2946.

[110] Schmidbaur, H.; Buchner, W.; Scheutzow, D. *Chem. Ber,* **1973**, *106*, 1251.

[111] Schmidbaur, H.; Richter, W.; Wolf, W.; Kohler, F. H. *Chem. Ber.* **1975**, *108*, 2649.

[112] Grim, S. O.; Davidoff, E. F.; Marks, T. J.; *Z. Naturforsch.* **1971**, *26B*, 184.

[113] Speziale, A. J.; Ratts, K. W. *J. Am. Chem. Soc.* **1963**, *85*, 2790.

[114] Schmidbaur, H.; Eberlein, J.; Richter, W. *Chem. Ber.* **1977**, *110*, 677.

[115] Grim, S. O.; Yankowsky, A. W.; Bruno, S. A.; Bailey, W. J.; Davidoff, E. F.; Marks, T. J. *J. Chem. Eng. Data* **1970**, *15*, 497.

[116] Ramirez, F.; Madan, O. P.; Smith, C. P. *Tetrahedron* **1966**, *22*, 567.

[117] Starzewski, K. A. O.; Feigel, M. *J. Organomet. Chem.* **1975**, *93*, C20.

[118] Albright, T. A.; Gordon, M. D.; Freeman, W. J.; Schweizer, E. E. *J. Am. Chem. Soc.* **1976**, *98*, 6249.

[119] Albright, T. A.; Freeman, W. J.; Schweizer, E. E., *J. Am. Chem. Soc.* **1975**, *97*, 2942.

[120] Fronza, G.; Bravo, P.; Ticozzi, C. *J. Organomet. Chem.* **1978**, *157*, 299.

[121] Froyen, P.; Morris, D. G. *Acta Chem. Scand.* **1977**, *B31*, 256.

[122] Gray, G. A. *J. Am. Chem. Soc.* **1973**, *95*, 5092.

[123] Seno, M.; Tsuchiya, S.; Kise, H.; Asahara, T.; *Bull. Chem. Soc. Jpn.* **1975**, *48*, 2001.

[124] Schier, A.; Schmidbaur, H. *Chem. Ber.* **1984**, *117*, 2314.

[125] Waack, R.; McKeever, L. D.; Doran, M. A. *J. Chem. Soc. Chem. Comm.* **1969**, 117.

[126] Albright, T. A.; DeVoe, S. V.; Freeman, W. J.; Schweizer, E. E. *J. Org. Chem.* **1975**, *40*, 1650.

[127] Luttke, W.; Wilhelm, K. *Angew. Chem.* **1965**, *4*, 875.

[128] Sawodny, W. *Z. Anorg. Allg. Chem.* **1969**, *368*, 284.

[129] Aksnes, G. *Acta Chem. Scand.* **1961**, *15*, 692.

[130] Chopard, P.; Salvadori, G. *Gazz. Chim. Ital.* **1963**, *93*, 668.

[131] Ding, W.; Zhang, P.; Pu, J. *Youji Huaxue* **1986**, 459; *Chem. Abstr.* **1987**, *107*, 198488.

[132] Grim, S. O.; Ambrus, J. H. *J. Org. Chem.* **1968**, *33*, 2993.

[133] Tomaschewski, G.; Geissler, G. *Z. Chem.* **1966**, *6*, 68.

[134] Shevchuk, M. I.; Dombrovskii, A. V. *J. Gen. Chem.* **1964**, *34*, 2738.

[135] Fischer, H.; Fischer, H. *Chem. Ber.* **1966**, *99*, 658.

[136] Lucken, E. A.; Mazeline, C. *J. Chem. Soc. (A)* **1966**, 1074.

[137] Starzewski, K. A. O.; Dieck, H. T.; Bock, H. *J. Organomet. Chem.* **1974**, *65*, 311.

[138] Starzewski, K. A. O.; Richter, W.; Schmidbaur, H. *Chem. Ber.* **1976**, *109*, 473.

[139] Starzewski, K. A. O.; Bock, H.; Dieck, H. T. *Angew. Chem.* **1975**, *14*, 173.

[140] Romanenko, E. A.; Marchenko, A. P.; Koidan, G. N.; Pinchuk, A. M. *J. Gen. Chem.* **1990**, *60*, 1992.

[141] Bestmann, H. J. *Chem. Ber.* **1962**, *95*, 58.

[142] Wohlleben, A.; Schmidbaur, H. *Angew. Chem.* **1977**, *16*, 417.

[143] Seyferth, D.; Singh, G. *J. Am. Chem. Soc.* **1965**, *87*, 4156.

[144] Schmidbaur, H.; Malisch, W. *Angew. Chem.* **1969**, *8*, 372.

[145] Fliszar, S.; Hudson, R. F.; Salvadori, G. *Helv. Chim. Acta* **1963**, *46*, 1580.

[146] Bordwell, F. G. *Acc. Chem. Res.* **1988**, *21*, 456.

[147] Issleib, K.; Linder, R. *Liebigs Ann. Chem.* **1967**, *707*, 120.

[148] Mastryukova, T.; Matveeva, A. G.; Grigoreva, A. A.; Litovchenko, G. F.; Matrosov, E. I.; Aladzheva, I. M.; Bukhovskaya, O. V.; Leonteva, K. V.; Kabachnik, M. I. *J. Gen. Chem.* **1991**, *61*, 2253.

[149] Ling-Chung, S.; Sales, K. D.; Utley, J. H. P. *J. Chem. Soc. Chem. Commun.* **1990**, 662.

[150] Alunni, S. *J. Chem. Res. Synopsis* **1986**, 231; *Chem. Abstr.* **1987**, *106*, 119957.

[151] Aksnes, G.; Songstad, J. *Acta Chem. Scand.* **1964**, *18*, 655.

152 Kabachnik, M. I.; Mastryukova, T. A. *J. Gen. Chem.* **1984**, *54*, 1931.

153 Johnson, A. W. In *Chemie Organique du Phosphore*; Colloques Internationaux du Centre de la Recherche Scientifique: Paris; 1969; pp. 229–234.

154 McEwen, W. E.; Smalley, A. W.; Sullivan, C. E. *Phosphorus,* **1972**, *1*, 259.

155 Randall, F. J. *Diss. Abstr. Int.* **1970**, *31B*, 2577.

156 Johnson, A. Wm.; Jones, H. L. *J. Am. Chem. Soc.* **1968**, *90*, 5232.

157 Bestmann, H. J.; Kratzer, O.; Simon, H. *Chem. Ber.* **1962**, *95*, 2750.

158 Schweizer, E. E.; Schaffer, E. T.; Hughes, C. T.; Berninger, C. J. *J. Org. Chem.* **1966**, *31*, 2907.

159 Wittig, G.; Schollkopf, U. *Chem. Ber.* **1954**, *87*, 1318.

160 Harrison, I. T.; Lythgoe, B. *J. Chem. Soc.* **1958**, 843.

161 Howe, R. K. *J. Am. Chem. Soc.* **1971**, *93*, 3457.

162 Hug, R.; Hansen, H. J.; Schmid, H. *Helv. Chim. Acta* **1972**, *55*, 1828.

163 Naf, F; Decorzant, R.; Thommen, W.; Willhalm, B.; Ohloff, G. *Helv. Chim. Acta* **1975**, *58*, 1016.

164 Kim, S.; Kim, Y. C. *Tetrahedron Lett.* **1990**, *31*, 2901.

165 Vedejs, E.; Bershas, J. P.; Fuchs, P. L. *J. Org. Chem.* **1973**, *38*, 3625.

166 Shen, Y.; Wang, T. *Tetrahedron Lett.* **1991**, *32*, 4353.

167 Corey, E. J.; Erickson, B. W. *J. Org. Chem.* **1974**, *39*, 82.

168 Bestmann, H. J.; Schulz, H. *Liebigs Ann. Chem.* **1964**, *674*, 11.

169 Capuano, L.; Triesch, T.; Willmes, A. *Chem. Ber.* **1983**, *116*, 3767.

170 Shen, Y.; Wang, T. *Tetrahedron Lett.* **1990**, *31*, 3161.

171 Hatanaka, M.; Himeda, Y.; Ueda, I. *J. Chem. Soc. Chem. Commun.* **1990**, 526.

172 Issleib, K.; Lischewski, M. *J. Prakt. Chim.* **1969**, *311*, 857.

173 Kim, S.; Kim, Y. C. *Synlett.* **1990**, 115.

174 Shen, Y.; Wang, T. *Tetrahedron Lett.* **1990**, *31*, 543.

175 Minami, T.; Nakayama, M.; Nakamura, T.; Okada, Y. *Chem. Lett.* **1989**, 1741.

176 Axelrod, E.; Milne, G. M.; Van Tamelen, E. E. *J. Am. Chem. Soc.* **1970**, *92*, 2139.

177 Zbiral, E. *Montash. Chem.* **1967**, *98*, 916.

178 Bestmann, H. J.; Rothe, O. *Angew. Chem.* **1964**, *76*, 569.

179 Dauben, W. G.; Kozikowski, A. P. *Tetrahedron Lett.* **1973**, 3711.

180 Hatanaka, M.; Yamamoto, Y.; Ishimaru, T. *J. Chem. Soc. Chem. Commun.* **1984**, 1705.

181 Buchi, G.; Wuest, H. *Helv. Chim. Acta* **1971**, *54*, 1767.

182 Dauben, W. G.; Hart, D. J.; Ipaktschi, J.; Kozikowski, A. P. *Tetrahedron Lett.* **1973**, 4425.

183 Dauben, W. G.; Ipaktschi, J. *J. Am. Chem. Soc.* **1973**, *95*, 5088.

184 Schmidbaur, H.; Tronich, W. *Chem. Ber.* **1968**, *101*, 3556.

185 Cramer, R. E.; Bruck, M. A.; Gilje, J. W. *Organometallics* **1986**, *5*, 1496.

186 Cristau, H. J.; Ribeill, Y.; Plenat, F.; Chiche, L. *Phosphorus Sulfur* **1987**, *30*, 135.

187 Cristau, H. J.; Ribeill, Y.; Chiche, L.; Plenat, F. *J. Organomet. Chem.* **1988**, *352*, C47.

188 Mikolajczyk, M.; Perlikowska, W.; Omelanczuk, J.; Cristau, H. J.; Perraud-Darcy, A. *Synlett.* **1991**, 913.

[189] Cristau, H. J.; Ribeill, Y. *J. Organomet. Chem.* **1988**, *352*, C51.

[190] McKenna, E. G.; Walker, B. J. *Tetrahedron Lett.* **1988**, *29*, 485.

[191] Schlosser, M.; Kadibelbon, T.; Steinhoff, G. *Angew. Chem.* **1966**, *5*, 968.

[192] McDowell, R. S.; Streitweiser, A. *J. Am. Chem. Soc.* **1984**, *106*, 4947.

[193] Corey, E. J.; Kang, J.; Kyler, K. *Tetrahedron Lett.* **1985**, *26*, 555.

[194] Schaub, B.; Jenny, T.; Schlosser, M. *Tetrahedron Lett.* **1984**, 4097.

[195] Schaub, B.; Schlosser, M. *Tetrahedron Lett.* **1985**, 1623.

[196] Bestmann, H. J.; Schmidt, M. *Angew. Chem.* **1987**, *26*, 79.

[197] Bestmann, H. J.; Schmidt, M. *Tetrahedron Lett.* **1987**, 2111.

[198] Ramirez, F.; Desai, N. B.; Hansen, B.; McKelvie, N. *J. Am. Chem. Soc.* **1961**, *83*, 3539.

[199] Ramirez, F.; Pilot, J. F.; Desai, N. B.; Smith, C. P.; Hansen, B.; McKelvie, N. *J. Am. Chem. Soc.* **1967**, *89*, 6273.

[200] Appel, R.; Knoll, F.; Scholer, H.; Wihler, H. D. *Angew. Chem.* **1976**, *15*, 701.

[201] Schmidbaur, H.; Gasser, O.; Hussain, M. S. *Chem. Ber.* **1977**, *110*, 3501.

[202] Fluck, E.; Neumuller, B.; Braun, R.; Heckmunn, G.; Simon, A.; Borrmann, H. *Z. Anorg. Allg. Chem.* **1988**, *567*, 23.

[203] Hardy, G. E.; Baldwin, J. C.; Zink, J. I.; Kaska, W. C.; Liu, P. H.; DuBois, L. *J. Am. Chem. Soc.* **1977**, *99*, 3552.

[204] Zink, J. I.; Kaska, W. C. *J. Am. Chem. Soc.* **1973**, *95*, 7510.

[205] Vincent, A. T.; Wheatley, P. J. *J. Chem. Soc. Dalton Trans.* **1972**, 617.

[206] Hardy, G. E.; Zink, J. H.; Kaska, W. C.; Baldwin, J. C. *J. Am. Chem. Soc.* **1978**, *100*, 8001.

[207] Ebsworth, E. A. V.; Fraser, T. E.; Rankin, D. W. H.; Gasser, O.; Schmidbaur, H. *Chem. Ber.* **1977**, *110*, 3508.

[208] Schubert, U.; Kappenstein, C.; Malewski-Mahrla, B.; Schmidbaur, H. *Chem. Ber.* **1981**, *114*, 3070.

[209] Appel, R.; Baumeister, U.; Knoch, F. *Chem. Ber.* **1983**, *116*, 2275.

[210] Glidewell, C. *J. Organomet. Chem.* **1978**, *159*, 23.

[211] Albright, T. A.; Hoffmann, T.; Rossi, A. R. *Z. Naturforsch.* **1980**, *35B*, 343.

[212] Schmidbaur, H.; Costa, T.; Milewski-Mahrla, B.; Schubert, U. *Angew. Chem.* **1980**, *19*, 555.

[213] Schmidbaur, H.; Costa, T. *Chem. Ber.* **1981**, 114, 3063.

[214] Schmidbaur, H.; Costa, T.; Milewski-Mahrla, B. *Chem. Ber.* **1981**, *114*, 1428.

[215] Bowmaker, G. A.; Herr, R.; Schmidbaur, H. *Chem. Ber.* **1983**, *116*, 3567.

[216] Schmidbaur, H.; Herr, R.; Zybill, C. E. *Chem. Ber.* **1984**, *117*, 3374.

[217] Schmidbaur, H.; Pollok, T. *Chem. Ber.* **1987**, *120*, 1911.

[218] Appel, R.; Erbelding, G. *Tetrahedron Lett.* **1978**, 2689.

[219] Gasser, O.; Schmidbaur, H. *J. Am. Chem. Soc.* **1975**, *97*, 6281.

[220] Bestmann, H. J. *Pure Appl. Chem.* **1980**, *52*, 771.

[221] Birum, G. H.; Matthews, C. N. *J. Am. Chem. Soc.* **1966**, *88*, 4198.

[222] Hussain, M. S.; Schmidbaur, H. *Z. Naturforsch.* **1976**, *31B*, 721.

[223] Schmidbaur, H.; Gasser, O.; Kruger, C.; Sekutowski, J. C. *Chem. Ber.* **1977**, *110*, 3517.

[224] Birum, G. H.; Matthews, C. N. *Chem. Ind.* **1968**, 653.

[225] Matthews, C. N.; Birum, G. H. *Acc. Chem. Res.* **1969**, *2*, 373.

[226] Bestmann, H. J.; Kloerters, W. *Tetrahedron Lett.* **1977**, 79.

[227] Birum, G. H.; Matthews, C. N. *J. Org. Chem.* **1967**, *32*, 3554.

[228] Matthews, C. N.; Driscoll, J. S.; Harris, J. E.; Wineman, R. J. *J. Am. Chem. Soc.* **1962**, *84*, 4349.

[229] Driscoll, J. S.; Grisley, D. W.; Pustinger, J. V.; Harris, J. E.; Matthews, C. N. *J. Org. Chem.* **1964**, *29*, 2427.

[230] Cox, D. G.; Burton, D. J. *J. Org. Chem.* **1988**, *53*, 366.

[231] Driscoll, J. S.; Matthews, C. N. *Chem. Ind.* **1963**, 1282.

[232] Bestmann, H. J. *Angew. Chem.* **1977**, *16*, 349.

[233] Bestmann, H. J.; Saalfrank, R. W.; Snyder, J. P. *Angew. Chem.* **1969**, *8*, 216.

[234] Burzlaff, H.; Voll, U.; Bestmann, H. J. *Chem. Ber.* **1974**, *107*, 1949.

[235] Bestmann, H. J.; Saalfrank, R. W.; Snyder, J. P. *Chem. Ber.* **1973**, *106*, 2601.

[236] Saalfrank, R. W. *Tetrahedron Lett.* **1973**, 3985.

[237] Bestmann, H. J.; Saalfrank, R. W. *Chem. Ber.* **1976**, *109*, 403.

[238] Matthews, C. N.; Driscoll, J. S.; Birum, G. H. *J. Chem. Soc. Chem. Commun.* **1966**, 736.

[239] Bestmann, H. J.; Sandmeier, D. *Angew. Chem.* **1975**, *14*, 634.

[240] Bestmann, H. J.; Schmid, G. *Chem. Ber.* **1980**, *113*, 3369.

[241] Bestmann, H. J.; Schmid, G. *Tetrahedron Lett.* **1975**, 4025.

[242] Ratts, K. W.; Partos, R. D. *J. Am. Chem. Soc.* **1969**, *91*, 6112.

[243] Daly, J. J.; Wheatley, P. J. *J. Chem. Soc. (A)* **1966**, 1703.

[244] Daly, J. J. *J. Chem. Soc. (A)* **1967**, 1913.

[245] Burzlaff, H.; Wilhelm, E.; Bestmann, H. J. *Chem. Ber.* **1977**, *110*, 3168.

[246] Burzlaff, H.; Haag, R.; Wilhelm, E.; Bestmann, H. J. *Chem. Ber.* **1985**, *118*, 1720.

[247] Bestmann, H. J.; Schmid, G.; Sandmeier, D.; Kisielowski, L. *Angew. Chem.* **1977**, *16*, 268.

[248] Matthews, C. N.; Birum, G. H. *Tetrahedron Lett.* **1966**, 5707.

[249] Bestmann, H. J.; Schmid, G.; Sandmeier, D.; Schade, G.; Oechsner, H. *Chem. Ber.* **1985**, *118*, 1709.

[250] Bestmann, H. J. Schobert, R. *Synthesis* **1989**, 419.

[251] Birum, G. H.; Matthews, C. N. *J. Am. Chem. Soc.* **1968**, *90*, 3842.

[252] Browne, N. R.; Brown, R. F. C.; Eastwood, F. W.; Fallon, G. D. *Aust. J. Chem.* **1987**, *40*, 1675.

[253] Van Woerden, H. F.; Cerfontain, H.; Van Valkenburg, C. F. *Rec. Trav. Chim.* **1969**, *88*, 158.

[254] Bestmann, H. J.; Schmid, G. *Tetrahedron Lett.* **1981**, 1679.

[255] Bestmann, H. J.; Siegel, B.; Schmid, G. *Chem. Lett.* **1986**, 1529.

[256] Kniezo, L.; Kristian, P.; Imrich, J.; Ugozzoli, F.; Andreetti, G. D. *Tetrahedron* **1988**, *44*, 543.

[257] Soliman, F. M.; Khalil, K. M. *Phosphorus Sulfur* **1987**, *29*, 165.

[258] Wittig, G.; Eggers, H.; Duffner, P. *Liebigs Ann. Chem.* **1958**, *619*, 10.

[259] Bestmann, H. J.; Haberlein, H.; Kratzer, O. *Angew. Chem.* **1964**, *3*, 226.

[260] Booth B. L.; Smith, K. G. *J. Organomet. Chem.* **1981**, *220*, 229.

[261] Blomquist, A. T.; Hruby, V. J. *J. Am. Chem. Soc.* **1967**, *89*, 4996.

[262] Stang, P. J.; Arif, A. M.; Zhdankin, V. V. *Tetrahedron* **1991**, *47*, 4539.

[263] Ford, J. A.; Wilson, C. V. *J. Org. Chem.* **1961**, *26*, 1433.

[264] McDonald, R. N.; Campbell, T. W. *J. Am. Chem. Soc.* **1960**, *82*, 4669.

[265] Griffin, C. E.; Martin, K. R.; Douglas, B. E. *J. Org. Chem.* **1962**, *27*, 1627.

[266] Denney, D. B.; Song, J. *J. Org. Chem.* **1964**, *29*, 495.

[267] Hercouet, A.; Le Corre, M. *Tetrahedron Lett.* **1974**, 2491.

[268] Bestmann, H. J.; Haberlein, H.; Wagner, H.; Kratzer, O. *Chem. Ber.* **1966**, *99*, 2848.

[269] Nesmeyanov, N. A.; Reutov, E. A. *Dokl. Akad. Nauk SSSR* **1966**, *171*, 111.

[270] Schmidbaur, H.; Paschalidis, C.; Steigelmann, O.; Muller, G. *Angew. Chem.* **1989**, *28*, 1700.

[271] Bestmann, H. J.; Kisielowski, L. *Tetrahedron Lett.* **1990**, *31*, 3301.

[272] Schmidpeter, A.; Jochem, G. *Tetrahedron Lett.* **1992**, *33*, 471.

[273] Schmidbaur, H.; Deschler, U.; Gasser, B. Z.; Neugebauer, D.; Schubert, U. *Chem. Ber.* **1980**, *113*, 902.

[274] Schmidbaur, H.; Deschler, U. *Chem. Ber.* **1981**, *114*, 2491.

[275] Appel, R.; Haubrich, G.; Knoch, F. *Chem. Ber.* **1984**, *117*, 2063.

[276] Wimmer, T.; Steigelmann, T.; Muller, G.; Schmidbaur, H. *Chem. Ber.* **1989**, *122*, 2109.

[277] Davies, M.; Hughes, A. N . *J. Heterocycl. Chem.* **1972**, *9*, 1.

[278] Savage, M. P.; Trippett, S. *J. Chem. Soc. (C)* **1968**, 591.

[279] Weiss, J.; Nuber, B. *Z. Anorg. Allg. Chem.* **1981**, *473*, 101.

[280] Keller, H.; Maas, G.; Regitz, M. *Tetrahedron Lett.* **1986**, 1903.

[281] Svara, J.; Fluck, E.; Riffel, H. *Z. Naturforsch.* **1985**, *40B*, 1258.

[282] Veszpremi, T.; Gleiter, R.; Fluck, E.; Svara, J.; Neumuller, B. *Chem. Ber.* **1988**, *121*, 2071.

[283] Plass, W.; Heckmann, G.; Fluck, E. *Phosphorus Sulfur* **1991**, *55*, 19.

[284] Fluck, E.; Braun, R.; Muller, A.; Bogge, H. *Z. Anorg. Allg. Chem.* **1992**, *609*, 99.

[285] Markl, G. *Z. Naturforsch.* **1963**, *18B*, 84.

[286] Schmidbaur, H.; Scherm, H. P.; Schubert, U. *Chem. Ber.* **1978**, *111*, 764.

[287] Schmidbaur, H.; Mortl, A. *J. Organomet. Chem.* **1983**, *250*, 171.

[288] Davies, M.; Hughes, A. N.; Jafry, S. W. S. *Can. J. Chem.* **1972**, *50*, 3625.

[289] Shaw, M. A.; Tebby, J. C.; Ward, R. S.; Williams, D. H. *J. Chem. Soc.* **1970**, 504.

[290] Barluenga, J.; Lopez, F.; Palacios, F. *J. Chem. Soc. Chem. Commun.* **1986**, 1574.

[291] Markl, G. *Angew. Chem.* **1963**, *2*, 153.

[292] Karsch, H. H. *J. Chem. Soc. Chem. Commun.* **1990**, 1621.

[293] (a) Markl, G. *Angew. Chem,* **1966**, *4*, 1023. (b) Markl, G. *J. Heterocycl. Chem.* **1972**, *9*, S-69. (c) Dimroth, K. *Topics Current Chem.* **1973**, *38*, 1. (d) Markl, G. *Phosphorus Sulfur* **1977**, *3*, 77. (e) Dimroth, K. *Acc. Chem. Res.* **1982**, *15*, 58.

[294] Schafer, W.; Schwerg, A.; Dimroth, K.; Kanter, H. *J. Am. Chem. Soc.* **1976**, *98*, 4410.

[295] Oehling H.; Schweig, A. *Tetrahedron Lett.* **1970**, 4941.

[296] Bundgaard, T.; Jakobsen, H. J.; Dimroth, K.; Pohl, H. H. *Tetrahedron Lett.* **1974**, 3179.

[297] Ashe, A. J.; Smith, T. W. *J. Am. Chem. Soc.* **1976**, *98*, 7861.

[298] Dimroth, K.; Berger, S.; Kaletsch, H. *Phosphorus Sulfur* **1981**, *10*, 305.

[299] Knecht, J. *Z. Naturforsch.* **1984**, *39B*, 795.

[300] Bird, C. W. *Tetrahedron* **1990**, *46*, 5697.

[301] (a) Daly, J. J. *J. Chem. Soc. (A)* **1970**, 1832. (b) Thewalt, U. *Angew. Chem.* **1969**, *8*, 769. (c) Thewalt, U.; Bugg, C. E. *Acta Crystallog.* **1972**, *28B*, 871. (d) Debaerdemaeker, T. *Cryst. Str. Commun.* **1979**, *8*, 309.

[302] Markl, G. *Angew. Chem.* **1963**, *2*, 479.

[303] Kieselack, P.; Dimroth, K. *Angew. Chem.* **1974**, *13*, 148.

[304] Markl, G.; Merz, A. *Tetrahedron Lett.* **1969**, 1231.

[305] Dimroth, K.; Stade, W. *Angew. Chem.* **1968**, *7*, 881.

[306] Kanter, H.; Dimroth, K. *Angew. Chem.* **1972**, *11*, 1090.

[307] Kanter, H.; Mach, W.; Dimroth, K. *Chem. Ber.* **1977**, *110*, 397.

[308] Markl, G.; Lieb, F.; Merz, A. *Angew. Chem.* **1967**, *6*, 87.

[309] Markl, G.; Baier, H.; Liebl, R. *Liebigs Ann. Chem.* **1981**, 919.

[310] Markl, G.; Hock, K.; Matthes, D. *Chem. Ber.* **1983**, *116*, 445.

[311] Markl, G.; Merz, A. *Tetrahedron Lett.* **1971**, 1215.

[312] Dimroth, K.; Pohl, H. H.; Wichmann, K. H. *Chem. Ber.* **1979**, *112*, 1272.

[313] Markl, G.; Hock, K. *Tetrahedron Lett.* **1983**, *24*, 2645.

[314] Markl, G.; Hock, K. *Tetrahedron Lett.* **1983**, *24*, 5051.

[315] Dimroth, K.; Luckoff, M.; Kaletsch, H. *Phosphorus Sulfur* **1981**, *3*, 285.

[316] Dimroth, K.; Berger, S.; Kaletsch, H. *Phosphorus Sulfur* **1981**, *10*, 295.

[317] Debaerdemaeker, T. *Acta Crystallog. (B)* **1979**, *35*, 1686.

[318] Dimroth, K.; Kaletsch, H. *Angew. Chem.* **1981**, *20*, 871; *Chem. Ber.* **1987**, *120*, 1249.

[319] Jongsma, C.; Freijee, F. J. M.; Bickelhaupt, F. *Tetrahedron Lett.* **1976**, 481.

[320] Facklam, T.; Wagner, O.; Heydt, H.; Regitz, M. *Angew. Chem.* **1990**, *29*, 314.

[321] Markl, G. *Z. Naturforsch.* **1963**, *18B*, 1136.

[322] Schmidbaur, H.; Paschalidis, C.; Steigelmann, O.; Muller, G. *Angew. Chem.* **1990**, *29*, 516.

[323] Dewar, M. J. S. *Angew. Chem.* **1971**, *10*, 761.

[324] Fluck, E.; Neumuller, B.; Heckmann, G.; Plass, W.; Jones, P. G. *New. J. Chem.* **1989**, *13*, 383.

[325] Fluck, E.; Becker, G.; Neumuller, B.; Knebl. R.; Heckmann, G.; Riffel, H. *Angew. Chem.* **1986**, *25*, 1002; *Z. Naturforsch.* **1987**, *42B*, 1213.

[326] Fluck, E.; Heckmann, G.; Plass, W.; Spahn, M.; Borrmann, H. *J. Chem. Soc. Perkin Trans. (1)* **1990**, 1223.

[327] Plass, W.; Heckmann, G.; Fluck, E. *Phosphorus Sulfur* **1990**, *54*, 181.

[328] Yoshida, Z.; Yoneda, S.; Hashimoto, H.; Murata, Y. *Tetrahedron Lett.* **1971**, 1527.

[329] Rigby, C. W.; Lord, E.; Hall, C. D. *J. Chem. Soc. Chem. Commun.* **1967**, 714.

330 Depoorter, H.; Nys, J.; Van Doermael, A. *Bull. Soc. Chim. Belg.* **1964**, *73*, 921.

331 Lloyd, D.; Singer, M. I. C. *Chem. Ind.* **1971**, 786.

332 Hall, C. D.; Parkins, A. W.; Nyburg, S. C. *Phosphorus Sulfur* **1991**, *63*, 231.

333 Cashman, D.; Lalor, F. J. *J. Organomet. Chem.* **1970**, *24*, C29.

334 Hall, C. D.; Speers, P.; Valero, R.; Pla, F. P.; Denney, D. B. *Phosphorus Sulfur* **1990**, *49/50*, 143; *J. Chem. Soc. Perkin Trans. (2)* **1991**, 1925; **1992**, 425.

335 Lloyd, D. *Non-Benzenoid Carbocyclic Compounds*; Elsevier: Amsterdam, 1984; pp. 32–42.

336 Smolii, O. B. *J. Gen. Chem.* **1988**, *58*, 2345.

337 Moore, A. J.; Bryce, M. R. *Synthesis* **1991**, 26.

338 Brovarets, V. S.; Smolii, O. B.; Vdovenko, S. I.; Drach, B. S. *J. Gen. Chem.* **1990**, *60*, 494.

339 Crofts, P. C.; Williamson, M. P. *J. Chem. Soc. (C)* **1967**, 1093.

340 Johnson, A. Wm.; LaCount, R. B. *Chem. Ind.* **1959**, 52.

341 Fletcher, T. L.; Namkung, M. J.; Dice, J. R.; Schaefer, S. K. *J. Med. Chem.* **1965**, *8*, 347.

342 Longone, D. T.; Alexander, E. S. *Tetrahedron Lett.* **1968**, 5815.

343 Battiste, M. A.; Sprouse, C. T. *Tetrahedron Lett.* **1969**, 3165, 3893.

344 Krivum, S. V.; Semenov, N. S.; Baranov, S. N.; Dulenko, V. I. *J. Gen. Chem.* **1970**, *40*, 1885.

345 Shen, Y.; Lin, Y.; Xin, Y. *Tetrahedron Lett.* **1985**, *26*, 5137.

346 Jones, G. H.; Moffatt, J. G. *J. Am. Chem. Soc.* **1968**, *90*, 5337.

347 Issleib, K.; Linder, R. *Liebigs Ann. Chem.* **1967**, *707*, 112.

348 Bykhovskaya, O. V.; Aladsheva, I. M.; Petrovski, P. V.; Matryukova, T. A.; Kabachnik, M. I. *Proceedings of International Conference on Phosphorus Chemistry,* Bonn; 1986, B-11.

349 Bykhovskaya, O. V. *Phosphorus Sulfur* **1990**, *51/52*, 262.

350 Gosselck, J.; Schenk, H.; Ahlbrecht, H. *Angew, Chem* **1967**, *6*, 249.

351 Denney, D. B.; Gross, F. J. *J. Org. Chem.* **1967**, *32*, 2445.

352 Bestmann, H. J.; Kratzer, O. *Chem. Ber.* **1962**, *95*, 1894.

353 Schmidbaur, H.; Scherm, H. P. *Chem. Ber. 1977*, *110*, 1576.

354 Campbell, I. G. M.; Cookson, R. C.; Hocking, M. B.; Hughes, A. N. *J. Chem. Soc.* **1965**, 2184.

355 Schmidbaur, H.; Blaschke, G.; Kohler, F. H. *Z. Naturforsch.* **1977**, *32B*, 757.

356 Schmidbaur, H.; Wolf, W. *Chem. Ber.* **1975**, *108*, 2851.

357 Wittig, G.; Weigmann, H. D.; Schlosser, M. *Chem. Ber.* **1961**, *94*, 676.

358 Oediger, H.; Eiter, K. *Liebigs Ann. Chem.* **1965**, *682*, 58.

359 Schmidbaur, H.; Pichl, R.; Muller, G. *Chem. Ber.* **1987**, *120*, 789.

360 Kolodiazhnyi, O. I. *Z. Chem.* **1989**, *29*, 396; *Russ. Chem. Revs.* **1991**, *60*, 391.

361 Kolodiazhnyi, O. I. *Tetrahedron Lett.* **1980**, *21*, 3983.

362 Kolodiazhnyi, O. I. *Phosphorus Sulfur* **1990**, *49/50*, 239.

363 Kolodiazhnyi, O. I. Golokhov, D. B. *J. Gen. Chem.* **1991**, *61*, 627.

364 Kolodiazhnyi, O. I. *J. Gen. Chem.* **1986**, *56*, 246.

[365] Kolodiazhnyi, O. I. *Tetrahedron Lett.* **1981**, *22*, 1231.

[366] Kolodiazhnyi, O. I. *Tetrahedron Lett.* **1987**, *28*, 881.

[367] Svara, J.; Fluck, E. *Phosphorus Sulfur* **1985**, *25*, 129.

[368] Fluck, E.; Braun, R. *Phosphorus Sulfur* **1988**, *40*, 83.

[369] Kolodiazhnyi, O. I.; Ustenko, S. N. *J. Gen. Chem.* **1990**, *60*, 2143; **1991**, *61*, 464.

[370] von Locquenghien, K. H.; Bacieredo, A.; Roese, R.; Bertrand, G. *J. Am. Chem. Soc.* **1991**, *113*, 5062.

[371] Mastryukova, T. A.; Aladzheva, I. M.; Leonteva, I. V.; Petrovski, P. V.; Fedin, E. I.; Kabachnik, M. I. *Pure Appl. Chem.* **1980**, *52*, 945.

[372] Kolodiazhnyi, O. I. *Tetrahedron Lett.* **1980**, 2269.

[373] Mastryukova, T. A.; Aladzheva, I. M.; Bykhovskaya, O. V.; Petrovski, P. V.; Antipin, M. Y.; Struchkov, Y. T.; Kabachnik, M. I. *Proc. Acad. Sci. USSR* **1982**, *264*, 182.

[374] Kolodiazhnyi, O. I. *J. Gen. Chem.* **1976**, *46*, 2285.

[375] Koster, R.; Simic, D.; Grassberger, M. A. *Liebigs Ann. Chem.* **1970**, *739*, 211.

[376] Mondon, A. *Liebigs Ann. Chem.* **1957**, *603*, 115.

[377] Maryanoff, B. E.; Reitz, A. B.; Duhl-Emswiler, B. A. *J. Am. Chem. Soc.* **1985**, *107*, 217.

[378] Kitihara, T.; Horiguchi, A.; Mari, K. *Tetrahedron* **1988**, *44*, 4713.

[379] Maercker, A. *Angew. Chem.* **1967**, *6*, 557.

[380] Minami, T.; Shikita, S.; Nakayama, M.; Yamamoto, I. *J. Org. Chem.* **1985**, *53*, 2937.

[381] Bestmann, H. J. *Angew. Chem.* **1960**, *72*, 34.

[382] Griffin, C. E.; Witschard, G. *J. Org. Chem.* **1964**, *29*, 1001.

[383] Bissing, D. E. *J. Org. Chem.* **1965**, *30*, 1296.

[384] Wasserman, H. H.; Kelly, T. A. *Tetrahedron Lett.* **1989**, *30*, 7117.

[385] House, H. O.; Babad, H. *J. Org. Chem.* **1963**, *28*, 90.

[386] Bremmer, M. L.; Khatri, N. A.; Weinreb, S. M. *J. Org. Chem.* **1983**, *48*, 3661.

[387] Danishefsky, S. J.; Cabal, M. P.; Chow, K. *J. Am. Chem. Soc.* **1989**, *111*, 3456.

[388] Ding, W.; Zhang, P.; Cao, W. *Tetrahedron Lett.* **1987**, *28*, 81.

[389] Evans, D. A.; Kaldor, S. W.; Jones, T. K.; Clardy, J.; Stout, T. J. *J. Am. Chem. Soc.* **1990**, *112*, 7001.

[390] Pauson, P. L.; Watts, W. E. *J. Chem. Soc.* **1963**, 2990.

[391] Oda, R.; Kawabata, T.; Tanimoto, S. *Tetrahedron Lett.* **1964**, 1653.

[392] Zinner, G.; Fehlhammer, W. P. *Angew. Chem.* **1985**, *24*, 979.

[393] Cristau, H. J.; Gasc, M. B. *Tetrahedron Lett.* **1990**, *31*, 341.

[394] Miyano, S.; Izumi, Y.; Fujii, K.; Ohno, Y.; Hashimoto, H. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 1197.

[395] Seyferth, D.; Heeren, J. K.; Singh, G.; Grim, S. O.; Hughes, W. B. *J. Organomet. Chem.* **1966**, *5*, 267.

[396] Stork, G.; Zhao, K. *Tetrahedron Lett.* **1989**, *30*, 2173.

[397] Schlosser, M.; Zimmerman, M. *Synthesis* **1969**, *1*, 75.

[398] Burton, D. J.; Greenlimb, P. E. *J. Org. Chem.* **1975**, *40*, 2796.

[399] Wittig, G.; Schlosser, M. *Chem. Ber.* **1961**, *94*, 1373.

400 Hellmann, H.; Bader, J. *Tetrahedron Lett.* **1961**, 724.

401 Schlessinger, R. H.; Poss, M. A.; Richardson, S.; Lin, P. *Tetrahedron Lett.* **1985**, *26*, 2391.

402 Abell, A. D.; Trent, J. O.; Whittington, B. I. *J. Org. Chem.* **1989**, *54*, 2763.

403 Bestmann, H. J.; Kranz, E. *Angew. Chem.* **1967**, *6*, 81.

404 Nagao, Y.; Shima, K.; Sakurai, H. *Tetrahedron Lett.* **1970**, 2221.

405 Horner, L.; Oediger, H. *Chem. Ber.* **1958**, *91*, 437.

406 Labuschagne, A. J. H.; Schneider, D. F. *Tetrahedron Lett.* **1983**, *24*, 743.

407 Burton, D. J.; Greenwald, J. R. *Tetrahedron Lett.* **1967**, 1535.

408 Maercker, A.; Theyson, W. *Liebigs Ann. Chem.* **1972**, *759*, 132.

409 Bestmann, H. J.; Schulz, H. *Tetrahedron Lett.* **1960**, 5.

410 Markl, G. *Tetrahedron Lett.* **1962**, 1027.

411 Chopard, P. A.; Searle, R. J. G.; Devitt, F. H. *J. Org. Chem.* **1965**, *30*, 1015.

412 Trippett, S.; Walker, D. M. *J. Chem. Soc.* **1961**, 1266.

413 Kobayashi, Y.; Yamashita, T.; Takahashi, K.; Kuroda, H.; Kumadaki, I. *Tetrahedron Lett.* **1982**, *23*, 343.

414 Denney, D. B.; Ross, S. T. *J. Org. Chem.* **1962**, *27*, 998.

415 Martin, D.; Niclas, H. J. *Chem. Ber.* **1967**, *100*, 187.

416 Zbiral, E.; Werner, E. *Monatsh. Chem.* **1966**, *97*, 1797.

417 Trippett, S.; Walker, D. M. *J. Chem. Soc.* **1959**, 3874.

418 Wittig, G.; Boll, W. *Chem. Ber.* **1962**, *95*, 2526.

419 Seebach, D. *Chem. Ber.* **1972**, *105*, 487.

420 Seebach, D.; Peleties, N. *Chem. Ber.* **1972**, *105*, 511.

421 Markl, G. *Z. Naturforsch.* **1962**, *17B*, 782.

422 Huang, Y. Z.; Shen, Y. C.; Ding, W.; Zheng, J. *Tetrahedron Lett.* **1981**, *22*, 5283.

423 Speziale, A. J.; Ratts, K. W. *J. Am. Chem. Soc.* **1962**, *84*, 854.

424 Burton, G.; Elder, J. S.; Fell, S. C. M.; Stachulski, A. V. *Tetrahedron Lett.* **1988**, *29*, 3003.

425 Lakhrissi, M.; Chapleur, Y. *Synlett.* **1991**, 583.

426 Olah, G. A.; Wu, A. H.; *Synthesis* **1990**, 885.

427 Bessard, Y.; Muller, U.; Schlosser, M. *Tetrahedron* **1990**, *46*, 5213.

428 Burton, D. J.; Krutzsch, H. C. *Tetrahedron Lett.* **1968**, 71.

429 Zinner, G. *J. Organomet. Chem.* **1989**, *368*, 23.

430 Wittig, G.; Weigmann, H. D.; Schlosser, M. *Chem. Ber.* **1961**, *94*, 676.

431 Denney, D. B.; Vill, J. J.; Boskin, M. J. *J. Am. Chem. Soc.* **1962**, *84*, 3944.

432 Schmidbaur, H.; Schnatterer, S. *Chem. Ber.* **1983**, *116*, 1947.

# 4

# PREPARATION OF PHOSPHONIUM YLIDES

In this chapter are described the various methods available for the preparation of phosphonium ylides. The most general method, the preparation of a phosphonium salt and then removal of an α-proton with base to form the ylide, is described in detail in Section 4.1. In succeeding sections are described more specialized methods, including nucleophilic addition to vinylphosphonium salts (Section 4.2), reaction of phosphines with carbenes (Section 4.3.1), addition of phosphines to alkenes and alkynes (Section 4.3.2), and several miscellaneous methods.

In addition to these direct methods, many phosphonium ylides of complex structure are best prepared from simpler ylides by their reaction with electrophiles. For example disubstituted ylides can often be prepared from monosubstituted ylides. This approach involves several reactions which are described in Chapter 6. Readers should refer to that chapter for halogenation (Section 6.2) as a route to α-haloylides, alkylation (Section 6.4) as a route to dialkyl ylides, and acylation (Section 6.5) as a route to acyl ylides. These are powerful alternatives to the direct synthesis of disubstituted ylides described in this chapter.

## 4.1 YLIDES FROM PHOSPHONIUM SALTS

The "salt method" for the formation of ylides involves two distinct steps, the formation of the phosphonium salt and the deprotonation of the latter to form the ylide (Eq. 4.1). These are discussed separately in the first two subsections, each of which identifies essential limitations and cautions. The third subsection

---

*Ylides and Imines of Phosphorus*, Edited by A. William Johnson.
ISBN 0-471-52217-1

$$R_3P + R^1R^2CHX \longrightarrow R_3\overset{+}{P}\text{-}CHR^1R^2 \quad X^- \xrightarrow{-H^+} R_3P{=}CR^1R^2 \qquad (4.1)$$

describes some specialized aspects of the salt method, including “salt-free” ylides, instant ylides, α-haloylides, and ylides from polyhalogen compounds.

### 4.1.1 Preparation of Phosphonium Salts

Trialkyl- or triarylphosphines react with alkyl halides in typical $S_N2$ quaternization reactions to form phosphonium halides which serve as precursors for phosphonium ylides. The usual order of halide reactivity is I > Br > Cl, typical of many substitution reactions. On occasion other leaving groups have been employed, such as the trimethylammonium group,[1,2] but the use of exotic alkylating reagents, such as the oxonium salts, seldom has been necessary because tertiary phosphines are reasonably good nucleophiles.

A wide variety of solvents have been employed in phosphonium salt synthesis (e.g., benzene, ether, acetone, acetonitrile, chloroform, dimethylformamide, and nitromethane), with the choice often determined by the desirability of having the phosphonium salt simply precipitate directly from the solution. The reaction conditions usually are very mild, but with some higher halides heat may be required. Maccarone et al.[3] determined that solvent electrophilicity, polarity, and polarizability all were important, but in that order in the formation of phosphonium salts.

Tertiary phosphines are much better nucleophiles than are similarly substituted amines. Since most ylide chemistry is designed to produce a phosphorus-free substance as the final product, the nature of the phosphine employed to form an ylide is virtually unlimited. However, the phosphine of choice for most ylides is triphenylphosphine for several reasons: (1) it is crystalline and safe to handle; (2) it is readily available at an economic price; (3) it is of the right nucleophilicity for quaternization; (4) it has no hydrogen atoms adjacent to the phosphorus that would compete in the deprotonation step; and (5) it is stable to air oxidation. Although trialkylphosphines also are effective, they are often liquids and less safe to handle, they pose the risk of competitive deprotonation at the α-position, and they have to be protected from ambient oxidation. In spite of this problem trialkylphosphines, and especially tri-*n*-butylphosphine, which is commercially available, occasionally are useful because they are more nucleophilic than the triarylphosphines, facilitating phosphonium salt formation, and the ylides obtained from them are also more nucleophilic.[4] Further, subsequent decomposition reactions, such as hydrolysis, may dictate a preference for having alkyl rather than phenyl groups on phosphorus (see Section 5.1).

The availability of triphenylphosphine and tri-*n*-butylphosphine suffices for most ylide reactions. For some specialized studies mixed aryl-alkylphosphines,[5] such as $(Me)_n(Ph)_{3-n}P$, and substituted triarylphosphines,[4] such as $(XC_6H_4)_3P$, have been useful and are readily converted into phosphonium salts. Optically active phosphines have been used to form optically active phosphonium salts and ylides.[6,7] The inability to quaternize a phosphonium salt seldom has been a major problem in phosphonium ylide chemistry, in contrast to ylides of other heteroatoms.

Michaelis and Gimborn[8] prepared the first ylide from triphenylcarbomethoxymethylphosphonium chloride, which had been prepared from methyl α-chloroacetate and triphenylphosphine. A wide variety of alkyl halides have been used since to quaternize triphenylphosphine to phosphonium salts, too many to attempt an exhaustive list, but a number of relatively ordinary examples is provided with exemplary citations: methyl iodide;[9] *n*-butyl bromide;[10] chloromethyl ether;[11] chloromethylthioethers;[12] phenacyl bromide;[13,14] chloroacetamides;[15] imidoyl chlorides;[16] benzylic bromides;[17] 9-bromofluorene;[18] cyclopropyl bromide;[19] and cyclohexyl bromide.[20] Substituents known on the α-carbon of phosphonium salts ($R{-}CH_2{-}PPh_3^+\ X^-$) include R = alkyl, aryl, alkoxyl, thioalkyl, carboalkoxyl, carbamido, keto, formyl, cyano, halo, alkenyl, alkynyl, and silyl. Formation of phosphonium salts and ylides from α-nitroalkyl halides generally is unsuccessful because of side reactions.[21,22] Tables 3.7 and 3.8 contain lists of exemplary ylides, often obtained by proton removal from phosphonium salts.

Triphenylphosphine reacts with dihalides to form mono- and/or bis-phosphonium salts. 1,2-Dibromoethane has been converted to the monophosphonium salt[17] and to the diphosphonium salt,[17,23] and it also has been cyclized in reaction with *cis*-1,2-diphosphoniodiphosphinoethene.[24] 1,2-Dibromobenzocyclobutene was converted to the bis-phosphonium salt.[25] 1,3-Dibromides[17,21,26] and 1,4-dibromides[17,27] also have afforded both mono- and diphosphonium salts. Di(bromomethyl)benzenes also afforded mono- and/or diphosphonium salts.[17]

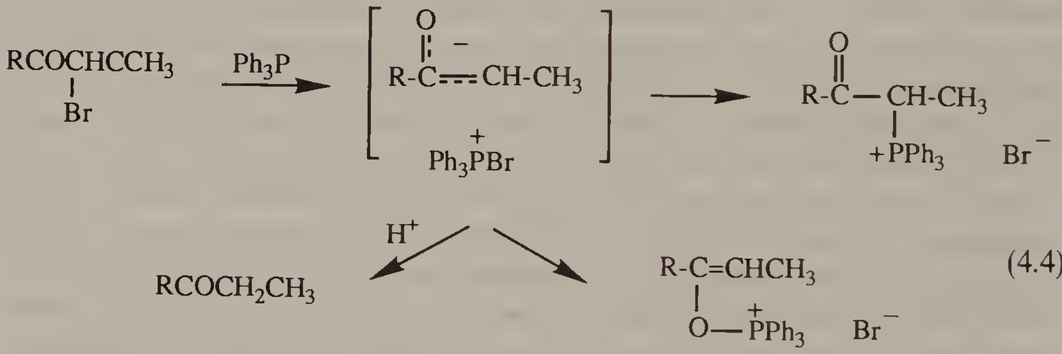
There have been many examples of the formation of phosphonium salts, and subsequently ylides, from allylic halides. From allyl chloride itself,[28] to 1,4-dibromo-2-butene[29] and farnesyl bromide,[30] the reactions proceeded well. In some instances, allylic displacements have occurred however. Although crotyl bromide was quaternized normally on the primary carbon,[31] 2-bromo-1-methylenecyclohexane underwent allylic quaternization to afford cyclohexenylmethyltriphenylphosphonium bromide[32] (Eq. 4.2).

(4.2)

Occasionally triphenylphosphine causes the elimination of HX from an alkyl halide, rather than effecting a substitution. Such was the case with 2-iodobutane[33] and with *β*-ionyl bromide,[34] but in the latter case triphenylphosphine added back to the triene to form the expected phosphonium salt! More recently Ullmann and Hannack[35] reported that 1,1,1-trifluoro-2-bromopropane afforded in good yield a rearranged phosphonium salt, probably resulting from the initial elimination of HBr followed by addition of triphenylphosphine (Eq. 4.3).

$$\underset{\text{Br}}{CF_3CHCH_3} \xrightarrow{Ph_3P} CF_3CH_2CH_2\overset{+}{P}Ph_3 \quad Br^- \qquad (4.3)$$

Reaction of triphenylphosphine with α-bromoketones to form α-triphenylphosphonioketones as precursors to acyl ylides is not always reliable. Whereas normal alkylation of the phosphine occurred in many cases, especially those involving α-bromoacetophenone-like substrates,[36–39] in others the starting ketone was debrominated,[39–41] and in some cases they appear to have been dehydrobrominated to alkenes to which triphenylphosphine added to produce an isomer of the sought-after phosphonium salt.[42] It has been proposed that triphenylphosphine initially attacked bromide to form an enolate ion pair which collapsed (a) to an enolphosphonium salt by O-attack, (b) to the sought-after phosphonium salt by C-attack, or (c) to debrominated ketone by protonation[43, 44] (Eq. 4.4). Aprotic solvents do favor phosphonium salt formation[43] and enolphosphonium salts are known.[40] Similar debromination of an α-sulfonyl compound has been reported.[45] Fukui et al.[46] found that the presence of triethylamine led to excellent yields of C-alkylation product, perhaps by temporary addition of amine to the carbonyl group, thereby preventing enolate formation.



(4.4)

## 4.1.2 Deprotonation of Phosphonium Salts

The conversion of a phosphonium salt to a phosphonium ylide involves the removal of an α-proton from the carbon destined to become the "ylidic" carbon (Eq. 4.5). The use of a triphenylphosphonium salt removes ambiguity about

$$RR'CH\text{-}\overset{+}{P}Ph_3 \quad X^- \xrightarrow{\text{Base:}} RR'C{=}PPh_3 + BH^+ + X^- \qquad (4.5)$$

which proton was removed. The reactions are conducted in a solvent using a base of the appropriate strength, with carbon, nitrogen, and oxygen bases commonly used. The solvents range widely in polarity from hexane, benzene, and ethers to dimethylformamide, nitromethane, and liquid ammonia. The solvent must be inert to reaction with the base and the ylide, thus usually eliminating chloroform, water, alcohols, and acetone, but some of these may be used with the more acidic phosphonium salts. Often a slurry of the phosphonium salt is treated with the base at low temperatures, with the slurry disappearing as the salt is converted into the ylide which invariably is colored, soluble, and ready for subsequent reaction. Two-phase systems have been employed for ylide formation preparatory to a Wittig reaction (see Section 8.1.5.1).

The base chosen to effect the proton removal is determined by the basicity needed and by the nature of the byproducts which can be tolerated by the ylide. The strength of the base required depends on the acidity of the phosphonium salt, which in turn depends on the nature of the phosphonium group and the nature of the carbon substituents (see Chapter 3). The strength of bases used ranges from organolithiums for the preparation of alkylides, to sodium methoxide for the preparation of the stabilized carbomethoxymethylides, to ammonia for the highly stabilized fluorenylides. The process of transylidation also may be used, taking advantage of the strongly basic character of triphenylphosphoniummethylide to remove a proton from a more acidic phosphonium salt (see Section 3.3 for a full discussion of this phenomenon).

It is essential that the selected base either not react with other functional groups in an ylide, or at least not irreversibly change them. For example, phenyllithium cannot be used with a carbomethoxyphosphonium salt because of competing reaction at the carbonyl group, but sodium methoxide is effective, and the use of two equivalents of sodium hydride or *n*-butyllithium is effective with $\omega$-carboxyalkylphosphonium salts. Table 4.1 lists the variety of bases and solvents reported, including examples of the types of ylides for which they have been used and a listing of exemplary references. The choice of base determines which counterions are present in solutions of ylides, unless the ylides are stable enough to be capable of isolation and separation from contaminants. It is well known that certain salts affect the Wittig and other reactions, and since many ylide reactions are performed in the same solution in which they were prepared, the choice of base may be determined by that limitation. In Section 4.1.3.1 is discussed the preparation of "salt-free" solutions of ylides, and the means of avoiding the presence of lithium cations, an especially complexing cation. There are a few complications and side reactions to the deprotonation of phosphonium salts to form ylides and these are discussed in the following three subsections.

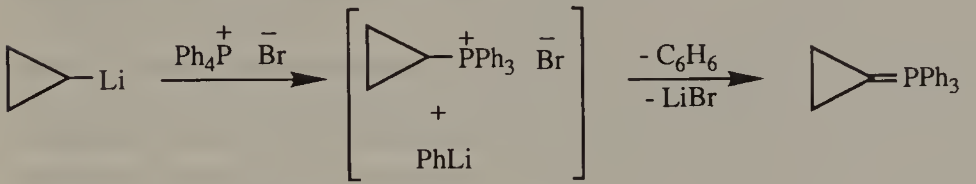
***4.1.2.1 Ligand Exchange.*** In 1962 Seyferth et al.[80] found that treatment of methyltriphenylphosphonium bromide with methyllithium afforded the expected methylene ylide, as demonstrated by trapping it with cyclophexanone in a Wittig reaction, but concluded that the ylide formation was not totally via $\alpha$-proton abstraction because a 21% yield of benzene also was obtained. Subsequent work[89] showed that about 30% of the reaction involved attack by methyllithium at *phosphorus* and 70% involved attack at the *$\alpha$-proton*. Reaction of tetraphenylphosphonium bromide with methyllithium afforded methylenetriphenylphosphorane, and subsequent experiments proved that the methyl car-

**TABLE 4.1 Bases for Converting Phosphonium Salts into Ylides ($RCH{=}PPh_3$)**

| Base | Reference | Solvent (s)[a] | Ylide Type (R group) |
|---|---|---|---|
| $Na_2CO_3$ | 13, 47, 48, 39 | Water | Ester, phenyl |
| $K_2CO_3$ | 49, 50 | Water, toluene | Acyl, vinyl |
| NaOH | 51, 52 | Water | Ester |
| LiOH | 53 | $CH_2Cl_2$ | Thiophenyl |
| KOH | 8, 54 | Water | Ester, phenyl |
| NaH | 55 | DMSO/THF | Alkylide |
| $NH_3$ | 18 | Ethanol | Fluorenylide |
| $N(C_2H_5)_3$ | 51, 56–58 | $CH_2Cl_2$, ethanol | Acyl, ester |
| Pyridine | 51, 57 | $CH_2Cl_2$, $CH_3NO_2$ | Ester, acyl |
| $NaOCH_3$ | 59, 69 | Methanol | Phenyl |
| $NaOC_2H_5$ | 38, 60, 61 | Ethanol | Phenyl, benzoyl |
| $NaOC(CH_3)_3$ | 62, 63 | Benzene, DMF | Phenyl, acyl |
| $NaOCH(CH_3)C_2H_5$ | 64 | Ether/benzene/THF | Alkyl |
| $NaOC(CH_3)_2C_2H_5$ | 65 | Benzene | Methyl |
| $KOC(CH_3)_3$ | 66–68 | THF | Alkyl, aryl |
| LiOMe | 69 | Methanol | Phenyl |
| LiOEt | 70 | Ethanol | Aryl |
| $NaNH_2$ | 21, 60, 71 | Ammonia, benzene | Alkyl, phenyl |
| $LiN(C_2H_5)_2$ | 72 | Toluene | Phenyl |
| Li piperidide | 21, 73 | Ether | Alkyl |
| $NaN(Si(CH_3)_3)_2$ | 74–76 | THF | Phenyl, alkyl |
| KHMDS | 77, 78 | THF | Alkyl |
| Li-1,3-diaminopropane | 79 | THF or HMPT | Alkyl |
| $LiCH_3$ | 80 | THF | Alkyl |
| $LiC_2H_5$ | 81 | THF | Alkyl |
| $Li\text{-}C_4H_9(n)$ | 9, 82 | Ether, ligroin | Alkyl |
| $Li\text{-}C_4H_9(t)$ | 83, 83a | THF | Alkyl |
| $LiC_6H_5$ | 30 | THF | Alkyl |
| $NaC(C_6H_5)_3$ | 82 | Ether | Alkyl, phenyl |
| $Na_2C_2$ | 84 | DMF | Alkyl |
| $NaCH_2SOCH_3$ | 85 | DMSO | Alkyl |
| Na metal | 86 | Ether | Phenyl |
| $Ph_3P{=}CH_2$ | 87, 88 | Toluene, ether | Phenyl, alkyl<br>Benzoyl |

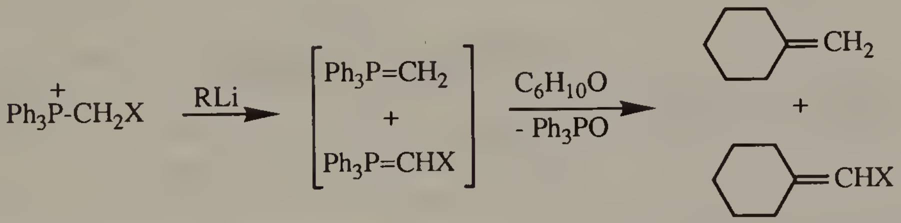
[a] DMF = dimethylformamide; DMSO = dimethylsulfoxide; THF = tetrahydrofuran; HMPT = hexamethylphosphorus triamide.

banion was attacking *phosphorus* to produce a pentavalent intermediate which collapsed to form phenyl anion and methyltriphenylphosphonium bromide, the overall result being an exchange of the ligands on phosphorus. Proton removal from the latter produced benzene and methylenetriphenylphosphorane, which converted cyclohexanone to methylenecyclohexane in 58% yield. A similar exchange of tetraphenylphosphonium bromide with ethyllithium and butyllithium was observed.[89] Also, *t*-butyltriphenylphosphonium bromide exchanged with methyl- or, ethyllithium to produce a methylide or ethylide, respectively.[81] Later, Schlosser et al.[90] observed exchange of *n*-butyllithium with pentaphenylphosphorus to form *n*-buytylidenetriphenylphosphorane, and Pilling and Sondheimer[91] observed traces of ligand exchange in the reaction of *n*-butyllithium with chloromethyltriphenylphosphonium chloride. Longone and Doyle[92] applied the exchange reaction as a synthetic route to cyclopropylidenetriphenylphosphorane by reaction of cyclopropyllithium with tetraphenylphosphonium bromide (Eq. 4.6). While *n*-butyllithium exchanged with methoxymethyltriphenylphosphonium chloride, *t*-butyllithium did not.[83a]



(4.6)

***4.1.2.2 α-H versus α-Halogen Attack.*** Two groups noted that reaction of organolithium reagents with mono-halomethyltriphenylphosphonium salts, and trapping of the resultant ylide(s) in a Wittig reaction with cyclohexanone, afforded a mixture of methylenecyclohexane and halomethylenecyclohexane, indicating that both a *methylide* and a *halomethylide* had been formed (Eq. 4.7).



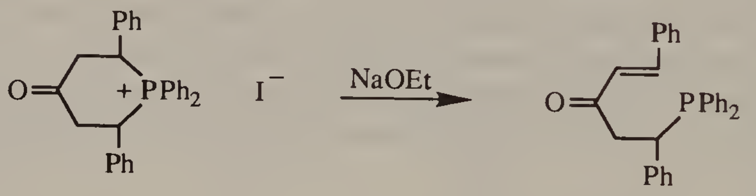
(4.7)

In other words, the base had attacked both the α-proton and the α-halogen. Seyferth et al.[93] showed that with phenyllithium the chlorophosphonium salt (X = Cl) underwent only proton removal, but that the bromo salt (X = Br) underwent attack at bromine as effectively as at hydrogen. The iodomethyl salt (X = I) resulted in a 3:1 ratio of attack at iodine compared to attack at hydrogen.

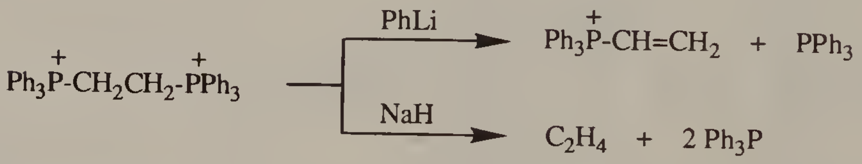
Kobrich et al.[73,94] observed similar results, determining that attack at bromine was more likely than at chlorine, but also that halogen attack was more likely using bases in the order butyllithium > phenyllithium > lithium piperidide. With butyllithium and the bromomethyl salt they obtained only attack at bromine, but with lithium piperidide they were able to exclude bromine attack completely. Smithers[95] later used this knowledge in the preparation of nonterminal vinyl bromides, otherwise obtainable only with difficulty. Readily accessible dibromomethylenetriphenylphosphorane was alkylated with an alkyl bromide and the resultant phosphonium bromide was debrominated with butyllithium to afford the mono-bromo ylide which was reacted with aldehydes to produce the desired products (Eq. 4.8). Recently Stork and Zhao found that using NaHMDS led to mainly proton attack on the iodomethyl salt.[78]

$$Ph_3P{=}CBr_2 \xrightarrow{RBr} Ph_3\overset{+}{P}\text{-}CRBr_2\ \ Br^- \xrightarrow[R'CHO]{BuLi} R'CH{=}CRBr \qquad (4.8)$$

*4.1.2.3* ***Competing Eliminations and Rearrangements.*** Since the phosphonium group can be an effective leaving group in an $E_2$ reaction it is not surprising that elimination reactions have been observed in attempted ylide formation reactions. Burger[96] obtained 1-triphenylphosphonio-1,3-butadiene and triphenylphosphine upon treatment of 1,4-bis(triphenylphosphonio)-2-butene with phenyllithium. Upon attempted ylide formation with sodium ethoxide, a cyclic $\beta$-ketophosphonium salt underwent elimination instead (Eq. 4.9).[97] $\beta$-Bromoethyltriphenylphosphonium bromide and $\beta$-triphenylphosphonioethyltriphenylphosphonium bromide underwent initial elimination of hydrogen bromide and triphenylphosphine, respectively, when treated with phenyllithium (Eq. 4.10).[98] The resulting vinyltriphenylphosphonium bromide reacted with additional phenyllithium to form a new ylide (see Section 4.2). The bis-phosphonium salt also underwent an elimination and displacement reaction when treated with sodium hydride.[99]

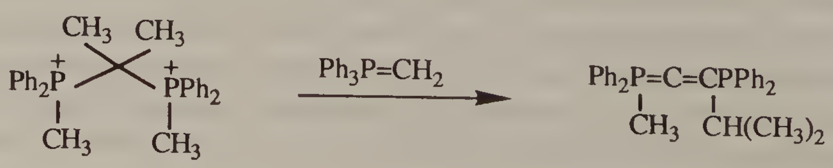


(4.9)

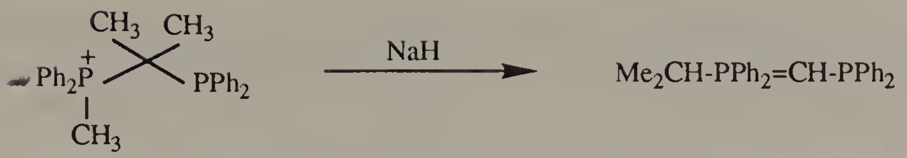


(4.10)

Rearrangements are rare in phosphonium ylide chemistry. A bis-phosphonium salt, when treated with methylenetriphenylphosphorane as the base, produced a carbodiphosphorane, probably via initial methylide formation and attack of that methylide at the other phosphorus atom (Eq. 4.11).[88] The monophosphonium salt afforded a rearranged monoylide when treated with



$$Ph_2\overset{+}{P}(CH_3)\text{-}C(CH_3)_2\text{-}\overset{+}{P}Ph_2(CH_3) \xrightarrow{Ph_3P=CH_2} \underset{CH_3}{Ph_2P}{=}C{=}\underset{CH(CH_3)_2}{CPPh_2} \qquad (4.11)$$



(4.12)

sodium hydride (Eq. 4.12). The highly sterically hindered methyltrimesitylphosphonium salt was deprotonated by sodium amide at an *ortho*-methyl group, rather than at the phosphonium methyl group, and afforded a rearranged phosphine. A dimesityl salt also rearranged but a di-*o*-tolylphosphonium salt was deprotonated normally to afford ylide.[100]

### 4.1.3 Special Cases

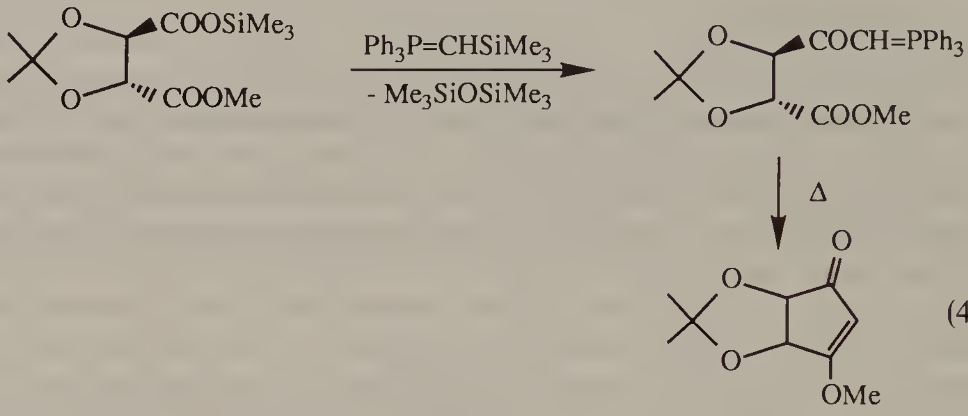
***4.1.3.1 "Salt-Free" Ylides.*** In the 1950's most ylides were prepared using organolithium reagents as the base, producing lithium halides as a byproduct, but it soon became known that lithium salts complexed with phosphonium ylides, and in the 1960s it was concluded that complexation also occurred in the course of the Wittig reaction. To avoid resulting complications both in syntheses and mechanism studies several methods were developed to produce so-called "salt-free" ylide solutions. Most of these were not free of salts, but were free of lithium cations and of a considerable portion of the salts. Albright and Schweizer[101] have shown that NMR spectroscopy distinguished "salt-free" ylides ($^{31}P \sim 2.0$ ppm; $J_{P-C} \sim 90$–$100$ Hz) from phosphonium salts or phosphonium ylides complexed with lithium, both of which exhibit similar spectra ($^{31}P \sim 22$ ppm; $J_{P-C} \sim 50$–$65$ Hz).

Bestmann and Arnason[102] prepared sodium amide in liquid ammonia and then added the phosphonium bromide. Subsequent addition of benzene, evaporation of the ammonia, and filtration of the insoluble NaBr under vacuum produced an approximately lithium-free solution of ylide. Later Koster et al.[103] modified this method to use the better solvent, tetrahydrofuran (THF), and others[104] employed it extensively to prepare and isolate nonstabilized ylides. Schmidbaur et al.[105] also employed sodium hydride in THF and filtration of the NaBr produced "salt-free" solutions which enabled the isolation of reactive ylides. More recently[74, 76] sodium hexamethyldisilazide [NaHMDS $= NaN(SiMe_3)_2$] has become a useful base in benzene, THF, hexane, or HMPT solvents, enabling the filtration of the sodium bromide and production of a salt-free solution of ylide. Schlosser et al.[106] described the preparation of an "instant ylide" which was lithium-free. Powdered sodium amide coated with paraffin was mixed with powdered phosphonium salt to form a storable dry mix which, upon addition of ether or THF, afforded a solution of ylide that could be used for various reactions in high yields.

The first nonstabilized ylides actually free of all salts were prepared by Schmidbaur and Tronich.[107] For example, trimethylsilylmethyl chloride and trimethylphosphine afforded a phosphonium salt which could be converted to trimethylsilylmethylide. Reaction of the silylated ylide with methanol or with trimethylsilanol resulted in a silicon exchange reaction to produce the corresponding silyl ether and methylenetrimethylphosphorane, which were separable by distillation (Eq. 4.13). Earlier Miller,[108] and later Schmidbaur and

$$Me_3SiCH_2Cl \xrightarrow[-\,HCl]{Me_3P} Me_3SiCH{=}PMe_3 \xrightarrow[-\,ROSiMe_3]{ROH} Me_3P{=}CH_2 \qquad (4.13)$$

Tronich,[109] described several routes to the silyl methylide. Bestmann and Moenius[110] recently used a similar silicon exchange reaction in a unique and selective manner to prepare a substituted ylide which led to a key synthetic intermediate precursor to hydroxylated cyclopentenones (Eq. 4.14).



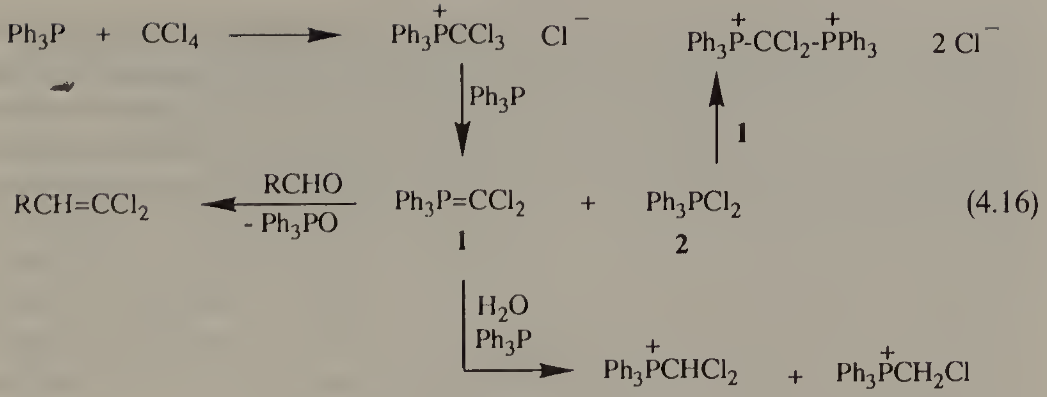
(4.14)

Finally, Vedejs et al.[111, 112] introduced a novel method to produce lithium-free phosphoniummethylides. Reaction of a tertiary phosphine with trimethylsilylmethyl triflate afforded a silylated methyltriphenylphosphonium salt. Simultaneous desilylation and ylide formation was effected cleanly by anhydrous cesium fluoride (Eq. 4.15). The method is not yet applicable to other than methylides.

$$Me_3SiCH_2OTf \xrightarrow{Ph_3P} Ph_3\overset{+}{P}CH_2SiMe_3 \xrightarrow[-\,Me_3SiF]{CsF} Ph_3P{=}CH_2 \qquad (4.15)$$

***4.1.3.2 α-Halo- and α,α-Dihaloylides.*** The preparation of α-halo- and α,α-dihaloylides, especially the methylides, has posed a special challenge but also has been possible through unusual routes. The difluoro-, dichloro-, and dibromomethylides are known, and the monofluoro-, monochloro-, monobromo-, and monoiodomethylides are known. One standard approach to the α-haloylides has been to halogenate methylenetriphenylphosphorane or a substituted derivative thereof, and this method is discussed in Chapter 6.2. For the dihalomethylides a potentially simpler route is the reaction of triphenylphosphine with carbon tetrahalides, and while reaction of these reagents can be quite complex,[113] it has become quite useful.

Reaction of triphenylphosphine with carbon tetrachloride can be summarized by Eq. 4.16, with the specific outcomes dependent on the relative amount of



(4.16)

triphenylphosphine used and the presence or absence of small amounts of water.[113] The initial adduct, trichloromethyltriphenylphosphonium chloride, has been isolated[114] and the dichloro- and monochloro salts have been obtained by addition of controlled amounts of water. Rabinowitz and Marcus[115] were the first to find that heating triphenylphosphine in carbon tetrachloride produced a solution of dichloromethylide (**1**), along with dichlorotriphenylphosphorane (**2**), and were able to trap the former in a Wittig reaction with benzaldehyde to form dichlorostyrene. Benzal chloride was a byproduct from the reaction of benzaldehyde with **2**, also present in the solution. Burton and Greenwald[116] extended the reaction to methyl trichloroacetate and obtained the expected α-chlorocinnamate from benzaldehyde, and to trichloroacetonitrile to obtain α-chlorocinnamonitrile. These reactions have been accounted for on the basis of phosphine attack on chlorine followed by formation of an ylide intermediate. Others[117–119] have claimed that a similar reaction, but using tris(dimethylamino)phosphine instead of triphenylphosphine, did *not* involve an ylide intermediate, but instead involved addition of trichloromethide anion to the aldehyde, followed by phosphine-catalyzed dehydrohalogenation and expulsion of triphenylphosphine oxide. The dichloro ylide (**1**) prepared by the $Ph_3P/CCl_4$ reaction has been used since for the preparation of a wide variety of dichlorovinyl systems.[120–123] A recent example reported using the dichlorophosphorane (**2**) present in the reaction mixture to first convert a carboxylic acid to an acid chloride which then acylated the ylide (**1**).[124] The ylide (**1**) could also be prepared from bromotrichloromethane, demonstrating that phosphine attack on bromine probably was involved,[115, 122] and acetonitrile solvent provided especially good results.

Ramirez et al.[125] reported the same overall reaction with carbon tetrabromide to afford $Ph_3P{=}CBr_2$, which could be trapped with benzaldehyde in a Wittig reaction in excellent yield. This method has been applied frequently,[126] recently by Olah and Wu[127] to convert 2-adamantanone to 2-dibromomethyleneadamantane, and earlier by Smithers[95] in an alkylation reaction.

The ylide $Ph_3P{=}CF_2$ was more difficult to obtain. Although initially reported in 1962[115] improved access became possible by Burton's method,[128] which was improved recently by Schlosser et al.,[129] involving the reaction of dibromodifluoromethane with triphenylphosphine. A solution of the ylide probably resulted,[130] but in the absence of an immediately available reactant, the ylide dissociated into difluorocarbene which could be trapped by alkenes.[128,129] In the presence of benzaldehyde a Wittig reaction occurred[131] to afford difluorostyrene, and in the presence of a more nucleophilic phosphine, such as tris(dimethylamino)phosphine, a new ylide was obtained,[130] probably by trapping of difluorocarbene.

The use of methylene bromide in reaction with triphenylphosphine led to di(triphenylphosphonio)methane instead of an ylide,[132] reflecting attack of phosphorus at carbon rather than at bromine as with $CBr_4$, and the use of bromoform led to dibromomethyltriphenylphosphonium bromide,[133] neither reaction being similar to the tetrahalomethane reactions.

All of the monohalomethylides are known. Chloromethylenetriphenylphosphorane ($Ph_3P{=}CHCl$) has been prepared from the chloromethylphosphonium salt using phenyllithium[134,135] or butyllithium.[93] Reaction of triphenylphosphine and iodochloromethane afforded the same salt, which was converted to ylide using potassium *t*-butoxide.[136]

Bromomethylenetriphenylphosphorane ($Ph_3P{=}CHBr$) has been prepared from the bromomethylphosphonium salt using phenyllithium,[92,93] but considerable debromination also occurred. The weaker base lithium piperidide converted the salt into the desired ylide.[93] The organomercury route to be described in Section 4.3 of this chapter seems better.

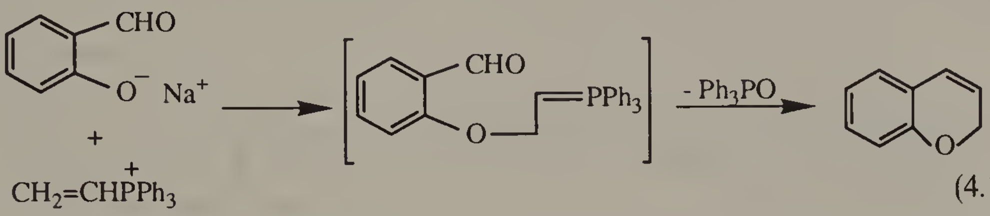
Iodomethylenetriphenylphosphorane ($Ph_3P{=}CHI$) has been prepared effectively from the iodomethylphosphonium salt only recently and using NaHMDS.[78,137] Seyferth et al.[93] earlier had reported that the iodomethyl salt underwent both deprotonation and deiodination with phenyllithium.

Fluoromethylenetriphenylphosphorane ($Ph_3P{=}CHF$) was first prepared by Schlosser and Zimmerman[138] by fluorinating methylenetriphenylphosphorane with $FClO_3$, and treating the resulting salt with phenyllithium. A somewhat safer, but lower yielding method, for preparing the fluoromethyl salt involved reacting triphenylphosphine with iodofluoromethane.[139] The ylide formation occurred in modest yields but was not without complications. A recent application of the same approach led to formation of the α-fluoro-α-carbethoxymethylide, probably by attack of phosphine on bromine (Eq. 4.17).[140] The preparation of *C*-fluoroylides has been reviewed.[141]

$$Ph_3P + FBrCHCOOEt \xrightarrow[2.\ BuLi]{1.\ CH_2Cl_2} Ph_3P{=}CFCOOEt \qquad (4.17)$$

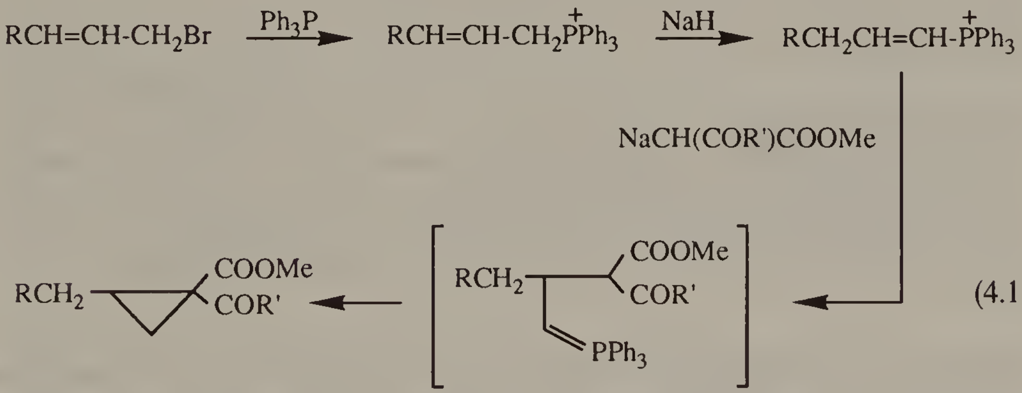
## 4.2 YLIDES FROM VINYLPHOSPHONIUM SALTS

Although the addition of nucleophiles to vinyltriphenylphosphonium salts had been known for some time, in 1964 two groups realized that the resulting ylides could be used to do subsequent chemistry. Seyferth et al.[96,142] found that phenyllithium would add to the vinylphosphonium salt and the intermediate ylide could be trapped, but generally in low yields, with ketones in a Wittig reaction. Recently it has been found that the use of dialkyllithium cuprates in place of alkyllithiums in the addition is much more effective.[143] Also in 1964 Schweizer[144, 145] effected the addition of the anion of salicylaldehyde to vinyltriphenylphosphonium bromide and obtained a 62% yield of chromene, resulting from initial oxyanion addition to form an ylide which then underwent an intramolecular Wittig reaction (Eq. 4.18).



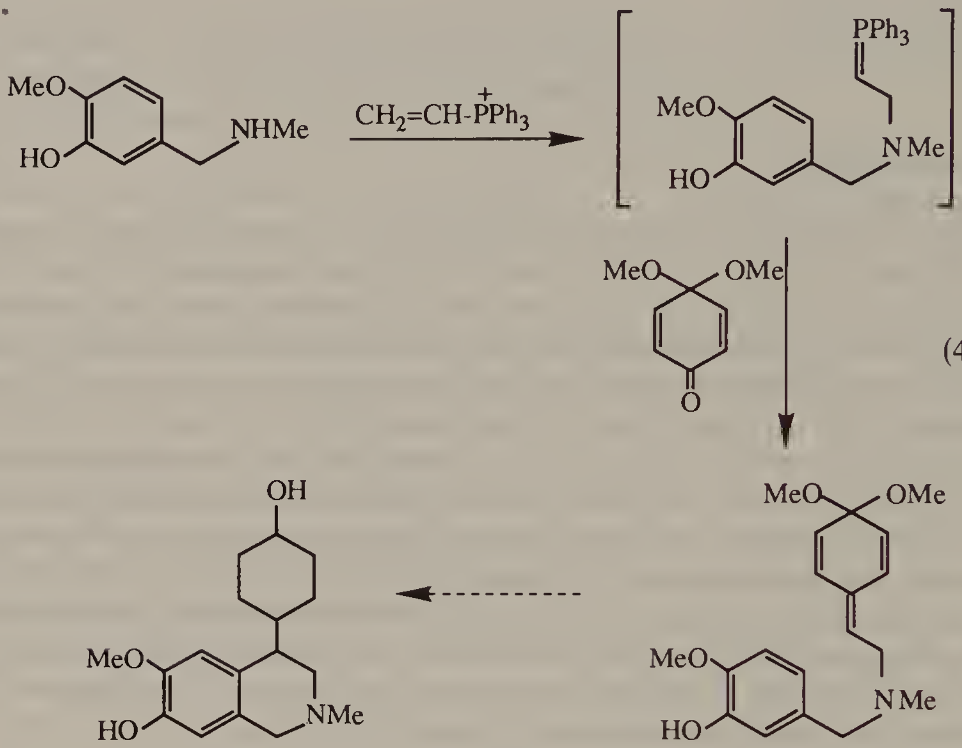
(4.18)

The potential scope of this type of reaction has increased markedly recently by the more ready availability of substituted vinylphosphonium salts. Hinkle et al.[146, 147] found that vinyltriflates, readily available from the reaction of alkynes with triflic acid, reacted with triphenylphosphine to afford good yields of the vinyltriphenylphosphonium salts essentially stereospecifically. Earlier Ohmari et al.[148] found that triphenylphosphine would add to alkenes in moderate yield under constant current electrolysis conditions, again producing alkenylphosphonium salts. Another approach to the vinyl salts is to prepare the more easily accessible allylic salts and effect an isomerization with base, as reported by Nesmeyanov et al.[149] using triethylamine, and by Jacoby et al.[150] using sodium hydride (Eq. 4.19). In the latter case the resulting ylide participated in a cyclization, with the overall process being similar to that reported earlier by McIntosh and Khalil.[151] Earlier Keough and Grayson[152] had reported that propenyl salts would not undergo nucleophilic addition.

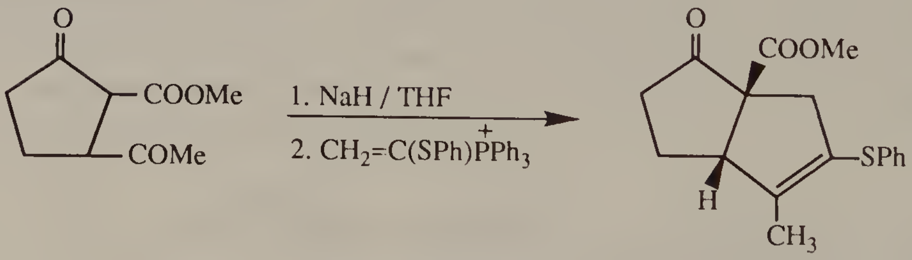


(4.19)

There have been many unique applications of the vinylphosphonium addition route to ylides, involving addition of a variety of nucleophiles: nitrogen, carbon, and oxygen. Zbiral[153] reviewed such additions resulting in the formation of heterocycles, many of which involved ylide formation followed by Wittig cyclization reactions. Minami and Yamamoto[154] recently reviewed the addition of nucleophiles to 1-cycloalkenyl phosphonium salts and subsequent Wittig reactions. Meyers et al.[155, 156] prepared a series of allyl amines by addition of amines followed by Wittig reaction of the resulting ylides. Hart et al.[157] used the same reaction in a key step enabling the coupling of the two major fragments necessary for the total synthesis of the isoquinoline alkaloid cherylline (Eq. 4.20). There are numerous examples of the addition of enolate anions,[158, 159] with that forming a highly functionalized (3,3,0)bicyclooctenone in 97% yield being especially attractive (Eq. 4.21).[160] Three groups[161–163] effected enolate additions to the terminal end of dienylidenephosphonium salts, leading eventually to 3 + 3 cyclizations, while others have added alkyllithium cuprates.[164] Minami et al.[165, 166] effected alkoxide and active methylene additions to cyclobutenyltriphenylphosphonium salts. Recently, White and Jensen[163] added enolates to a trienylidene phosphonium salt with the two original double bonds retaining their E configuration.



(4.20)



(4.21)

## 4.3 OTHER METHODS

### 4.3.1 Ylides from Carbenes

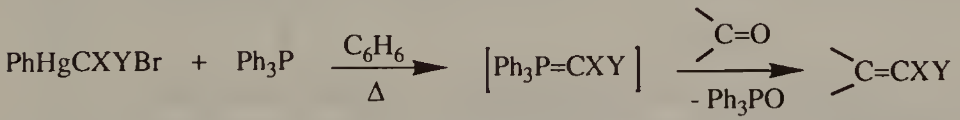
If an ylide could be formed by direct coupling of two chemical species, they would be a phosphine and a carbene. This reaction is known, is of some interest, but is only of modest synthetic usefulness. Nearly all of the applications known involve the preparation of variously substituted halomethyl- or dihalomethyl ylides. Padwa and Hornbuckle[167] recently reviewed the formation of ylides from carbenes but excluded phosphonium ylides from consideration.

Reaction of chloroform with potassium *t*-butoxide in the presence of triphenylphosphine afforded dichloromethylenetriphenylphosphorane, as evidenced by its being trapped in a Wittig reaction with benzophenone.[168] The reaction was proposed to occur by proton extraction from chloroform, loss of a chloride ion, and direct coupling of the resulting carbene ($:CCl_2$) with triphenylphosphine. In a similar manner bromoform afforded $Ph_3P{=}CBr_2$ and fluorodichloromethane afforded $Ph_3P{=}CFCl$, but bromodichloromethane would not afford either $Ph_3P{=}CCl_2$ or $Ph_3P{=}CBrCl$.

At about the same time two groups found that methylene chloride could be dehydrohalogenated with organolithiums, perhaps to a carbene ($:CHCl$), which would couple with triphenylphosphine to form the ylide ($Ph_3P{=}CHCl$). The latter was trapped in a Wittig reaction but in modest to low yields.[134, 169]

A few years later a decarboxylative route to carbenes and ylides was discovered and provided access to the previously unknown $Ph_3P{=}CF_2$. Heating of sodium difluorochloroacetate in diglyme with triphenylphosphine and a carbonyl compound led to the evolution of carbon dioxide and the formation of triphenylphosphine oxide and a difluorovinyl compound.[170] Use of tri-*n*-butylphosphine and *N*-methylpyrrolidone as solvent resulted in much more reactive ylides,[171] but the yields remained modest. Using sodium fluorodichloroacetate the chlorofluoromethylide ($Ph_3P{=}CFCl$) was produced in modest yield, and in the absence of triphenylphosphine the carbene could be trapped with tetramethylethylene.[172]

The smoothest and most widely applicable route to phosphonium ylides through a carbene or carbene-type reaction is that involving organomercury compounds. Seyferth et al.[92] found that phenyldihalomercuric bromides, when refluxed in benzene solution in the presence of triphenylphosphine and a carbonyl compound, afforded good yields of halovinyl compounds (Eq. 4.22).

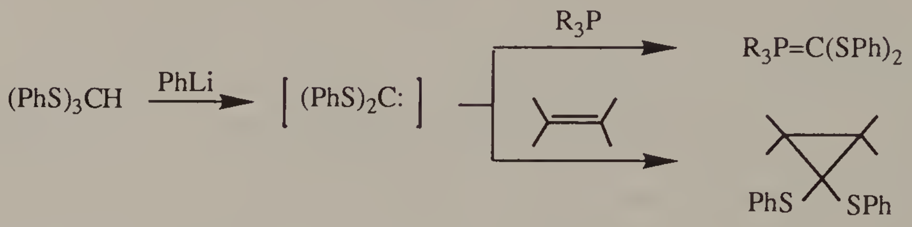


$$\mathrm{PhHgCXYBr} + \mathrm{Ph_3P} \xrightarrow[\Delta]{C_6H_6} \left[\mathrm{Ph_3P{=}CXY}\right] \xrightarrow[-\,\mathrm{Ph_3PO}]{>C{=}O} \;>C{=}CXY \qquad (4.22)$$

They prepared a variety of ylides, including X=Y=Br; X=H, Y=Br; X=H, Y=Cl; X=Y=Cl. This route to halomethylides is better than the reaction of phosphines with perhaloalkanes because there is no $Ph_3PCl_2$ present as a byproduct, and because the yields usually are at least as good.

Finally, two groups have reported the preparation of dithio- or diselenomethylides by routes probably involving carbenes. Lemal and Banitt[173] reacted a tosylhydrazone with sodium hydride in the presence of triphenylphosphine to produce an ylide which was trapped in a Wittig reaction (Eq. 4.23). In the

$$\mathrm{TsNHN{=}C(SEt)_2} \xrightarrow{\mathrm{NaH}} \left[\mathrm{:C(SEt)_2}\right] \xrightarrow{\mathrm{Ph_3P}} \mathrm{Ph_3P{=}C(SEt)_2} \qquad (4.23)$$

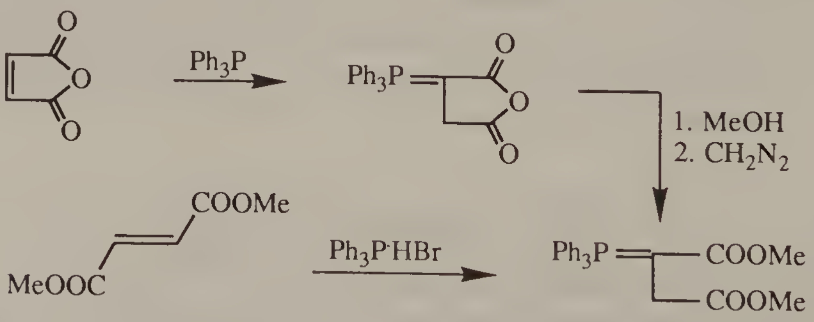


(4.24)

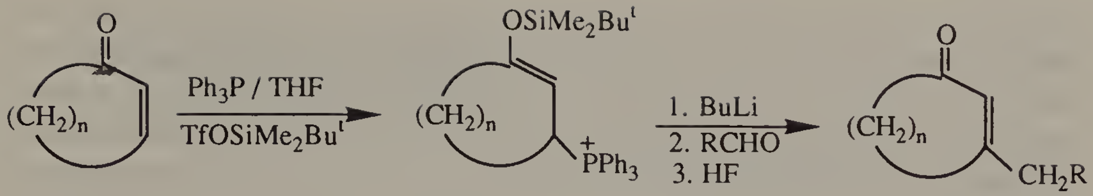
absence of the phosphine, a dimer of the carbene was produced, but the carbene could not be trapped by cyclohexene. However, Seebach[174] produced the similar di(phenylthio)carbene (Eq. 4.24), from which the triphenylphosphonium- and tri-*n*-butylphosphonium ylides could be isolated, and the carbene could be trapped with an alkene if phosphine was absent. Similarly, tri(phenylseleno)methane afforded the expected ylide, $\mathrm{Ph_3P{=}C(SePh)_2}$.[175]

### 4.3.2 Addition of Phosphines to Alkenes and Alkynes

*4.3.2.1* ***Ylides from Alkenes.*** Tertiary phosphines will effect a nucleophilic addition to an activated alkene, and the initially formed carbanion intermediate will undergo prototropy to afford an ylide, with the effectiveness of the process being a function of the presence of an ylide-stabilizing group. Reaction of triphenylphosphine with maleic anhydride[176–179] afforded a stable ylide, and the addition of triphenylphosphine hydrobromide to dimethylfumarate[180,181] and to many other similarly unsaturated compounds proceeded likewise (Eq. 4.25). Ramirez et al.[182] found that several phosphines added to dibenzoylethylene to afford stabilized ylides. Recently two groups have reported application of this addition reaction to effect substitution at the *β*-position of enones (Eq. 4.26)[183,184] but in these instances the intermediate adduct had to be



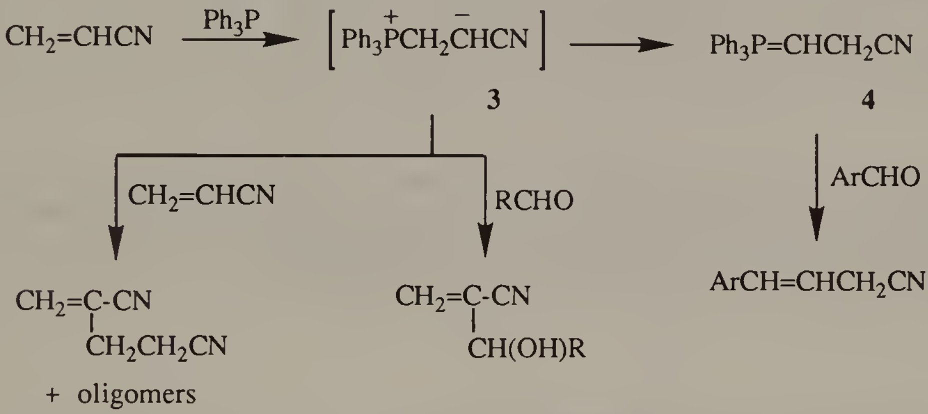
(4.25)



(4.26)

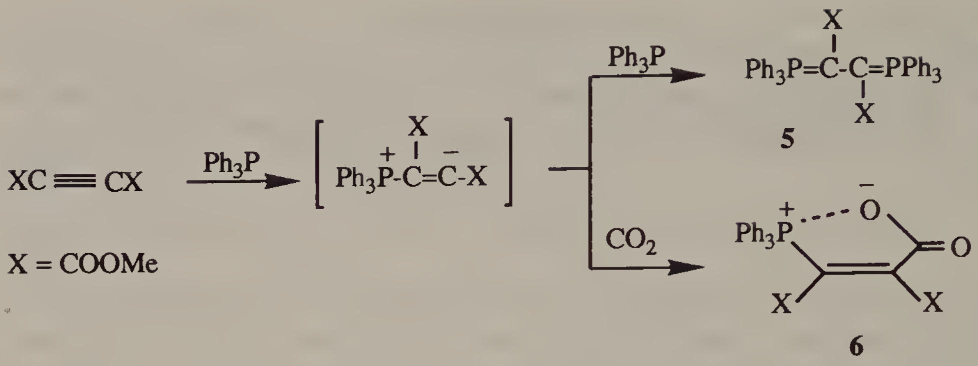
trapped as the enolate silylether because of the absence of a stabilizing group on the "ylidic" carbon. Ylides recently have been detected from the addition of phosphines to phosphaalkenes.[185]

Reaction of phosphines with acrylonitrile is not as straightforward as implied by the examples described above. Oda et al.[186] originally found that triphenylphosphine added to acrylonitrile in the presence of benzaldehyde to afford the product of a Wittig reaction involving the ylide (**4**). McClure[187] elaborated much better conditions for the reaction, demonstrating that a small amount of proton source, such as *t*-butyl alcohol or triethylsilanol, significantly assisted the essential proton transfer to form ylide (Eq. 4.27). Earlier it had been shown that triphenylphosphine would catalyze the hexamerization of acrylonitrile,[188] and later Baizer found that in acetonitrile solvent a dimer and/or higher oligomers of acrylonitrile resulted.[189] Here again the presence of an effective proton transfer agent such as triethylsilanol inhibited oligomer formation and favored ylide formation. The use of trialkylphosphines, and/or the addition of a small amount of triethylaluminum, resulted in the initially formed anion (**3**), adding to aldehyde and expelling triphenylphosphine to eventually afford a carbinol adduct.[190–193]



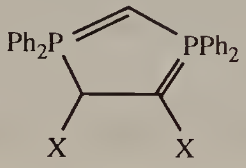
(4.27)

**4.3.2.2** ***Ylides From Alkynes.*** Although Hoffmann and Diehr[194] found that triphenylphosphine would add to activated alkynes in the presence of HBr, the products were alkenylphosphines, useful perhaps as substrates in nucleophilic addition to form ylides, but not as ylides themselves. Later, Shaw et al.[195] found that excess triphenylphosphine reacted with dimethyl acetylenedicarboxylate (DMAD) (Eq. 4.28) to afford a bis-ylide (**5**), and Caesar et al.[196] recently

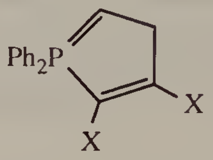


(4.28)

redetermined the structure of the $CO_2$ adduct (**6**) of the intermediate. A similar bis-ylide was obtained with dibenzoylacetylene,[197] and di (diphenylphosphino) methane with DMAD afforded the corresponding cyclic bis-ylide (**7**).[198] Use of diphenylvinylphosphine with DMAD resulted in an internal cyclization after the first addition of the phosphine to produce a cyclic ylide (**8**).[199]



**7**

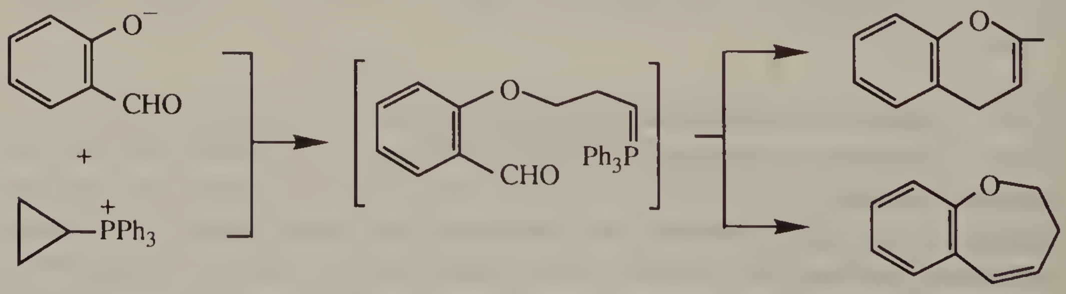


**8**

Reaction of triphenylphosphine with excess DMAD[200, 201] or with excess dicyanoacetylene[202] produced more complex structures, some of which were ylides and some of which appeared to be phosphacycles, but in any event such reactions are not effective means for ylide synthesis.

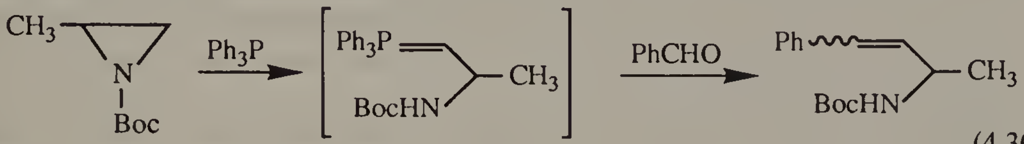
### 4.3.3 Miscellaneous Preparative Methods

***4.3.3.1 Ring Opening.*** Schweizer et al.[203] serendipitously noted that while cyclopropyltriphenylphosphonium bromide reacted at the α-proton or at phosphorus when treated with strong bases, reaction with the anion of salicylaldehyde led to ring opening followed by reaction of the resulting phosphonium ylide with the carbonyl group to form two oxacycles in a 60/40 ratio (Eq. 4.29).



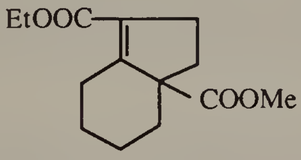
(4.29)

The obtaining of two ring systems indicated that the opening of the cyclopropane ring occurred in both possible directions, the first to produce an ylide directly, and the second to produce a β-carbanion which underwent a proton shift to form an α-methyl ylide. Cyclobutyltriphenylphosphonium salts would not undergo similar ring opening,[204] but aziridines would, with reaction of the resulting β-aminoylide with a carbonyl compound providing an entry to the allylamine system (Eq. 4.30).[205] Optically active aziridine produced an allylamine with 98% retention of activity and a 2:1 ratio of $E$:$Z$ isomers.

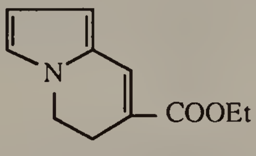


(4.30)

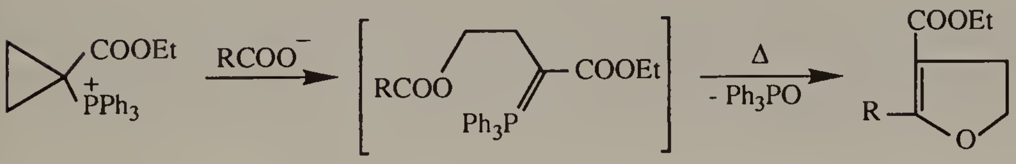
Three groups subsequently have utilized α-carbethoxycyclopropyltriphenylphosphonium salts, obtainable from the cyclopropyl ylide and ethyl chloroformate, as a more effective ylide precursor. Fuchs reported reactions of nitrogen, oxygen, and carbon nucleophiles with this substrate to produce ring systems, such as enolate addition of 2-carbomethoxycyclohexanone to afford **9** and addition of 2-pyrrolaldehyde to form **10**.[206] The thiolate anion[207] and even the carboxylate anion[208] have been added to the cyclopropane ring, and in the latter instance the intermediate ylide could be isolated (Eq. 4.31).



**9**



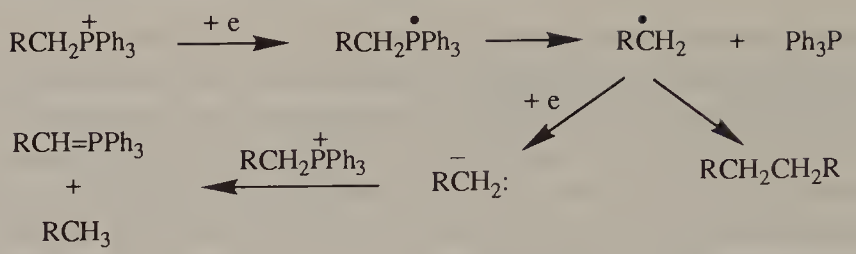
**10**



(4.31)

### 4.3.3.2 *Electrolytic Methods.*

Phosphonium salts have for some time been known to undergo electrolytic reduction with the major results being cleavage of one of the phosphorus substituents to afford a hydrocarbon and a phosphine,[209, 210] but a coupling reaction of the cleaved group also has been observed, and the ratio of the two depends on solution and electrode conditions.[211] These generally have been viewed as the result of one-electron reductions. Later Shono and Mitani[212] found that electrolysis at a carbon electrode in the presence of a carbonyl compound led to the product of a Wittig reaction, and later workers have concluded that a two-electron transfer was involved and

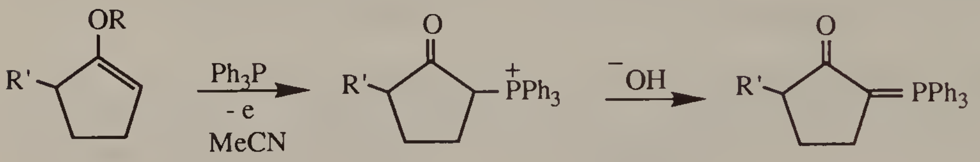


(4.32)

resulted in ylide formation, perhaps as shown in Eq. 4.32.[213–215] Saveant and Binh[216] concluded that in the presence of a small amount of water the ylide was hydrolyzed to produce phosphine oxide and hydrocarbon. Thus, under the appropriate conditions phosphonium ylides can be generated from phosphonium salts by electrolysis.

Recently a Japanese group have found that constant current electrolysis of triphenylphosphine in the presence of cyclic or acyclic alkenes resulted in good yields of alkenylphosphonium salts from addition of phosphine at the double bond.[148, 217] A two-step oxidation was proposed for this useful method of preparing "vinylic" phosphonium salts (Eq. 4.33) (see Section 4.2). Application of

$$Ph_3P \xrightarrow{-e} Ph_3\overset{+}{P}\bullet \xrightarrow{C=C} Ph_3\overset{+}{P}\text{-}C\text{-}\overset{\bullet}{C} \xrightarrow[-H^+]{-e} Ph_3\overset{+}{P}\text{-}C=C \qquad (4.33)$$



(4.34)

this method to cyclic enol ethers provided good yields of $\beta$-ketophosphonium salts, obtainable only with uncertainty by the usual alkylation method (see Section 4.1.1), and which were readily convertible into ylides (Eq. 4.34).[218] Use of $\beta$-diketones in the presence of lutidine as a deprotonating agent afforded modest yields of $\alpha,\alpha$-diacylmethylides directly,[219] presumably via phosphine addition to the enols.

***4.3.3.3 Historically Interesting Methods.*** Finally, brief mention will be made of three methods of phosphonium ylide synthesis which have little general synthetic use but which are either historically significant or which have been applied successfully to the preparation of ylides other than phosphorus.

The first phosphonium ylide recognized as such, diphenylmethylenetriphenylphosphorane ($Ph_3P{=}CPh_2$), was prepared by heating the product of diphenyldiazomethane and triphenylphosphine, an azine, to 195°C, leading to the expulsion of nitrogen (Eq. 4.35).[220] This reaction, if generally applicable, would

$$Ph_2CN_2 \xrightarrow{Ph_3P} Ph_2C=N\text{-}N=PPh_3 \xrightarrow[-N_2]{\Delta} Ph_2C=PPh_3 \qquad (4.35)$$

be most significant as a general preparative method, but such was not to be the case. Wittig initially failed to obtain a methylide[61] from the azine $CH_2{=}N{-}N{=}PPh_3$, but later was able to obtain low yields of the methylide conjugate acid upon heating the azine with cuprous chloride.[221] The azine from diazocyclopentadiene and triphenylphosphine also could not be converted into the known and very stable ylide.[222] Later, it was found possible to convert the triphenylphosphineazine from di-,[223] tri-,[224] or tetraphenyldiazocyclopentadienes[223, 225] into the corresponding ylides by thermal elimination of nitrogen, often using a copper catalyst. The severity of the necessary reaction conditions preclude general applicability of this method.

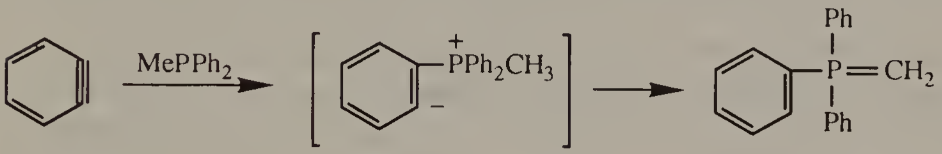
The reaction of active methylenes with dichlorotriphenylphosphorane in the presence of triethylamine produced good yields of highly stabilized ylides (Eq. 4.36).[226, 227] The method is not generally applicable because the necessity

$$Ph_3PCl_2 \quad + \quad CH_2XY \quad \xrightarrow{Et_3N} \quad Ph_3P{=}CXY \qquad (4.36)$$

$$X,Y = COOR,\ CN,\ SO_2Ph,\ COR$$

for active methylenes dictates that only highly stabilized, and generally unreactive, ylides can be produced.

Wittig and Geissler[9] had reacted benzyne with triphenylphosphine and obtained 9-phenyl-9-phosphafluorene. Later, Seyferth and Burlitch[228] found that tertiary phosphines with an α-proton would add to benzyne to produce ylides (Eq. 4.37) which could be trapped in a Wittig reaction. Presumably the



(4.37)

zwitterionic adduct underwent proton transfer to form the ylide. This method has not been investigated for its general applicability but the severity of the benzyne-forming reaction conditions makes general usefulness unlikely.

## REFERENCES

[1] Hellman, H.; Schumacher, O. *Liebigs Ann. Chem.* **1961**, *640*, 79.
[2] Pauson, P. L.; Watts, W. E. *J. Chem. Soc.* **1963**, 2990.
[3] Maccarone, E.; Perrini, G.; Torre, M. *Gazz. Chim. Ital.* **1982**, *112*, 25.
[4] Johnson, A. Wm.; Lee, S. Y.; Swor, R. A.; Royer, L. D. *J. Am. Chem. Soc.* **1966**, *88*, 1953.
[5] Trippett, S.; Walker, D. M. *Chem. Ind.* **1960**, 933.
[6] McEwen, W. E.; Wolf, A. P. *J. Am. Chem. Soc.* **1962**, *84*, 676.
[7] Horner, L.; Winkler, H. *Liebigs Ann. Chem.* **1965**, *685*, 1.

[8] Michaelis, A.; Gimborn, H. V. *Chem. Ber.* **1894**, *27*, 272.

[9] Wittig, G.; Geissler, G. *Liebigs Ann. Chem.* **1953**, *580*, 44.

[10] Mechoulam, R.; Sondheimer, F. *J. Am. Chem. Soc.* **1958**, *80*, 4386.

[11] Levine, S. G. *J. Am. Chem. Soc.* **1958**, *80*, 6150.

[12] Gosselck, J,; Schenk, H.; Ahlbrecht, H. *Angew. Chem.* **1967**, *6*, 249.

[13] Michaelis, A.; Kohler, E. *Chem. Ber.* **1899**, *32*, 1566.

[14] Ramirez, F.; Dershowitz, S. *J. Org. Chem.* **1957**, *22*, 41.

[15] Evans, D. E.; Kaldor, S. W.; Jones, T. K.; Clardy, J.; Stout, T. J. *J. Am. Chem. Soc.* **1990**, *112*, 7001.

[16] Yoshida, H.; Ogata, T.; Inokawa, S. *Synthesis* **1977**, 626.

[17] Friedrich, K.; Henning, H. J. *Chem. Ber.* **1959**, *92*, 2756.

[18] Pinck, L. A.; Hilbert, G. E. *J. Am. Chem. Soc.* **1947**, *69*, 723.

[19] Schweizer, E. E.; Thompson, J. G. *J. Chem. Soc. Chem. Commun.* **1966**, 666.

[20] Bestmann, H. J.; Schulz, H. *Angew. Chem.* **1961**, *73*, 27.

[21] Trippett, S.; Walker, B. J.; Hoffman, H. *J. Chem. Soc.* **1965**, 7140.

[22] Asunskis, J. P. *Diss. Abstr. Int.* **1971**, *31B*, 5250.

[23] Wittig, G.; Eggers, H.; Duffner, P. *Liebigs Ann. Chem.* **1958**, *619*, 10.

[24] Aguiar, A. M.; Aguiar, H. *J. Am. Chem. Soc.* **1966**, *88*, 4090.

[25] Blomquist, A. T.; Hruby, V. J. *J. Am. Chem. Soc.* **1967**, *89*, 4996.

[26] Markl, G. *Z. Naturforsch.* **1963**, *18B*, 1136.

[27] Mondon, A. *Liebigs Ann. Chem.* **1957**, *603*, 115.

[28] Buchi, G.; Wuest, H. *Helv. Chim. Acta* **1971**, *54*, 1767.

[29] Heitman, H.; Wieland, J. H. S.; Huisman, H. O. *Proc. Koninkl. Ned. Akad. Wetenschap* **1961**, *64B*, 165; *Chem. Abstr.* **1961**, *55*, 17562.

[30] Axelrod, E.; Milne, G. M.; Van Tamelen, E. E. *J. Am. Chem. Soc.* **1970**, *92*, 2139.

[31] Bohlmann, F.; Mannhardt, H. J. *Chem. Ber.* **1956**, *89*, 1307.

[32] Inhoffen, H. H.; Bruckner, K.; Domagk, G. F.; Erdmann, H. M. *Chem. Ber.* **1955**, *88*, 1415.

[33] Trippett, S. *Quart. Rev.* **1963**, *17*, 412.

[34] Pommer, H. *Angew. Chem.* **1960**, *72*, 811.

[35] Ullmann, J.; Hanack, M. *Synthesis* **1989**, 685.

[36] Gough, S. T. D.; Trippett, S. *Proc. Chem. Soc.* **1961**, 302.

[37] Dombrovskii, V. A.; Shevchuk, M. I.; Dombrovskii, A. V. *J. Gen. Chem.* **1964**, *34*, 3741.

[38] Hercouet, A.; Le Corre, M.; Le Floch, Y. *Synthesis* **1982**, 597.

[39] Trippett, S. *J. Chem. Soc.* **1962**, 2337.

[40] Speziale, A. J.; Partos, R. D. *J. Am. Chem. Soc.* **1963**, *88*, 3312.

[41] Hudson, R. F.; Salvadori, G. *Helv. Chim. Acta* **1966**, *49*, 96.

[42] Borowitz, I.; Kirgy, K. C.; Rusek, P. E.; Virkhaus, R. *J. Org. Chem.* **1968**, *33*, 3686.

[43] Borowitz, I.; Virkhaus, R. *J. Am. Chem. Soc.* **1963**, *85*, 2183.

[44] Chopard, P. A.; Hudson, R. F.; Klopman, G. *J. Chem. Soc.* **1965**, 1379.

[45] Hoffmann, H.; Forster, H. *Tetrahedron Lett.* **1963**, 1547.

[46] Fukui, K.; Sudo, R.; Masaki, M.; Ohta, M. *J. Org. Chem.* **1968**, *33*, 3504.

[47] Kröhnke, F. *Chem. Ber.* **1950**, *83*, 291.

[48] Schlosser, M. *Chem. Ber.* **1964**, *97*, 3219.

[49] Trost, B. M.; Curran, D. P. *J. Am. Chem. Soc.* **1980**, *102*, 5699.

[50] Attra, T. B.; LeBigot, Y.; El Gharbi, R.; Delmas, M.; Gaset, A. *Synth. Comm.* **1992**, *22*, 1421.

[51] Denney, D. B.; Ross, S. T. *J. Org. Chem.* **1962**, *27*, 998.

[52] Angelova, O.; Kirilov, E. M. G.; Kirilov, M.; Petrov. G.; Kaneti, J.; Macicek, J. *J. Chem. Soc. Perkin Trans. (2)* **1989**, 1405.

[53] Nicolaides, D. N.; Litinas, K.; Argyropoulos, N. G. *J. Chem. Soc. Perkin Trans. (1)* **1986**, 415.

[54] Mizrakh, L. I.; Polonskaya, L. Y. *J. Gen. Chem.* **1990**, *59*, 1299.

[55] Corey, H. S.; McCormick, J. R. D.; Swensen, W. E. *J. Am. Chem. Soc.* **1964**, *86*, 1884.

[56] Markl, G. *Chem. Ber.* **1962**, *95*, 3003.

[57] Trippett, S.; Walker, D. M. *J. Chem. Soc.* **1961**, 1266.

[58] Lang, R. W.; Bestmann, H. J. *Helv. Chim. Acta* **1980**, *63*, 438.

[59] Eyles, C. T.; Trippett, S. *J. Chem. Soc.* **1966**, 67.

[60] Grayson, M.; Keough, P. T. *J. Am. Chem. Soc.* **1960**, *82*, 3919.

[61] Wittig, G.; Haag, W. *Chem. Ber.* **1955**, *88*, 1654.

[62] Markl, G. *Tetrahedron Lett.* **1961**, 807.

[63] Markl, G. *Z. Naturforsch.* **1963**, *18B,* 84.

[64] Wnuk, S. F.; Rabins, M. J. *Can. J. Chem.* **1991**, *69*, 334.

[65] Conia, J. M.; Limasset, J. C. *Bull. Soc. Chim. Fr.* **1967**, 1937.

[66] Boden, R. M. *Synthesis* **1975**, 784.

[67] Dauben, W. G.; Takasugi, J. J. *Tetrahedron Lett.* **1987**, *28*, 4377.

[68] Dondoni, A.; Fantin, G.; Fogagnolo, M.; Medici, A.; Pedrini, P. *Tetrahedron* **1988**, *44*, 2021.

[69] Bottin-Strzalko, T.; Seyden-Penne, J.; Tchoubar, B. *C. R. Seances Acad. Sci.* **1971**, *272*, 728.

[70] Drefahl, G.; Horhold, H. H.; Kuhne, K. *Chem. Ber.* **1965**, *98*, 1826.

[71] Schlosser, M.; Christmann, K. F. *Liebigs Ann. Chem.* **1967**, *708*, 1.

[72] Hoffmann, H. *Chem. Ber.* **1962**, *95*, 2563.

[73] Kobrich, G. *Angew. Chem.* **1962**, *74*, 33.

[74] Anders, E.; Clark, T.; Gassner, T. *Chem. Ber.* **1986**, *119*, 1350.

[75] Zaltsman, I. S.; Bespalko, G. K.; Marchenko, A, P.; Pinchuk, A. M. *J. Gen. Chem.* **1990**, *60*, 613.

[76] Bestmann, H. J.; Stransky, W.; Vostroswsky, O. *Chem. Ber.* **1976**, *109*, 1694.

[77] Chhen, A.; Vaultier, M.; Carrie, R. *Tetrahedron Lett.* **1989**, *30*, 4953.

[78] Stork, G.; Zhao, K. *Tetrahedron Lett.* **1989**, *30*, 2173.

[79] Streinz, L.; Saman, D.; Konecny, K.; Romanuk, M. *Collect. Czech. Chem. Commun.* **1990**, *55*, 1555.

[80] Seyferth, D.; Heeren, J. K.; Hughes, W. B. *J. Am. Chem. Soc.* **1962**, *84*, 1764.

[81] Seyferth, D.; Eisert, M. A.; Heeren, J. K. *J. Organomet. Chem.* **1964**, *2*, 101.

[82] Coffmann, D. D.; Marvel, C. S. *J. Am. Chem. Soc.* **1929**, *51*, 3496.

[83] Fyles, T. M.; Leznoff, C. C.; Weatherston, J. *Can. J. Chem.* **1978**, *56*, 1031.

[83a] Anderson, C. L.; Soderquist, J. A.; Kabalka, G. W. *Tetrahedron Lett.* **1992**, *33*, 6915.

[84] Wittig, G.; Pommer, H. German Patent 954,247; *Chem. Abstr.* **1959**, *53*, 2279.

[85] Greenwald, R.; Chaykovsky, M.; Corey, E. J. *J. Org. Chem.* **1963**, *28*, 1128.

[86] Parfentev, L. N.; Shamshurin, A. A. *Zh. Obshch. Khim.* **1939**, *9*, 865; *Chem. Abstr.* **1940**, *34*, 392.

[87] Bestmann, H. J. *Chem. Ber.* **1962**, *95*, 58.

[88] Wohlleben, A.; Schmidbaur, H. *Angew. Chem.* **1977**, *16*, 417.

[89] Seyferth, D.; Hughes, W. B.; Heeren, J. K. *J. Am. Chem. Soc.* **1965**, *87*, 3467.

[90] Schlosser, M.; Kadibelban, T.; Steinhoff, G. *Angew. Chem.* **1966**, *5*, 968.

[91] Pilling, G. W.; Sondheimer, F. *J. Am. Chem. Soc.* **1971**, *93*, 1970.

[92] Longone, D. T.; Doyle, R. R. *J. Chem. Soc. Chem. Commun.* **1967**, 300.

[93] Seyferth, D.; Heeren, J. K.; Singh, G.; Grim, S. O.; Hughes, W. B. *J. Organomet. Chem.* **1966**, *5*, 267.

[94] Kobrich, G.; Trapp, H.; Flory, K.; Drischel, W. *Chem. Ber.* **1966**, *99*, 689.

[95] Smithers, R. H. *J. Org. Chem.* **1978**, *43*, 2833.

[96] Burger, H. Dissertation at Tubingen University, **1957**.

[97] Welcher, R. P.; Day, N. E. *J. Org. Chem.* **1962**, *27*, 1824.

[98] Seyferth, D.; Fogel, J. *J. Organomet. Chem.* **1966**, *6*, 205.

[99] Brophy, J. J.; Gallagher, M. J. *J. Chem. Soc.* **1966**, 531.

[100] Schmidbaur, H.; Schnatterer, S. D. *Chem. Ber.* **1983**, *116*, 1947.

[101] Albright, T. A.; Schweizer, E. E. *J. Org. Chem.* **1976**, *41*, 1168.

[102] Bestmann, H. J.; Arnason, B. *Chem. Ber.* **1962**, *95*, 1513.

[103] Koster, R.; Simic, D.; Grassberger, M. A. *Liebigs Ann. Chem.* **1970**, *739*, 211.

[104] Schmidbaur, H.; Blaschke, G.; Kohler, F. H. *Z. Naturforsch.* **1977**, *32B*, 757.

[105] Schmidbaur, H.; Stuhler, H.; Vornberger, W. *Chem. Ber.* **1972**, *105*, 1084.

[106] Schaub, B.; Blaser, G.; Schlosser, M. *Tetrahedron Lett.* **1985**, *26*, 307.

[107] Schmidbaur, H.; Tronich, W. *Chem. Ber.* **1968**, *101*, 595.

[108] Miller, N. E. *Inorg. Chem.* **1965**, *4*, 1458.

[109] Schmidbaur, H.; Tronich, W. *Chem. Ber.* **1967**, *100*, 1032.

[110] Bestmann, H. J.; Moenius, T. *Angew. Chem.* **1986**, *25*, 994.

[111] Vedejs, E.; Martinez, G. R. *J. Am. Chem. Soc.* **1979**, *101*, 6452.

[112] Vedejs, E.; West, F. G. *Chem. Rev.* **1986**, *86*, 941.

[113] Appel, R. In *Organophosphorus Reagents in Organic Synthesis*; Cadogan, J. I. G., Ed.; Academic: London, 1979, Chapter 9, pp. 387–431; *Angew. Chem.* **1975**, *14*, 801.

[114] Appel, R.; Morbach, W. *Synthesis* **1977**, 679.

[115] Rabinowitz, R.; Marcus, R. *J. Am. Chem. Soc.* **1962**, *84*, 1312.

[116] Burton, D. J.; Greenwald, J. R. *Tetrahedron Lett.* **1967**, 1535.

[117] Combret, J. C.; Villieras, J.; Lavielle, G. *Tetrahedron Lett.* **1971**, 1035.

[118] Chapleur, Y. *J. Chem. Soc. Chem. Commun.* **1984**, 449.

[119] Motherwell, W. B.; Tozer, M. J.; Ross, B. C., *J. Chem. Soc. Chem. Commun.* **1989**, 1437.

[120] Soulen, R. L.; Clifford, D. B.; Chim, F. F.; Johnson, J. A. *J. Org. Chem.* **1971**, *36*, 3386.

[121] Gadreau, C.; Foucaud, A. *Bull. Soc. Chim. Fr.* **1976**, 2068.

[122] Burton, G.; Elder, J. S.; Fell, S. C. M.; Stachulski, A. V. *Tetrahedron Lett.* **1988**, *29*, 3003.

[123] Lakhrissi, M.; Chapleur, Y. *Synlett.* **1991**, 583.

[124] Vorbruggen, H.; Bohn, B. D.; Krolikiewicz, K. *Tetrahedron* **1990**, *46*, 3489.

[125] Ramirez, F.; Desai, N. B.; McKelvie, N. *J. Am. Chem. Soc.* **1962**, *84*, 1745.

[126] Corey, E. J.; Fuchs, P. L. *Tetrahedron Lett.* **1972**, 3769.

[127] Olah, G.; Wu, A. H. *Synthesis* **1990**, 885.

[128] Burton D. J.; Naae, D. G. *J. Am. Chem. Soc.* **1973**, *95*, 8467.

[129] Bessard, Y.; Muller, U.; Schlosser, M. *Tetrahedron* **1990**, *46*, 5213.

[130] Burton, D. J.; Naae, D. G.; Flynn, R. M.; Smart, B. E.; Britelli, D. R. *J. Org. Chem.* **1983**, *48*, 3616.

[131] Riesel, L.; Vogt, H.; Kolleck, V. *Z. Anorg. Allg. Chem.* **1989**, *574*, 143.

[132] Ramirez, F.; McKelvie, N. *J. Am. Chem. Soc.* **1957**, *79*, 5829.

[133] Ramirez, F.; Pilot, J. F.; Desai, N. B.; Smith, C. P.; Hansen, B.; McKelvie, N. *J. Am. Chem. Soc.* **1967**, *89*, 6273.

[134] Seyferth, D.; Grim, S. O.; Read, T. O. *J. Am. Chem. Soc.* **1961**, *83*, 1617.

[135] Schlosser, M. *Angew. Chem.* **1962**, *74*, 291.

[136] Miyano, S.; Izumi, Y.; Fujii, K.; Ohno, Y.; Hashimoto, H. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 1197.

[137] Bestmann, H. J.; Rippell, H. C.; Dostalek, R. *Tetrahedron Lett.* **1989**, *30*, 5261.

[138] Schlosser, M.; Zimmerman, M. *Synthesis* **1969**, *1*, 75.

[139] Burton, D. J.; Greenlimb, P. E. *J. Org. Chem.* **1975**, *40*, 2796.

[140] Thenappan, A.; Burton, D. J. *J. Org. Chem.* **1990**, *55*, 2311.

[141] Tyuleneva, V. V.; Rokhlin, E. M.; Knunyants, I. L. *Russ. Chem. Revs.* **1981**, *50*, 280; **1982**, *51*, 1.

[142] Seyferth, D.; Fogel, J. S.; Heeren, J. K. *J. Am. Chem. Soc.* **1964**, *86*, 307.

[143] Just, C.; O'Connor, B. *Tetrahedron Lett.* **1985**, *26*, 1799.

[144] Schweizer, E. E. *J. Am. Chem. Soc.* **1964**, *86*, 2744.

[145] Schweizer, E. E.; Smucker, L. D.; Votral, R. J. *J. Org. Chem.* **1966**, *31*, 467.

[146] Kowalski, M. H.; Hinkle, R. J.; Stang, P. J. *J. Org. Chem.* **1989**, *54*, 2783.

[147] Hinkle, R. J.; Stang, P. J.; Kowalski, M. H. *J. Org. Chem.* **1990**, *55*, 5033.

[148] Ohmari, H.; Takanami, T.; Masui, M. *Tetrahedron Lett.* **1985**, 2199; *Chem. Pharm. Bull.* **1987**, *35*, 4960.

[149] Nesmeyanov, N. A.; Mikulshina, V. V.; Kharitonov, V. G.; Petrovskii, P. V.; Reutov, O. A. *Izv. Akad. Nauk SSSR* **1989**, 1182; *Chem. Abstr.* **1990**, *112*, 56086.

[150] Jacoby, D.; Celerier, J. P.; Petit, H.; Lhommet, G. *Synthesis*, **1990**, 301.

[151] McIntosh, J. M.; Khalil, H. *Can. J. Chem.* **1978**, *56*, 2134.

[152] Keough, P. T.; Grayson, M. *J. Org. Chem.* **1964**, *29*, 631.

[153] Zbiral, E. In *Organophosphorus Reagents in Organic Synthesis*; Cadogan, J. I. G., Ed.; Academic: London, 1979; Chapter 5, pp. 250–266.

[154] Minami, T.; Yamamoto, I. *Revs. Heteroatom Chem.* **1991**, *5*, 270.

[155] Meyers, A. I.; Lawson, J. P.; Carver, D. R. *J. Org. Chem.* **1981**, *46*, 3119.

[156] Linderman, R. J.; Meyers, A. I. *Tetrahedron Lett.* **1983**, *24*, 3043.

[157] Hart, D. J.; Cain, P. A.; Evans, D. A. *J. Am. Chem. Soc.* **1978**, *100*, 1548.

[158] Kawamoto, I.; Muramatsu, S.; Yura, Y. *Tetrahedron Lett.* **1974**, 4223.

[159] Cameron, A. G.; Hewson, A. T. *J. Chem. Soc. Perkin Trans. (1)* **1983**, 2979.

[160] Hewson, A. T.; MacPherson, D. T. *Tetrahedron Lett.* **1983**, *24*, 5807.

[161] Fuchs, P. L. *Tetrahedron Lett.* **1974**, 4055.

[162] Buchi, G.; Pawlak, M. *J. Org. Chem.* **1975**, *40*, 100.

[163] White, J. D.; Jensen, M. S. *Tetrahedron Lett.* **1992**, *33*, 577.

[164] Scheuplein, S. W.; Bruckner, R. *Chem. Ber.* **1991**, *124*, 1871.

[165] Minami, T.; Sako, H.; Ikehira, T.; Hanamoto, T.; Hirao, I. *J. Org. Chem.* **1983**, *48*, 2569.

[166] Okada, Y.; Minami, T.; Yahiro, S.; Akinaga, K. *J. Org. Chem.* **1989**, *54*, 974.

[167] Padwa, A.; Hornbuckle, S. F. *Chem. Rev.* **1991**, *91*, 263.

[168] Speziale, A. J.; Ratts, K. W. *J. Am. Chem. Soc.* **1962**, *84*, 854.

[169] Wittig, G.; Schlosser, M. *Chem. Ber.* **1961**, *94*, 1373.

[170] Fuqua, S. A.; Duncan, W. G.; Silverstein, R. M. *J. Org. Chem.* **1965**, *30*, 1027.

[171] Fuqua, S. A.; Duncan, W. G.; Silverstein, R. M. *J. Org. Chem.* **1965**, *30*, 2543.

[172] Burton, D. J.; Kratsch, H. C. *Tetrahedron Lett.* **1968**, 71.

[173] Lemal, D. M.; Banitt, E. H. *Tetrahedron Lett.* **1964**, 245.

[174] Seebach, D. *Angew. Chem.* **1967**, *6*, 443; *Chem. Ber.* **1972**, *105*, 487.

[175] Seebach, D.; Peleties, N. *Chem. Ber.* **1972**, *105*, 511.

[176] Hedaya, E.; Theodoropulos, S. *Tetrahedron* **1968**, *24*, 2241.

[177] Hudson, R. F.; Chopard, P. A. *Helv. Chim. Acta* **1963**, *46*, 2178.

[178] Aksnes, G. *Acta Chem. Scand.* **1961**, *15*, 692.

[179] Schonberg, A.; Ismail, A. F. A. *J. Chem. Soc.* **1940**, 1374.

[180] Hoffmann, H. *Chem. Ber.* **1961**, *94*, 1331.

[181] Osuch, C.; Franz, J. E.; Zienty, F. B. *J. Org. Chem.* **1964**, *29*, 3721.

[182] Ramirez, F.; Madan, O. P.; Smith, C. P. *Tetrahedron Lett.* **1965**, 201; *Tetrahedron* **1966**, *22*, 567.

[183] Kozikowski, A. P.; Jung, S. H. *J. Org. Chem.* **1986**, *51*, 3402.

[184] Kim, S.; Lee, P. H. *Tetrahedron Lett.* **1988**, *29*, 5413.

[185] Grobe, J.; Le Van, D.; Althoff, U.; Lange, G. *Chem. Ber.* **1992**, *125*, 567.

[186] Oda, R.; Kawabata, T.; Tanimoto, S. *Tetrahedron Lett.* **1964**, 1653.

[187] McClure, J. D. *Tetrahedron Lett.* **1967**, 2401; *J. Org. Chem.* **1970**, *35*, 3045.

[188] Takashina, N.; Price, C. C. *J. Am. Chem. Soc.* **1962**, *84*, 489.

[189] Baizer, M. M. *J. Org. Chem.* **1965**, *30*, 1357.

[190] Morita, K.; Suzuki, Z.; Hirose, H. *Bull. Chem. Soc. Jpn.* **1968**, *41*, 2815.

[191] Imagawa, T.; Memura, K.; Nagai, Z.; Kawanisi, M. *Synth. Commun.* **1984**, *14*, 1267.

[192] Bertenshaw S. *Tetrahedron Lett.* **1989**, *30*, 2731.

[193] Drewes, S. E.; Roos, G. H. P. *Tetrahedron* **1988**, *44*, 4653.

[194] Hoffmann, H.; Diehr, H. J. *Chem. Ber.* **1965**, *98*, 363.

[195] Shaw, M. A.; Tebby, J. C.; Ward, R. S.; Williams, H. *J. Chem. Soc. (C)* **1967**, 2442.

[196] Caesar, J. C.; Griffiths, D. V.; Griffiths, P. A.; Tebby, J. C. *J. Chem. Soc. Perkin Trans. (1)* **1989**, 2425.

[197] Shaw, M. A.; Tebby, J. C. *J. Chem. Soc.* **1970**, 5.

[198] Shaw, M. A.; Tebby, J. C.; Ward, R. S.; Williams, D. H. *J. Chem. Soc.* **1970**, 504.

[199] Hughes, A. N.; Davies, M. *Chem. Ind.* **1969**, 138.

[200] Johnson, A. W.; Tebby, J. C. *J. Chem. Soc.* **1961**, 2126.

[201] Waite, N. E.; Tebby, J. C.; Ward, R. S.; Williams, D. H. *J. Chem. Soc. (C)* **1969**, 1100.

[202] Shaw, M. A.; Tebby, J. C.; Ward, R. S.; Williams, D. H. *J. Chem. Soc. (C)* **1968**, 1609.

[203] Schweizer, E. E.; Berninger, C. J.; Thompson, J. G. *J. Org. Chem.* **1968**, *33*, 336.

[204] Schweizer, E. E.; Thompson, J. G.; Ulrich, T. A. *J. Org. Chem.* **1968**, *33*, 3082.

[205] Delloria, J. F.; Sallin, K. J. *Tetrahedron Lett.* **1990**, *31*, 2661.

[206] Fuchs, P. L. *J. Am. Chem. Soc.* **1974**, *96*, 1607.

[207] Barreau, M.; Ponsinet, G. *Tetrahedron Lett.* **1985**, *26*, 5451.

[208] Dauben, W. G.; Hart, D. J. *Tetrahedron Lett.* **1975**, 4353.

[209] Horner, L.; Mentrup, A. *Liebigs Ann. Chem.* **1961**, *646*, 65.

[210] Horner, L.; Haufe, J. *Chem. Ber.* **1968**, *101*, 2903.

[211] Utley, J. H. P.; Webber, A. *J. Chem. Soc. Perkin Trans. (1)* **1980**, 1154.

[212] Shono, T.; Mitani, M. *J. Am. Chem. Soc.* **1968**, *90*, 2728.

[213] Saveant, J. M.; Binh, S. K. *Bull. Soc. Chim. Fr.* **1972**, 3549.

[214] Pardini, V. L.; Roullier, L.; Utley, J. H. P.; Webber, A. *J. Chem. Soc. Perkin Trans. (1)* **1981**, 1520.

[215] Hall, T. J.; Hargis, J. H. *Abstracts of Papers*, 189th National Meeting of the American Chemical Society, Miami Beach, FL; American Chemical Society: Washington, D. C. 1985; ORGN 233.

[216] Saveant, J. M.; Binh, S. K. *J. Org. Chem.* **1977**, *42*, 1242.

[217] Takanami, T.; Suda, K.; Ohmori, H.; Masui, M. *Chem. Lett.* **1987**, 1335.

[218] Takanami, T.; Abe, A.; Suda, K.; Ohmori, H. *J. Chem. Soc. Chem. Commun.* **1990**, 1310.

[219] Ohmori, H.; Maeda, H.; Tamaoka, M.; Masui, M. *Chem. Pharm. Bull.* **1988**. *36*, 613.

[220] Staudinger, H.; Meyer, J. *Helv. Chim. Acta* **1919**, *2*, 619.

[221] Wittig, G.; Schlosser, M. *Tetrahedron* **1962**, *18*, 1023.

[222] Ramirez, F.; Levy, S. *J. Org. Chem.* **1958**, *23*, 2036.

[223] Regitz, M.; Liedhegener, A. *Tetrahedron* **1967**, *23*, 2701.

[224] Lloyd, D.; Singer, M. I. C. *Tetrahedron* **1972**, *28*, 353.

[225] Lloyd, D.; Singer, M. I. C.; Regitz, M.; Liedhegener, A. *Chem. Ind.* **1967**, 324.

[226] Horner, L.; Oediger, H. *Chem. Ber.* **1958**, *91*, 437.

[227] Diefenbach, H.; Ringsdorf, H.; Wilhelms, R. E. *J. Polym. Sci. B* **1967**, *5*, 1039.

[228] Seyferth, D.; Burlitch, J. M. *J. Org. Chem.* **1963**, *28*, 2463.

# 5

# REACTIONS OF PHOSPHONIUM YLIDES I. CLEAVAGES AND DECOMPOSITIONS

Because of their unique molecular and electronic structure, phosphonium ylides undergo a wide variety of reactions. Some reactions depend simply on the carbanionic nature of such ylides, and the reactions are typical of carbon nucleophiles in general. The presence of the adjacent phosphonium group has little effect on such reactions, at least in the initial step. Other reactions depend on the unique ylide structure and involve both the carbanion portion and the phosphonium portion of the ylide, though not necessarily simultaneously. Both kinds of reactions are very important in synthetic chemistry, and are discussed in detail in this book, but the distinction between the two is not the most useful basis for cataloging and presenting such chemistry. Instead, the organization used to present the reaction chemistry of phosphonium ylides depends on the kind of reagent with which the ylide reacts.

The reactions of phosphonium ylides are presented in this chapter, Chapters 6–9 and Chapter 14. In this chapter are discussed reactions that result in cleavage of the carbon–phosphorus bond. In Chapter 6 are described the reactions of phosphonium ylides with various electrophilic reagents, generally substitution-type reactions. Chapter 7 presents addition-type reactions typically found with multiply bonded reagents. Chapters 8 and 9 are devoted to the Wittig reaction of phosphonium ylides with aldehydes and ketones—Chapter 8 describes the scope of the reaction and it's applications, and Chapter 9 describes the mechanism and stereochemical control available for the reaction. In Chapter 14 the relatively new area of the reaction of phosphonium ylides with metal complexes is discussed.

The cleavage reactions applicable to phosphonium ylides can be very important and useful in synthetic chemistry, and are discussed in this chapter. After

---

*Ylides and Imines of Phosphorus*, Edited by A. William Johnson.
ISBN 0-471-52217-1

using a phosphonium ylide as a template on which to create new bonds, usually between the ylide carbanion and another reagent, it is often desirable to remove the phosphorus group that activated the ylide. Hydrolysis, oxidation, reduction, and electrolysis reactions have been used for this purpose and will be described.

Some phosphonium ylides are sensitive to a variety of other reaction conditions, such as heat and light. Accordingly, the nature of the products resulting from such decompositions are also described in this chapter.

## 5.1 HYDROLYSIS OF YLIDES

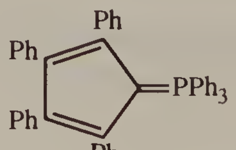
Phosphonium ylides generally are susceptible to hydrolytic cleavage, producing a hydrocarbon and a phosphine oxide (Eq. 5.1). The uncertainties involve the ease of such a reaction and the question of which carbon–phosphorus bond is broken (i.e., which phosphonium substituent appears as the hydrocarbon).

$$R_3P{=}CHR' \xrightarrow{H_2O} \begin{array}{c} R_3PO \quad + \quad R'CH_3 \\ \text{or} \\ R_2(R'CH_2)PO \quad + \quad RH \end{array} \tag{5.1}$$

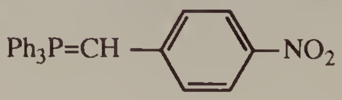
The susceptibility to hydrolysis varies with the reactivity of the ylide, with some ylides so susceptible that they need to be prepared and handled in the complete absence of moisture while others resist hydrolysis under severe conditions. Alkylidenetriphenylphosphoranes, generally classified as nonstabilized or reactive ylides, react so rapidly with water that they need to be prepared in an inert atmosphere. For example, Coffmann and Marvel[1] found that ethylidenetriphenylphosphorane was immediately decolorized in the presence of water (Eq. 5.2) and afforded ethyldiphenylphosphine oxide; benzene presumably

$$Ph_3P{=}CHCH_3 \xrightarrow{H_2O} Ph_2P(O)C_2H_5 \quad + \quad C_6H_6 \tag{5.2}$$

was the other product. On the other hand, a highly stabilized ylide such as 2,3,4,5-tetraphenylcyclopentadienylidenetriphenylphosphorane (**1**) was unchanged after lengthy reflux in alcoholic sodium hydroxide.[2] Of intermediate stability to hydrolysis are the so-called semistabilized ylides, those containing electron-withdrawing substituents on the ylidic carbon. Thus, *p*-nitroben-



**1**



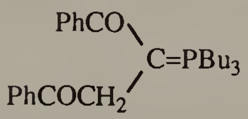
**2**

zylidenetriphenylphosphorane (**2**) was sufficiently stable that it could be prepared from its precursor salt by treatment with cold aqueous sodium hydroxide, but on extended contact or heating hydrolysis to triphenylphosphine oxide and *p*-nitrotoluene occurred.[3] Similarly, ylides such as the phenacylidene-, acetylidene-, carbethoxymethylene-, and fluorenylidenetriphenylphosphoranes could be prepared in aqueous media, but hydrolyzed upon extended exposure to water or heating in basic media. In general, the stability of an ylide toward hydrolysis parallels its basicity, with the most basic being the most susceptible to hydrolysis. Thus, hydrolysis is a reaction to be guarded against in much ylide chemistry, but, as shown below, can be a useful P–C cleavage reaction under controlled conditions.

There is a consistent pattern to the hydrolytic cleavage of the carbon–phosphorus bond in ylides, with the group leaving phosphorus generally being that which can produce the most stable carbanion. Thus, benzoylmethylenetriphenylphosphorane (**3**) hydrolyzed to acetophenone and triphenylphosphine oxide,[4] the tributylphosphonium ylide (**4**) hydrolyzed to phenacylacetophenone and tributylphosphine oxide,[5] and the fluorenylidenephosphoranes (**5**) hydrolyzed to fluorene and trimethyl-,[6] tri-*n*-butyl,[7] or triphenylphosphine oxides.[8]

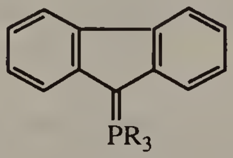
$PhCOCH{=}PPh_3$

**3**



$(PhCO)(PhCOCH_2)C{=}PBu_3$

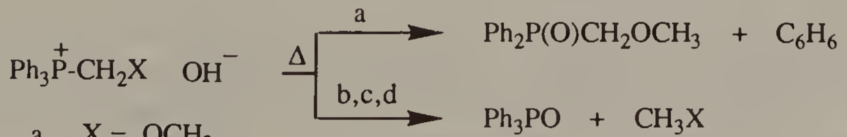
**4**



**5**

The preceding paragraph also cites examples of ylide hydrolyses in which the preference for hydrocarbon formation was phenyl > alkyl. In all of these instances, and in many more, the group ejected from the phosphonium group was that group expected to form the most stable carbanion.

Fenton and Ingold[9] studied the base-catalyzed hydrolysis of a series of quaternary phosphonium salts and found that the group ejected from the phosphonium atom as a hydrocarbon was that which formed the most stable carbanion. Thus, the preference for hydrocarbon formation was benzyl > phenyl > alkyl. Finally, a series of phosphonium salts was hydrolyzed by Schlosser,[10] with two different reaction paths being followed, depending on the nature of the methyl substituent (Eq. 5.3). The methylene–phosphorus bond was cleaved in those instances (compounds b, c, and d) where stabilization was



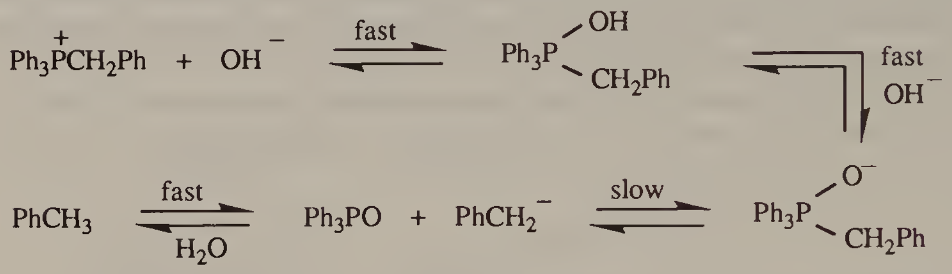
$$Ph_3\overset{+}{P}\text{-}CH_2X \quad OH^- \xrightarrow{\Delta} \begin{cases} \xrightarrow{a} Ph_2P(O)CH_2OCH_3 + C_6H_6 \\ \xrightarrow{b,c,d} Ph_3PO + CH_3X \end{cases} \tag{5.3}$$

a. $X = OCH_3$
b. $X = SCH_3$
c. $X = Cl$
d. $X = Br$

available to the substituted methyl carbanion, but the phenyl–phosphorus bond was broken in the case of the methoxy substituent (a) which would, relatively, destabilize a methyl carbanion.

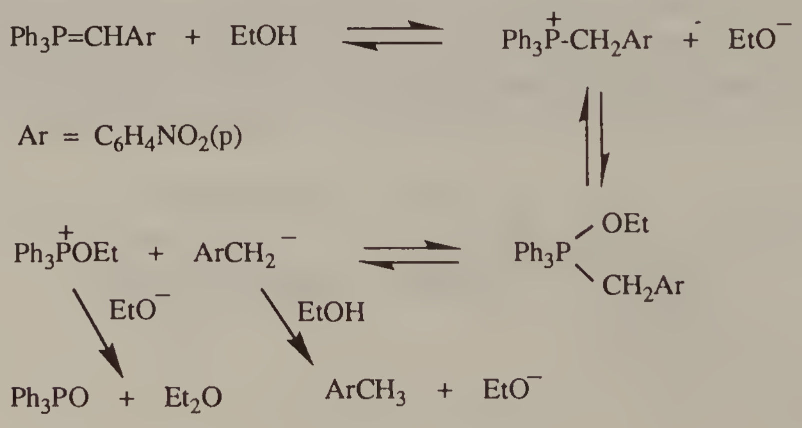
From the examples given above, it is apparent that the nature of the leaving group was similarly determined whether the species undergoing hydrolysis was a phosphonium ylide or a phosphonium salt. Largely on that basis it has been concluded that the hydrolysis of ylides proceeds via initial protonation to a phosphonium salt, followed by hydrolysis of the salt to hydrocarbon and phosphine oxide.

The mechanism of the hydrolysis of phosphonium salts was established by VanderWerf et al. in 1959[11] and confirmed thereafter by Aksnes and Songstad.[12] The reactions generally followed third-order kinetics, first order in phosphonium salt and second order in hydroxide, as shown in Eq. (5.4). In addition, the reaction normally occurred stereospecifically with inversion of configuration at phosphorus resulting from the initial direct hydroxide attack on phosphorus.[13] The mechanistic and stereochemical details of this reaction were reviewed in 1965 by McEwen.[14]



(5.4)

The alcoholysis of phosphonium ylides and phosphonium salts seems to occur by a similar mechanism. Grayson and Keough[15] found that *p*-nitrotoluene, triphenylphosphine oxide, and diethyl ether were the products of ethoxide-catalyzed decomposition of *p*-nitrobenzyltriphenylphosphonium bromide, and the same products were obtained by heating *p*-nitrobenzylidenetriphenylphosphorane in ethanol. They rationalized that the first step was an equilibrium between phosphonium ylide and phosphonium salt, with the slow step of the reaction being the attack of ethoxide on tetravalent phosphorus. The resulting



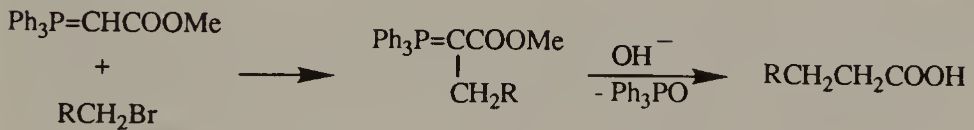
(5.5)

pentavalent phosphorane was proposed to eject the most stable carbanion, in this instance the *p*-nitrobenzyl anion, with ethoxide reacting with the tetravalent phosphorus cation to form phosphine oxide and diethyl ether (Eq. 5.5). Evidence for the initial equilibrium between ylide and salt was the fact that carrying out the reaction between preformed ylide and O-deuteroethanol resulted in the formation of di- and tri-deutero-*p*-nitrotoluene.

Aksnes et al.[16] compared the third-order basic hydrolysis and methanolysis of phosphonium salts and concluded, on the basis of quite different activation parameters for the two similar reactions, that the mechanisms must be different. They concurred with the previous proposals for a pentavalent phosphorus intermediate in the hydrolysis, but suggested a hexavalent phosphorus intermediate $[R_4P(OMe)_2]$ for the methanolysis reaction.

In a few instances alcoholysis of phosphonium ylides derived from phosphines other than triphenylphosphine has led to some cleavage of other than the ylide carbon–phosphorus bond. Thus, Burgada et al.[17] found that during methanolysis of an ylide methoxy groups were ejected to some extent in competition with a stabilized carbanion. More recently dialkylamino groups were found to cleave in preference to the benzyl group upon hydrolysis with potassium hydroxide.[18] A number of P-chloro ylides are now known and they invariably are cleaved at the chlorine–phosphorus bond upon hydrolysis,[19] resulting in a phosphine oxide with the ylidic carbon–phosphorus bond intact.

In summary, hydrolysis is an effective means of cleaving the carbanion–phosphorus bond. This reaction is useful in many synthetic sequences as a final step after new carbon–carbon bonds have been formed, as will be seen in Chapter 6. For example, carboxylic acids were synthesized from phosphonium ylides and alkyl halides in a two-step reaction (Eq. 5.6), both of which occurred in good yields.[20]



$$\begin{matrix}\mathrm{Ph_3P{=}CHCOOMe}\\ +\\ \mathrm{RCH_2Br}\end{matrix} \longrightarrow \mathrm{Ph_3P{=}\underset{\underset{\displaystyle CH_2R}{|}}{C}COOMe} \xrightarrow[-\,\mathrm{Ph_3PO}]{\mathrm{OH^-}} \mathrm{RCH_2CH_2COOH} \qquad (5.6)$$

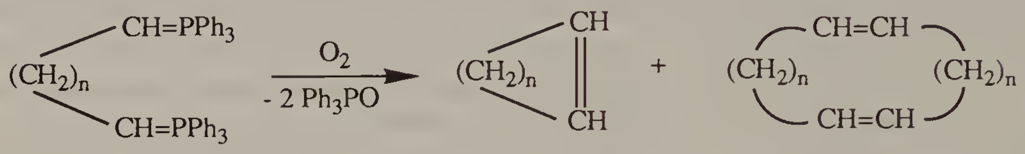
## 5.2 OXIDATION OF YLIDES

Oxidation of phosphonium ylides results in cleavage of the carbanion–phosphorus bond, and the discovery of newer reagents permits this reaction to be very specific. The carbanion portion of the ylide is converted to a carbonyl group in most instances,while the phosphorus portion appears as a phosphine oxide. In other instances reaction of the carbonyl product with unconverted ylide produces a symmetrical alkene, the alkene being effectively a "dimer" of the carbanion portion of the starting ylide. The driving force in all of the oxidations probably is the formation of the high-energy phosphorus–oxygen bond.

The so-called "autoxidation" of ylides with molecular oxygen was first and extensively employed by Bestmann to cleave ylides either to carbonyl compounds or to olefinic dimers of the carbanion portion of the ylide. Reaction of monosubstituted ylides with a limited amount of oxygen, approximately one-half an equivalent, afforded alkene and two equivalents of phosphine oxide (Eq. 5.7). For example, benzylidenetriphenylphosphorane (R = phenyl) afforded

$$2\,RCH{=}PPh_3 \xrightarrow{O_2} RCH{=}CHR + 2\,Ph_3PO \qquad (5.7)$$

a 72% yield of stilbene[21] and vitamin A alcohol, after conversion to the corresponding phosphonium ylide (R = retinyl), afforded a 35% yield of all trans-$\beta$-carotene.[22] The reaction is especially useful in forming cyclic olefins if the ring size is at least five members and no greater than seven members (Eq. 5.8). Thus, the bis-ylide **6** (n = 3) afforded cyclopentene in 68% yield, with

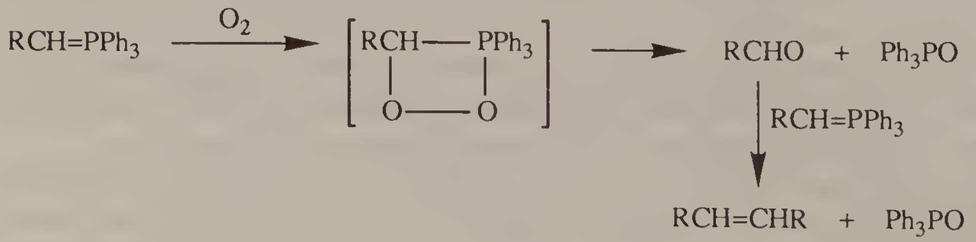


**6**

(5.8)

similar results being reported for the C-6 and C-7 rings. Also, acenaphthylene was obtained in 30% yield,[23] phenanthrene in 45% yield,[23] dibenzoxepine in 52% yield,[23] and bicyclo(4.3.0)-nona-3,6-diene in 53% yield[24] using the same reaction with the appropriate bis-ylide. As the ring size increased, competition from dimer and oligomer formation detracted from the usefulness of the cyclization reaction. Thus, bis-ylide **6** (n = 6) afforded only 2% cyclooctene, 12% dimer (1,9-cyclohexadecadiene), and 11% of higher oligomers.[24]

The autoxidation–dimerization reaction only is applicable to relatively reactive ylides, not to stabilized ylides, and the reaction was ineffective with disubstituted ylides. The latter afford one equivalent of ketone and phosphine oxide under the same conditions. For example, isopropylidenetriphenylphosphorane afforded a 60% yield of acetone and benzhydrylidenetriphenylphosphorane produced a 70% yield of benzophenone.[21] All of these observations have been accounted for by proposing initial oxidation of the ylide, via oxygen addition across the ylide bond, to afford aldehyde and phosphine oxide. The aldehyde is then thought to be trapped by a rapid Wittig reaction with unconverted ylide to afford the alkene and another equivalent of phosphine oxide (Eq. 5.9). This trapping would be expected to be much slower in the case of

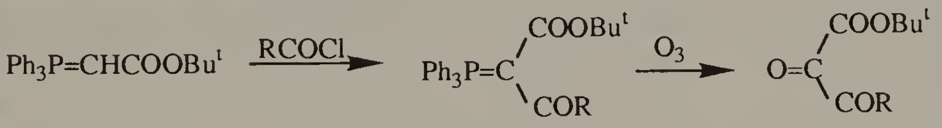


(5.9)

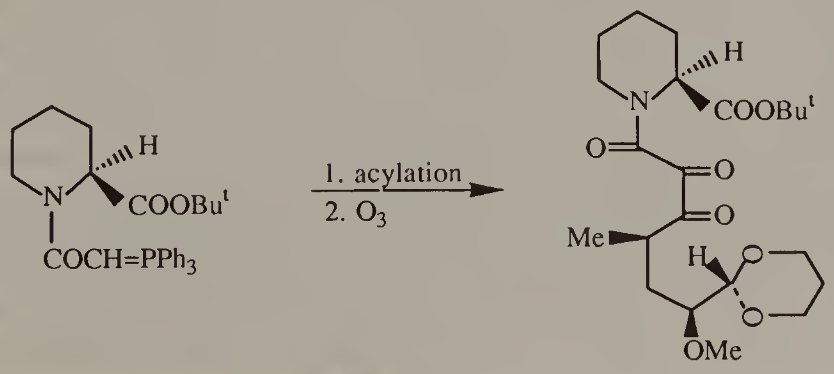
disubstituted ylides, permitting the faster autoxidation to proceed, resulting in complete conversion of ylide to ketone. In the case of bis-ylides, the initially formed aldehyde–ylide has the choice of intramolecular cyclization or intermolecular dimerization, depending on ring size. Finally, these observations indicate that in the preparation of reactive phosphonium ylides, and in their subsequent reactions, oxygen should be rigorously excluded from the environment.

Photochemical oxidation, using singlet oxygen, accomplished identical bond cleavage with stabilized ylides, affording either carbonyl or Wittig reaction product (dimer) as a function of the amount of oxygen supplied to the reaction.[25] The cleavage could be effected even in the presence of alkene groups in the ylide.[26] The initial ylide–oxygen adduct has been detected by $^{31}P$ NMR spectroscopy recently.[27]

An alternative and complementary oxidation of ylides can be accomplished with ozone, typically used at − 70°C in methylene chloride. These conditions are sufficient to oxidize even stabilized ylides to carbonyl compounds and phosphine oxides. Ramirez et al.[28] first reported this reaction with phenacylidenetriphenylphosphorane obtaining phenylglyoxal in 88% yield and the α-phenyl counterpart produced benzil in 80% yield. Addition of ozone across the P–C ylide bond was proposed as the initial step in this oxidation. There have been no reports of alkenes resulting from this reaction, although if any were formed they probably would be immediately oxidatively cleaved to the same expected ketone. The ozonolysis of ylides has been applied recently by Wasserman to the synthesis of several tricarbonyl compounds useful in natural products synthesis. For example, acylation of an ester-ylide with a variety of acyl halides produced α,α-diacylylides which, upon ozonolysis, afforded vicinal tricarbonyl compounds (Eq. 5.10).[29] Similarly, the $C_1$–$C_{15}$ α,β-diketoamide subunit of the immunosuppressant FK 506 has been prepared by a similar acylation and ozonolysis of the appropriate ylide (Eq. 5.11).[30]

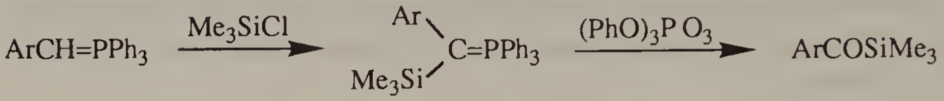


$$Ph_3P{=}CHCOOBu^t \xrightarrow{RCOCl} Ph_3P{=}C\begin{matrix} COOBu^t \\ COR \end{matrix} \xrightarrow{O_3} O{=}C\begin{matrix} COOBu^t \\ COR \end{matrix} \qquad (5.10)$$



(5.11)

A convenient reagent for the oxidation of ylides is triphenylphosphite ozonide, which results in alkenes when monosubstituted ylides are employed, and ketones when the starting ylides are disubstituted. The reagent is equally effective with reactive and stabilized ylides, affording β-carotene in 75% yield, stilbene in 89% yield, dibenzoylethylene in 62% yield, benzophenone in 73% yield, and methyl phenyl diketone in 81% yield from the appropriate ylides.[31]. More recently, acyl silanes have been prepared by silylation of arylidenetriphenylphosphoranes followed by oxidation with triphenylphosphite ozonide (Eq. 5.12).[32] The advantages of this reagent over autoxidation with oxygen or ozonolysis are the low temperature conditions, reaction with both reactive and stabilized ylides, accurate dosage, and excellent yields.

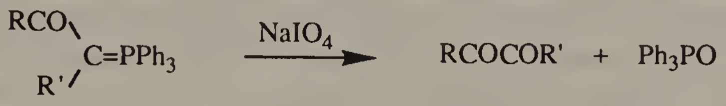


$$\mathrm{ArCH{=}PPh_3} \xrightarrow{\mathrm{Me_3SiCl}} \mathrm{(Ar)(Me_3Si)C{=}PPh_3} \xrightarrow{\mathrm{(PhO)_3P\,O_3}} \mathrm{ArCOSiMe_3} \qquad (5.12)$$

Davis and Chen[33] recently announced a very effective aprotic oxidation technique using N-sulfonyloxaziridines as the oxygen source. The advantages are that the reagents are storable, and even commercially available, and the yields are very high. The outcomes of the reaction are the same as for the triphenylphosphite ozonide method, that is, monosubstituted ylides afforded alkenes, disubstituted ylides afforded ketones, and the reaction proceeded effectively both with reactive and stabilized ylides. The reaction is thought to proceed by oxygen transfer to the ylide, followed by ejection of triphenylphosphine and resulting in formation of the carbonyl compound. The carbonyl compound is thought to be converted to alkene in a Wittig reaction as fast as it is formed. One equivalent of the oxidizing reagent is necessary for each equivalent of ylide, with half being used to cleave the ylide and half being used to oxidize the phosphine to phosphine oxide, a more easily separated byproduct.

Several other methods have been used to oxidatively cleave the carbanion–phosphorus bond in ylides. Nurrenbach et al.[34] found that 30% hydrogen peroxide would convert long chain precarotenoid phosphonium salts, in the presence of mild base, to the corresponding carotenoids in good yield. For example, a very dilute solution of triphenylretinylphosphonium hydrogen sulfate and hydrogen peroxide, when treated slowly with aqueous sodium carbonate, afforded an 80% yield of all-trans β-carotene. Wasserman and Vu[26] employed oxone, a commercial version of potassium peroxymonosulfate, as a selective oxidant usable in the presence of alkene groups. Rihter and Masnovi[35] found that a mixture of alkene and carbonyl was formed when monosubstituted ylides were oxidized with oxo(salen) chromium(V) complex. The formation of the mixture limited the usefulness of the reaction, but it was effective with disubstituted ylides which afforded ketones in good yield. Denney et al.[36] used peracetic acid to oxidize stabilized monosubstituted ylides to the corresponding alkenes, but the protic nature of the reaction and the lower yields make this procedure less useful than those mentioned above. The use of benzoyl peroxide as an aprotic oxidant turned out not to be straightforward or effective.[37] Other oxidants, such as ethyl nitrite,[38] lead tetraacetate,[39] potassium permanganate,[40] diacetoxyiodosobenzene[41] and lead dioxide[37] did react, but also were not reliable compared to the newer methods previously described.

Finally, Bestmann et al.[42] reported some usefulness of periodate as an ylide oxidant, although the method seems not to have been employed by others who are relying instead on the newer methods. α-Keto disubstituted ylides invariably produced α,β-dicarbonyl compounds upon reaction with sodium periodate under reflux conditions, with yields of 28–100% (Eq. 5.13). These conditions



$$\begin{matrix}\mathrm{RCO}\diagdown \\ \mathrm{R'}\diagup\end{matrix}\mathrm{C{=}PPh_3} \xrightarrow{\mathrm{NaIO_4}} \mathrm{RCOCOR'} + \mathrm{Ph_3PO} \qquad (5.13)$$

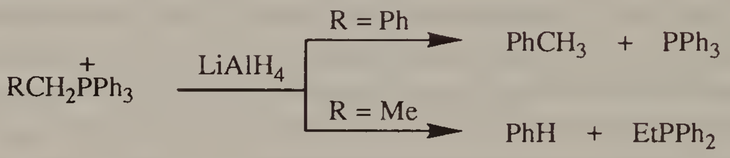
also afforded several α-ketoaldehydes, the aldehyde group surprisingly not reacting further with unchanged ylides. Use of the hydrohalide salt of a monosubstituted phosphonium ylide, converting it to the periodate, and then refluxing the solution with sodium ethoxide, sodium amide, or organolithiums to convert the phosphonium salt to the ylide, led to the formation of generally good yields of alkene, an outcome similar to that using other oxidants. This reaction was successful with both reactive and stabilized ylides, but only with monosubstituted ylides. Ring closures of bis-ylides to five-, six-, and seven-membered ring systems also were effected using this procedure.

In summary, the carbanion–phosphorus bond of phosphonium ylides can be cleaved by a number of oxidizing reagents, both protic and aprotic. Monosubstituted ylides invariably result in alkenes which are dimers of the carbanion portion of the ylide, apparently resulting from capture of initially formed aldehyde by unreacted ylide. Disubstituted ylides undergo the same cleavage to afford ketones, but the Wittig reaction does not occur with the ketone, resulting in its isolation as the major product.

## 5.3 REDUCTION OF YLIDES

A third method for cleaving the carbanion–phosphorus bond in ylides involves reduction. This method, however, is not as regiospecific as hydrolysis and oxidation methods, and the presence of other reducible groups in many ylides also leads to complications. Since it also is possible to reduce phosphonium salts, and since conversion of an ylide to its conjugate acid, the phosphonium salt, is facile, reduction of ylides can be approached either by direct reduction, or via the phosphonium salt. Both of these approaches are described. Reduction of phosphonium salts or phosphonium ylides usually leads to an alkane resulting from the cleaved group and a residual tertiary phosphine (under some workup conditions the phosphine is oxidized to the phosphine oxide). The problem usually is to predict which carbon–phosphorus bond will be cleaved.

Phosphonium salts are not reduced under catalytic conditions, and reduction reactions with sodium and liquid ammonia, sodium in benzene, or sodium in ethanol all proceeded in a somewhat unpredictable manner and in highly variable yields.[43,44] Lithium in ethylamine was an effective reductant, cleaving tributylphosphine from alkyltributylphosphonium salts.[45] The method of choice for reducing phosphonium salts is lithium aluminum hydride (LAH), with the resultant hydrocarbon and tertiary phosphine usually being obtained in high yield.[43] For example, dibenzyldimethylphosphonium bromide was cleaved to benzyldimethylphosphine in 81% yield, with the other product being toluene. Cleavage of a series of alkyltriphenylphosphonium salts revealed the fact that the group usually cleaved from phosphorus as a hydrocarbon was that group which could be the most stable carbanion.[46] Thus, the benzyl salt afforded toluene and triphenylphosphine whereas the ethyl salt afforded benzene and ethyldiphenylphosphine (Eq. 5.14).



$$\mathrm{RCH_2\overset{+}{P}Ph_3} \xrightarrow{\mathrm{LiAlH_4}} \begin{cases} \xrightarrow{\mathrm{R = Ph}} \mathrm{PhCH_3} + \mathrm{PPh_3} \\ \xrightarrow{\mathrm{R = Me}} \mathrm{PhH} + \mathrm{EtPPh_2} \end{cases}$$

(5.14)

However, isopropyltriphenylphosphonium bromide afforded a modest yield of triphenylphosphine, a fact as yet unexplained other than to suggest steric inhibition of attack at phosphorus.[47] Since most ylides are used as the triphenylphosphonium derivative, the effectiveness of LAH reduction of the conjugate acid as a regiospecific cleavage reaction depends on the ylide carbon being part of a potentially stable carbanion fragment, more stable than the competing phenyl carbanion.

The mechanism of the LAH reduction of phosphonium salts is not clearly understood. Bailey and Buckler[43] suggested that hydride attacked the carbon of the leaving group, ejecting phosphine. However, later workers[48] surmised that the mechanism was similar to that of hydrolysis whereby the nucleophile, in this instance hydride, attacked phosphorus to form a pentavalent species which then spontaneously lost the most stable carbanion. The latter proposal has been generally accepted, but the fact that optically active phosphonium salts, which are optically stable to LAH, are reduced to mainly racemic phosphines which also are optically stable to LAH, has led to the suggestion that pseudorotation of phosphorus must occur during the pentavalency stage.[49]

Electrolytic reduction of phosphonium salts also may lead to phosphorus–carbon cleavage and formation of a tertiary phosphine and an alkane. Which carbon–phosphorus bond is broken seems to depend somewhat on the choice of cathode material (mercury, lead, platinum, or copper), but mainly on the potential stability of the leaving group as a carbanion.[50] Thus, the order of preference for leaving seems to be benzyl > alkyl > phenyl ~ methyl.[51] Electrolytic reduction of optically active phosphonium salts afforded optically active phosphines. Maier[52] suggested that a pentavalent intermediate is not involved in this reduction—if it were, racemization would be expected as with LAH (see discussion above)—and that instead a two-electron transfer to phosphorus, followed by carbanion ejection, was more likely. Ylides also have been formed from phosphonium salts under electrolytic reduction conditions (see Section 4.3.3.2).

There have been several reports of the reduction of phosphonium ylides to tertiary phosphines and alkanes, but the technique leaves much to be desired because of low yields. Most reductions of triphenylphosphonium ylides result in cleavage of a phenyl–carbon bond and the formation of benzene and a tertiary phosphine (or its corresponding oxide) containing the ylide carbanion fragment (Eq. 5.15). Saunders and Burchman[53] found that methylene-, acetonylidene-, and phenacylidenetriphenylphosphorane all underwent cleavage at the

$$\mathrm{RCH{=}PPh_3} \xrightarrow{\mathrm{LiAlH_4}} \mathrm{RCH_2PPh_2} + \mathrm{C_6H_6} \tag{5.15}$$

phenyl–carbon bond when reacted with LAH. Gough and Trippett[44] reported that benzylidene- and isopropylidenetriphenylphosphorane also underwent phenyl–phosphorus cleavage with LAH. The mechanism of this cleavage must be different than that of phosphonium salts because of the different product mix, and cannot result in carbanion stabilization being an important factor in determining the leaving group. There may be initial complexation of the aluminum group with the ylide carbon, followed by direct substitution on phosphorus by hydride, expelling a phenyl group as a carbanion.

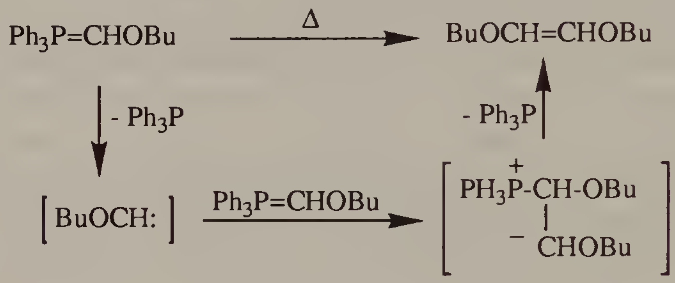
Schonberg et al.[54] found that Raney nickel and hydrogen reduced fluorenylidenetriphenylphosphorane to fluorene and triphenylphosphine, but the extent of this catalytic reduction reaction has not been fully explored. The same authors reported that zinc and hydrochloric acid would effect the same result. Similarly, Trippett and Walker[55] found that phenacylidenetriphenylphosphorane was reduced by zinc and acetic acid to triphenylphosphine and acetophenone, but that no reduction occurred with several other reducing reagents, including sodium borohydride and hydrogen over platinum. It is likely that the actual substrate in these acidic reductions was the conjugate acid, not the ylide.

In summary, reduction of phosphonium ylides as a means to cleave the carbanion–phosphorus bond is not a straightforward and fully predictable chemical process. If the ylide carbanion is substituted with electron-withdrawing groups that can withstand the reducing agent, it is best cleaved by conversion to the conjugate acid and then reduction with LAH. Alternatively, electrolytic reduction of the same conjugate acid may be feasible.

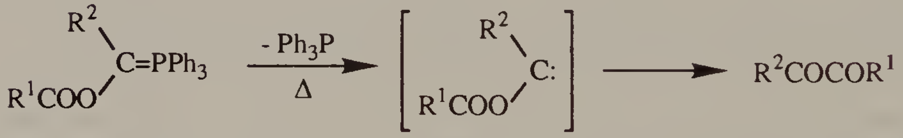
## 5.4 THERMAL DECOMPOSITION

In contrast to ylides of many other heteroatoms, phosphonium ylides have not usually shown a propensity for spontaneous thermal decomposition. Thus, it has usually not been essential to carry out reactions with these ylides at low temperatures for reasons of ylide stability, although many ylide reactions are performed at low temperature for other reasons. Three classes of thermal decomposition reactions are known and will be discussed in this section: decomposition to form transient carbenes, rearrangements, and elimination of phosphine oxide from *β*-ketoylides to form alkynes.

In their early work on trimethylphosphoniumfluorenylide Wittig and Laib[6] reported that the ylide was stable at least to 100°C in solution, in spite of the well-known tendency of fluorenyl derivatives to decompose to fluorenylidene. Nine years later the same laboratory reported that the *n*-butoxymethylide would decompose to a mixture of products, the major component being di-*n*-butoxyethylene, after heating to 45°C for 20 hours.[56] These products were accounted for by proposing fragmentation of the ylide to triphenylphosphine and *n*-butoxycarbene, the latter forming alkene by coupling with additional ylide to form a zwitterion which ejected phosphine (Eq. 5.16). In 1986 there was a second report of alkoxycarbene formation when the ylide solution temperature rose above – 30°C, the major product being a rearranged diketone (Eq. 5.17).[57] Below that temperature, the ylide was sufficiently stable to participate in a Wittig Reaction with aryl aldehydes. Nagao et al.[58] found that carbethoxytriphenylphosphorane was surprisingly, but not totally, resistant to thermal decomposition in degassed cyclohexene for 40 hours at 180°C. There was no increase in decomposition in the presence of added peroxide, but slightly more in the presence of added oxygen. What little decomposition occurred resulted in fracture of the ylide bond (P=C). In a similar vein Bestmann and Denzel[59] reported that cyclopropylidenetriphenylphosphorane decomposed to triphenylphosphine and allene only when heated above 150°C. Flash vacuum pyrolysis of α-sulfonyl phosphonium ylides resulted in P=C cleavage and formation of transient sulfonylcarbenes.[60]



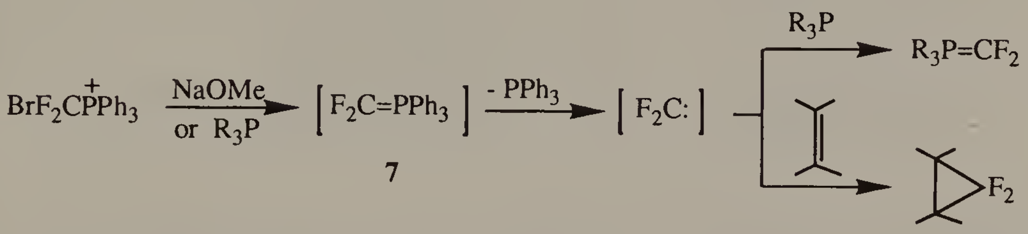
(5.16)



(5.17)

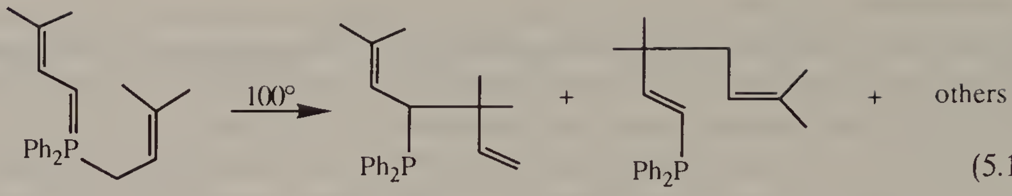
While dichloro- and dibromomethylenetriphenylphosphorane are well known and show no inherent instability, [61] it has been known for a long time that the difluoro analog (7) was rather different, and showed evidence of spontaneous dissociation to difluorocarbene. Fuqua et al.[62] finally were able to prepare the difluoro ylide in solution from decomposition of sodium chlorodifluoroacetate in the presence of triphenylphosphine, the ylide being trapped by Wittig Reaction with an aldehyde.

It became clear that while the difluoroylide (7) now could be prepared, it had a short lifetime and tended to dissociate to difluorocarbene. Burton's group[63] found that treatment of bromodifluorotriphenylphosphonium bromide with sodium methoxide presumably formed the ylide (7) which rapidly decomposed to difluorocarbene which was, in turn, trapped by tetramethylethylene to afford a 1,1-difluorocyclopropane (Eq. 5.18). In addition, the alternate method of reacting triphenylphosphine with dibromodifluoromethane, in the presence of fluoride ion as the base, produced an even higher yield of cyclopropanes. Bessard et al.[64] improved this technique even further as a means of :$CF_2$ generation. Burton et al.[65] showed that it was possible to transfer :$CF_2$ between phosphines. Using bromodifluorotriphenylphosphonium salt as the starting material, they proposed that ylide formation occurred by nucleophilic attack of added phosphine, followed by ylide dissociation to :$CF_2$, which then was trapped by a more nucleophilic phosphine (Eq. 5.18). Riesel et al.,[66] using a zinc amalgam reduction of the same starting phosphonium salt, also concluded that the decomposition reaction of the ylide (7) was favored. Finally, Dixon and Smart[67] calculated that the P–C bond is so long (3.54 Å), and that fluorine on carbanion tends to destabilize ylides so much (in this instance by about 25 kcal/mol), that the hypothetical molecule $H_3P{=}CF_2$ would behave more as a dissociated carbene than as an ylide, consistent with the experimental evidence cited above.



(5.18)

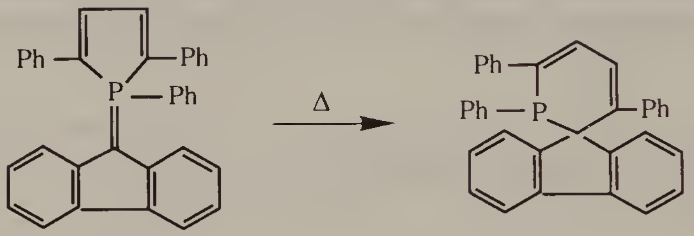
Because some ylides, most notably sulfur and nitrogen ylides, undergo rearrangements under relatively mild thermal conditions, the question naturally arises regarding rearrangements of phosphonium ylides. As a follow-up to their earlier work with sulfonium ylides, which demonstrated a proclivity for Steven's and 1,5-sigmatropic rearrangements, Baldwin and Armstrong[68] studied the stability of the red phosphonium ylide **8**. The ylide was stable to 90°C but at 100°C in benzene it was converted to a myriad of products, most of which seemed to be the result of radical dissociation and recombination. However, they did find some (7%) product (**9**) corresponding to a sigmatropic rearrangement and some (15%) product (**10**) which might arise from a homo-Steven's rearrangement. No Steven's rearrangement product was observed. Others[69] in



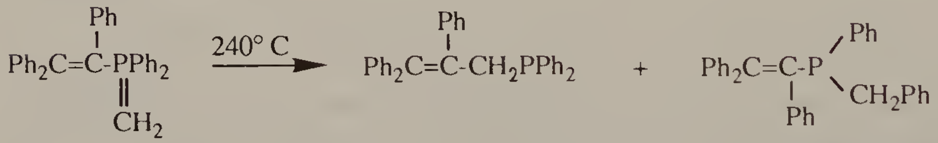
(5.19)

**8** **9** **10**

1972 claimed to have observed a Steven's rearrangement of methylenetrimesitylphosphorane, but the structural assignment of the product, and therefore the conclusion, later was found to be in error.[70] In 1984 the apparently first example of a Steven's rearrangement of a phosphonium ylide was reported, in which a heterocyclic ylide underwent ring expansion upon refluxing in toluene (Eq. 5.20).[71] Recently[72] a second "phospha-Steven's" rearrangement was reported (Eq. 5.21). Rearrangement of an "isolated" bis-ylide into a carbodiphosphorane has also been reported.[73]



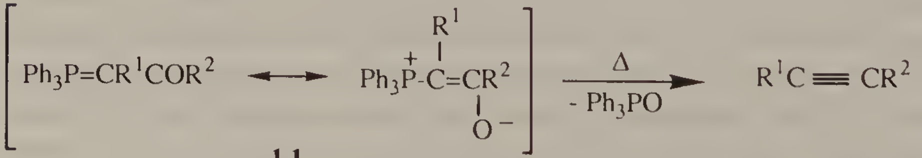
(5.20)



$$\underset{\underset{\displaystyle CH_2}{\|}}{Ph_2C{=}\overset{\overset{\displaystyle Ph}{|}}{C}\text{-}PPh_2} \xrightarrow{240^\circ C} Ph_2C{=}\overset{\overset{\displaystyle Ph}{|}}{C}\text{-}CH_2PPh_2 + Ph_2C{=}\underset{\underset{\displaystyle Ph}{|}}{C}\text{-}P\begin{smallmatrix}/Ph\\ \backslash CH_2Ph\end{smallmatrix}$$

(5.21)

The one category of phosphonium ylide that is predictably susceptible to thermal decomposition is the $\beta$-ketoylides, although even these require very high temperatures. Trippett and Walker[74] were the first to observe the reaction when they heated $\alpha$-phenylphenacylidenetriphenylphosphorane (**11**, $R^1 = R^2 = Ph$) to 300°C and obtained a 59% yield of diphenylacetylene and triphenylphosphine oxide (Eq. 5.22). The driving force for the reaction probably is the



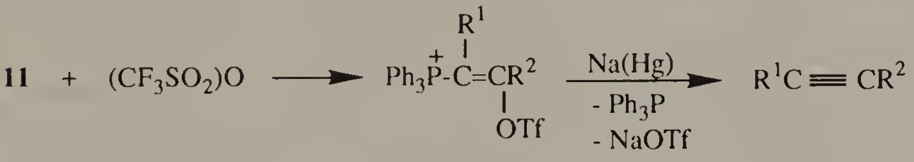
$$\left[ Ph_3P{=}CR^1COR^2 \longleftrightarrow Ph_3\overset{+}{P}\text{-}\overset{\overset{\displaystyle R^1}{|}}{C}{=}\underset{\underset{\displaystyle O^-}{|}}{C}R^2 \right] \xrightarrow[-\ Ph_3PO]{\Delta} R^1C{\equiv}CR^2$$

(5.22)

**11**

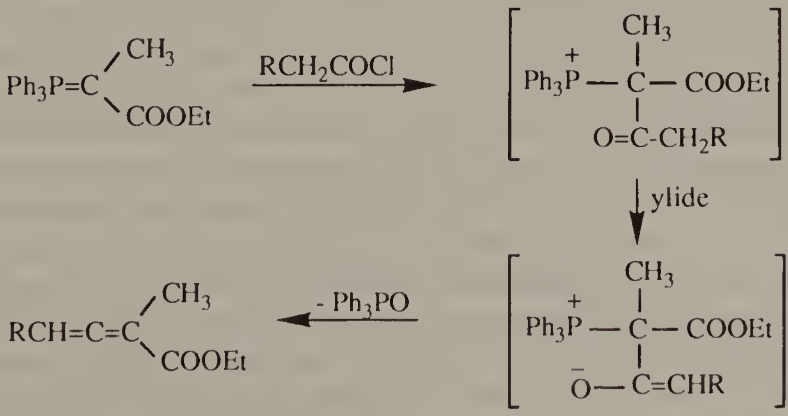
elimination of triphenylphosphine oxide, just as in the Wittig Reaction, of which this is a kind of intramolecular example. Many other examples of this thermolysis reaction followed and it soon was realized that the method provided an overall useful synthesis of alkynes, starting with readily available primary alkyl halides (to produce the initial monosubstituted ylide) and carboxylic acids (to produce the acyl halide which could acylate that ylide) to afford the necessary β-ketoylide (**11**). Successful reactions were obtained with the following kinds of ylides (**11**) to produce the corresponding disubstituted alkynes: $R^1$ = aryl;[74–76] $R^1$ = carboalkoxy;[75,77,78] $R^1$ = cyano;[78–80] $R^1$ = diphenylphosphonate;[81] $R^1$ = SeAr;[82] $R^1$ = SR or SAr.[83] There was virtually no limit on the nature of the $R^2$ group. However, a limitation soon appeared—the reaction was successful only with $R^1$ groups that were electron-withdrawing, thus making it impossible to prepare dialkylalkynes via this route.

Aitken and Atherton[84] later found that flash vacuum pyrolysis (750°C, $10^{-2}$ mm Hg) produced from 59 to 85% yields of alkynes where $R^1$ was hydrogen or an alkyl group. Bestmann et al.[85] devised a slight variant on the reaction which also permitted the preparation of dialkylalkynes. The same ylide starting material (**11**) was converted to an enol triflate ester in high yield, and reduction of the latter over long periods of time with sodium amalgam in THF gave 47–80% yields of alkyne, accompanied by triphenylphosphine and sodium triflate (Eq. 5.23). With these two newer techniques, the decomposition of β-ketoylides to alkynes is virtually without limit.



$$\mathbf{11} + (CF_3SO_2)O \longrightarrow Ph_3\overset{+}{P}\text{-}\underset{\text{OTf}}{\overset{R^1}{C}}=CR^2 \xrightarrow[\text{- Ph}_3\text{P} \;\; \text{- NaOTf}]{\text{Na(Hg)}} R^1C\equiv CR^2 \qquad (5.23)$$

In a slight variant of the alkyne synthesis it is possible to prepare allenes. A α,α-disubstituted ylide was acylated with an acyl halide having at least one α-hydrogen to produce a phosphonium salt. The latter was converted in situ, presumably by a second equivalent of starting ylide, to an enolate ion which then underwent Wittig-type elimination of triphenylphosphine oxide to afford allenes[86] (Eq. 5.24). It was later shown that the use of chiral ylides and chiral acyl halides resulted in partial kinetic resolution and the production of optically active allenes.[87] Using these reactions, an extensive series of allenic esters were prepared.



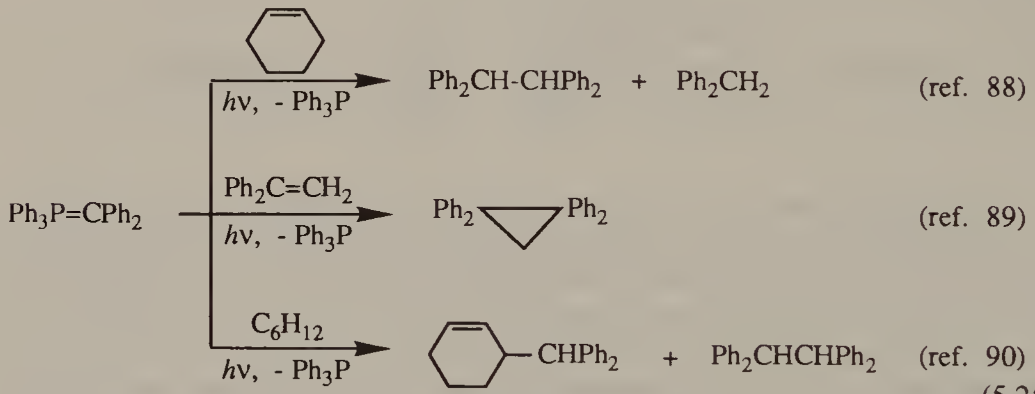
(5.24)

In summary, with the exception of $Ph_3P{=}CF_2$, thermal decomposition of phosphonium ylides usually is not spontaneous. It is only synthetically useful with $\beta$-keto ylides that can be converted to a wide variety of alkynes at high temperatures.

## 5.5 PHOTOLYTIC DECOMPOSITION

Relatively little work has been reported on the photochemical decomposition of phosphonium ylides, but the results available lead to a consistent picture of the chemistry involved. Factors important in determining the course of photochemical cleavage of phosphonium ylides seem to include (1) the nature of the carbanion substituents, and (2) the wavelength of the irradiation. The ylides normally cleave at the carbanion–phosphorus bond to produce a tertiary phosphine and a carbene.

Diphenylmethylenetriphenylphosphorane first was photolyzed by Tschesche[88] in 1965, and doing so in cyclohexene solution with a quartz immersion lamp led to an 83% yield of triphenylphosphine, a 64% yield of 1,1,2,2-tetraphenylethane, and a 33% yield of diphenylmethane (Eq. 5.25). It was proposed that the P=C ylide bond fractured to afford triphenylphosphine and diphenylcarbene, with the latter extracting hydrogen from cyclohexene at the allylic position to afford the diphenylmethyl and cyclohexenyl radicals. Three years later it was reported that the same ylide, when photolyzed at > 300 nm in the presence of 1,1-diphenylethylene, afforded triphenylphosphine and 1,1,2,2-tetraphenylcyclopropane in 73% yield[89] (Eq. 5.25). Still later, Nagao et al.[90] found that irradiation at > 320 nm in cyclohexene also afforded 3-diphenylmethylcyclohexene along with the triphenylphosphine and tetraphenylethane reported earlier by Tschesche[88] (Eq. 5.25). In all of the above instances it is clear that the ylidic P=C bond was cleaved, probably to produce a carbene, but it is not apparent from the experimental conditions why the cyclopropane-type adduct was obtained by only one of the three groups.

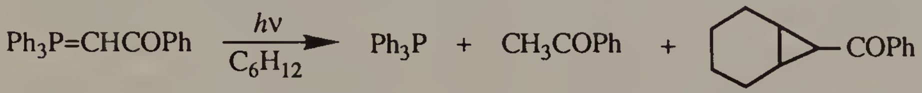


(5.25)

Nagao et al.[90] showed that at lower wavelength in a quartz apparatus the major cleavage of the same ylide was at a phenyl–phosphorus bond, affording a

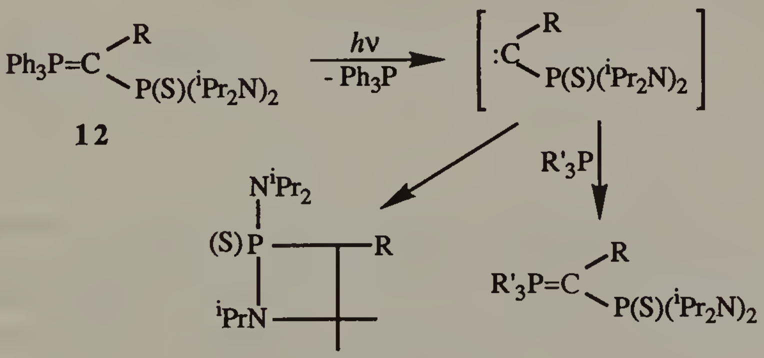
78% yield of benzene but with no triphenylphosphine formation. This same group[58] reported that carbethoxymethylenetriphenylphosphorane also underwent P-phenyl cleavage, producing a 100% yield of benzene and no triphenylphosphine, but also a number of insertion products which reflect the intermediacy of a triplet carbethoxymethylene group. The latter logically could only have arisen from P=C cleavage, leaving questions about the material balance reported and the fate of the phosphorus.

The nature of the carbene entity in ylide photolyses became clearer following the report by DaSilva et al.[91] that photolysis in pyrex vessels of phenacylidenetriphenylphosphorane in cyclohexene afforded a mixture of triphenylphosphine, acetophenone, and the cyclopropyl adduct (Eq. 5.26). The ratio of acetophenone to adduct was 1:1.2, but the ratio inverted to 6.5:1 when the irradiation was at 366 nm and was sensitized by Michler's ketone. It is likely that the former photolysis occurred by formation of the singlet carbene (PhCOCH:) which would be expected to add readily to the alkene, while the latter photolysis involved formation of the triplet carbene.



(5.26)

Recently Grutzmacher and his colleagues[92] found that the stabilized ylide **12** was cleaved photolytically (benzene solution, > 300 nm) at the P=C bond to form triphenylphosphine and a carbene intermediate which inserted into an isopropyl group to form a tetracycle (Eq. 5.27). If a phosphine more nucleophilic than triphenylphosphine, such as tris(dimethylamino)phosphine, was present it would capture the carbene intermediate to afford a new ylide, and none of the tetracycle was formed.[93] The trapping of a carbene by a phosphine is known as an ylide preparative method (see Section 4.3.1).



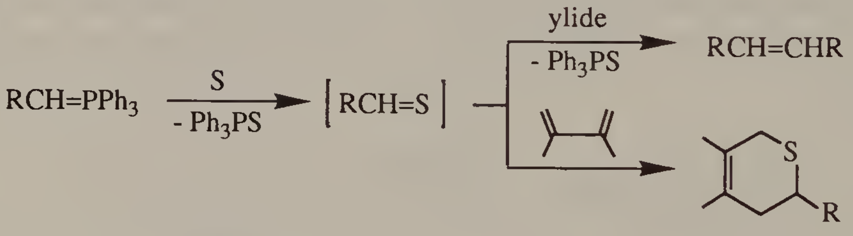
(5.27)

In summary, it is apparent that ylides can be photolytically cleaved in good yield at the carbanion–phosphorus (C=P) bond and the resultant carbene can be produced in the singlet or the triplet state. However, all of the examples reported involve ylides carrying powerful carbanion-stabilizing groups, so it cannot be stated with certainty that the photochemical cleavage applies to all types of phosphonium ylides. Caution is indicated in contemplating such a conclusion by the recent interesting observation that the unsulfidized precursor of **12**, a nonstabilized ylide, could not be photolyzed.[93]

## 5.6 MISCELLANEOUS CLEAVAGE REACTIONS

Just as phosphonium ylides reacted with oxygen (see Section 5.2) they have also been found to react with sulfur, selenium, and tellurium. In these instances the P=C bond is cleaved to afford a phosphine sulfide, selenide, or telluride and a thio-, seleno-, or tellurocarbonyl compound, these latter usually not being isolated but instead being trapped by external agents or by unconverted ylide. In these latter instances the product actually isolated is an alkene, resulting from overall "dimerization" of the carbanion portion of the starting ylide.

As early as 1919 the stabilized ylide diphenylmethylenetriphenylphosphorane was shown to react when heated with sulfur to afford triphenylphosphine sulfide and thiobenzophenone,[94] and in 1962 the corresponding fluorenylide similarly was converted to thiofluorenone.[95] These two thiones did not react with unconverted ylide to afford alkenes because of the unreactivity of the ylides. Later Glanzstoff[96] and then Magerlein and Meyer[97] found that using semistabilized ylides (R = phenyl, *p*-anisyl, 1-naphthyl-) in the reaction resulted in high yields of alkene and triphenylphosphine sulfide (Eq. 5.28). A nonstabilized ylide (R = Et) also reacted, but only in 28% yield. A paper by Tokunaga et al.[98] followed and reported attempts to react a variety of phosphonium ylides with sulfur, confirming Staudinger's work[94] but reporting confusing, generally unsuccessful, results with other ylides. Finally, Okuma et al.[99] showed by two separate experiments that a thiocarbonyl compound was, in fact, an initial product of the sulfur cleavage of ylides. The first experiment involved trapping it with 2,3-dimethyl-1,3-butadiene to form the thiacyclohexene (**13**), and the second involved preparing the thiocarbonyl by another route and showing that it reacted with the ylide to afford alkene (Eq. 5.28). The thioaldehydes also have been trapped in reactions with secondary amines to produce thioamides.[100] The use of sulfidation, rather than oxidation, to convert an ylide into an alkene may be advantageous in industrial processes because it is easier to recycle the phosphorus byproduct to phosphine when it is a sulfide rather than an oxide. The overall reaction seems very effective with monosubstituted semistabilized

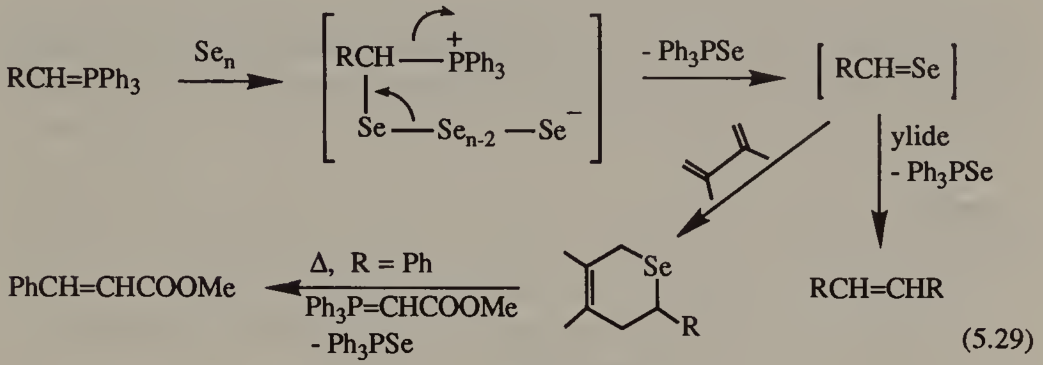


**13**

(5.28)

ylides, unsuccessful with highly stabilized ylides, and really has not been effectively explored with nonstabilized ylides. Reaction of stabilized ylides with benzopentathiepin also resulted in similar sulfur transfer to the ylides producing thioaldehydes or thioketones.[101]

Two research groups have recently, almost simultaneously, explored the reaction of phosphonium ylides with elemental selenium. Both stabilized and reactive ylides reacted with excess selenium to afford alkenes that were dimers of the carbanion portion of the starting ylide (Eq. 5.29). Okuma et al.[102] established the intermediacy of the selenocarbonyl compound, examples of which are rarely isolable, by trapping it with 2,3-dimethyl-1,3-butadiene in a Diels–Alder reaction, and by reduction with sodium borohydride to afford diphenyldiselenide. The same group[103] found that a retro Diels–Alder reaction of the adduct could be effected in the presence of another ylide which would trap the selenocarbonyl compound, forming alkene (Eq. 5.29).



(5.29)

The mechanism of the reaction was proposed [102, 103] to involve nucleophilic attack of the ylide carbanion on selenium to produce a zwitterionic intermediate, followed by ejection of triphenylphosphine, the selenocarbonyl, and selenium. Although not stated, presumably the phosphine would later react with selenium to form the isolated $Ph_3PSe$. Interestingly, the reaction also was found to proceed with only a catalytic quantity of selenium, in which case triphenylphosphine was a final product and its selenide was absent.[104] Since $Ph_3PSe$ should have been produced in the second step of the reaction (Eq. 5.29), its absence indicates that it must have been consumed in the reaction. This led to the observation[104] that triphenylphosphine selenide would serve as a catalyst in the conversion of ylide to alkene, although the Okuma group[103] was not able to effect such a reaction with stabilized ylides. The mechanism by which such a catalysis occurs has not even been the subject of speculation, and is unknown. The reaction of an ylide with a tertiary phosphine selenide, effecting the necessary transfer of selenium from phosphorus to carbon, would be unusual, to say the least!

The first preparation of a tellurobenzaldehyde recently was accomplished through the similar reaction of benzylidenetriphenylphosphorane with tellurium powder. The use of catalytic quantities of tellurium afforded the expected stilbene in 61% yield.[105]

In summary, tellurium, selenium, and sulfur can be used as alternatives to oxygen for the "dimerization" of the carbanion portion of phosphonium ylides to produce alkenes. In fact, the catalytic selenium or tellurium process may be especially advantageous in that it produced the phosphorus byproduct in a trivalent state, permitting its recycling. The overall result could be the conversion of alkyl halide to "dimeric" alkene via an ylide, avoiding the net consumption of phosphine (Eq. 5.30). In addition, phosphonium ylides now provide a convenient route to thio-, seleno-, and tellurocarbonyl compounds.

$$RCH_2Br \xrightarrow[\substack{\text{2. Base} \\ \text{3. Se or Te}}]{\text{1. } Ph_3P} RCH{=}CHR \qquad (5.30)$$

## REFERENCES

[1] Coffman, D. D.; Marvel, C. S. *J. Am. Chem. Soc.* **1929**, *51*, 3496.

[2] Freeman, B. H.; Lloyd, D.; Singer, M. I. C. *Tetrahedron* **1972**, *28*, 343.

[3] Krohnke, F. *Chem. Ber.* **1950**, *83*, 291.

[4] Ramirez, F.; Dershowitz, S. *J. Org. Chem.* **1957**, *22*, 41.

[5] Ramirez, F.; Madan, O.P.; Smith, C. P. *Tetrahedron Lett.* **1965**, 201.

[6] Wittig, G.; Laib, H. *Liebigs Ann. Chem.* **1953**, *580*, 57.

[7] Johnson, A. Wm.; LaCount, R. B. *Tetrahedron* **1960**, *9*, 130.

[8] Johnson, A. Wm. *J. Org. Chem.* **1959**, *24*, 282.

[9] Fenton, G. W.; Ingold, C. K. *J. Chem. Soc.* **1929**, 2342.

[10] Schlosser, M. *Angew. Chem.* **1962**, *74*, 291.

[11] VanderWerf, C. A.; McEwen. W. E.; Zanger, M. *J. Am. Chem. Soc.* **1959**, *81*, 3806.

[12] Aksnes, G.; Songstad, J. *Acta Chem. Scand.* **1962**, *16*, 1426.

[13] McEwen, W. E.; Kumli, K. F.; Blade-Font, A.; Zanger, M.; VanderWerf, C. A. *J. Am. Chem. Soc.* **1964**, *86, 2378.*

[14] McEwen, W. E. In *Topics in Phosphorus Chemistry*; Grayson, M. and Griffith, E. J., Eds.; Interscience: New York, 1965, Vol. 2, pp. 5–9.

[15] Grayson, M.; Keough, P. T. *J. Am. Chem. Soc.* **1960**, *82*, 3919.

[16] Aksnes, G.; Khalil, F.; Majewski, P. J. *Phosphorus Sulfur* **1977**, *3*, 157.

[17] Burgada, R.; El Khoshnieh, Y. O., Leroux, Y. *Phosphorus Sulfur* **1985**, *22*, 225.

[18] Mizrakh, L. I.; Polonskaya, L. Y. *J. Gen. Chem. USSR* **1990**, *59*, 1299.

[19] Marchenko, A. P.; Koldan, G. N.; Oleinik, V. O.; Zaltsman, I. S.; Pinchuk, A. M. *J. Gen. Chem. USSR* **1988**, *58*, 1485.

[20] Bestmann, H. J.; Schulz H. *Tetrahedron Lett.* **1960**, No. 4, 5.

[21] Bestmann, H. J.; Kratzer, O. *Chem. Ber.* **1963**, *96*, 1899.

[22] Bestmann, H. J.; Kratzer, O.; Armsen, R.; Maekawa, E. *Liebigs Ann. Chem.* **1973**, 760.

[23] Bestmann, H. J.; Haberlein, H.; Kratzer, O. *Angew. Chem.* **1964**, *76*, 226.

[24] Bestmann, H. J.; Pfuller, H. *Angew. Chem.* **1972**, *11*, 508.

[25] Jefford, C. W.; Barchietto, G. *Tetrahedron Lett.* **1977**, 4531.

[26] Wasserman, H. H.; Vu, C. B. *Tetrahedron Lett.* **1990**, *31*, 5205.

[27] Akasaka, T.; Sato, R.; Ando, W. *J. Am. Chem. Soc.* **1985**, *107*, 5539.

[28] Ramirez, F.; Mitra, R. B.; Desai, N. B. *J. Am. Chem. Soc.* **1960**, *82*, 5763.

[29] Wasserman, H. H.; Kelly, T. A. *Tetrahedron Lett.* **1989**, *30*, 7117.

[30] Wasserman, H. H.; Rotello, V. M.; Williams, D. R.; Benbow, J. W. *J. Org. Chem.* **1989**, *54*, 2785.

[31] Bestmann, H. J.; Kisielowski, L.; Distler, W. *Angew. Chem.* **1976**, *15*, 298.

[32] Ricci, A.; Fiorenza, M.; Degl'Innocenti, A.; Secani, G.; Dembech, A.; Witzgall, K.; Bestmann, H. J. *Angew. Chem.* **1985**, *24*, 1068.

[33] Davis, F. A.; Chen, B. C. *J. Org. Chem.* **1990**, *55*, 360.

[34] Nurrenbach, A.; Paust, J.; Pommer, H.; Schneider, J.; Schulz, B. *Leibigs Ann. Chem.* **1977**, 1146.

[35] Rihter, B.; Masnovi, J., *J. Chem. Soc. Chem. Commun.* **1988**, 35.

[36] Denney, D. B.; Smith, L. S.; Song, J.; Rossi, C. J.; Hall, C. D. *J. Org. Chem.* **1963**, *28*, 778.

[37] Denney, D. B.; Valega, T. M. *J. Org. Chem.* **1964**, *29*, 440.

[38] Zbiral, E.; Fenz, L. *Monatsh. Chem.* **1965**, *96*, 1983.

[39] Zbiral, E.; Werner, E. *Tetrahedron Lett.* **1966**, 2001.

[40] Zbiral, E.; Rasberger, M. *Tetrahedron* **1968**, *24*, 2419.

[41] Zbiral, E.; Werner, E. *Monatsh. Chem.* **1966**, *97*, 1797.

[42] Bestmann, H. J.; Armsen, R.; Wagner, H. *Chem. Ber.* **1969**, *102*, 2259.

[43] Bailey, W. J.; Buckler, S. A. *J. Am. Chem. Soc.* **1957**, *79*, 3567.

[44] Maier, L. In *Organic Phosphorus Compounds*, Kosolapoff, G. M. and Maier, L., Eds.; Wiley-Interscience: New York, 1972; Vol. 1, Chapter 1, p. 56.

[45] Axelrod, E.; Milne, G. M.; Van Tamelen, E. E. *J. Am. Chem. Soc*, **1970**, *92*, 2139.

[46] Gough, S. T. D.; Trippett, S. *J. Chem. Soc.* **1961**, 4263.

[47] Maier, L. In *Progress in Inorganic Chemistry*, Cotton, F. A. Ed.; Interscience: New York, 1963; Vol. 5, Chapter 2, p. 106.

[48] McEwen, W. E.; Keldsen, G.; Blade-Font, A.; Zanger, K.; VanderWerf, C. A. *J.Am. Chem. Soc.* **1964**, *86*, 2378.

[49] Horner, L.; Ernst, M. *Chem. Ber.* **1970**, *103*, 318.

[50] Horner, L.; Haufe, J. *Chem. Ber.* **1968**, *101*, 2903.

[51] Horner, L.; Mentrup, A. *Liebigs Ann. Chem.* **1961**, *646*, 65.

[52] Reference 47, p. 110.

[53] Saunders, M.; Burchman, G. *Tetrahedron Lett.* **1959**, no. 1, 8.

[54] Schonberg, A.; Brosowski, K. H.; Singer, E. *Chem. Ber.* **1962**, *95*, 2984.

[55] Trippett, S.; Walker, D. M. *J. Chem. Soc.* **1961**, 1266.

[56] Wittig, G.; Boll, W. *Chem. Ber.* **1962**, *95*, 2526.

[57] Anders, E.; Clark, T.; Gaßner, T. *Chem. Ber.* **1986**, *119*, 1350.

[58] Nagao, Y.; Shima, K.; Sakurai, H. *Bull. Chem. Soc. Jpn.* **1970**, *34*, 1885.

[59] Bestmann, H. J.; Denzel, T. *Tetrahedron Lett.* **1966**, 3591.

[60] Aitken, R. A.; Drysdale, M. J. *J. Chem. Soc. Chem. Commun.* **1991**, 512.

[61] Speziale, A. J.; Ratts, K. W. *J. Am. Chem. Soc.* **1962**, *84*, 854.

[62] Fuqua, S. A.; Duncan, W. G.; Silverstein, R. M. *J. Org. Chem.* **1965**, *30*, 1027.

[63] Burton, D. J.; Naae, D. G. *J. Am. Chem. Soc.* **1973**, *95*, 8467.

[64] Bessard, Y.; Muller, U.; Schlosser, M. *Tetrahedron* **1990**, *46*, 5213; *Tetrahedron* **1991**, *47*, 7323.

[65] Burton, D. J.; Naae, D. G.; Flynn, R. M.; Smart, B. E.; Britelli, D. R. *J. Org. Chem.* **1983**, *48*, 3616.

[66] Riesel, L.; Vogt, H.; Kolleck, V. *Z. Anorg. Allg. Chem.* **1989**, *574*, 143.

[67] Dixon, D. A.; Smart, B. E. *J. Am. Chem. Soc.* **1986**, *108*, 7172.

[68] Baldwin, J. E.; Armstrong, M. C. H. *J. Chem. Soc. Chem. Commun.* **1970**, 631.

[69] Heydenreich, F.; Mollach, A.; Wilke, G.; Dreeskamp, H.; Hoffmann, E. G.; Schroth, G.; Seevogel, K.; Stempfle, W., *Isr. J. Chem.* **1972**, *10*, 293.

[70] Schmidbaur, H.; Schnatterer, S. *Chem. Ber.* **1983**, *116*, 1947.

[71] Gilheany, D. G.; Kennedy, D. A.; Malone, J. F.; Walker, B. J. *J. Chem. Soc. Chem. Commun.* **1984,** 1217.

[72] Maercker, A.; Bsata, A.; Jung, R. *Main Group Met. Chem.* **1987**, *10*, 11.

[73] Wohlleben, A.; Schmidbaur, H. *Angew. Chem.* **1977**, *16*, 417.

[74] Trippett, S.; Walker, D. M. *J. Chem. Soc.* **1959**, 3874.

[75] Gough, S. T. D.; Trippett, S. *Proc. Chem. Soc.* **1961**, 302.

[76] Kobayashi, Y.; Yamashita, K.; Takahashi, K.; Kuroda, H.; Kumadaki, I. *Tetrahedron Lett.* **1982**, 343.

[77] Markl, G. *Chem. Ber.* **1961**, *94*, 3005.

[78] Gough, S. T. D.; Trippett, S. *J. Chem. Soc.* **1962**, 2333.

[79] Rehman, H.; Rao, J. M. *Synth. Commun.* **1987**, *17*, 1119; *Tetrahedron* **1987**, *43*, 5335.

[80] Huang, Y. Z.; Shen, Y. C.; Ding, W.; Zheng, J. *Tetrahedron Lett.* **1981**, *22*, 5283.

[81] Shen, Y.; Lin, Y.; Xin, Y. *Tetrahedron Lett.* **1985**, *26*, 5137.

[82] Braga A. L.; Comasseto, J. V.; Petragnini, N. *Synthesis* **1984**, 240.

[83] Braga A. L.; Comasseto, J. V.; Petragnini, N. *Tetrahedron Lett.* **1984**, *25*, 111.

[84] Aitken, R. A.; Atherton, J. I. *J. Chem. Soc. Chem. Commun.* **1985**, 1140.

[85] Bestmann, H. J.; Kumar, K.; Schaper, W. *Angew. Chem.* **1983**, *22*, 167.

[86] Bestmann, H. J.; Hartrung, H. *Angew. Chem.* **1963**, *2*, 214; *Chem. Ber.* **1966**, *99*, 1198.

[87] Tomoskozi, I.; Bestmann, H. J. *Tetrahedron Lett.* **1964**, 1293; *Tetrahedron* **1968**, *24*, 3299.

[88] Tschesche, H. *Chem. Ber.* **1965**, *98*, 3318.

[89] Ritter, A.; Kim, B. *Tetrahedron Lett.* **1968**, 3449.

[90] Nagao, Y.; Shima, K.; Sakurai, H. *Tetrahedron Lett.* **1970**, 2221.

[91] DaSilva, R. R.; Toscano, V. G.; Weiss, R. G. *J. Chem. Soc. Chem. Commun.* **1973**, 567.

[92] Sicard, G.; Grutzmacher, H.; Baceiredo, A.; Fischer, J.; Bertrand, G. *J. Org. Chem.* **1989**, *54*, 4426.

[93] Grutzmacher, H. *Z. Naturforsch.* **1990**, *45B*, 170.

[94] Staudinger, H.; Meyer, J. *Helv. Chim. Acta* **1919**, *2*, 635.

[95] Schonberg, A.; Brosowski, K. H.; Singer, E. *Chem. Ber.* **1962**, *95*, 2144.

[96] Glanzstoff, A. G. Netherlands Patent Application 6612260; *Chem. Abstr.* **1967**, *67*, 90516.

[97] Magerlein, H.; Meyer, G. *Chem. Ber.* **1970**, *103*, 2995.

[98] Tokunaga, H.; Akiba, K.; Inamoto, N. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 506.

[99] Okuma, K.; Tachibana, Y.; Sakata, J. I.; Komiya, T.; Kaneko, I.; Komiya, Y.; Yamasaki, Y.; Yamamoto, S. I.; Ohta, H. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 4323.

[100] Okuma, K.; Komiya, Y.; Ohta, H. *Chem. Lett.* **1988**, 1145; *Bull. Chem. Soc. Jpn.* **1991**, *64*, 2402.

[101] Sato, R.; Satoh, S. I. *Synthesis* **1991**, 785.

[102] Okuma, K.; Sakata, J.; Tachibana, Y.; Honda, T.; Ohta, H. *Tetrahedron Lett.* **1987**, *28*, 6649.

[103] Okuma, K.; Komiya, Y.; Kaneko, I.; Tachibana, Y.; Iwata, E.; Ohta, H. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 1653.

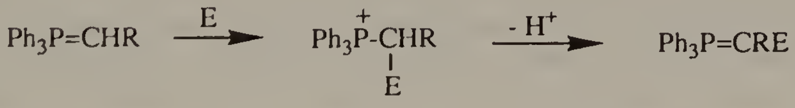
[104] Erker, G.; Hock, R.; Nolte, R. *J. Am. Chem. Soc.* **1988**, *110*, 624.

[105] Erker, G.; Hock, R. *Angew. Chem.* **1989**, *28*, 179.

# 6

# REACTIONS OF PHOSPHONIUM YLIDES II. WITH ELECTROPHILIC REAGENTS

Ylides have the potential to react with almost any electrophile in view of their strong nucleophilicity, and this chapter describes such reactions with trivalent boron compounds, halogens, nontransition metal halides, alkylating reagents, acylating reagents, carbenes, diazo compounds (including diazonium salts), and sulfur and nitrogen oxides. The major use of such reactions is for converting relatively simple ylides into more complex ylides which subsequently may be used in synthesis reactions (Eq. 6.1). This sequence provides a very effective means for placing a particular substituent at a particular point in a synthetic target molecule.



$$Ph_3P{=}CHR \xrightarrow{E} Ph_3\overset{+}{P}\text{-}\underset{\displaystyle E}{\underset{|}{C}}HR \xrightarrow{-\,H^+} Ph_3P{=}CRE \qquad (6.1)$$

## 6.1 REACTION WITH TRIVALENT BORON COMPOUNDS

Hawthorne[1] was the first to discover that phosphonium ylides would react with diborane to afford a 1:1 adduct (Eq. 6.2) which could be recrystallized and

$$Ph_3P{=}CHR \xrightarrow{B_2H_6} Ph_3\overset{+}{P}\text{-}CHR\text{-}\overset{-}{B}H_3 \qquad (6.2)$$

handled in the presence of water and air, but which was hydrolyzed by hydrochloric acid to methyltriphenylphosphonium chloride, hydrogen, and boric acid. Substituted ylides, such as the ethylide and the benzylide, reacted in

---

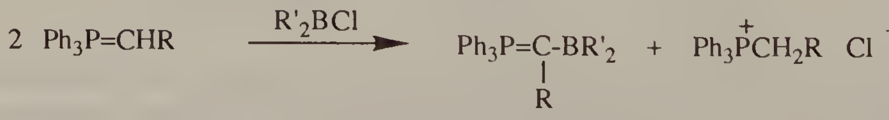
*Ylides and Imines of Phosphorus*, Edited by A. William Johnson.
ISBN 0-471-52217-1 © 1993 John Wiley & Sons, Inc.

the same manner. More recently Schmidbaur et al.[2] have studied the analogous adducts obtained from reaction of borane–tetrahydrofuran complex with a series of trialkylphosphoniummethylides, with the trialkyl groups being methyl, ethyl, isopropyl, and *t*-butyl. The same group[3] reported the X-ray structural analysis of the adduct $Me_3P^+{-}CH_2{-}BH_3^-$ and found that the bond angles about phosphorus were closer to tetrahedral in the adduct than in the precursor ylide, and that the P–$CH_2$ distance of 1.756 Å was typical of phosphonium salts, much longer than the ylidic P=$CH_2$ bond (1.64 Å). The $^{13}C$ NMR spectra showed evidence of relief in the tri-*t*-butyl ylide adduct with $BH_3$ of the rotational hindrance which had been detected in the uncomplexed ylide.[2]

Hawthorne[4] and Seyferth and Grim[5] both reported the reaction of triphenylphosphoniummethylide with substituted boranes, the former with methyl- and phenylborane, and the latter group with triphenylborane, to form similar adducts. Both groups also showed that amine complexes of the boranes would react with ylides, the latter displacing the amines. Three groups[5–7] have shown that $BF_3$ gas or $BF_3$ etherate also reacted with phosphonium ylides in a similar manner to form stable adducts. Lithium aluminum hydride reduction of the $BF_3$ adduct of triphenylphosphoniummethylide resulted in its conversion to the $BH_3$ adduct.[5] Reaction of the $BF_3$ adduct with $BBr_3$ or $BI_3$ resulted in displacement of $BF_3$ and formation of the new adduct,[6] and the $BCl_3$ adduct also could be formed directly from $BCl_3$ and the ylide.[5] Thus, adducts of all four of the trihaloboranes are known.

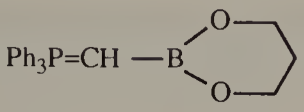
Only a few higher boranes have been reacted with ylides. Lower boranes, such as $B_3H_7$, formed crystalline 1:1 zwitterionic adducts ($Ph_3P^+{-}CHR{-}B_3H_7^-$)[8] with a carbon–boron bond, a triangular boron structure, and two bridging hydrogen atoms.[9] Higher boranes, such as $B_5H_9$[10] and $B_9H_{13}$,[11] did not form adducts with phosphonium ylides. Instead, they were deprotonated by the ylide acting as a base to form crystalline salts, such as $Ph_3P^+{-}CH_3B_5H_8^-$, which were stable in air and moisture. The first reaction of a phosphonium ylide with a carborane resulted in cage opening by ylide attack at boron,[12] resulting in a zwitterion whose structure was shown to contain a phosphorus–carbon distance of 1.776 Å, close to that reported by Schmidbaur et al.[3] for the $BH_3$ adduct.

Bestmann and Arenz[13] found that phosphonium ylides would displace chloride from a dialkylchloroborane to afford a new boro-substituted phosphonium ylide after subsequent deprotonation (transylidation) (Eq. 6.3). In a



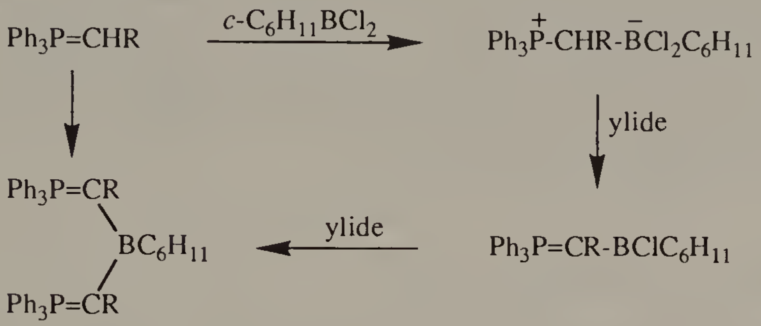
$$2\ Ph_3P{=}CHR \xrightarrow{R'_2BCl} Ph_3P{=}\underset{\displaystyle R}{\underset{|}{C}}{-}BR'_2 + Ph_3\overset{+}{P}CH_2R\ \ Cl^- \qquad (6.3)$$

similar manner Matteson and Majumda[14] reacted methylenetriphenylphosphorane with a monochloroborate to afford a precipitate, which, when treated with lithium diisopropylamide (LDA), presumably afforded the boro-ylide (**1**) as evidenced by its double "Wittig-type" reaction with aldehydes or ketones.



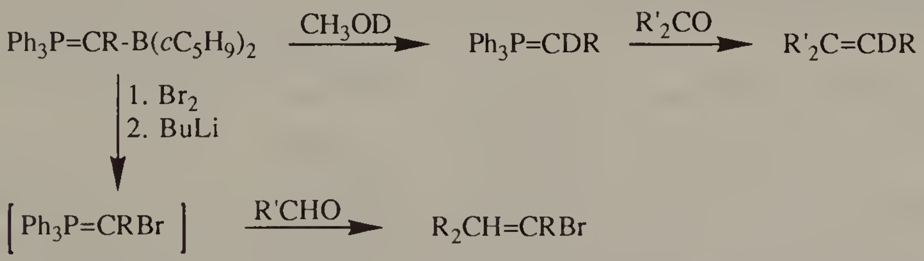
**1**

Alkylation of phosphonium ylides with dichlorocyclohexylborane resulted in an initial adduct which was isolable.[15] Treatment with additional ylide resulted in proton abstraction to afford a boro-ylide which reacted with yet additional ylide to afford a bis-ylide (Eq. 6.4). The latter also could be obtained directly from the starting materials by using a fourfold excess of ylide.



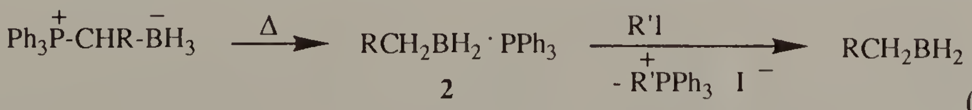
(6.4)

Boron-substituted phosphonium ylides have found few uses to date. Recently it has proved possible to cleave the ylides with O-deuteriomethanol to reform the parent phosphonium ylide, but with deuterium in place of hydrogen.[16] Use of these labelled ylides in Wittig reactions has led to deuterio-alkenes (Eq. 6.5). Similarly, cleavage of the boro-ylide with bromine afforded an α,α-dibromophosphonium salt which, with butyllithium, produced an α-bromoylide that could be used in a Wittig reaction (Eq. 6.5).[16]



(6.5)

At an early date Koster and Rickborn[17] reported that the adduct of $BH_3$ and triphenylphosphoniummethylide rearranged upon heating to 130°C (Eq. 6.6),



(6.6)

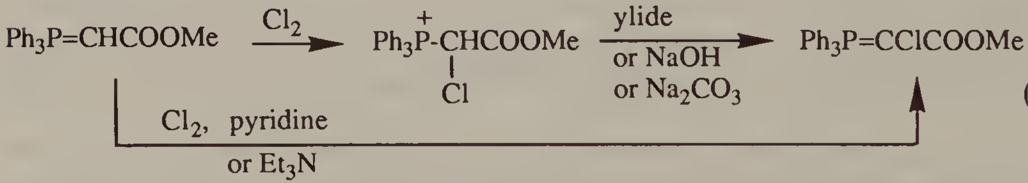
probably to **2**, with the isolated products being triphenylphosphine–borane, trimethylborane, and triphenylphosphine, probably the result of disproportionation. Starting with the benzylide adduct they obtained similar disproportionation products, but reaction of the solution of **2** with hydrogen peroxide led to benzyl alcohol, indicating a borane had been produced in the rearrangement. More recently, Bestmann et al.[18] confirmed these results and refined the process to enable isolation and purification of the rearranged borane–phosphine complex (**2**). The rearranged borane could be freed from the phosphine by precipitating the latter as its phosphonium salt, and subsequent chemistry could be performed on the borane. For example, it could be used in hydroboration of alkenes and dienes. No mechanistic speculation has been advanced for the rearrangement of the ylide adduct.

It is clear that ylides can be a route to variously substituted monoalkylboranes, $RR'CH{-}BH_2$. The limits of the nature of the R and R′ groups, which come from the original ylide, are not known. Thus far, no rearrangements have been reported on ylide adducts of mono- or dialkyl boranes. Further, only one unsuccessful attempt has been documented of attempted rearrangement of adducts of ylides with higher boranes.[8]

## 6.2 REACTION WITH HALOGENS

Phosphonium ylides have been shown to react with a variety of halogenating agents, providing direct accessibility to α-halo ylides. This route to such ylides is important since access via the normal salt method of ylide preparation is unpredictable because of the tendency of many bases to attack halogen rather than proton in an α-haloalkylphosphonium salt (see Section 4.1.3.2). However, most halogenations have been studied with stabilized ylides, usually β-keto or α-carbalkoxy ylides, and relatively little is known about the behavior of other types of ylides. α-Haloylides are important precursors to vinyl halides through the Wittig reaction (Eq. 6.7).

$$Ph_3P{=}CHR \xrightarrow{X_2} Ph_3P{=}CXR \xrightarrow{R'CHO} R'CH{=}CXR \qquad (6.7)$$



$$Ph_3P{=}CHCOOMe \xrightarrow{Cl_2} Ph_3\overset{+}{P}\text{-}\underset{\underset{Cl}{|}}{C}HCOOMe \xrightarrow[\text{or NaOH} \atop \text{or Na}_2\text{CO}_3]{\text{ylide}} Ph_3P{=}CClCOOMe \qquad (6.8)$$

$$Ph_3P{=}CHCOOMe \xrightarrow[\text{or Et}_3\text{N}]{Cl_2,\ \text{pyridine}} Ph_3P{=}CClCOOMe$$

Reaction of carbomethoxymethylenetriphenylphosphorane with chlorine in benzene solution lead to a mixture of chloroylide and the conjugate acid of the original ylide[19] (Eq. 6.8). This resulted from nucleophilic attack of ylide on chlorine, presumably forming a chlorophosphonium salt intermediate, which underwent deprotonation (transylidation) by the starting ylide, which was more basic.

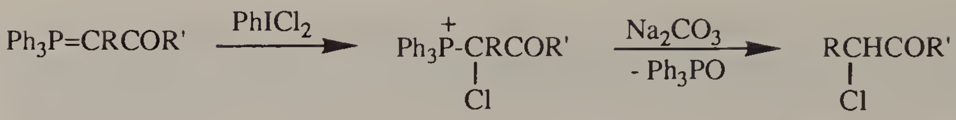
To avoid "loss" of one-half of the starting ylide through its serving as a base, three approaches subsequently have been developed. The first involved the use of excess chlorine, which has the effect of chlorinating both the starting ylide and the conjugate phosphonium salt, such that the product was completely α-chlorophosphonium salt, usually in high yield.[20, 21] The latter then was converted to α-chloroylide using sodium carbonate or sodium hydroxide. The second approach utilized pyridine or triethylamine as external bases present in the original reaction mixture at low temperatures, these bases serving to deprotonate the initially formed salt.[20] There were no complications from double chlorination. A third approach was discovered by Denney and Ross,[20] who found that use of *t*-butyl hypochlorite as a chlorinating agent resulted in complete conversion of a stabilized ylide to α-chloro ylide, the reagent serving both as a source of chlorine and as the source of internal base (*t*-butoxide) for conversion of chlorophosphonium salt to chloro ylide.

Bromination of stabilized phosphonium ylides appears to proceed identically with the chlorination. Markl[19] obtained a 77% yield of one-half equivalent of α-bromo ylide, but Speziale[21] and Grigorenko et al.[22] obtained nearly quantitative yields of the α-bromophosphonium salts which subsequently were converted to α-bromoylide using hydroxide bases.

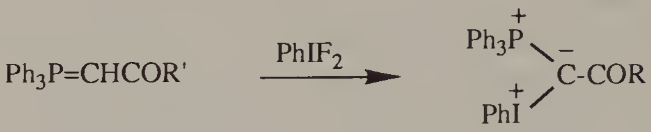
Iodination of stabilized phosphonium ylides proceeds similarly, with Markl[19] isolating the α-iodo ylide directly, but only one-half equivalent thereof. Grigorenko et al.[23] and Iman et al.[24] both isolated the intermediate α-iodophosphonium salts in high yield, and separately converted them to α-iodo ylides with external bases. Interestingly, Markl[19] found that treatment of the α-bromo ylide with methanolic potassium iodide resulted in high yield conversion to the α-iodo ylide. Iman et al.[23] used the iodination process as a means of converting triphenylphosphoniumphenacylide to a series of benzoylalkynes, proceeding through the iodo ylide and a Wittig reaction to a vinyl iodide, followed by elimination of HI, all in a "two-pot" reaction (Eq. 6.9). Corey et al. did likewise to prepare alkynes, but also reacted the vinyl iodides with cuprate reagents to produce trisubstituted alkenes.[25]

$$\mathrm{Ph_3P{=}CHCOPh} \xrightarrow{\mathrm{I_2}} \mathrm{Ph_3\overset{+}{P}CHICOPh} \xrightarrow[\mathrm{RCHO}]{\mathrm{K_2CO_3}} \mathrm{RC{\equiv}CCOPh} \qquad (6.9)$$

Halogenation also occurs with other reagents. Markl,[19] Corey et al.,[25] and Zbiral and Rashberger,[26] found that phenyliodide dichloride was an effective chlorinating agent, but again one half of the ylide was lost owing to transylidation. Starting with a disubstituted ylide, which could be tailor-made, the latter group carried out the chlorination, which stopped at the phosphonium salt stage because of the absence of α-hydrogen. The salt was hydrolytically cleaved under mild conditions to afford good yields of α-chloroketones (Eq. 6.10). Moriarty et al.,[27] using the similar phenyliodide difluoride, found that fluorination did not occur, the ylide instead attacking the iodine atom, resulting in the formation of double (iodonium–phosphonium) ylides (Eq. 6.11).

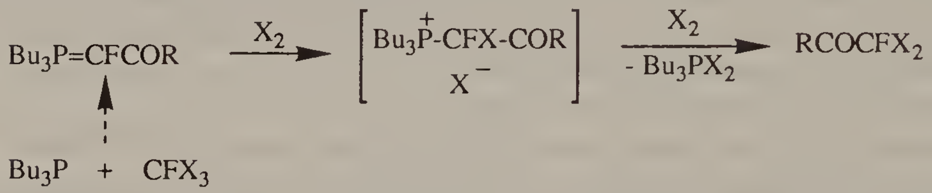


$$Ph_3P{=}CRCOR' \xrightarrow{PhICl_2} Ph_3\overset{+}{P}\text{-}\underset{\underset{Cl}{|}}{C}RCOR' \xrightarrow[-\,Ph_3PO]{Na_2CO_3} R\underset{\underset{Cl}{|}}{C}HCOR' \qquad (6.10)$$



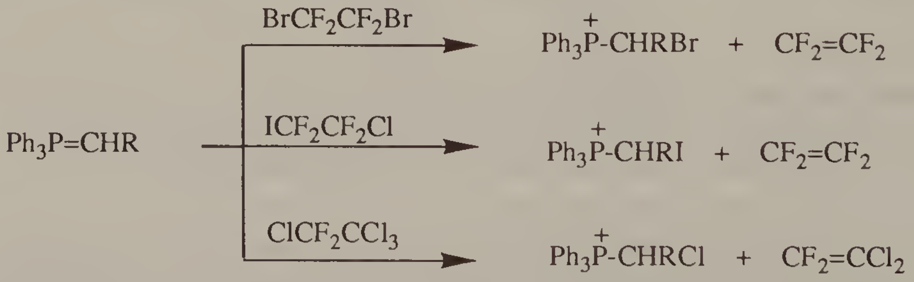
$$Ph_3P{=}CHCOR' \xrightarrow{PhIF_2} \begin{matrix} Ph_3\overset{+}{P} \diagdown \\ \phantom{x}\overset{-}{C}\text{-COR} \\ Ph\overset{+}{I} \diagup \end{matrix} \qquad (6.11)$$

The Burton group[28] recently reported a combination of the Zbiral cleavage approach mentioned above[26] and halogenation to prepare a series of α-fluoro-α,α-dihaloketones. Intermediate in the process was an α-fluoro ylide, which, upon bromination or chlorination, probably was converted to the α-halophosphonium salt which then was cleaved with more halogen to the final product (Eq. 6.12). The net effect was to use the intermediacy of an ylide and its halogenation to fuse an acyl halide and a perhalogen compound.



$$\underset{\underset{Bu_3P \;+\; CFX_3}{\uparrow}}{Bu_3P{=}CFCOR} \xrightarrow{X_2} \left[\begin{matrix} Bu_3\overset{+}{P}\text{-}CFX\text{-}COR \\ X^- \end{matrix}\right] \xrightarrow[-\,Bu_3PX_2]{X_2} RCOCFX_2 \qquad (6.12)$$

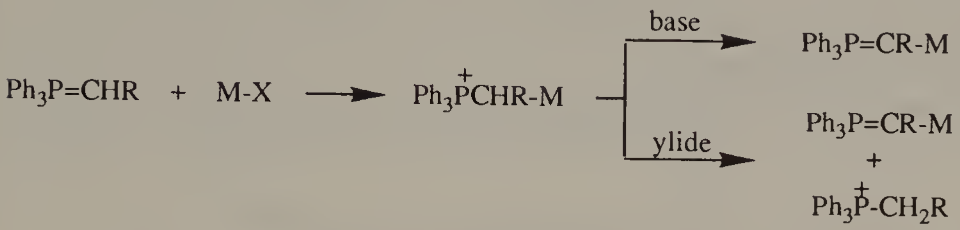
As mentioned earlier, most of the α-halophosphonium ylides known are those in which the ylide is highly stabilized, usually with a carbonyl group. It simply is not known whether direct halogenation is a generally effective route to other ylides. Li and Hu[29] reported an interesting, and very mild, alternative process for halogenating triphenylphosphoniumalkylides to produce α-halophosphonium salts. Reaction of the alkylide with a series of iodo-, bromo-, and chlorofluorocarbons resulted in attack of the ylide carbanion on halogen, ejecting a perhalocarbanion which in turn lost halide to form a perhalo, usually perfluoro, alkene (Eq. 6.13). Use of excess halide minimized transylidation reactions, resulting in yields of 70–93%, although the unsubstituted ylide ($Ph_3P{=}CH_2$) gave poor yields.



$$Ph_3P{=}CHR \begin{cases} \xrightarrow{BrCF_2CF_2Br} Ph_3\overset{+}{P}\text{-}CHRBr \;+\; CF_2{=}CF_2 \\ \xrightarrow{ICF_2CF_2Cl} Ph_3\overset{+}{P}\text{-}CHRI \;+\; CF_2{=}CF_2 \\ \xrightarrow{ClCF_2CCl_3} Ph_3\overset{+}{P}\text{-}CHRCl \;+\; CF_2{=}CCl_2 \end{cases} \qquad (6.13)$$

## 6.3 REACTION WITH METAL HALIDES

In view of their nucleophilicity, phosphonium ylides would be expected, and are known to react with a wide variety of metalloid and metal halides, usually carrying out a displacement reaction resulting in a new phosphonium salt. This is known as a metallation reaction. In a number of instances these new salts have been deprotonated to form metal-substituted phosphonium ylides (Eq. 6.14). In some cases this deprotonation occurs spontaneously through "transylidation" effected by the basicity of the original unconverted ylide, but only in those instances in which the original ylide is more basic than the new metal-substituted ylide.

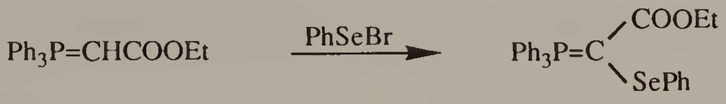


$$\mathrm{Ph_3P{=}CHR} + \mathrm{M{-}X} \longrightarrow \mathrm{Ph_3\overset{+}{P}CHR{-}M} \begin{cases} \xrightarrow{\text{base}} \mathrm{Ph_3P{=}CR{-}M} \\ \xrightarrow{\text{ylide}} \mathrm{Ph_3P{=}CR{-}M} + \mathrm{Ph_3\overset{+}{P}{-}CH_2R} \end{cases} \qquad (6.14)$$

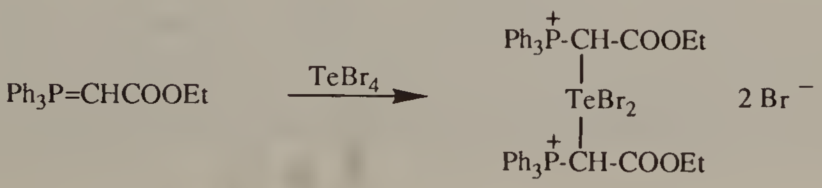
The metallation reaction is known with a wide variety of metal halides, and in some instances the products of these reactions have become very useful and significant, but in many other cases no special significance has resulted. In this section are discussed such metallation reactions; it is organized into subsections, each of which deals with elements of a particular group from the periodic table, proceeding from right (group VIA) to left (group IB), from the less "metallic" to the more "metallic" elements. In this chapter the reaction of phosphonium ylides with transition metals is not discussed, saving that discussion for a later chapter on the topic because of its prominence over the last 15 years.

### 6.3.1 Group VIA Halides

Group VIA halides and ylides react uneventfully to result in ordinary substitution products. Petragnini and Campos[30] found that phenylbromoselenide reacted with a carbethoxy ylide to afford selenated ylide, transylidation having occurred (Eq. 6.15). The metallated ylide was less nucleophilic and basic than the original ylide and too unreactive to undergo a Wittig reaction. More recently Minami et al.[31] reported the same selenation reaction using allylic ylides which resulted in a similar selenation, but at the $\gamma$-carbon of the ylide. Metallation of the carbethoxy ylide with tellurium tetrabromide afford a bis-phosphonium salt (Eq. 6.16), the result of displacement of two of the four bromine atoms.[30]



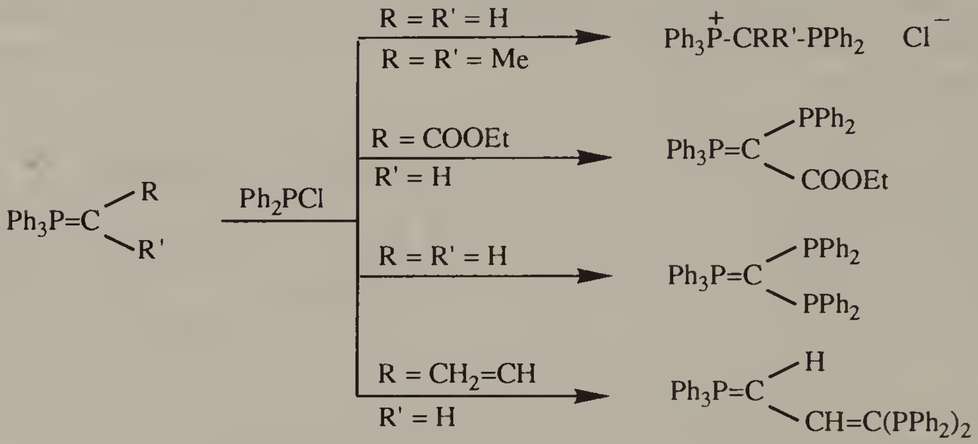
$$\mathrm{Ph_3P{=}CHCOOEt} \xrightarrow{\text{PhSeBr}} \mathrm{Ph_3P{=}C}\begin{array}{l} \diagup \mathrm{COOEt} \\ \diagdown \mathrm{SePh} \end{array} \qquad (6.15)$$



$$\mathrm{Ph_3P{=}CHCOOEt} \xrightarrow{\mathrm{TeBr_4}} \begin{array}{c} \mathrm{Ph_3\overset{+}{P}{-}CH{-}COOEt} \\ | \\ \mathrm{TeBr_2} \\ | \\ \mathrm{Ph_3\overset{+}{P}{-}CH{-}COOEt} \end{array} \quad 2\,\mathrm{Br}^- \qquad (6.16)$$

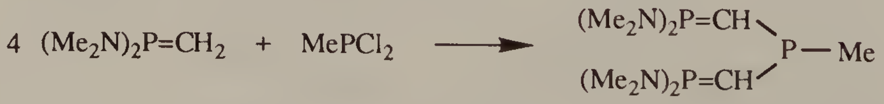
### 6.3.2 Group VA Halides

Numerous phosphorus halides react readily with phosphonium ylides, often providing entry to bis-ylides of various types (Eq. 6.17). Seyferth and Brandle[32] were the first to report the reaction of a phosphonium ylide (R = R′ = H) with a monohalophosphine, diphenylbromophosphine, and to isolate the phosphonium salt. Issleib and Linder[33] effected the same reaction with a disubstituted ylide (R = Me or Ph, R′ = Me) and diphenylchlorophosphine. The latter group also found that using a monosubstituted stabilized ylide (R = COOEt, R′ = H) afforded the diphenylphosphino-substituted ylide as a result of transylidation. Reaction of four equivalents of the unsubstituted ylide (R = R′ = H) with three equivalents of $Ph_2PCl$ afforded a new diphosphino ylide. Several other groups also found that replacement of hydrogen from the ylide carbon was quite straightforward, regardless of the P-substituents or the ylidic carbon substituents.[34–36] Issleib and Lischewski[37] obtained similar results with the vinyl-substituted ylide (R = $-CH{=}CH_2$, R′ = H), except that metallation occurred on the γ-carbon rather than the α-carbon (Eq. 6.17).

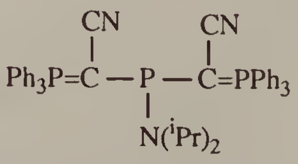


(6.17)

Dihalophosphines also reacted with ylides, and in all instances both halogens were displaced by the ylide acting as a nucleophile. In some instances, only the diphosphonium salt was obtained,[32] but in others conversion to a new ylide was effected[36, 38] by transylidation. Thus, four equivalents of a methylide reacted with one equivalent of methyldichlorophosphine to afford a bis-ylide (Eq. 6.18),[38] and in a similar manner a cyanomethylide afforded a very stable bis-ylide (**3**).[34]



(6.18)



$$Ph_3P{=}\overset{CN}{\overset{|}{C}}-\underset{\underset{N(^iPr)_2}{|}}{P}-\overset{CN}{\overset{|}{C}}{=}PPh_3$$

**3**

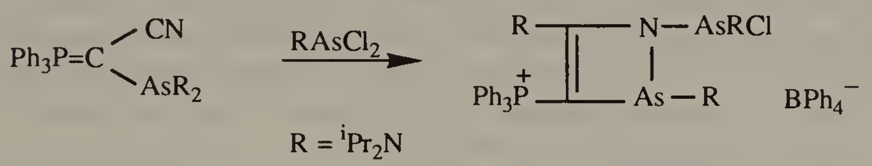
Phosphorus trichloride has been shown to undergo triple substitution by ylides, with transylidation resulting in the formation of tri-ylides.[37, 38] For example, six equivalents of triphenylphosphoniummethylide afforded $(Ph_3P{=}CH)_3P$. Phosphorus oxychloride afforded the similar ylide $(Ph_3P{=}CH)_3PO$ in a reaction parallel to that of diphenylphosphinous chloride which afforded the stabilized ylide $(Ph_3P{=}C(P(O)Ph_2)_2$.[39]

Recently, Markl and Bauer[40] reported the first example of the reaction of phosphonium ylides with an arylhalophosphine, ArPHCl, in which the initial step appeared to be normal metallation to a phosphonium salt. However, this was followed by an ylide-catalyzed elimination of triphenylphosphine to afford a phosphaalkene (Eq. 6.19). This may be a useful synthesis of the latter group of compounds which are presently of considerable interest.

$$Ph_3P{=}CRR' \xrightarrow{ArPHCl} \left[Ph_3\overset{+}{P}\text{-}CRR'\text{-}PHAr\right] \xrightarrow{-\,Ph_3P} RR'C{=}PAr \qquad (6.19)$$

Haloarsines reacted with ylides in a manner similar to the halophosphines. Although the Schmidbaur group[35] had prepared an arsino-substituted phosphonium ylide in 1968 by a desilylation reaction, it was not until 1984 that the metallation route involving transylidation was reported (Eq. 6.20).[41] Grutzmacher and Pritzkow[42] recently reported a metallation using a dichloroarsine which resulted in an unusual ring closure (Eq. 6.21).

$$Ph_3P{=}CH_2 \xrightarrow{Ph_2AsCl} Ph_3P{=}CHAsPh_2 \longrightarrow Ph_3P{=}C(AsPh_2)_2 \qquad (6.20)$$



(6.21)

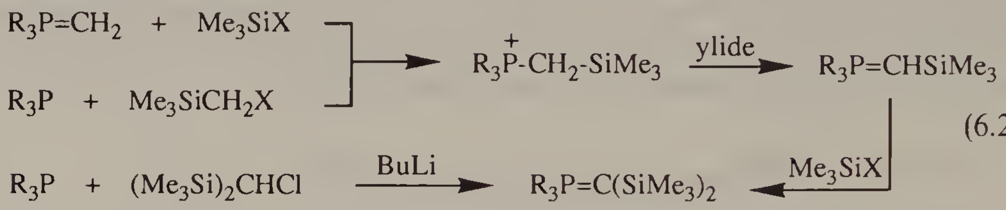
Metallation of triphenylphosphoniummethylide with dimethylbromostibine afforded the expected phosphonium salt, with no report of subsequent ylide formation.[32] Use of the lithio anion of trimethylphosphoniummethylide with dimethylchlorostibine afforded the antimony-substituted ylide resulting from transylidation (Eq. 6.22).[33] The new ylide underwent disproportionation upon heating to form a diantimony-substituted phosphonium ylide.

(6.22)

### 6.3.3 Group IVA Halides

This section deals with the reaction of phosphonium ylides with halides of Group IVA elements: C, Si, Ge, Sn, and Pb. However, the reaction of phosphonium ylides with carbon halides is discussed as alkylation reactions in Section 6.4.

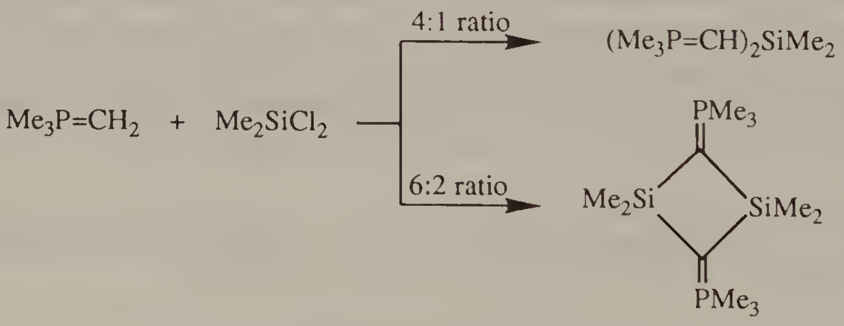
Considerable chemistry is now known of silylphosphonium ylides, the entry to which usually is via metallation (i.e., silylation) of a phosphonium ylide. This reaction is of considerable significance because of the subsequent desilylation and trans-silylation reactions which are known, including the preparation of salt-free ylides (see Chapter 4). Seyferth and Grim[43] reacted bromotrimethylsilane with triphenylphosphoniummethylide to obtain the expected salt (Eq. 6.23),



(6.23)

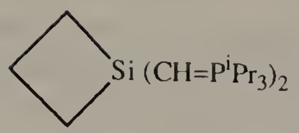
which they also obtained from bromomethyltrimethylsilane and triphenylphosphine. Later[44, 45] it was found that the salt could be converted into the silylated ylide using triphenylphosphoniummethylide as the base, and shortly thereafter the silylated ylide was prepared directly from the original ylide and the silyl chloride by using two equivalents of ylide and relying on transylidation.[46] Reaction of the silylated ylide (R = $CH_3$) with additional trimethylsilyl chloride afforded a bis-silylated ylide,[46] which also could be obtained by direct ylide preparation. Many examples are known of silylation of phosphonium ylides, and these reactions have been reviewed.[47–49]

The reaction of phosphonium ylides with dialkyldihalosilanes can produce bis-ylides or cyclic ylides. The reaction of four equivalents of trimethylphosphoniummethylide with one equivalent of dimethyldichlorosilane afforded an acylic bis-ylide, but the same reaction in a 6:2 ratio of reactants resulted in a cyclic bis-ylide,[50] with the authors proposing that the former reacted with a second equivalent of $Me_2SiCl_2$ to afford the latter after transylidation (Eq. 6.24).



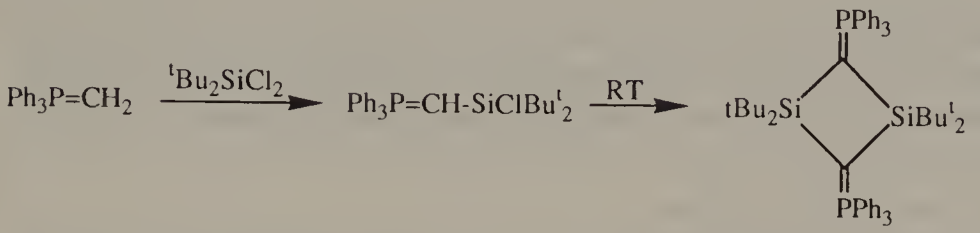
(6.24)

The same group[51] later found that 1,1-dichlorosilacyclobutane reacted with tri(iso-propyl)phosphoniummethylide to afford the bis-ylide **4**. Reaction of triphenylphosphoniummethylide with di-*t*-butyl-dichlorosilane afforded a silylated ylide which, on standing, spontaneously dehydrohalogenated and cyclized



**4**

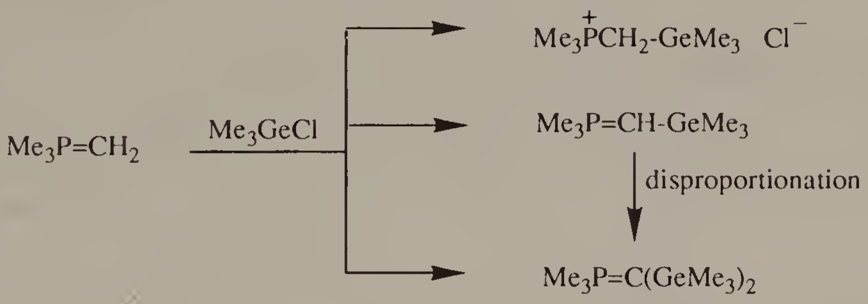
to a bis-ylide (Eq. 6.25). On the other hand, treatment of a similar silyl ylide with *t*-butyllithium resulted in intramolecular silylation, affording a cyclic ylide (Eq. 6.26).[52]



(6.25)

(6.26)

Germanylation of ylides is very similar to silylation, with one equivalent of triphenylphosphoniummethylide reacting with triphenylgermanyl bromide to afford the phosphonium salt.[43] Use of two equivalents afforded the corresponding germanyl-substituted ylide.[35] Use of three equivalents of ylide and two equivalents of trimethylgermanyl chloride resulted in a bis-germanyl ylide.[46, 53] The mono-germanyl ylide probably underwent disproportionation to the digermanyl ylide (Eq. 6.27).[35]

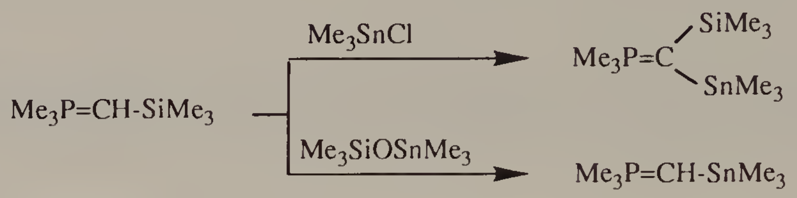


(6.27)

Reaction of trimethylstannyl bromide with triphenylphosphoniummethylide gave the monosubstituted salt, and use of dimethyldibromostannane resulted in a double displacement.[43] Use of three equivalents of ylide with two equivalents of trimethylstannyl chloride resulted in transylidation and formation of the distannyl-substituted ylide (Eq. 6.28).[46] Trimethylphosphonium(trimethylsilyl)-

$$Ph_3P{=}CH_2 \xrightarrow{Me_3SnCl} Ph_3P{=}C(SnMe_3)_2 \qquad (6.28)$$

methylide gave a mixed ylide via normal metallation and transylidation when reacted with trimethylstannylchloride,[34] but when reacted with a siloxane trans-silylation resulted to afford a stannyl-substituted ylide (Eq. 6.29).[35] The same



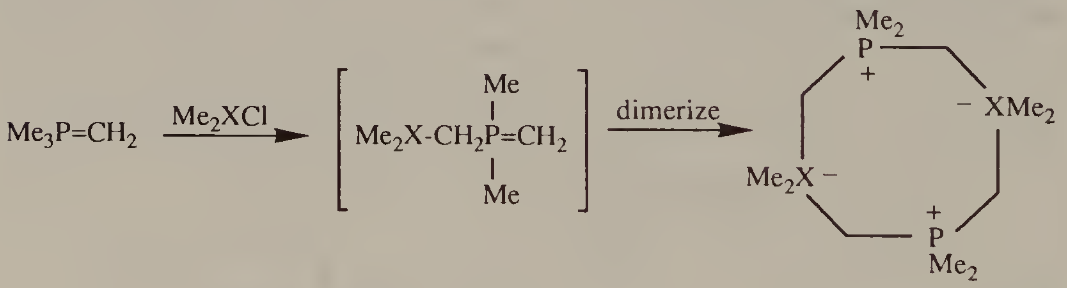
(6.29)

trans-silylation reaction was used with the trimethyllead siloxane, and probably produced the mono-lead-substituted ylide, but disproportionation probably occurred, resulting in the isolation of a di-lead-substituted ylide.[53]

### 6.3.4 Group IIIA–IB Halides

*6.3.4.1* ***Group IIIA Halides.*** The reaction of organoboron halides with phosphonium ylides was discussed in Section 6.1. Several authors found that metallation occurred and new mono- and di-boron-substituted ylides resulted.[13–15] No aluminum metallations have been reported.

Schmidbaur and Fuller[54] found that dimethylchloro-gallium, -indium, and -thallium all were metallated similarly using two equivalents of trimethylphosphoniummethylide. Each formed an eight-membered ring complex, probably the result of dimerization of the new ylide product of transylidation (Eq. 6.30). The dimers are electronically similar to the zwitterionic borane complexes (Eq. 6.2) discussed in Section 6.1 and to the known aluminum complex.[55]



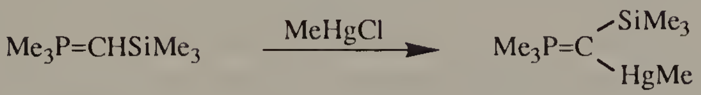
(6.30)

*6.3.4.2* ***Group IIB Halides.*** Wittig and Schwarzenbach[56] found that zinc chloride metallated two equivalents of triphenylphosphoniummethylide to $Ph_3P^+–CH_2–Zn–CH_2–{}^+PPh_3\ 2Cl^-$, and that the same double salt could be obtained from triphenylphosphine and bis-chloromethylzinc. No cadmium metallations have been reported.

Mercuric compounds have long been known to metallate phosphonium ylides. Mercuric bromide reacted with two equivalents of triphenylphosphoniummethylide to afford a mercury bis-phosphonium salt[43] (Eq. 6.31), but

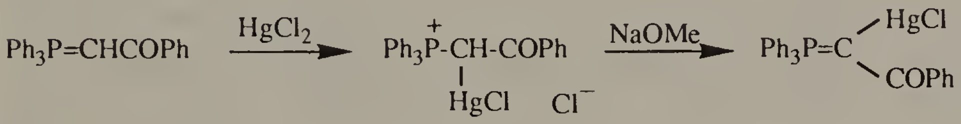
$$Ph_3P{=}CH_2 \xrightarrow{HgBr_2} (Ph_3\overset{+}{P}CH_2)_2Hg \quad 2\,Br^- \qquad (6.31)$$

$$Me_3P{=}CHSiMe_3 \xrightarrow{HgI_2} Me_3\overset{+}{P}\text{-}CH_2\text{-}HgI \quad I^- \qquad (6.32)$$



$$Me_3P{=}CHSiMe_3 \xrightarrow{MeHgCl} Me_3P{=}C(SiMe_3)(HgMe) \qquad (6.33)$$

mercuric iodide stopped at the monosubstitution stage when trans-silylated with a silyl ylide (Eq. 6.32).[34] The same silyl ylide reacted with methylchloromercury without trans-silylation (Eq. 6.33).[32] Nesmeyanov and his colleagues extensively studied the reaction of stabilized ylides with mercuric chloride, finding that phenacylidenetriphenylphosphorane afforded a complex which could be converted to a mercurated ylide (Eq. 6.34).[57,58] The complex could be



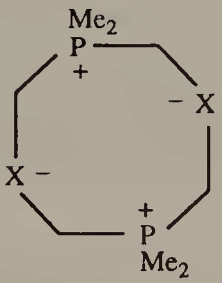
$$Ph_3P{=}CHCOPh \xrightarrow{HgCl_2} Ph_3\overset{+}{P}\text{-}\underset{HgCl}{CH}\text{-}COPh \quad Cl^- \xrightarrow{NaOMe} Ph_3P{=}C(HgCl)(COPh) \qquad (6.34)$$

caused to revert to unsubstituted ylide in a polar solvent, and would even undergo a Wittig reaction in a solvent such as DMF. Similar complexes could be obtained with a variety of β-keto or β-carbalkoxy ylides, and such complexes underwent O-acylation, rather than the C-acylation undergone by the uncomplexed ylide.[59]

***6.3.4.3 Group IB Halides.*** After others failed to identify the product of reacting trimethylsilylmethylenetrimethylphosphorane with cuprous iodide,[34] Schmidbaur et al.[60] obtained the dimeric complex (**5a**) from cuprous chloride and

**5**

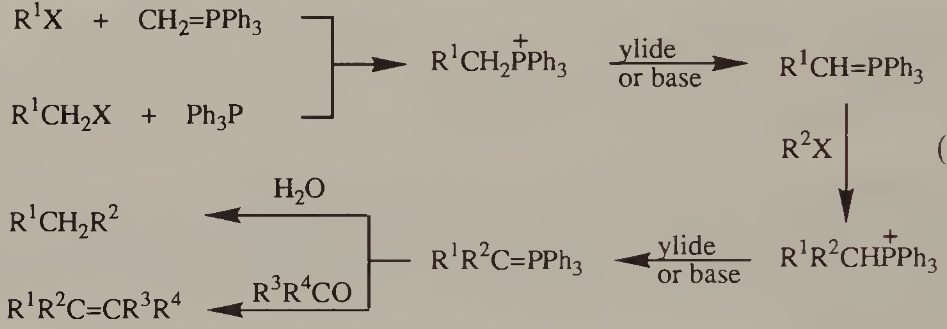
(**a**) X = Cu
(**b**) X = Ag
(**c**) X = Au



trimethylphosphoniummethylide in benzene at room temperature and the similar silver complex (**5b**) was obtained from trimethylphosphine·silver chloride. Trimethylphosphine·gold chloride[61] complex initially formed a 1:1 adduct ($Me_3P{\cdot}AuCH_2P^+Me_3Cl^-$), but with additional ylide the 1:2 adduct [$(Me_3P^+CH_2)_2Au\ 2Cl^-$] was formed. Reaction of $Me_3PAuCl$ with either of these adducts, or with excess starting ylide, produced the cyclic gold complex (**5c**). No chemistry has been reported for these complexes.

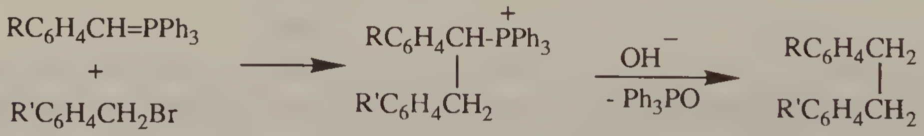
## 6.4 ALKYLATION

Alkylation of phosphonium ylides is one of the most widely explored and useful means involving ylides for elaborating carbon frameworks previously only obtained with difficulty. The reaction depends on the nucleophilicity of the ylide carbanion and attack at an electrophilic carbon, usually an alkyl halide. The reaction is used for two major purposes, as illustrated in Eq. 6.35: (1) to use the ylide carbon as a carbanion to which may be attached different alkyl groups, the phosphonium group eventually being cleaved by methods discussed in Chapter 5, and (2) to prepare mono- and disubstituted ylides for subsequent use in the Wittig reaction, thereby sequentially controlling the nature of the substituents on one end of the eventual double bond. Many ingenious applications of these two basic approaches have been discovered and applied to acyclic and cyclic syntheses.



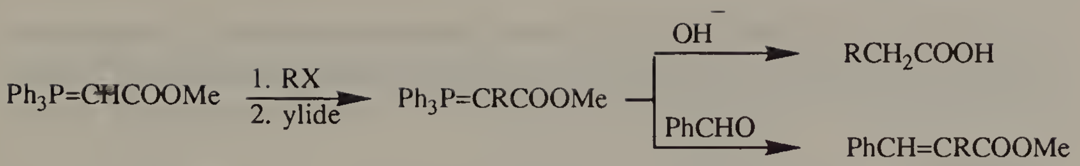
(6.35)

Alkyl halides, especially bromides, but also chlorides and iodides, seem to be the favorite alkylating agent, with the alkyl groups usually being primary, occasionally secondary, but virtually never tertiary because of competing elimination reactions. As part of their initial identification of ylides as a species, Wittig and Rieber[62] alkylated trimethylphosphoniummethylide with methyl iodide and obtained ethyltrimethylphosphonium iodide. Isopropyl iodide also afforded the corresponding phosphonium salt.[63] A series of triphenylphosphoniumbenzylides were alkylated in good yield by a series of benzyl halides, and the resulting phosphonium salts were de-phosphorylated to afford a series of 1,2-di-(substituted-phenyl)ethanes[64] (Eq. 6.36).



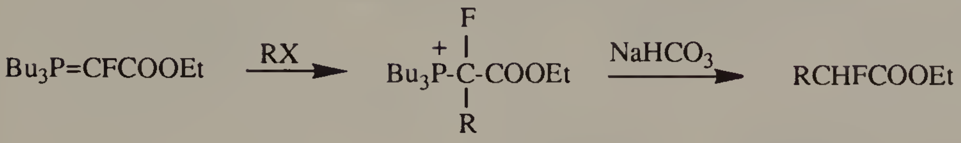
(6.36)

Bestmann and Schulz[65] alkylated triphenylcarbomethoxymethylenephosphorane with a series of primary alkyl bromides and obtained the corresponding alkylated ylides in good yield, the result of a transylidation reaction, necessitating the use of two equivalents of starting ylide. Hydrolysis of the new ylides afforded a series of alkane carboxylic acids, while reaction of the ylides with



$$\mathrm{Ph_3P{=}CHCOOMe} \xrightarrow[\text{2. ylide}]{\text{1. RX}} \mathrm{Ph_3P{=}CRCOOMe} \begin{cases} \xrightarrow{\mathrm{OH^-}} \mathrm{RCH_2COOH} \\ \xrightarrow{\mathrm{PhCHO}} \mathrm{PhCH{=}CRCOOMe} \end{cases}$$

(6.37)

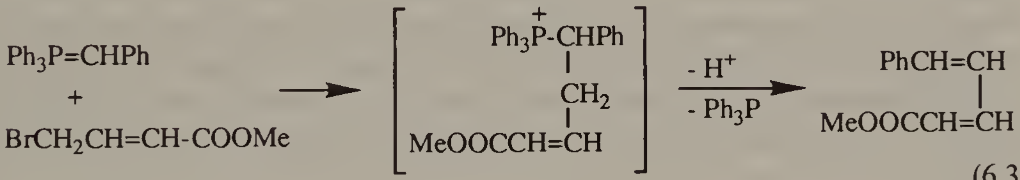


$$\mathrm{Bu_3P{=}CFCOOEt} \xrightarrow{\mathrm{RX}} \mathrm{Bu_3\overset{+}{P}\text{-}\underset{R}{\overset{F}{C}}\text{-}COOEt} \xrightarrow{\mathrm{NaHCO_3}} \mathrm{RCHFCOOEt}$$

(6.38)

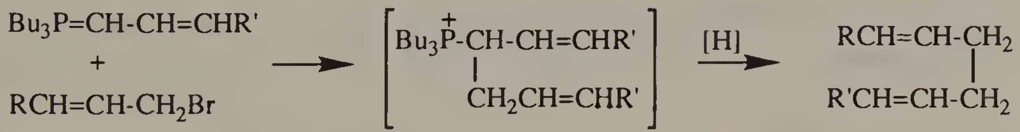
benzaldehyde provided a series of substituted cinnamates (Eq. 6.37). More recently Thenappan and Burton[66] alkylated tri-*n*-butylcarbethoxyfluoromethylenephosphorane with a series of primary alkyl halides and hydrolyzed the reaction mixture to obtain the desired and otherwise difficult to obtain α-fluoroacetates (Eq. 6.38). Secondary bromides, tosylates, and iodides did not afford alkylation products.

A number of other alkylating agents have been employed in this kind of reaction. Bestmann[67] used primary tosylates in many alkylations, and others[68] have used Mannich bases. Markl[69] obtained excellent yields with triethyloxonium tetrafluoroborate, although with certain ylides other reactions occur with this reagent. The use of allylic halides leads to normal substitution at the α-carbon,[65, 66, 70] although in one instance Bestmann et al.[71] found that the initially formed alkylation product underwent an elimination of triphenylphosphine to afford the highly conjugated ester (Eq. 6.39). The van Tamelen group[72]



$$\begin{matrix}\mathrm{Ph_3P{=}CHPh}\\ +\\ \mathrm{BrCH_2CH{=}CH\text{-}COOMe}\end{matrix} \longrightarrow \left[\begin{matrix}\mathrm{Ph_3\overset{+}{P}\text{-}CHPh}\\ |\\ \mathrm{CH_2}\\ |\\ \mathrm{MeOOCCH{=}CH}\end{matrix}\right] \xrightarrow[\mathrm{-\,Ph_3P}]{\mathrm{-\,H^+}} \begin{matrix}\mathrm{PhCH{=}CH}\\ |\\ \mathrm{MeOOCCH{=}CH}\end{matrix}$$

(6.39)



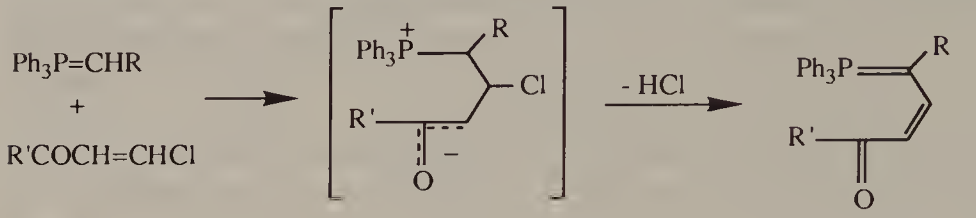
$$\begin{matrix}\mathrm{Bu_3P{=}CH\text{-}CH{=}CHR'}\\ +\\ \mathrm{RCH{=}CH\text{-}CH_2Br}\end{matrix} \longrightarrow \left[\begin{matrix}\mathrm{Bu_3\overset{+}{P}\text{-}CH\text{-}CH{=}CHR'}\\ |\\ \mathrm{CH_2CH{=}CHR'}\end{matrix}\right] \xrightarrow{[\mathrm{H}]} \begin{matrix}\mathrm{RCH{=}CH\text{-}CH_2}\\ |\\ \mathrm{R'CH{=}CH\text{-}CH_2}\end{matrix}$$

(6.40)

used the alkylation route as a means of coupling two allyl groups to form 1,5-dienes, first forming an allylide which was then allylated, followed by the phosphonium group being reductively removed (Eq. 6.40). They applied this technique to the conversion of farnesol to all-trans-squalene, and avoided any γ-allylation reactions.

Vinylic halides also have been used in the "alkylation" reaction. Zbiral[70] found that a series of chlorovinyl ketones could be attached to the ylide carbanion in what appeared to be an "alkylation" reaction, but in reality was a Michael addition–elimination reaction sequence followed by transylidation

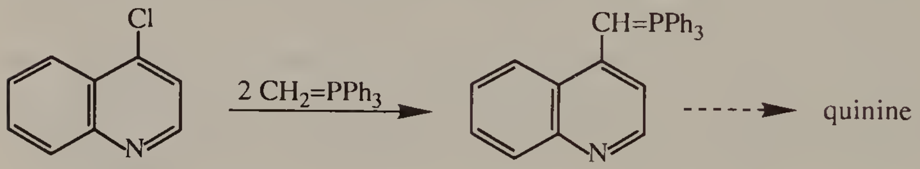
(Eq. 6.41). In a somewhat related reaction Bestmann and Frey[73] reported the preparation of a series of allenes by reacting a vinyl dibromide or an alkynyl



(6.41)

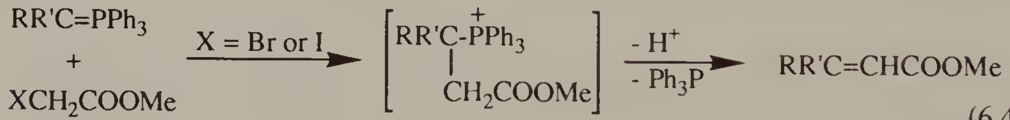
$$\begin{array}{l} RCH{=}CBr_2 \xrightarrow{3\ CH_2{=}PPh_3} \\ RC{\equiv}CBr \xrightarrow{2\ CH_2{=}PPh_3} \end{array} \longrightarrow RC{\equiv}CCH{=}PPh_3 \xrightarrow{H_2O} RCH{=}C{=}CH_2 \qquad (6.42)$$

bromide with three or two equivalents, respectively, of methylenetriphenylphosphorane, and then hydrolyzing the resultant ylide (Eq. 6.42). Taylor and Martin[74] used the same type of reaction to heteroarylate phosphonium ylides, using the resulting ylide in a Wittig reaction to couple the two components which eventually led to quinine (Eq. 6.43).

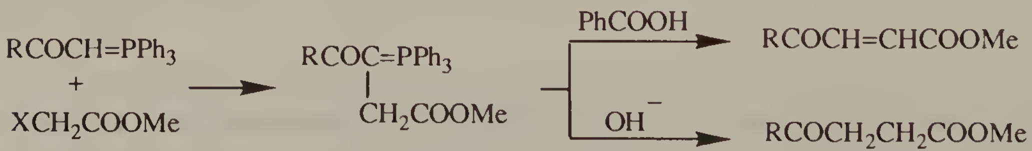


(6.43)

Alkylation of ylides with α-halo esters, usually acetates, leads to different products depending on the nature of the halogen. α-Iodo- and α-bromo acetates with two equivalents of phosphonium ylides normally afforded acrylates as a result of initial alkylation followed by a β-elimination of triphenylphosphine, effected by the second equivalent of ylide (Eq. 6.44).[71,75] The *trans*-alkene



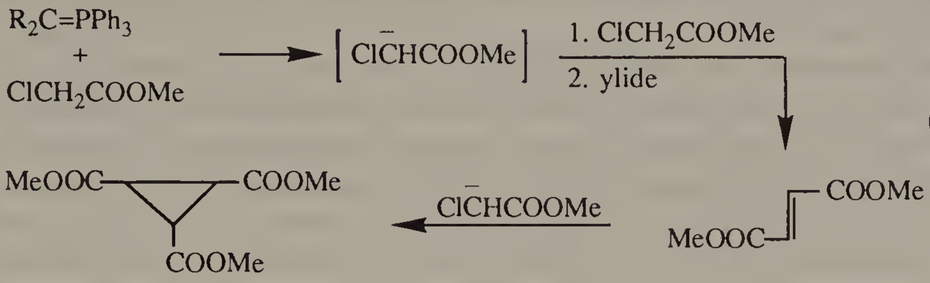
$$\begin{array}{c} RR'C{=}PPh_3 \\ + \\ XCH_2COOMe \end{array} \xrightarrow{X\,=\,Br\ or\ I} \left[ \begin{array}{l} RR'\overset{}{C}\text{-}\overset{+}{P}Ph_3 \\ \quad | \\ \quad CH_2COOMe \end{array} \right] \xrightarrow[-\,Ph_3P]{-\,H^+} RR'C{=}CHCOOMe \qquad (6.44)$$



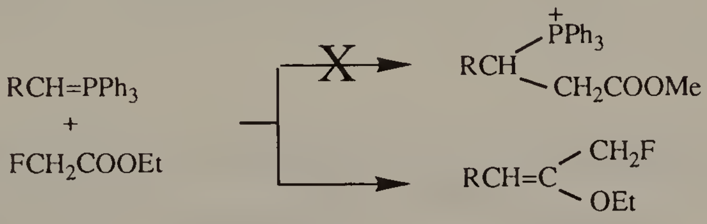
$$\begin{array}{c} RCOCH{=}PPh_3 \\ + \\ XCH_2COOMe \end{array} \longrightarrow \begin{array}{l} RCOC{=}PPh_3 \\ \quad | \\ \quad CH_2COOMe \end{array} \begin{array}{l} \xrightarrow{PhCOOH} RCOCH{=}CHCOOMe \\ \\ \xrightarrow{OH^-} RCOCH_2CH_2COOMe \end{array} \qquad (6.45)$$

usually dominated.[71] If one of the ylide substituents was a keto group, the elimination reaction was α- rather than β-, affording a new stabilized ylide. However, it too could be converted to an acrylate by protonation to its benzoate salt and heating, resulting in the β-elimination of triphenylphosphine, or it could be hydrolyzed in base to a γ-keto ester (Eq. 6.45).[76]

The use of α-chloroacetate led to the formation of a *trans*-cyclopropane triester and an equivalent amount of the ylide conjugate acid (Eq. 6.46).[75,77] It was surmised that the ylide served only as a base, forming first the carbanion of the ester which reacted with additional α-chloroester to form a fumarate, which has been shown to add ester carbanion to form a cyclopropane. The reaction of α-fluoroacetate with phosphonium ylides does not result in alkylation. Instead, and probably because fluorine is a poor leaving group but an effective activator of the carbonyl group, the ylide effected a Wittig reaction on the carbonyl group, resulting in α-fluoromethylvinyl ethers (Eq. 6.47).[75,78]

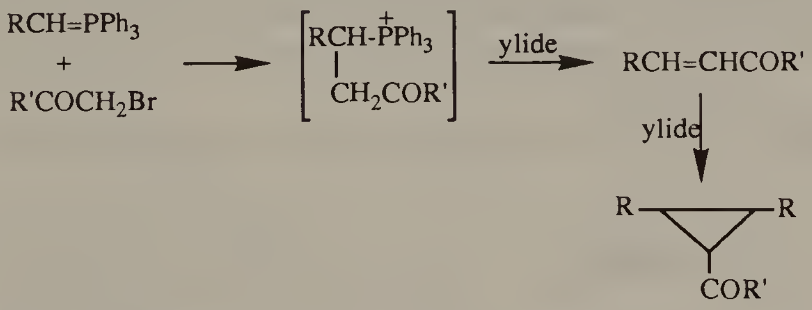


(6.46)



(6.47)

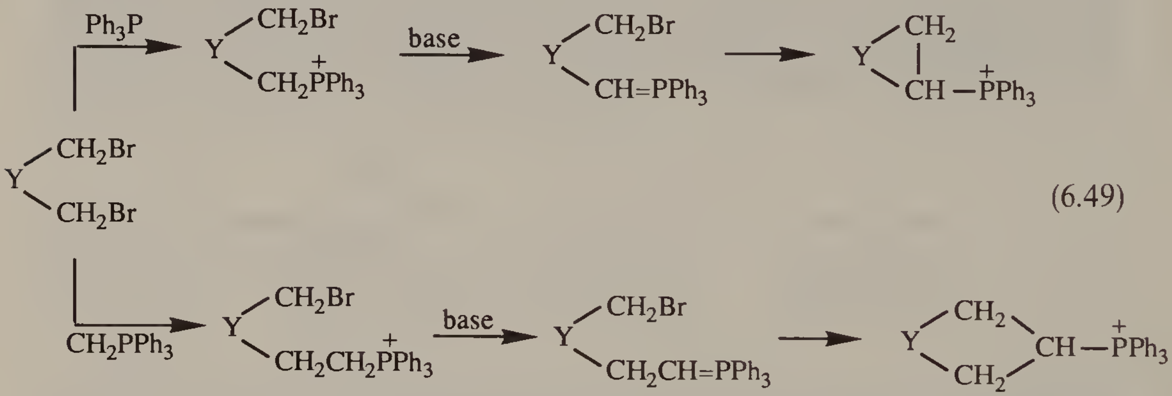
Alkylation of ylides with α-haloketones usually leads to α,β-unsaturated ketones, the conjugate acid of the ylides, and triphenylphosphine, the result of initial alkylation followed by β-elimination effected by a second equivalent of ylide (Eq. 6.48). Thus, phenacyl bromide with ester ylides afforded γ-ketoacrylates.[79] Earlier workers[80] also obtained tribenzoylcyclopropane as a minor product, and proposed that benzoylcarbene was involved in the reaction, but that is unlikely. Instead, the acrylate probably underwent the known Michael addition by ylide.[81] Pasto et al.[82] found that $Ph_3P{=}CH_2$ reacted with phenacyl chloride to afford a mixture of products, including dibenzoylethylene, 1,2,3-tribenzoylcyclopropane, some Wittig reaction products, and some ethers, and



(6.48)

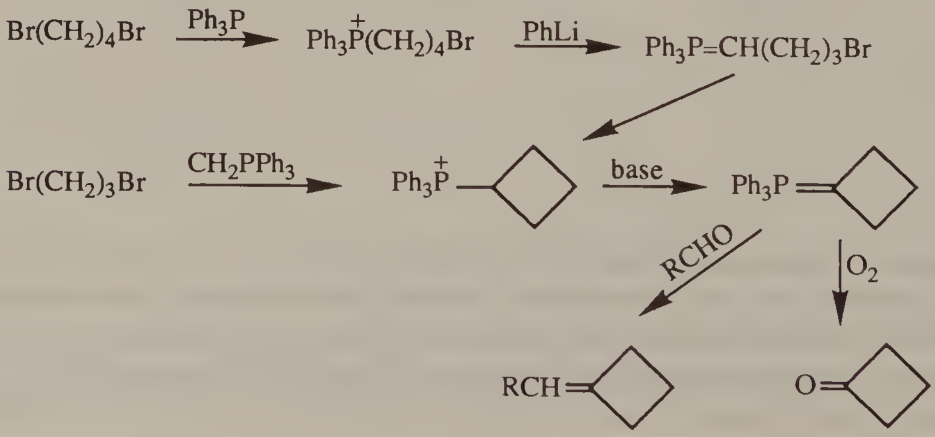
proposed that enolate formation was involved. Finally, Bose et al.[83] found that 2-halo-3-keto steroids would react with some phosphonium ylides but only at the carbonyl group to form alkenes, there being no sign of alkylation of the ylide. Thus, alkylation reactions with α-haloketones are possible but must be used with caution.

The *intramolecular* alkylation reaction has been used extensively to form cyclic systems. One concept is to use an α,ω-dibromoalkane in reaction with a tertiary phosphine to first form a monophosphonium salt, which then is converted to an ylide for alkylation by the remaining alkyl bromide group at the end of the chain to close the ring. A second concept is to react an α,ω-dibromoalkane with a methylide to effect, in sequence, an alkylation, ylide reformation, and another alkylation. The first approach produces a ring with the same number of carbons as were in the starting alkane, while the second produces a ring with one more carbon (Eq. 6.49).



(6.49)

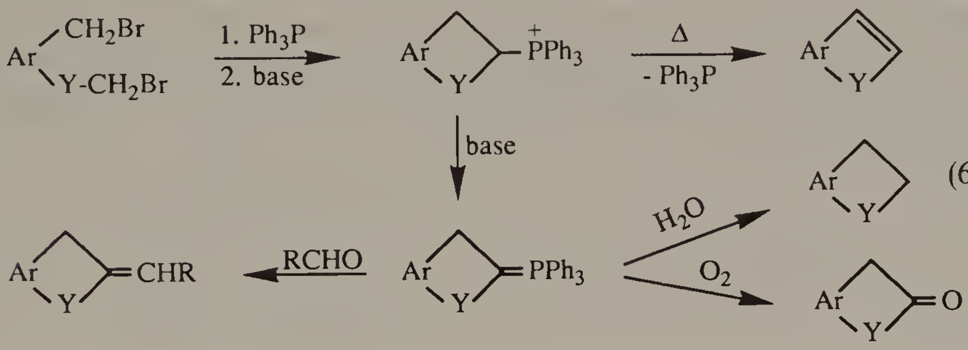
The first application of the concepts described above was the formation of a four-membered ring by the reaction of a monophosphonium salt, obtained from the reaction of 1,4-dibromobutane with triphenylphosphine, with excess phenyllithium to afford a red-colored solution of ylide which was thought to intramolecularly alkylate to the cyclobutyltriphenylphosphonium salt.[84] Later, Scherer and Lunt[85] verified this reaction, isolated the ring-closed salt, and converted it into the cyclobutylidene ylide which was used in subsequent



(6.50)

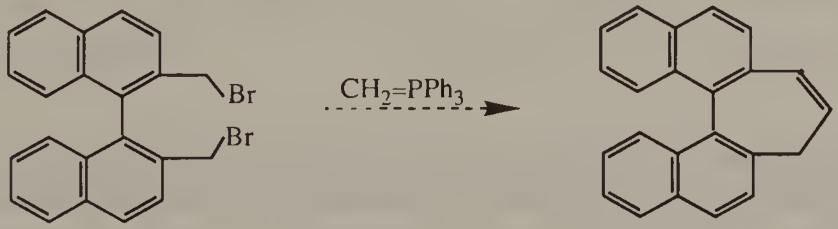
reactions. Bestmann and Kranz[65, 86] obtained the same ylide by effecting a double alkylation of methylenetriphenylphosphorane by 1,3-dibromopropane, and Baldwin and Fleming[87] did likewise with 1,3-dibromobutane (Eq. 6.50).

Rings varying in size from three to seven carbons have been prepared using intramolecular alkylation. Three-membered rings have been formed from 1,3-dibromopropane[88] and also from 1,2-dibromoethane[89] using the approaches described above. Bestmann and Kranz[67] have demonstrated the ability to effect cyclizations using methylenetriphenylphosphorane and double alkylations with α,ω-dibromo-propanes, -butanes, -pentanes, and -hexanes. They were unable to obtain rings larger than seven members by that process.

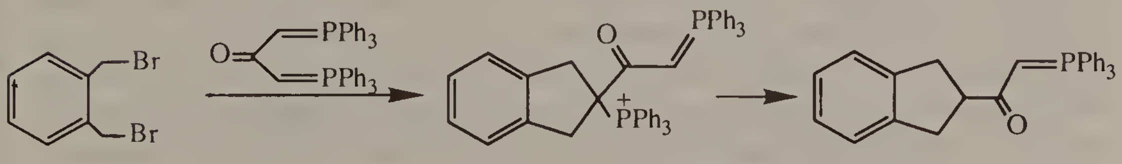


(6.51)

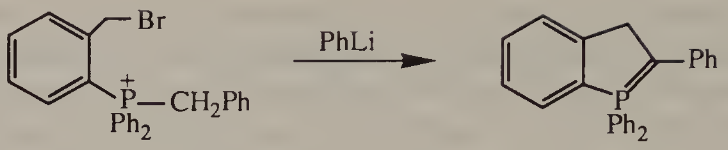
It has proven possible to obtain cyclic systems incorporating aromatic rings through intramolecular alkylation reactions. Use of di-(bromoalkyl) aromatics with triphenylphosphine and appropriate external bases has been an effective method (Eq. 6.51). Examples are the use of 1,8-di-(bromomethyl)naphthalene to prepare acenapthylene, 2,2′-di-(bromomethyl)biphenyl to prepare phenanthrene,[90, 91] and 1-bromo-2-(2-bromomethyl)phenylethane to prepare indane.[92] In each of these instances the cyclic ylide also could be reacted with carbonyl compounds or hydrolyzed to an alkane. The dinaphthocycloheptatriene (Eq. 6.52)[93] was prepared by double alkylation of methylenetriphenylphosphorane, and an indanoyl ylide (Eq. 6.53) was prepared from α,α′-dibromo-o-xylene.[89]



(6.52)



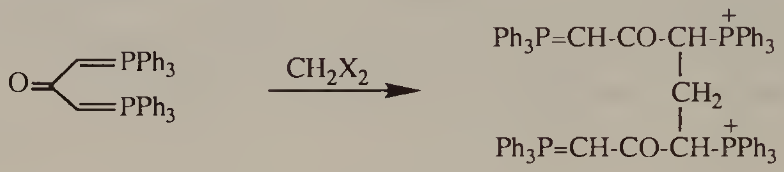
(6.53)



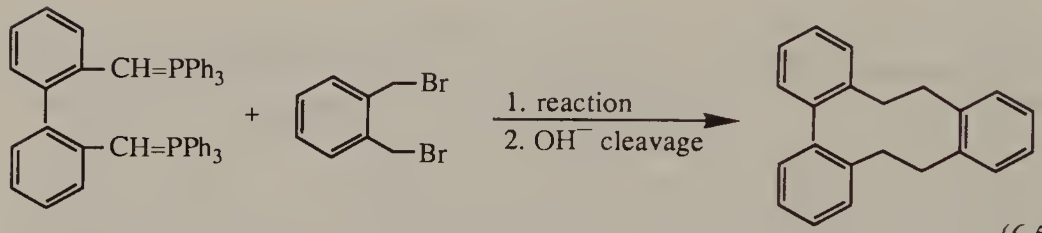
(6.54)

Markl[94,95] used a similar intramolecular alkylation route to prepare early examples of ylidic phosphacycles such as Eq. 6.54.

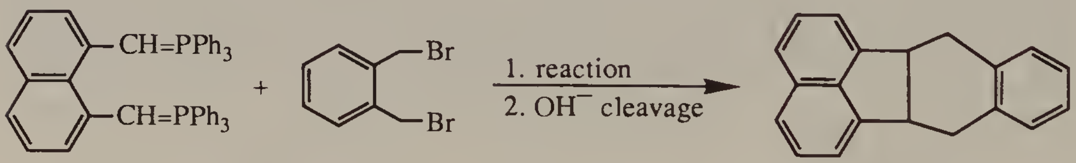
Two kinds of *intermolecular* reactions of dibromides with phosphonium ylides have been reported. Methylene bromide or iodide reacted with two equivalents of bis-ylide to afford a "cross-linked" double phosphonium ylide salt which was converted to a number of useful substances (Eq. 6.55).[89] Bestmann et al.[96,97] reported a number of examples of reactions of bis-ylides with bis-halomethylene compounds, some cases involving only intermolecular alkylations (Eq. 6.56) and others involving initial intermolecular alkylations followed by an intramolecular alkylation (Eq. 6.57).



(6.55)

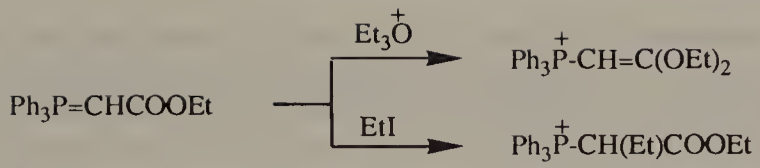


(6.56)



(6.57)

The paragraphs above indicated no ambiguity about the point of attachment of the alkylating agent to the ylide—it is only on the carbanion carbon, with regioselective C-alkylation occurring. However, two structural environments can produce ambiguity: those ylides with an $\alpha$-carbalkoxy group (ester ylides) and those with a $\beta$-keto group. Ester ylides undergo C-alkylation in all instances except those where a very active alkylating agent such as triethyloxonium tetrafluoroborate is employed. Thus, the carbethoxy ylide afforded the O-ethylated phosphonium salt with this reagent, whereas with alkyl bromides it afforded the C-alkylated product (Eq. 6.58).[98,99]



(6.58)

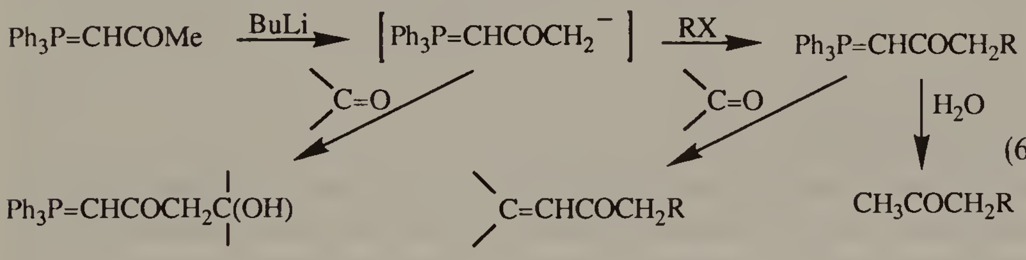
Phenacylidenetriphenylphosphorane reacted under mild conditions with methyl iodide to afford the O-methylated product, but on heating the latter rearranged to the C-methylated product (Eq. 6.59).[100] Earlier workers reported

$$\mathrm{Ph_3P{=}CHCOPh} \xrightarrow{\mathrm{MeI}} \mathrm{Ph_3\overset{+}{P}\text{-}CH{=}C(OMe)Ph} \xrightarrow{\Delta} \mathrm{Ph_3\overset{+}{P}\text{-}CH(Me)COPh} \tag{6.59}$$

only the latter product, but they carried out the reaction at high temperatures and undoubtedly effected the rearrangement unknowingly.[101] Ethyl iodide,[100-102], propyl iodide,[100] triethyloxonium salts,[99] and benzyl iodide[100] also initially O-alkylated the phenacylide. The O-benzyl derivative rearranged to the C-benzyl derivative, but the ethyl and propyl derivatives did not.[100] Other $\beta$-keto ylides behaved similarly.[99, 103] Nesmeyanov et al.[104] found that diphenyliodonium tetrafluroborate served as an effective O-phenylating agent with $\beta$-keto ylides (Eq. 6.60), and Issleib and Linder[39] reported the similar O-"phosphinylation" of the acetonylide by diphenylphosphinous chloride.

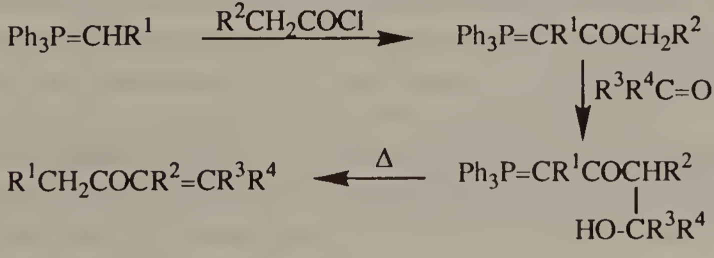
$$\mathrm{Ph_3P{=}CHCOMe} \xrightarrow{\mathrm{Ph_2\overset{+}{I}\ BF_4^-}} \mathrm{Ph_3\overset{+}{P}\text{-}CH{=}C(OPh)Me\ \ BF_4^-} \tag{6.60}$$

Finally, $\beta$-keto ylides could be alkylated at the $\gamma$-position. Reaction of triphenylphosphoniumacetonylide with *n*-butyllithium in THF produced a colored carbanion which was alkylated to a new phosphonium ylide (Eq. 6.61).[105] The latter could be hydrolyzed,[106] producing the same product



(6.61)

obtainable through an acetoacetic ester synthesis but under milder conditions, or could be used in a Wittig reaction. The $\gamma$-carbanion also could be added to



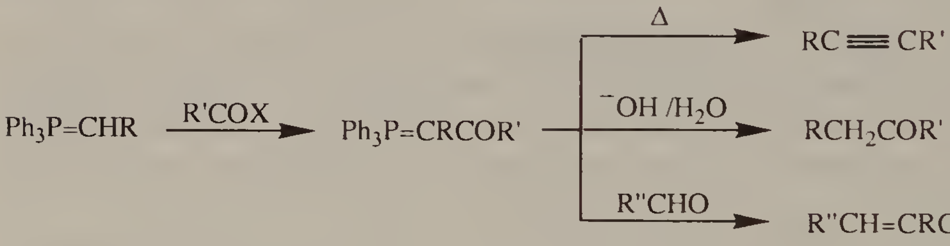
(6.62)

carbonyl compounds. LeRoux and LeCorre[107] recently applied this approach to the preparation of a series of α,β-unsaturated ketones in which the substituents on all noncarbonyl carbons could be separately chosen (Eq. 6.62).

In summary, alkylation is a varied and useful reaction of phosphonium ylides with the possibility of forming a wide variety of new ylides for subsequent use, for creating cyclic systems, and for elaborating carbon frameworks such as with β-keto ylides which can be alkylated at the α-, β-, and γ-positions.

## 6.5 ACYLATION

The acylation of phosphonium ylides, involving the attachment of an acyl group to the ylide carbanion, is a very widely used reaction for the same purposes listed in the preceding section. It is additionally useful, even necessary, because the preparation of β-keto ylides by quaternization of triphenylphosphine with α-bromoketones is an unreliable reaction. Through the acylation reaction can be obtained access to ketones,[28, 108–110] alkenones,[108, 111] aldehydes,[112–114] alkenals,[115] carboxylic acids,[110, 116–118] unsaturated carboxylic acids,[116] alkynes,[119–123] and allenes[124, 125] by following the initial acylation with thermolytic expulsion of triphenylphosphine oxide, by a Wittig reaction, or by cleavage of the ylide (Eq. 6.63). A variety of acylating reagents have been employed in the initial step of such reactions and are discussed separately.

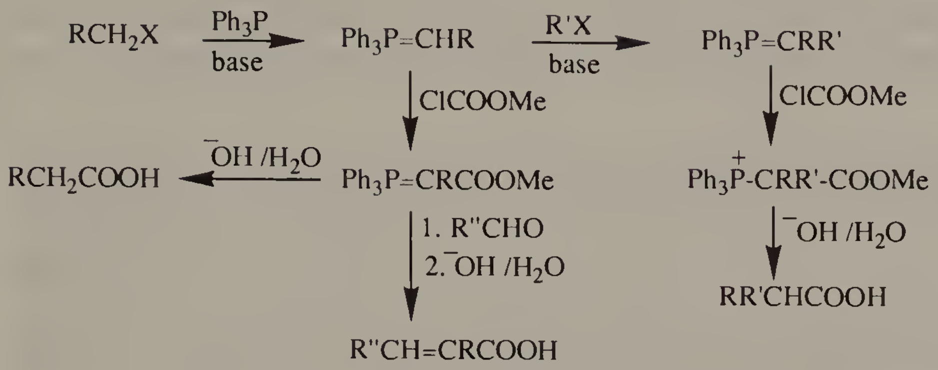


(6.63)

### 6.5.1 Acid Halides

Reaction of a phosphonium ylide with an acid chloride normally results in nucleophilic displacement of the chloride by the ylide carbanion, resulting in a phosphonium salt.[112] However, this salt seldom is isolated because it is more acidic than the starting ylide, and gives up a proton to form a new acylated ylide and the conjugate acid of the starting ylide (i.e., a transylidation). Separation is relatively easy because of the usual insolubility of the conjugate acid. However, this reaction suffers from the obvious disadvantage that a 1:1 ratio of ylide to acyl halide will result in a maximum of 0.5 equivalent of acylated ylide (Eq. 6.64).[109, 116] There appears to be virtually no limit to the nature of the acyl halide, examples existing of R′ = alkyl,[109] aryl,[126] perfluoroalkyl,[28] haloalkyl,[127] and alkoxy (e.g., chloroformate).[106, 112, 114, 128, 129] The use of chloroformate has been especially attractive as a means to convert alkyl halides to

$$\mathrm{Ph_3P{=}CHR} \xrightarrow{\mathrm{R'COCl}} \left[\mathrm{Ph_3\overset{+}{P}\text{-}CHRCOR'}\quad \mathrm{Cl}^-\right] \xrightarrow{\text{ylide}} \begin{matrix}\mathrm{Ph_3P{=}CRCOR'}\\ +\\ \mathrm{Ph_3\overset{+}{P}CH_2R\quad Cl^-}\end{matrix} \qquad (6.64)$$

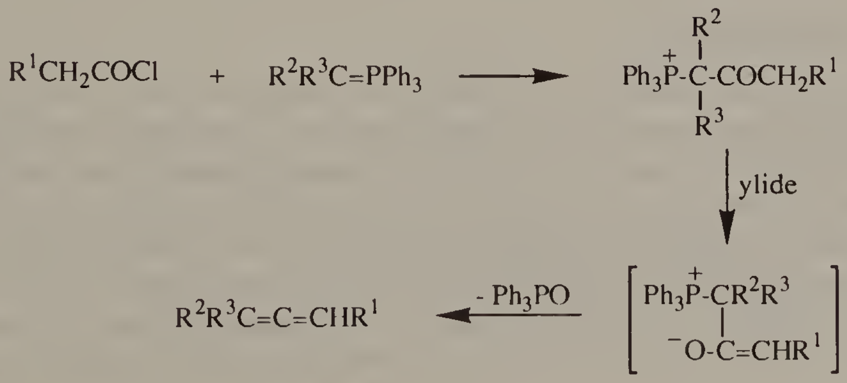


$$\begin{tikzcd}
\mathrm{RCH_2X} \arrow[r, "\mathrm{Ph_3P}", "\text{base}"'] & \mathrm{Ph_3P{=}CHR} \arrow[r, "\mathrm{R'X}", "\text{base}"'] \arrow[d, "\mathrm{ClCOOMe}"] & \mathrm{Ph_3P{=}CRR'} \arrow[d, "\mathrm{ClCOOMe}"] \\
\mathrm{RCH_2COOH} & \mathrm{Ph_3P{=}CRCOOMe} \arrow[l, "{}^-\mathrm{OH\,/H_2O}"'] \arrow[d, "{1.\ \mathrm{R''CHO} \atop 2.\ {}^-\mathrm{OH\,/H_2O}}"] & \mathrm{Ph_3\overset{+}{P}\text{-}CRR'\text{-}COOMe} \arrow[d, "{}^-\mathrm{OH\,/H_2O}"] \\
 & \mathrm{R''CH{=}CRCOOH} & \mathrm{RR'CHCOOH}
\end{tikzcd} \qquad (6.65)$$

complex carboxylic acids (Eq. 6.65).[116] The acylated ylide could be hydrolyzed,[108] reduced,[112] or electrolyzed[130] to a ketone, or used in a Wittig reaction with an aldehyde or ketone to produce an $\alpha,\beta$-unsaturated ketone.[102, 116]

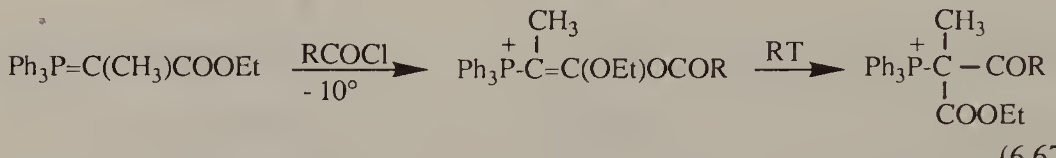
Several techniques have been evolved to avoid the loss of one-half equivalent of starting ylide owing to transylidation. Gough and Trippett[121] conducted the acylation in the presence of triethylamine. More recently, Listvan et al.[131] reported a two-phase system for the reaction, with sodium hydroxide in the aqueous phase to effect proton removal from the initial product. However, the most usual means of solving this problem is to use a different acylating agent, one in which the group displaced is a sufficiently strong base to effect the subsequent proton transfer. Reagents such as esters, thioesters, and acylimidazoles have been employed to this end and are discussed later in this section.

Use of an acid chloride containing $\alpha$-hydrogens, and an ylide without $\alpha$-hydrogens, produced an adduct that could not be transylidated in the usual manner. The resulting phosphonium salt was stable, could be isolated, and could be converted by hydrolysis or electrolysis to ketones. However, if the salt was left in solution and heated a proton was removed from the $\gamma$-carbon to form an enolate from which triphenylphosphine oxide was eliminated, resulting in an allene (Eq. 6.66).[124]



$$\begin{tikzcd}
\mathrm{R^1CH_2COCl} + \mathrm{R^2R^3C{=}PPh_3} \arrow[r] & \mathrm{Ph_3\overset{+}{P}\text{-}\underset{\displaystyle R^3}{\overset{\displaystyle R^2}{C}}\text{-}COCH_2R^1} \arrow[d, "\text{ylide}"] \\
\mathrm{R^2R^3C{=}C{=}CHR^1} & \left[\begin{matrix}\mathrm{Ph_3\overset{+}{P}\text{-}CR^2R^3}\\ \mathrm{{}^-O\text{-}C{=}CHR^1}\end{matrix}\right] \arrow[l, "-\ \mathrm{Ph_3PO}"']
\end{tikzcd} \qquad (6.66)$$

Just as in the alkylation reaction discussed in the preceding section, β-carbonyl ylides present the potential for C- and O-acylation. α-Carboalkoxymethylenetriphenylphosphoranes normally are acylated on the ylide carbon (C-acylation) by acid chlorides.[119, 122, 124, 125, 132] However, Abell et al.[133] recently have shown for the first time that at low temperatures O-acylation occurred and the enol ester–ether could be detected, rearranging to the usually isolated C-acylation product upon warming to room temperature (Eq. 6.67). In

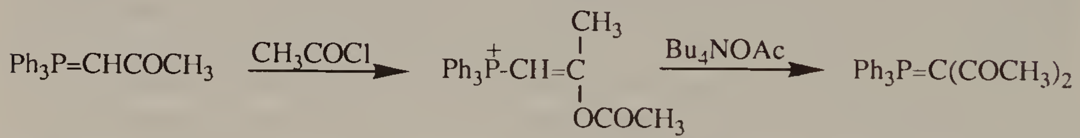


$$Ph_3P{=}C(CH_3)COOEt \xrightarrow[-10°]{RCOCl} Ph_3\overset{+}{P}\text{-}\overset{CH_3}{C}{=}C(OEt)OCOR \xrightarrow{RT} Ph_3\overset{+}{P}\text{-}\underset{COOEt}{\overset{CH_3}{C}}-COR$$

(6.67)

1965 Nesmeyanov and Novikov[58] had shown that while an ester ylide normally underwent C-acylation with acetyl chloride, the $HgCl_2$ complex of the ylide underwent O-acylation.

β-Keto ylides have been known for some time to undergo O-acylation readily. Chopard et al.[134] were able to isolate the O-acetyl product from acetyl chloride and acetonylidenetriphenylphosphorane, and showed that it rearranged in the presence of tetrabutylammonium acetate to the C-acetylated product (Eq. 6.68).



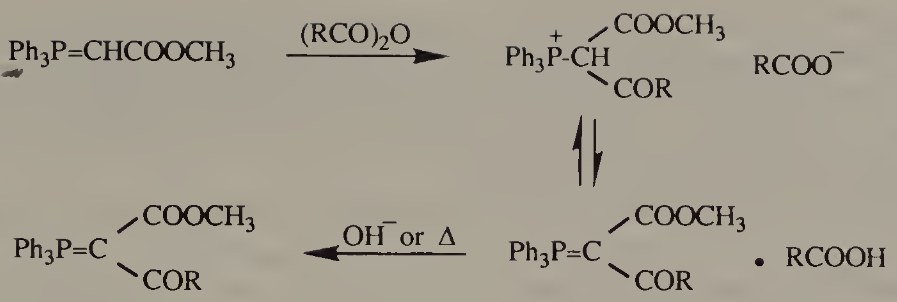
$$Ph_3P{=}CHCOCH_3 \xrightarrow{CH_3COCl} Ph_3\overset{+}{P}\text{-}CH{=}\underset{OCOCH_3}{\overset{CH_3}{C}} \xrightarrow{Bu_4NOAc} Ph_3P{=}C(COCH_3)_2$$

(6.68)

They surmized that the O-acetyl product was the kinetically controlled product, whereas the C-acetyl derivative was the thermodynamically controlled product. Listvan et al.[129] recently have isolated additional examples of O-acylated products, and have effected cleavage of the phosphonium group to produce enol esters. Earlier, Nesmeyanov et al.[59] had shown that the $HgCl_2$ complex of β-keto ylides underwent exclusive O-acylation, but removal of the mercury anion also led to removal of the acetyl group, so the reaction was of no synthetic value.

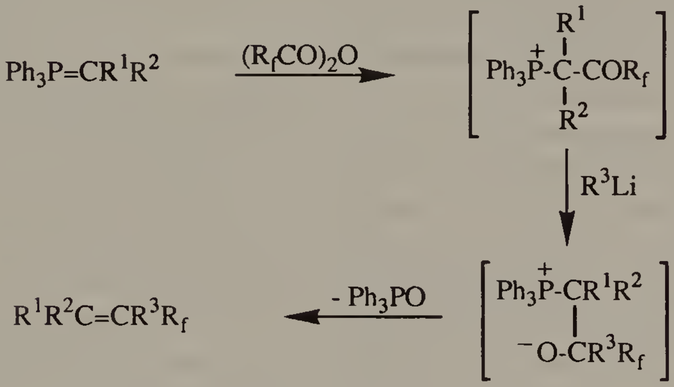
### 6.5.2 Acid Anhydrides

With the notable exception of certain cyclic anhydrides, acid anhydrides are effective acylating agents for phosphonium ylides. Chopard et al.[134] reacted α-carboalkoxymethylenetriphenylphosphorane with several linear anhydrides, including acetic and benzoic anhydrides, and produced the phosphonium salts, which could be isolated in some instances as the carboxylate salts. The carboxylate anion was thought not to be sufficiently basic to remove the α-proton from the ylide salt. Usually either heating the salt to evolve the carboxylic acid, if volatile, or treating the salt with aqueous sodium hydroxide



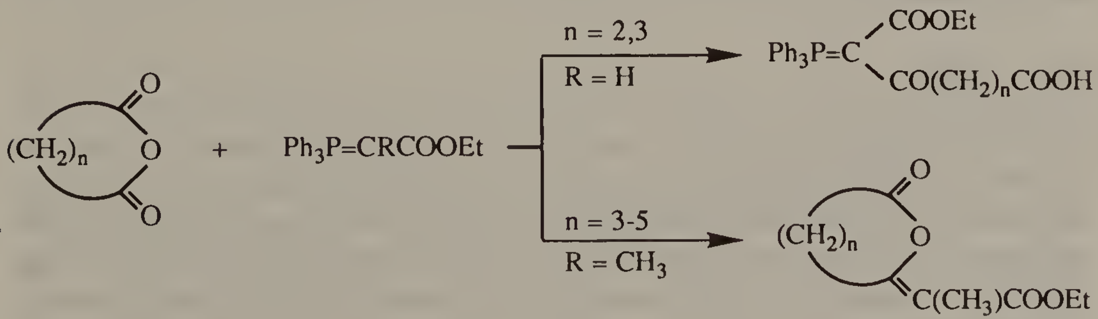
(6.69)

afforded the acylated ylide (Eq. 6.69). Just recently Abell et al.[135] showed by spectral analysis in solution and by X-ray analysis in the solid state that the originally formed phosphonium carboxylate (see Eq. 6.69, R = $CH_3$) should be reformulated as the phosphorane with a molecule of acetic acid in the crystal structure. This explains the thermal conversion of the original acetylation product to ylide. The acylation reaction is reliable, as illustrated by its recent application with perfluoroanhydrides[127,136,137] to the synthesis of substituted fluoroalkenes in a synthesis allowing separate introduction of all four alkene substituents (Eq. 6.70).



(6.70)

Cyclic anhydrides react differently with phosphonium ylides. In their original report, Chopard et al.[134] reported that glutaric anhydride reacted analogously to the linear anhydrides, undergoing ring opening to a phosphonium carboxylate. However, they shortly found that phthalic anhydride reacted with the same ylide to afford the product of a Wittig reaction on the carbonyl group, an enol lactone (Eq. 6.71).[138] A similar result was reported by Ingham et al.,[139] who



(6.71)

were the first to demonstrate that succinic and maleic anhydrides also underwent Wittig reactions with their carbonyl groups. Many years later Tsuboi et al.[140] confirmed the ring-opening reaction of glutaric anhydride initially reported by Chopard et al.,[134] but found that use of a disubstituted ylide resulted in the Wittig reaction instead.

The exclusive formation of cyclic enol lactones from reaction of ylides with cyclic anhydrides seems now relatively well understood. Most reactions have provided alkenation of only one carbonyl group, but, the use of stronger conditions has forced dialkenation to cyclic divinyl ether.[141,142] There have been extensive studies of the regio- and stereochemistry of the reactions of ester ylides with substituted succinic,[143,144] maleic,[145,146] and phthalic anhydrides.[147,148] The general conclusions are that (1) alkene formation occurs at the carbonyl group farthest from any substituents, but the presence of a methoxy group can attract that ylide to attack the adjacent carbonyl group, perhaps by special coordination between the methoxy group and the phosphonium ion, and (2) the dominant, and frequently exclusive, stereochemistry of the enol lactones is the $E$-alkene, which is a product of kinetic control. In the interesting case of 3,6-dimethylphthalic anhydride, however, the $E$:$Z$ ratio was 1:15, presumably as a result of overpowering steric effects.[149]

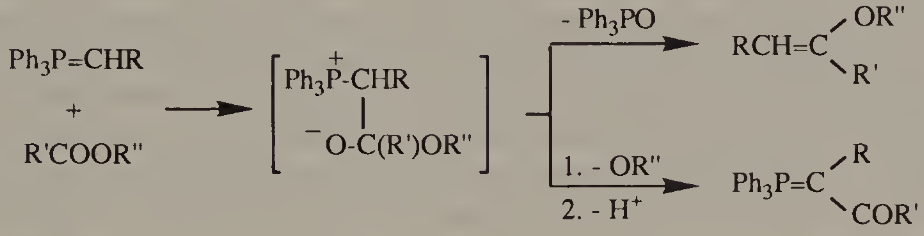
The Abell group have isolated the proposed intermediate carboxylic acid–ylide in the case of the reaction of succinic anhydride with carbethoxymethylenetriphenylphosphorane,[149] have prepared it by an alternate route,[150] have proven its ready transformation (i.e., warming to 40°C) to the enol lactone with no evidence for the intermediacy of the corresponding phosphonium salt,[150] and have determined the structure of the intermediate by X-ray crystallographic analysis.[151] Interestingly, no intermediate could be detected when the ylide was disubstituted (i.e., α-carbethoxyethylidenetriphenylphosphorane), even when the alternate route was explored.[150,151] Kayser et al.[151a] have proven the reversible opening of phthalic anhydride by ylides but could not prove whether the enol-lactone product arose from the initial betaine adduct or from a separately formed oxaphosphetane.

In summary, the use of linear anhydrides as acylating agents is effective and uncomplicated, whereas $C_4$ and $C_5$ cyclic anhydrides are not useful in acylation because of formation of enol lactones instead. Readers should refer to the excellent recent review by Murphy and Brennan for more detailed discussion and examples.[152]

### 6.5.3 Esters

The first acylating reagent ever reacted with a phosphonium ylide was an ester, but the now-known duality of ester reactions with ylides has led to the use of acyl halides as the acylating reagent of choice in most instances. Wittig and Schollkopf[153] found that methylenetriphenylphosphorane, prepared from the precursor bromide salt with phenyllithium, reacted with ethyl benzolate to produce phenacyltriphenylphosphonium bromide in 53% yield, and the latter could be deprotonated by reaction with hydroxide into what is now known to be triphenylphosphoniumphenacylide. More recently Cristau and Ribeill[154] obtained the same product in 96% yield by reacting the diylide, lithium diphenylmethylenephosphoniummethylide [$Ph_2P(CH_2)CH_2Li$], with ethyl benzoate.

Reaction of esters with phosphonium ylides normally follow one of two pathways (Eq. 6.72). Both reactions can be represented by initial attack of the ylide carbanion on the ester carbonyl group to afford an intermediate betaine, which might be complexed or "free." If the betaine is uncomplexed it is free to transfer oxygen to phosphorus in a Wittig reaction, affording an enol ether as product. If the oxygen is complexed, particularly with lithium, such transfer is slowed and ejection of alkoxide becomes the dominant route. The alkoxide, or other bases in the solution, remove the acidic proton from the carbon alpha to phosphorus, forming a new acylated ylide. It is clear that a number of factors can influence the balance between these two reactions.[152]



(6.72)

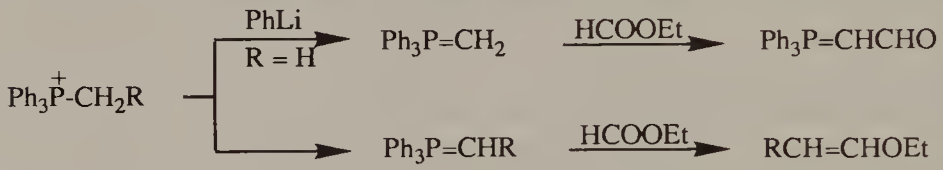
There is no absolute evidence regarding the existence of a betaine or an oxaphosphetane intermediate in those reactions involving a Wittig reaction with an ester. In other words, olefination of an ester may or may not proceed via the same mechanism as olefination of an aldehyde or ketone (see Chapter 9). However, recently Begue et al.[137] reported observing the first betaine ($\delta_p 31 = +24$–$28$ ppm) and then the oxaphosphetane ($\delta_p 31 = -64.9$ ppm) in the reaction of ethyl trifluoroacetate with $Ph_3P{=}CH(CH_2)_2Ph$.

The presence or absence of lithium salts in the reaction has a major effect on its outcome.[137] Bestmann et al.[75] obtained good yields of enol ethers when a series of alkylides (Eq. 6.72, R = alkyl), generated by the salt-free process, were reacted with esters. However, similar alkylides generated with organolithium reagents and then reacted with esters resulted in acylation of the ylides to afford acyl ylides.[114, 155, 156] Only one report exists of the reaction of an organolithium-produced ylide with an ester producing an enol ether, and that was done at – 78°C.[156]

The nature of the ester involved also affects the course of the reaction, with those esters having more "ketonic" carbonyl groups (i.e., with strong electron-withdrawing groups attached to the carbonyl group) being more reactive and producing enol ethers via a Wittig reaction. A wide-ranging series of salt-free ylides reacted with ethyl trifluoroacetate and ethyl α-fluoroacetate to afford enol ethers.[78] The ester ylide (Eq. 6.72, R = COOEt) reacted with diethyl oxalate (R′ = COOEt) to afford the corresponding enol ether[157] and various benzylides did likewise.[158] Le Corre[155] and Ploder and Tavares[159] have shown that other esters with α-electron withdrawing groups, such as –CN, –OPh, and COCOOEt, also tended to form enol ethers when reacted with ylides.

The nature of the ylide also affects the course of the reaction with esters. Subramanyan et al.[156] and Le Corre[155] showed that stabilized and semi-stabilized ylides, in the absence of lithium, afforded enol ethers as products. However, there is some evidence that even nonstabilized ylides will produce ethers. A phenyllithium-produced alkylide reacted with ethyl formate at – 78°C to give a low yield of the enol ether, but at room temperature the same reactants afforded a good yield of the formylated product.[156] Changing the phosphonium group from triphenyl to tri-*n*-butyl led to an increase in the production of acylation products, and a decrease in the production of enol ethers.[155] The $n$-$Bu_3P$ group made the Wittig reaction less likely as expected, reducing the ease with which the oxyanion attacked tetravalent phosphorus in the intermediate. It is unlikely that the change had any effect on the stability of the intermediate as claimed.[152]

The use of ethyl formate as an acylating reagent provides an interesting case study. Trippett and Walker[112] and LeCorre[155] obtained moderate yields of the formyl ylide (Eq. 6.73) from reaction with the phenyllithium-generated meth-



(6.73)

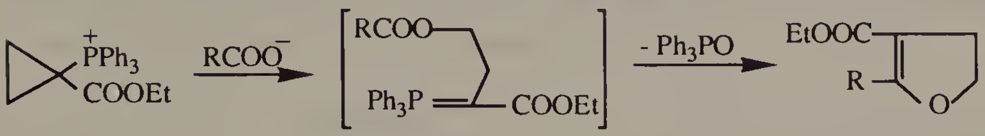
ylide, and the procedure has been improved now to provide yields of about 80%.[114] On the other hand, reaction of ethyl formate with a variety of substituted ylides (R = COOEt, CH=CHPh, COOEt) afforded good yields of the enol ether.[155, 156] There seems to be no report of the reaction of salt-free methylide with ethyl formate, but the reaction would be expected to afford enol ether. There is no demanding evidence that the sequence of addition of the formate ester to ylide, or vice versa, or the presence of an excess of formate, are significant controlling factors as sometimes claimed.

Both reactions of esters with ylides (Eq. 6.72) have been applied to the synthesis of cyclic compounds. In the course of attempting to prepare fatty acids via the Wittig reaction, Bergelson et al.[160] found that an intramolecular acylation had occurred in 70% yield (Eq. 6.74, n = 3), and in the absence of

(6.74)

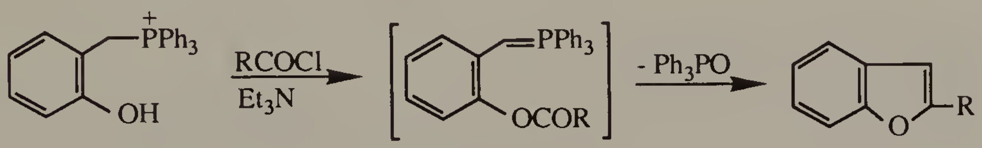
lithium! At about the same time House and Babad[161] extended the application of the reaction to the formation of 5- to 7-membered rings.

The enol ether result of the reaction of esters with ylides has been extensively applied to the synthesis of oxygenated heterocycles. Using the ring-opening method of forming an ylide in proximity to an ester group, Dauben and Hart[162] first applied this approach in preparing a series of dihydrofurans (Eq. 6.75).

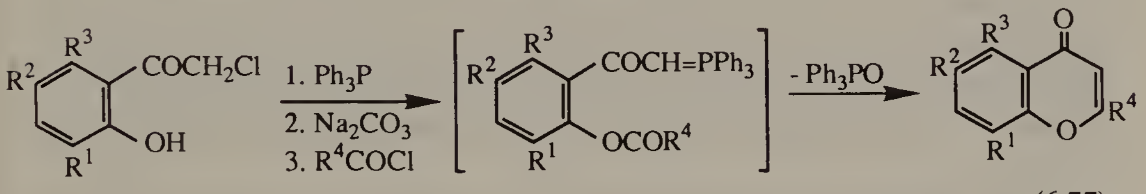


(6.75)

Dihydrofurans and dihydropyrans have been prepared from ω-acyloxy alkylides.[163] The same group[164] later prepared benzofurans from *o*-cresols using enol ether formation as the final step of the one-pot reaction (Eq. 6.76). *o*-Hydroxyphenacylides similarly produced benzopyranones[165] and this approach more recently has been applied to the synthesis of flavones (Eq. 6.77).[166, 167] Esters of *o*-thiolbenzylides have afforded benzothiophenes by Wittig reaction cyclization as well.[168]



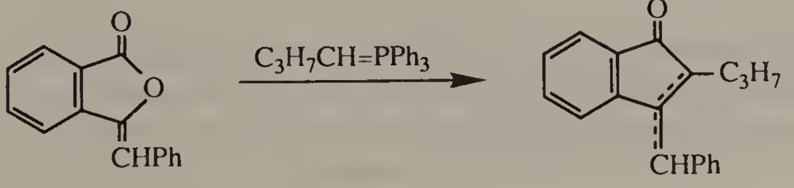
(6.76)



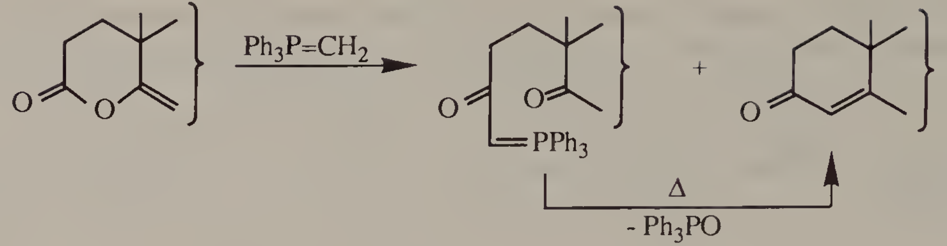
(6.77)

### 6.5.4 Miscellaneous Acylating Reagents

*6.5.4.1 Lactones.* There have been few reports of the reaction of phosphonium ylides with lactones, which are but special forms of esters and thereby should be capable of acylating an ylide. Henrick et al.[169] found that enol γ-lactones underwent attack by ylide at the carbonyl group, presumably to form an acylated ylide intermediate which then effected an intramolecular Wittig reaction, with the overall result being the replacement of oxygen by the ylide alkyl group (Eq. 6.78). Application to a steroidal enol δ-lactone, using methylenetriphenylphosphorane, afforded a mixture of testosterone acetate and the intermediate ylide, the latter being convertible to the former by heating in toluene, resulting in an overall 50% yield (Eq. 6.79).[169]

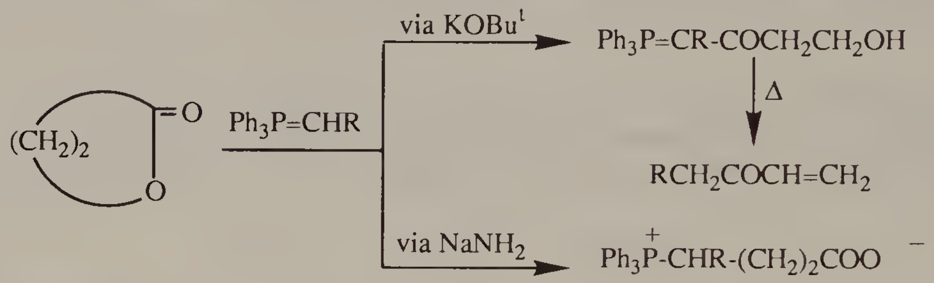


(6.78)



(6.79)

Attack of ylide at the carbonyl group and ring opening also has been reported recently for β-lactones, producing δ-hydroxy acylated ylides which underwent thermolytic triphenylphosphine oxide elimination to afford α,β-unsaturated ketones (Eq. 6.80).[170] More recently the same acylated intermediate has been

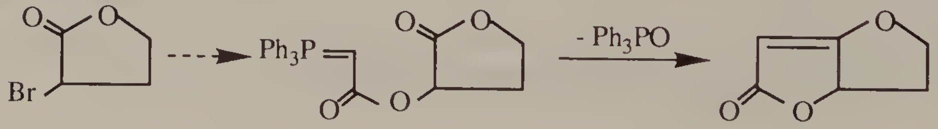


(6.80)

prepared by normal acylation of ylides, generation of the γ-carbanions according to the method of Taylor and Wolf,[105] and reaction with aldehydes or ketones.[107] γ-Butyrolactone also underwent carbonyl attack and ring opening.[170]

In contrast to the reports mentioned above, Kise et al.[171] earlier had reported that β-propiolactone and γ-butyrolactone both underwent ylide attack at the methylene group, rather than the carbonyl group, to effect ring opening and formation of the phosphonium carboxylates (Eq. 6.80). This discrepancy has not been clarified other than to note that the ylide-forming base was $\mathrm{NaNH_2/THF}$ for the attack at methylene and $\mathrm{KOBu^t}$/toluene for attack at carbonyl.[172]

In the first example reported to date, Brennan and Murphy[173] found that a phosphonium ylide would react with a lactone at the carbonyl group to effect an intramolecular Wittig reaction to result in the formation of an enol ether (Eq. 6.81), reminiscent of the reaction of ylides with esters and with some cyclic

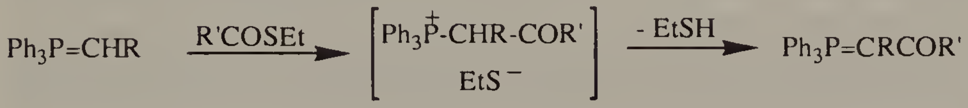


(6.81)

anhydrides. Perhaps the potential fusion of two five-membered rings, as well as the formation of the phosphine oxide, was a sufficient driving force. Erba et al.[174] have reported both Wittig reactions and ring openings to result from the reaction of several ylides with oxazolones.

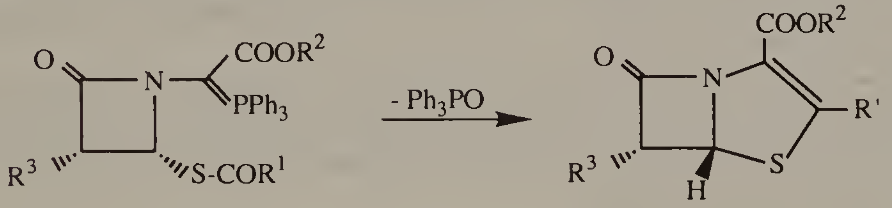
The brief work reported to date on lactones reveals instances of all possible kinds of reactions—acylation, Wittig reaction to form enol ethers, and ring opening at the alkyl group. Thus, the use of lactones as ylide acylating agents cannot be considered fully predictable at this time.

*6.5.4.2* ***Thiolesters.*** Bestmann and Arnason[109, 175] found that reaction of phosphonium ylides with thiolesters was an effective means of improving the efficiency of the acylation reaction because the thiolate anion produced in the first step was sufficiently basic to convert the initially formed salt to its ylide, thereby avoiding the consumption of one half of the starting ylide in a transylidation reaction (Eq. 6.82).



$$Ph_3P{=}CHR \xrightarrow{R'COSEt} \left[\begin{array}{c} Ph_3\overset{+}{P}\text{-}CHR\text{-}COR' \\ EtS^- \end{array}\right] \xrightarrow{-\,EtSH} Ph_3P{=}CRCOR' \qquad (6.82)$$

In contrast to these reports, Woodward and colleagues[176] found that thiolesters in a potential cyclic environment did not acylate phosphonium ylides. Instead they effected an intramolecular Wittig reaction typical of many ordinary esters to produce an enol thioether in 6–90% yields, and this reaction was a key cyclization step for the synthesis of many examples of the bicyclic penem system (Eq. 6.83). Benzothiophenes recently have been prepared by this route[168] and a thiolester is attacked in preference to an ester.[177] The review article by Murphy and Brennan contains many more examples of this kind of Wittig reaction.[152]



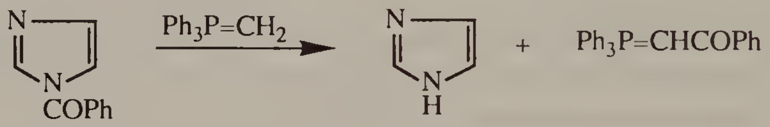
(6.83)

*6.5.4.3* ***Amides and Imides.*** Reaction of ordinary amides with phosphonium ylides is a recent phenomenon—the first reports were seen in 1981, two described intramolecular Wittig reactions at the carbonyl group to form pyrroles,[178, 179] and the third a Wittig reaction at the carbonyl group of a $\beta$-lactam,[180] all rather than acylation reactions. The Le Corre group reported the reaction of a variety of ylides, both stabilized and reactive, with oxamic esters and obtained exclusively the product of Wittig reaction at the amide carbonyl group.[181] Ring closure of *o*-amidobenzylides has provided a route to indoles.[182, 183] However, Cristau and Rebeill[154] recently found that the diylide $[Ph_2P(CH_2)_2^- Li^+]$ reacted with N,N-dimethylbenzamide to produce only 20% of the Wittig reaction product, 80% being benzoylated ylide. Another example of acylation by an amide was the reaction of an aziridylphenyl urea with an ester ylide in which initial attack at the carbonyl group led to ejection of the aziridine

(6.84)

moiety and resultant acylation of the original ylide (Eq. 6.84).[184] N,N-Disubstituted amides of perfluoro carboxylic acids reacted with phosphonium ylides to afford only enamines via a Wittig reaction with the amide carbonyl group.[137] Thus, use of ordinary amides generally is not an absolutely predictable process for acylating ylides, but often is an effective means of preparing nitrogenous heterocycles.

In the early days of ylide chemistry, when acylations normally were conducted using acyl halides in spite of the maximum 50% conversion limited by transylidation, it was discovered that use of acylimidazoles was an attractive alternative. Thus, N-formylimidazole with methylenetriphenylphosphorane gave an 81% yield of formylmethylenetriphenylphosphorane.[115] N-Benzoylimidazole similarly gave a quantitative yield of the phenacylide (Eq. 6.85).[185] In both



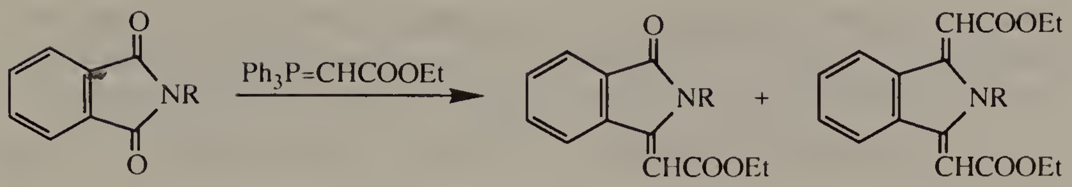
(6.85)

instances, the imidazole anion ejected upon ylide attack at the carbonyl group was sufficiently basic to remove the proton from the newly formed acylmethylenephosphonium salt, avoiding the consumption of an equivalent of ylide for that purpose. Miyano and Stealy[186] exploited this process to enable the use of virtually any acyl group by initial reaction of an acid chloride with imidazole, followed by addition of ylide.

Masked amides also have been used to effect acylations. Mark[169] used dimethylformamide chloride, and more recently Bestmann et al.[113] used tetramethylformamidine chloride, as effective formylation reagents with reactive or semistabilized ylides (Eq. 6.86).

$$RCH{=}PPh_3 \xrightarrow{H\overset{+}{C}(NMe_2)_2\ Cl^-} Ph_3\overset{+}{P}CR{=}CHNMe_2 \xrightarrow[2.\ NaOH]{1.\ HCl} Ph_3P{=}CRCHO \qquad (6.86)$$

Imides are not an effective source of acyl groups for transfer to ylides. In all instances reported to date the result of such an attempt has been a Wittig reaction to alkenate one or both of the imide carbonyl groups. Flitsch and Peters[187] found that phthalimide and succinimide reacted with the ester ylide to afford mono- or dialkenated products (Eq. 6.87). The mono product was mainly of *E* configuration when the imide was N-substituted and of *Z* configuration when unsubstituted. Imides also have undergone intramolecular Wittig reactions.[188] Gossauer et al.[189] and, more recently, Bishop et al.[190] observed only Wittig reactions with monothioimides, the reactions occurring preferentially

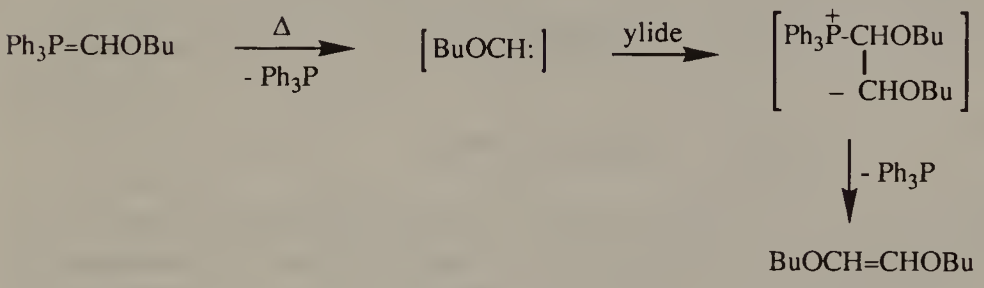


(6.87)

with the thio-carbonyl group (see also Section 7.2.2.3). Natsune et al.[191] reported that N-tosyl cyclic amides (e.g., N-tosylpyrrolidone) reacted similarly, producing Wittig reaction products, and removal of the tosyl group afforded exocyclic enamines. Flitsch and Schindler,[192] as well as Murphy and Brennan,[152] have reviewed these reactions.

## 6.6 REACTION WITH MISCELLANEOUS ELECTROPHILES

Carbenes are known to react with phosphonium ylides. To account for the formation of 1,2-dibutoxyethene from the thermal decomposition of *n*-butoxymethylenetriphenylphosphorane, Wittig and Boll[193] proposed initial fragmentation of the ylide to *n*-butoxycarbene, followed by its reaction with unchanged ylide to form a carbanion which eliminated triphenylphosphine, forming the alkene (Eq. 6.88). Oda et al.[194, 195] verified such a possibility when



$$Ph_3P{=}CHOBu \xrightarrow[-\,Ph_3P]{\Delta} \left[BuOCH{:}\right] \xrightarrow{\text{ylide}} \left[\begin{array}{l} Ph_3\overset{+}{P}\text{-}CHOBu \\ \quad -\ CHOBu \end{array}\right] \xrightarrow{-\,Ph_3P} BuOCH{=}CHOBu \qquad (6.88)$$

$$Ph_3P{=}CHR \ + \ R'\text{-}\ddot{C}\text{-}Cl \longrightarrow RCH{=}CClR' \ + \ Ph_3P \qquad (6.89)$$

they discovered that separately generated mono- or dihalo carbenes would react as electrophiles with a variety of stabilized ylides to form alkenes (Eq. 6.89). The overall effect was to couple the carbene with the carbanion portion of the ylide, ejecting triphenylphosphine. Chromium carbene complexes have reacted with stabilized yields in the presence of carbon monoxide to afford transient allenes, probably via initial ketene formation followed by a Wittig reaction. In the absence of carbon monoxide, low yields of carbene–ylide coupling products were obtained.[196]

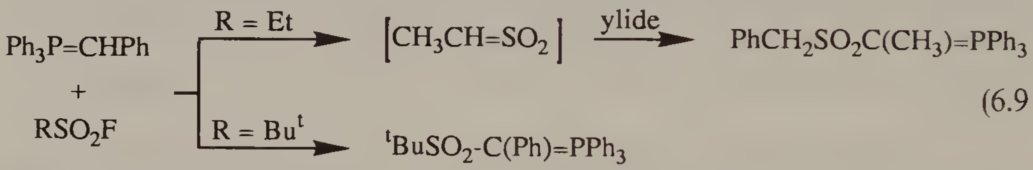
Ylides also react with diazo compounds to afford similar coupling products, but which retain the nitrogen. Triphenylphosphoniumbenzylide reacted with diazo compounds to produce an azine and a phosphine azine, the latter from subsequent reaction of eliminated triphenylphosphine with unreacted diazo compound (Eq. 6.90).[197, 198] Acylides and fluorenylides afforded similar direct

$$\mathrm{Ph_3P{=}CHPh} \; + \; \mathrm{R^1R^2CN_2} \xrightarrow{-\,\mathrm{Ph_3P}} \mathrm{R^1R^2C{=}N{-}N{=}CHPh} \qquad (6.90)$$

coupling products with the ylide carbanion bonding to the terminal nitrogen in a mechanism similar to that for carbenes.[199] Somewhat later, Strzelecka et al.[200] reacted triphenylphosphoniumphenacylide with diazoacetophenone and obtained an initially unknown substance which later was proposed to be 2,6-diphenyl-4-benzylidenepyran.

Diazonium salts reacted with phosphonium ylides in a direct coupling to afford phosphonium salts, from which a proton easily was removed to produce diazo-substituted ylides, $Ph_3P{=}C(R)N{=}N{=}Ph$.[201, 202] Such ylides also could be obtained from reaction of hydrazonoyl chlorides with triphenylphosphine in the presence of triethylamine.[203] In the presence of moisture the diazo ylides hydrolyzed to hydrazones.[204] In one instance two diazo groups were added to the ylide carbanion and oxidation of the bis-diazo ylide afforded a tetrazolium salt.[205]

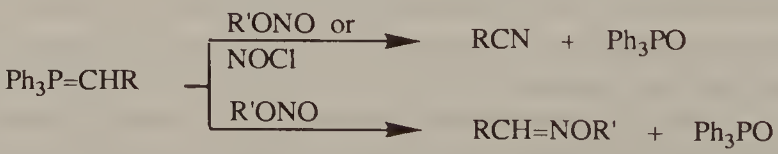
Sulfonation of phosphonium ylides with sulfonyl chlorides was ineffective, leading to rearrangement, but the fluoride was effective.[30, 206] Even then, however, dehydrofluorination to sulfenes and rearranged products occurred when using a sulfenyl fluoride carrying α-hydrogen (Eq. 6.91).[207]



$$\mathrm{Ph_3P{=}CHPh} + \mathrm{RSO_2F} \begin{cases} \xrightarrow{R\,=\,Et} \left[\mathrm{CH_3CH{=}SO_2}\right] \xrightarrow{\text{ylide}} \mathrm{PhCH_2SO_2C(CH_3){=}PPh_3} \\ \xrightarrow{R\,=\,Bu^t} \mathrm{{}^tBuSO_2\text{-}C(Ph){=}PPh_3} \end{cases} \qquad (6.91)$$

Nesmeyanov et al.[208] found that sulfur trioxide directly coupled with stabilized phosphonium ylides although the products were not well characterized. Sulfur dioxide and ylides afforded good yields of sulfines and triphenylphosphine oxide, reminiscent of the Wittig reaction.[209]

Oxides of nitrogen also served as electrophiles toward ylides. Stabilized and semistabilized ylides attacked alkyl nitrites on nitrogen, ejecting alkoxide and triphenylphosphine oxide to result in the formation of nitriles (Eq. 6.92).[210]



$$\mathrm{Ph_3P{=}CHR} \begin{cases} \xrightarrow[\mathrm{NOCl}]{\mathrm{R'ONO\ or}} \mathrm{RCN} + \mathrm{Ph_3PO} \\ \xrightarrow{\mathrm{R'ONO}} \mathrm{RCH{=}NOR'} + \mathrm{Ph_3PO} \end{cases} \qquad (6.92)$$

With reactive ylides, however, a Wittig-type reaction occurred to form an alkoxyimine and triphenylphosphine oxide. Reaction of ylides with nitrosyl chloride also resulted in nitriles, the mechanism indicating that only monosubstituted ylides could react in that manner (Eq. 6.92).[211, 212] Nitrous oxide also reacted with phosphonium ylides but produced a complex mixture of products.[213]

Ylides reacted with cyanogen bromide through attack at bromine or at cyano, often producing mixtures of α-bromo and α-cyano ylides.[214]

## REFERENCES

[1] Hawthorne, M. F. *J. Am. Chem. Soc.* **1958**, *80*, 3480.

[2] Schmidbaur, H.; Muller, G.; Blaschke, G. *Chem. Ber.* **1980**, *113*, 1480.

[3] Schmidbaur, H.; Muller, G.; Milewski-Mahrla, B.; Schubert, U. *Chem. Ber.* **1980**, *113*, 2575.

[4] Hawthorne, M. F. *J. Am. Chem. Soc.* **1961**, *83*, 367.

[5] Seyferth, D.; Grim, S. O. *J. Am. Chem. Soc.* **1961**, *83*, 1613.

[6] Siebert, W. *Z. Naturforsch.* **1970**, *25B*, 314.

[7] Fluck, E.; Bayha, H.; Heckmann, G. *Z. Anorg. Allg. Chem.* **1976**, *421*, 1.

[8] Choi, P. C.; Morris, J. H. *J. Chem. Soc. Dalton Trans.* **1984**, 2119.

[9] Andrews, S. J.; Welch, A. J. *Acta Cryst.* **1985**, *C41*, 1496.

[10] Barton, L.: Rush, P. K.; Zhu, T.; Nevels, P.; Owens, M. H. *Inorg. Chem.* **1989**, *28*, 381.

[11] Graybill, B. M.; Pitochelli, A. B.; Hawthorne, M. F. *Inorg. Chem.* **1962**, *1*, 626.

[12] Su, K.; Fazen, P. J.; Carroll, P. J.; Snedden, L. G. *Organometallics* **1992**, *11*, 2715.

[13] Bestmann, H. J.; Arenz, T. *Angew. Chem.* **1984**, *23*, 381.

[14] Matteson, D. S.; Majumda, D. *Organometallics* **1983,** *2*, 230.

[15] Bestmann, H. J.; Arenz, T. *Angew. Chem.* **1986**, *25*, 559.

[16] Bestmann, H. J.; Arenz, T. *Tetrahedron Lett.* **1986** *27*, 1995.

[17] Koster, R.; Rickborn, B. *J. Am. Chem. Soc.* **1967**, *89*, 2783.

[18] Bestmann, H. J.; Suhs, K.; Roder, T. *Angew. Chem.* **1981**, *20*, 1038; *Chem. Ber.* **1988**, *121*, 1509.

[19] Markl, G. *Chem. Ber.* **1961**, *94*, 2996.

[20] Denney, D. B.; Ross, S. T. *J. Org. Chem.* **1962**, *27*, 998.

[21] Speziale, A. J.; Ratts, K. W. *J. Org. Chem.* **1963**, *28*, 465.

[22] Grigorenko, A. A.; Shevchuk, M. I.; Dombrovskii, A. V. *J. Gen. Chem.* **1965**, *35*, 1232.

[23] Grigorenko, A. A.; Shevchuk, M. I.; Dombrovskii, A. V. *Zh. Obshch. Khim.* **1966**, *36*, 1121.

[24] Iman, M.; Bouysson, P.; Chenault, J. *Synthesis* **1990**, 631.

[25] Corey, E. J.; Shulman, J. I.; Yamamoto, H. *Tetrahedron Lett.* **1970**, 447.

[26] Zbiral, E.; Rashberger, M. *Tetrahedron* **1969**, *25*, 1871.

[27] Moriarty, R. M.; Prakash, I.; Prakash, O.; Freeman, W. A. *J. Am. Chem. Soc.* **1984**, *106*, 6082.

[28] Jeong, I. H.; Burton, D. J.; Cox D. G. *Tetrahedron Lett.* **1986**, *27*, 3709.

[29] Li, X.; Hu, J. S. *Tetrahedron Lett.* **1987**, *28*, 6317.

[30] Petragnini, N.; Campos, M. M. *Chem. Ind.* **1964**, 1461.

[31] Minami, T.; Nakayama, M.; Nakamura, T.; Okada, Y. *Chem. Lett.* **1989**, 1741.

[32] Seyferth, D.; Brandle, K. A. *J. Am. Chem. Soc.* **1961**, *83*, 2055.

[33] Issleib, K; Linder, R. *Liebigs Ann. Chem.* **1966**, *699*, 40.

[34] Mathiason, D. R.; Miller, N. E. *Inorg. Chem.* **1968**, *7*, 709.

[35] Schmidbaur, H.; Tronich, W. *Chem. Ber.* **1968**, *101*, 3545.

[36] Grutzmacher, H.; Pritzkow, H. *Chem. Ber.* **1989**, *122*, 1411.

[37] Issleib, K.; Lischewski, M. *J. Prakt. Chem.* **1969**, *311*, 857.

[38] Issleib, K.; Lischewski, M. *J. Prakt. Chem.* **1970**, *312*, 135.

[39] Issleib, K.; Linder, R. *Liebigs. Ann. Chem.* **1967**, *707*, 112.

[40] Markl, G.; Bauer, W. *Angew. Chem.* **1989**, *28*, 1695.

[41] Schmidbaur, H.; Nuβstein, P.; Muller, G. *Z. Naturforsch.* **1984**, *39B*, 1456.

[42] Grutzmacher, H.; Pritzkow, H. *Chem. Ber.* **1989**, *122*, 1417.

[43] Seyferth, D.; Grim, S. O. *J. Am. Chem. Soc.* **1961**, *83*, 1610.

[44] Seyferth, D.; Singh, G. *J. Am. Chem. Soc.* **1965**, *87*, 4156.

[45] Seyferth, D.; Singh, G.; Suzuki, R. *Pure Appl. Chem.* **1966**, *13*, 159.

[46] Schmidbaur, H.; Tronich, W. *Chem. Ber.* **1967**, *100*, 1032.

[47] Schmidbaur, H. *In Advances in Organometallic Chemistry*; Stone, F. G. A; West, R. Eds.; Academic: New York, 1970, Vol. 9, p. 260.

[48] Schmidbaur, H. *Acc. Chem. Res.* **1975**, *8*, 62.

[49] Kaska, W. C. *Coord. Chem. Revs.* **1983**, *48*, 1.

[50] Schmidbaur, H.; Molisch, W. *Chem. Ber.* **1970**, *103*, 97.

[51] Schmidbaur, H.; Wolf, W. *Chem. Ber.* **1975**, *108*, 2851.

[52] Schmidbaur, H.; Pichl, R.; Muller, G. *Chem. Ber.* **1987**, *120*, 789.

[53] Schmidbaur, H.; Eberlein, J.; Richter, W. *Chem. Ber.* **1977**, *110*, 677.

[54] Schmidbaur, H.; Fuller, H. J. *Chem. Ber.* **1974**, *107*, 3674.

[55] Schmidbaur, H.; Tronich, W. *Angew. Chem.* **1967**, *6*, 448.

[56] Wittig, G.; Schwarzenbach, K. *Liebigs Ann. Chem.* **1961**, *650*, 1.

[57] Nesmeyanov, N. A.; Novikov, V. M.; Reutov, O. A. *Bull. Acad. Sci. USSR* **1964**, 724.

[58] Nesmeyanov, N. A.; Novikov, V. M.; *Proc. Acad. Sci. USSR* **1965**, *162*, 471.

[59] Nesmeyanov, N. A.; Novikov, V. M.; Reutov, O. A. *J. Organomet. Chem.* **1965**, *4*, 202.

[60] Schmidbaur, H.; Adlkofer, J.; Buchner, W. *Angew. Chem.* **1973**, *12*, 415.

[61] Schmidbaur, H.; Franke, R. *Angew. Chem.* **1973**, *12*, 416.

[62] Wittig, G.; Reiber, M. *Liebigs Ann. Chem.* **1949**, *562*, 177.

[63] Eyles, C. T.; Trippett, S. *J. Chem. Soc.* **1966**, 67.

[64] Bestmann, H. J.; Vilsmaier, E.; Graf, G. *Liebigs Ann. Chem.* **1967**, *704*, 109.

[65] Bestmann, H. J.; Schulz, H. *Chem. Ber.* **1962**, *95*, 2921.

[66] Thenappan, A.; Burton, D. J. *J. Org. Chem.* **1990**, *55*, 2311; *Tetrahedron Lett.* **1989**, *30*, 3641.

[67] Bestmann, H. J.; Kranz, E. *Chem. Ber.* **1969**, *102*, 1802.

[68] von Strandtmann, M.; Cohen, M. P.; Puchalski, C.; Shavel, J. *J. Org. Chem.* **1968**, *33*, 4306.

[69] Markl, G. *Tetrahedron Lett.* **1962**, 1027.

[70] Zbiral, E. *Angew. Chem.* **1967**, *6*, 877.

[71] Bestmann, H. J.; Dornauer, H.; Rostock, K. *Chem. Ber.* **1970**, *103*, 685.

[72] Axelrod, E.; Milne, G. M.; van Tamelen, E. E. *J. Am. Chem. Soc.* **1970**, *92*, 2139.

[73] Bestmann, H. J.; Frey, H. *Synthesis* **1984**, 243.

[74] Taylor, E. C.; Martin, S. F. *J. Am. Chem. Soc.* **1972**, *94*, 2874, 6281.

[75] Bestmann, H. J.; Rostock, K.; Dornauer, H. *Angew. Chem.* **1966**, *5*, 308.

[76] Bestmann, H. J.; Graf, G.; Hartung, H. *Liebigs Ann. Chem.* **1967**, *706*, 68.

[77] Bestmann, H. J.; Dornauer, H.; Rostock, K. *Liebigs Ann. Chem.* **1970**, *735*, 52.

[78] Bestmann, H. J.; Dornauer, H.; Rostock, K. *Chem. Ber.* **1970**, *103*, 2011.

[79] Bestmann, H. J.; Seng, F.; Schulz, H. *Chem. Ber.* **1963**, *96*, 465.

[80] Siemiatycki, M. S.; Strzelecka, H. *C. R. Seances Acad. Sci.* **1960**, *250*, 3489.

[81] Bestmann, H. J.; Seng, F. *Angew. Chem.* **1962**, *74*, 154.

[82] Pasto, D. J.; Garves, K.; Sevenair, J. P. *J. Org. Chem.* **1968**, *33*, 2975.

[83] Bose, A. K.; Dahill, R. T.; Ramer, R. M. *Tetrahedron Lett.* **1966**, 6263.

[84] Mondon, A. *Liebigs Ann. Chem.* **1957**, *603*, 115.

[85] Scherer, K. V.; Lunt, R. S. *J. Org. Chem.* **1965**, *30*, 3215.

[86] Bestmann, H. J.; Kranz, E. *Angew. Chem.* **1967**, *6*, 1967.

[87] Baldwin, J. E.; Fleming, R. H. *J. Am. Chem. Soc.* **1972**, *94*, 2140.

[88] Bestmann, H. J.; Kranz, E. *Chem. Ber.* **1972**, *105*, 2098.

[89] Hercouet, A.; Le Corre, M. *Tetrahedron Lett.* **1974**, 2491.

[90] Bestmann, H. J.; Haberlein, H. *Z. Naturforsch.* **1962**, *17B*, 787.

[91] Bestmann, H. J.; Haberlein, H.; Eisele, W. *Chem. Ber.* **1966**, *99*, 28.

[92] Bestmann, H. J.; Hartl, R.; Haberlein, H. *Liebigs Ann. Chem.* **1968**, *718*, 33.

[93] Bestmann, H. J.; Both, W. *Chem. Ber.* **1974**, *107*, 2926.

[94] Markl, G. *Angew. Chem.* **1963**, *2*, 153.

[95] Markl, G. *Z. Naturforsch.* **1963**, *18B*, 84.

[96] Bestmann, H. J.; Ruppert, D. *Angew. Chem.* **1968**, *7*, 637.

[97] Bestmann, H. J.; Schaper, W.; Ruppert, D.; Zimmerman, R.; Burzlaff, H. *Chem. Ber.* **1991**, *124*, 2761.

[98] Bestmann, H. J.; Saalfrank, R. W.; Snyder, J. P. *Angew. Chem.* **1969**, *8*, 216.

[99] Kayser, M. M.; Hatt, K. L.; Hooper, D. L. *Can. J. Chem.* **1991**, *69*, 1929.

[100] Nesmeyanov, N. A. *Bull. Acad. Sci. USSR* **1975**, *24*, 2737.

[101] Grigorenko, A. A.; Shevchuk, M. I.; Dombrovskii, A. V. *Zh. Obshch. Khim.* **1966**, *36*, 506; *Chem. Abstr.* **1966**, *65*, 737.

[102] Ramirez, F.; Dershowitz, S. *J. Org. Chem.* **1957**, *22*, 41.

[103] Issleib, K.; Linder, R. *Liebigs Ann. Chem.* **1967**, *707*, 120.

[104] Nesmeyanov, N. A.; Zhuzhlikova, S. T.; Reutov, O. A. *Bull. Acad. Sci. USSR* **1965**, 183.

[105] Taylor, J. D.; Wolf, J. W. *J. Chem. Soc., Chem. Commun.* **1972**, 876.

[106] Cooke, M. P. *J. Org. Chem.* **1973**, *38*, 4082.

[107] LeRoux, J.; Le Corre, M. *Tetrahedron Lett.* **1990**, *31*, 2591.

[108] Bestmann, H. J. *Tetrahedron Lett.* **1960**, 7.

[109] Bestmann, H. J.; Arnason, B. *Chem. Ber.* **1962**, *95*, 1513.

[110] Bestmann, H. J.; Denzel, T. *Tetrahedron Lett.* **1966**, 3591.

[111] Capuano, L.; Triesch, T.; Willmes, A. *Chem. Ber.* **1983**, *116*, 3767.

[112] Trippett, S.; Walker, D. M. *J. Chem. Soc.* **1961**, 1266.

[113] Bestmann, H. J.; Schmid, G.; Oechsner, H.; Ermann, P. *Chem. Ber.* **1984**, *117*, 1561.

[114] Schlessinger, R. H.; Poss, M. A.; Richardson, S.; Lin, P. *Tetrahedron Lett.* **1985**, *26*, 2391.

[115] Staab, H. A.; Sommer, N. *Angew. Chem.* **1962**, *74*, 294.

[116] Bestmann, H. J.; Schulz, H. *Liebigs Ann. Chem.* **1964**, *674*, 11.

[117] Maercker, A. *Angew. Chem.* **1967**, *6*, 557.

[118] Maercker, A.; Theysohn, W. *Liebigs Ann. Chem.* **1972**, *759*, 132.

[119] Bohlmann, F.; Skuballa, W. *Chem. Ber.* **1973**, *106*, 497.

[120] Braga, A. L.; Comasetto, J. V.; Petragnini, N. *Tetrahedron Lett.* **1984**, *25*, 111.

[121] Gough, S. T. D.; Trippett, S. *J. Chem. Soc.* **1964**, 543.

[122] Markl, G. *Chem. Ber.* **1961**, *94*, 3005.

[123] Shen, Y.; Lin, Y.; Xin, Y. *Tetrahedron Lett.* **1985**, *26*, 5137.

[124] Bestmann, H. J.; Hartung, H. *Chem. Ber.* **1966**, *99*, 1198.

[125] Bestmann, H. J.; Graf, G.; Hartung, H.; Kolewa, S.; Vilsmaier, E. *Chem. Ber.* **1970** *103*, 2794.

[126] Gough, S. T. D.; Trippett, S. *Proc. Chem. Soc.* **1961**, 302.

[127] Hamper, B. *J. Org. Chem.* **1988**, *53*, 5558.

[128] Capuana, L.; Triesch, T.; Schramm, V.; Hiller, W. *Chem. Ber.* **1984**, *117*, 2785.

[129] Listvan, V. N.; Stasyuk, A. P.; Bolyukh, A. N. *J. Org. Chem. USSR* **1989**, *25*, 392.

[130] Bestmann, H. J.; Graf, G.; Hartung, H. *Angew. Chem.* **1965**, *4*, 596.

[131] Listvan, V. N.; Stasyuk, A. P.; Kurgan, L. N. *J. Gen. Chem.* **1987**, *57*, 1366.

[132] Gough, S. T. D.; Trippett, S. *J. Chem. Soc.* **1962**, 2333.

[133] Abell, A. D.; Trent, J. O.; Whittington, B. I. *J. Org. Chem.* **1989**, *54*, 2763.

[134] Chopard, P. A.; Searle, R. J. G.; Devitt, F. H. *J. Org. Chem.* **1965**, *30*, 1015.

[135] Abell, A. D.; Clark, B. M.; Robinson, W. T. *Aust. J. Chem.* **1989**, *42*, 1161.

[136] Shen, Y.; Qui, W. *J. Chem. Soc. Chem. Commun.* **1987**, 703; *Tetrahedron Lett.* **1987**, *28*, 449; *J. Fluorine Chem.* **1988**, *38*, 249.

[137] Begue, J. P.; Bonnet-Delpon, D.; Mesurer, D.; Nee, G.; Wu, S. W. *J. Org. Chem.* **1992**, *57*, 3807.

[138] Chopard, P. A.; Hudson, R. F.; Searle, R. J. G. *Tetrahedron Lett.* **1965**, 2357.

[139] Ingham, C. F.; Massy-Westropp, R. A.; Reynolds, G. D.; Thorpe, W. D. *Aust. J. Chem.* **1975**, *28*, 2499.

[140] Tsuboi, S.; Fukumoto, H.; Wada, H.; Takeda, A.; Fukuyama, K. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 689.

[141] Babidge, P. J.; Massy-Westropp, R. A. *Aust. J. Chem.* **1977**, *30*, 1629.

[142] Boulos, L. S.; Shabama, R. *Phosphorus Sulfur* **1990**, *53*, 81; **1991**, *61*, 131.

[143] Abell, A. D.; Doyle, I. R.; Massy-Westropp, R. A. *Aust. J. Chem.* **1982**, *35*, 2270.
[144] Kayser, M. M.; Breau, L. *Can. J. Chem.* **1989**, *67*, 1401.
[145] Knight, D. W.; Pattenden, G. *J. Chem. Soc. Perkin Trans. (1)* **1979**, 62.
[146] Kayser, M. M.; Breau, L. *Tetrahedron Lett.* **1988**, *29*, 6203.
[147] Allahdad, A.; Knight, D. W. *J. Chem. Soc. Perkin Trans. (1)* **1982**, 1855.
[148] Breau, L.; Kayser, M. M. *Can. J. Chem.* **1989**, *67*, 569.
[149] Abell, A. D.; Massy-Westropp, R. A. *Aust. J. Chem.* **1982**, *35*, 2077.
[150] Abell, A. D.; Morris, K. B.; Litten, J. C. *J. Org. Chem.* **1990**, *55*, 5217.
[151] Abell, A. D.; Clark, B. C.; Robinson, W. T. *Aust. J. Chem.* **1988**, *41*, 1243.
[151a] Kayser, M. M.; Hatt, K. L.; Hooper, D. L. *Can. J. Chem.* **1992**, *70*, 1985.
[152] Murphy, P. J.; Brennan, J. *Chem. Soc. Revs.* **1988**, *17*, 1.
[153] Wittig, G.; Schollkopf, U. *Chem. Ber.* **1954**, *87*, 1318.
[154] Cristau, H. J.; Ribeill, Y. *J. Organomet. Chem.* **1988**, *352*, C51.
[155] Le Corre, M. *Bull. Soc. Chim. Fr.* **1974**, 2005.
[156] Subramanyan, V.; Silver, E. H.; Solway, A. H. *J. Org. Chem.* **1976**, *41*, 1272.
[157] Grell, W.; Machleidt, H. *Liebigs Ann. Chem.* **1966**, *693*, 134.
[158] Aitken, R. A.; Thom, G. L. *Synthesis* **1989**, 958.
[159] Ploder, W. H.; Tavares, D. F. *Can. J. Chem.* **1970**, *48*, 2446.
[160] Bergelson, L. D.; Vaver, V. A.; Borsukov, L. I.; Shemyakin, M. M. *Bull. Acad. Sci. USSR* **1963**, 1037.
[161] House, H. O.; Babad, H. *J. Org. Chem.* **1963**, *28*, 90.
[162] Dauben, W. G.; Hart, D. J. *Tetrahedron Lett.* **1975**, 4353.
[163] Hercouet, A.; Le Corre, M. *Tetrahedron* **1981**, *37*, 2855, 2861.
[164] Hercouet, A.; Le Corre, M. *Tetrahedron Lett.* **1979**, 2145; *Tetrahedron* **1981**, *37*, 2867.
[165] Hercouet, A.; Le Corre, M.; Le Floch, Y. *Synthesis* **1982**, 597.
[166] Le Floch, Y; Lefeuvre, M. *Tetrahedron Lett.* **1986**, *27*, 2751, 5503.
[167] Zammattio, F.; Brion, J. D.; Ducrey, P.; Le Baut, G. *Synthesis* **1992**, 375.
[168] Hsiao, C. N.; Kolasa, T. *Tetrahedron Lett.* **1992**, *33*, 2629.
[169] Henrick, C. A.; Bohme, E.; Edwards, J. A.; Fried, J. H. *J. Am. Chem. Soc.* **1968**, *90*, 5926.
[170] Le Roux, J.; Le Corre, M. *J. Chem. Soc. Chem. Commun.* **1989**, 1464.
[171] Kise, H.; Arase, Y.; Shiraishi, S.; Semo, M.; Asahara, T. *J. Chem. Soc. Chem. Commun.* **1976**, 299.
[172] Le Corre, M.; Le Roux, J. *Phosphorus Sulfur* **1990**, *51/52*, 257.
[173] Brennan, J.; Murphy, P. J. *Tetrahedron Lett.* **1988**, *29*, 2063.
[174] Erba, E.; Gelmi, M. L.; Pocar, D. *Chem. Ber.* **1988**, *121*, 1519.
[175] Bestmann, H. J.; Arnason, B. *Tetrahedron Lett.* **1961**, 455.
[176] Ernest, I.; Greengrass, C. W.; Holick, W.; Jackman, D. E.; Pfaendler, H. R.; Woodward, R. B. *J. Am. Chem. Soc.* **1978**, *100*, 8214.
[177] Bestmann, H. J.; Roth, D. *Angew. Chem.* **1990**, *29*, 99.
[178] Le Corre, M.; Hercouet, A.; Le Baron, H. *J. Chem. Soc. Chem. Commun.* **1981**, 14.
[179] Cooney, J. V.; McEwen, W. E. *J. Org. Chem.* **1981**, *46*, 2570.

[180] Gilpin, M. L.; Harbridge, J. B.; Howarth, T. T.; King, T. J. *J. Chem. Soc. Chem. Commun.* **1981**, 929.

[181] Bazureau, J. P.; Le Corre, M. *Tetrahedron Lett.* **1990**, *29*, 1919.

[182] Le Corre, M.; Hercouet, A.; Le Stanc, Y.; Le Baron, H. *Tetrahedron* **1985**, *41*, 5313.

[183] Eitel, M.; Pindur, U. *Synthesis* **1989**, 364.

[184] Heine, H. W.; Lowrie, G. B.; Irving, K. C. *J. Org. Chem.* **1970**, *35*, 444.

[185] Bestmann, H. J.; Sommer, N.; Staab, H. A. *Angew. Chem.* **1962**, *1*, 270.

[186] Miyano, M.; Stealy, M. A. *J. Org. Chem.* **1975**, *40*, 2840.

[187] Flitsch, W.; Peters, H. *Tetrahedron Lett.* **1969**, 1161.

[188] Couture, A.; Cornet, H.; Grandclaudon, P. *Tetrahedron* **1992**, *48*, 3857.

[189] Gossauer, A.; Ruebler, F.; Zilch, H. *Liebigs Ann. Chem.* **1979**, 1309.

[190] Bishop, J. E.; O'Connell, J. F.; Rapoport, H. *J. Org. Chem.* **1991**, *56*, 5079.

[191] Natsune, M.; Takahashi, M.; Kiuchi, K.; Sugaya, H. *Chem. Pharm. Bull.* **1971**, *19*, 2648.

[192] Flitsch, W.; Schindler, S. R. *Synthesis* **1975**, 685.

[193] Wittig, G.; Boll, W. *Chem. Ber.* **1962**, *95*, 2526.

[194] Oda, R.; Ito, Y.; Okano, M. *Tetrahedron Lett.* **1964**, 7.

[195] Ito, Y.; Okano, M.; Oda, R. *Tetrahedron* **1966**, *22*, 2615.

[196] Sestrick, M. R.; Miller, M.; Hegedus, L. S. *J. Am. Chem. Soc.* **1992**, *114*, 4079.

[197] Markl, G. *Tetrahedron Lett.* **1961**, 811.

[198] Wittig, G.; Schlosser, M. *Tetrahedron* **1962**, *18*, 1023.

[199] Ege, G.; Gilbert, K. *Tetrahedron Lett.* **1979**, 1567; *J. Heterocycl. Chem.* **1981**, *18*, 675.

[200] Strzelecka, H. *C. R. Seances Acad. Sci.* **1962**, *255*, 731.

[201] Markl, G. *Tetrahedron Lett.* **1961**, 807.

[202] Alemagna, A.; Buttero, P. D.; Licandro, E.; Maiorana, S.; Guastini, C. *J. Chem. Soc. Chem. Commun* **1983**, 337.

[203] Dalla Croce, P.; Buttero, P. D.; Licandro, E.; Maiorana, S. *Synthesis* **1979**, 279.

[204] Froyen, P.; Jurvik, P. *Phosphorus Sulfur* **1992**, *69*, 83.

[205] Markl, G. *Z. Naturforsch.* **1962**, *17B*, 782.

[206] van Leusen, A. M.; Reith, B. A.; Iedema, A. J. W.; Strating, J. *Rec. Trav. Chim.* **1972**, *91*, 37.

[207] Reith, B. A.; Strating, J.; van Leusen, A. M. *J. Org. Chem.* **1974**, *39*, 2728.

[208] Nesmeyanov, N. A.; Zhuzhlikova, S. T.; Reutov, O. A. *Dokl. Akad. Nauk. SSSR* **1963**, *151*, 856.

[209] Zwanenburg, B.; Venier, C. G.; Porskamp, P. A. T.; Vanderbeij M. *Tetrahedron Lett.* **1978**, 807.

[210] Zbiral, E.; Fenz, L. *Monatsh. Chem.* **1965**, *96*, 1983.

[211] Akiba, K.; Eguchi, C.; Inamoto, N. *Bull. Chem. Soc. Jpn.* **1967**, *40*, 2983.

[212] van Leusen, A. M.; Iedema, A. J. W.; Strating, J. *J. Chem. Soc. Chem. Commun* **1968**, 440.

[213] Akiba, K.; Imanari, M.; Inamoto, N. *J. Chem. Soc. Chem. Commun.* **1969**, 166.

[214] Martin, D.; Niclas, H. J. *Chem. Ber.* **1967**, *100*, 187

# 7

# REACTIONS OF PHOSPHONIUM YLIDES III. WITH MULTIPLE-BONDED COMPOUNDS AND THREE-MEMBERED RINGS

Phosphonium ylides (P=C) react with a wide variety of multiple bonded compounds (A=B) in addition reactions to initially afford, formally, if not really, betaine intermediates ($^+$P–C–A–B$^-$) which can follow a variety of routes to products, including proton transfer to produce new ylides, displacement of phosphine to afford three-membered rings, covalent bond formation to afford ring systems, or transfer of B to phosphorus to afford multiple bonded products such as P=B and C=A. The best known such reaction is the Wittig reaction in which A=B is a carbonyl compound, usually an aldehyde or ketone, and the reaction proceeds to completion by transfer of oxygen from carbonyl to phosphorus, producing an alkene (C=A) and a phosphine oxide (P=B). Because of the major importance of that specific reaction, by itself justifying the award of the Nobel Prize for 1979 to Georg Wittig for its development, it will be discussed separately in the following two chapters.

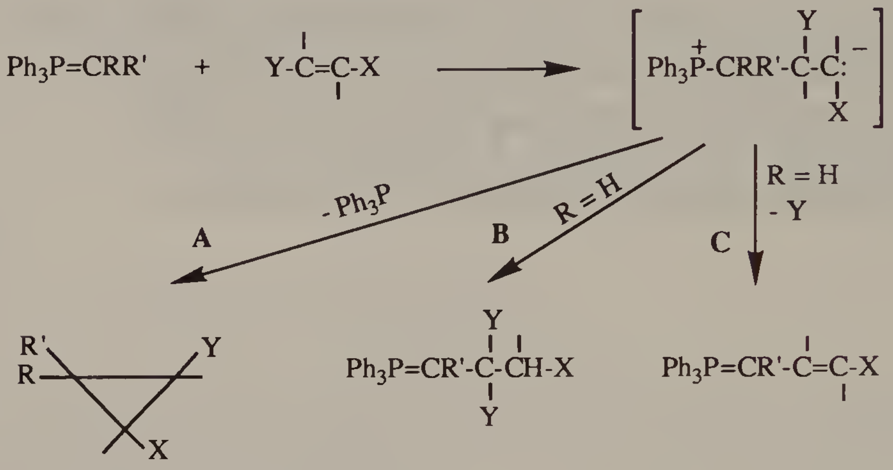
In this chapter are discussed addition reactions of other than carbonyl compounds, compounds where A and B are combinations of carbon, nitrogen, oxygen, and sulfur, the elements best known for multiple bonding. Sections will deal with additions to carbon–carbon multiple bonds (A = B = carbon), carbon–nitrogen systems (A = carbon; B = nitrogen), carbon–sulfur systems (A = carbon; B = sulfur), and nitrogen systems (A = nitrogen; B = nitrogen or oxygen). In Section 7.3 are covered reactions with cumulene-type compounds such as ketenes and isocyanates, as well as reactions with 1,3-dipolar compounds. In section 7.4 are discussed the reactions of phosphonium ylides with the three-membered rings: oxiranes, thiiranes, and aziridines.

*Ylides and Imines of Phosphorus*, Edited by A. William Johnson.
ISBN 0-471-52217-1

## 7.1 CARBON–CARBON MULTIPLE-BONDED SYSTEMS

### 7.1.1 Alkenes

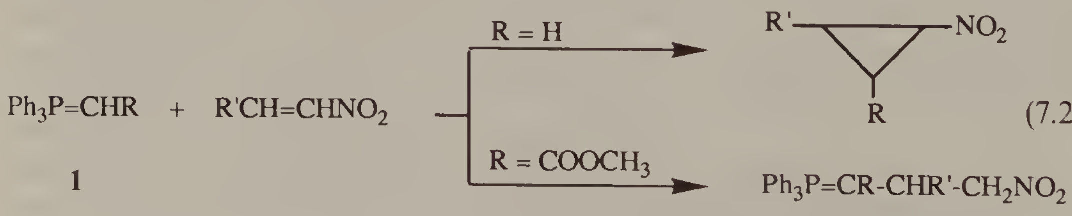
Phosphonium ylides do not react with isolated alkenes, but do react with a variety of conjugated alkenes and in this section the various kinds of alkene substrates are discussed. Virtually all such reactions can be explained by a single comprehensive mechanism (Eq. 7.1)[1,2] involving an initial Michael addition by



(7.1)

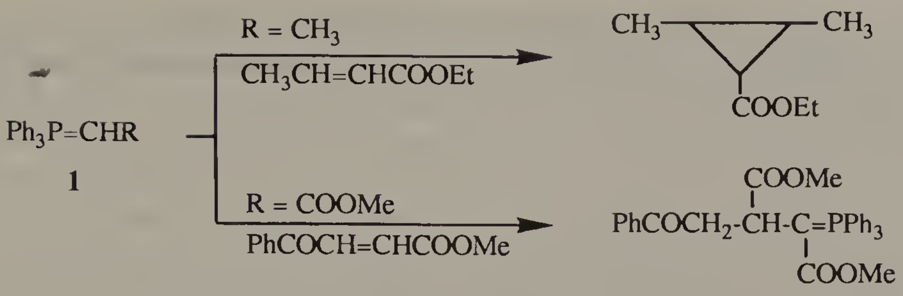
the ylide followed by three separate routes to completion: **A** (cyclopropane formation by expulsion of phosphine); **B** (ylide formation by proton transfer); and **C** (ejection of a leaving group followed by proton loss to form a new ylide). Route **A** is usually followed by ylides which are nonstabilized whereas route **B** usually is followed by stabilized ylides, the α-proton being especially acidic. The reversibility of route **B** addition has been demonstrated.[3,4] Route **C** can be followed by both kinds of ylides, but only when the alkene carries a good leaving group Y.

Reaction of the unsubstituted ylide (**1**, R = H) with nitroalkenes followed path **A** and afforded low yields of nitrocyclopropanes,[3] but reaction of the stabilized ester ylide (**1**, R = COOMe) with the same nitroalkenes followed path **B** and afforded moderate yields of new ylides (Eq. 7.2)[3,4]



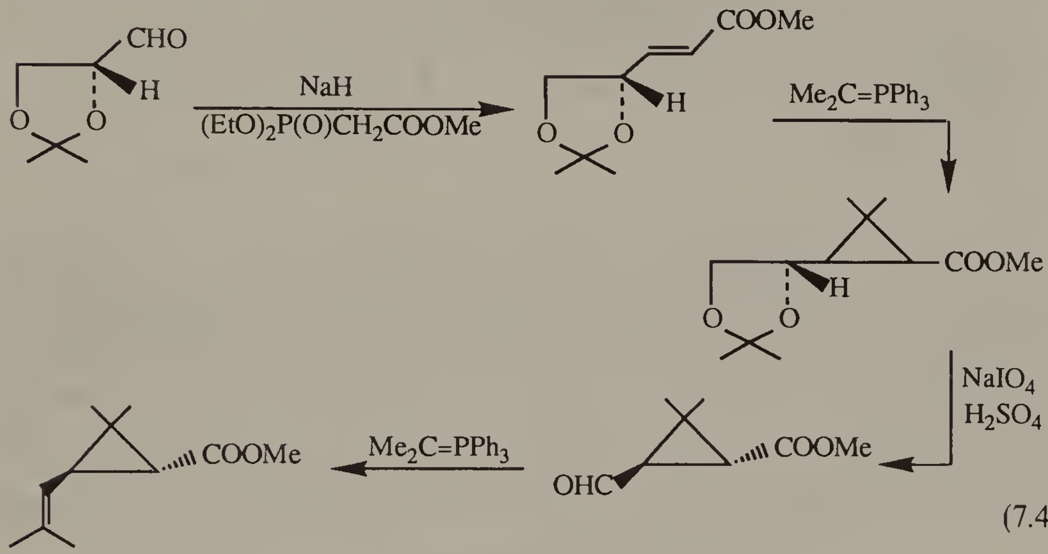
(7.2)

A similar pattern occurred in reaction of ylides with α,β-unsaturated esters. The ethylide (**1**, R = $CH_3$) reacted with ethyl crotonate to afford a 91% yield of ethyl 2,3-dimethylcyclopropane carboxylate and triphenylphosphine, whereas the ester ylide (**1**, R = COOMe) reacted with methyl benzoylacrylate to produce



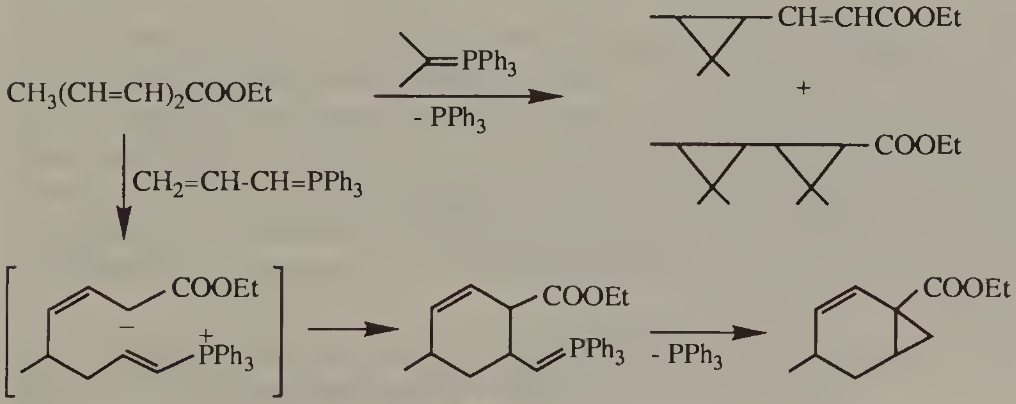
(7.3)

a new ylide in 92% yield (Eq. 7.3).[5] Grieco and Finkelhor[6] prepared a number of 1,1-dimethylcyclopropanes by reacting isopropylidenetriphenylphosphorane with α,*β*-unsaturated esters, and more recently Devos et al.[7] and Bernardi et al.[8] used this same ylide in stereoselective syntheses of chrysanthemic ester precursors via route A. In both instances *trans*-alkenes were converted to *trans*-cyclopropanes. Starting with R-glyceraldehyde Mulzer and Kappert[9] obtained 99% ee chrysanthemic ester, involving as a key step an enantioselective cyclopropanation with the isopropylidene ylide (Eq. 7.4).



(7.4)

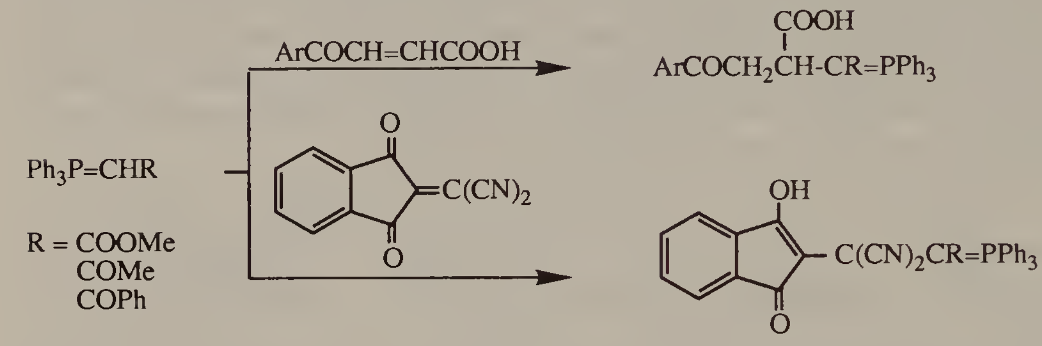
Conjugated dienoates react with phosphonium ylides via route A. Dauben[10] originally reported that the isopropylidene ylide reacted with ethyl sorbate to



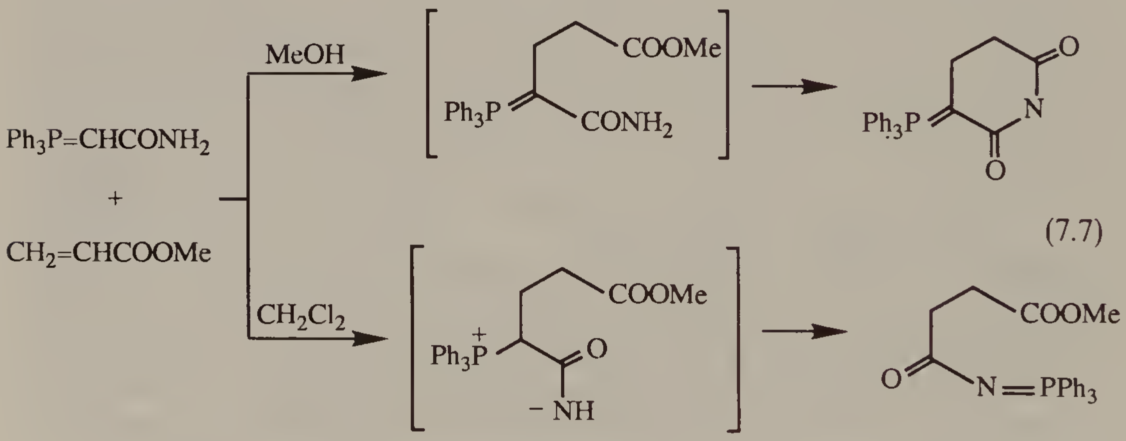
(7.5)

afford a 1:1 mixture of the $\gamma,\delta$-monocyclopropanated product and the $\alpha,\beta,\gamma,\delta$-dicyclopropanated product (Eq. 7.5). He also proposed $\delta$-attack by the allylidene ylide (using its $\gamma$-position) and a mechanism as shown to account for formation of a norcarene product. However, two more recent reports of the reaction of the isopropylidene ylide with similar dienoates reported only $\beta$-attack to form monocyclopropanated products in moderate yields.[7,11]

Several examples of route **B** reactions have appeared in the recent literature, all involving stabilized ylides[12,13] (Eq. 7.6). Wanner and Koomen[14] found that $Ph_3P{=}CHCONH_2$ reacted with methyl acrylate to afford glutarimide ylides in methanol, the first step being a route **B** addition. However, in an aprotic solvent a rearrangement followed to produce an iminophosphorane (Eq. 7.7).

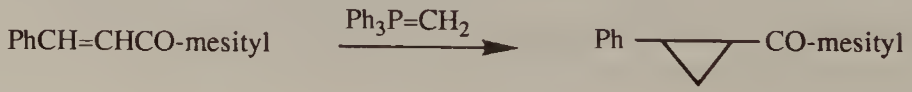


(7.6)

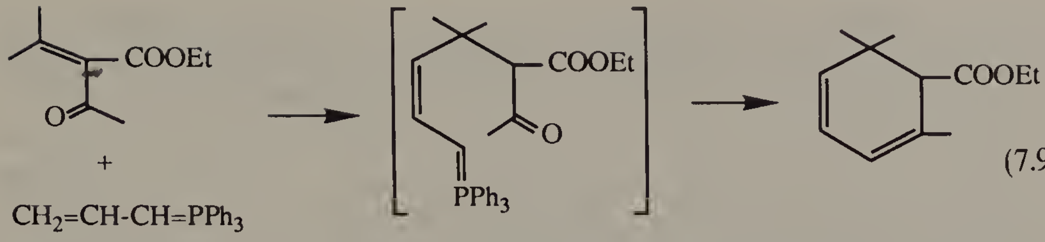


(7.7)

Ylides invariably react with $\alpha,\beta$-unsaturated aldehydes at the carbonyl group in a normal Wittig reaction.[15]. Few conjugate additions of ylides to $\alpha,\beta$-unsaturated ketones are known because of the preference for ylide attack at the carbonyl group in a Wittig reaction. However, Freeman[2] showed that steric blocking of the carbonyl group would force attack at the $\beta$-carbon and a route **A** reaction (Eq. 7.8). Later, Buchi and Wuest[16] reported the attack of an allylidene ylide (using its $\gamma$-position) on the $\beta$-position of an unsaturated keto-ester in a



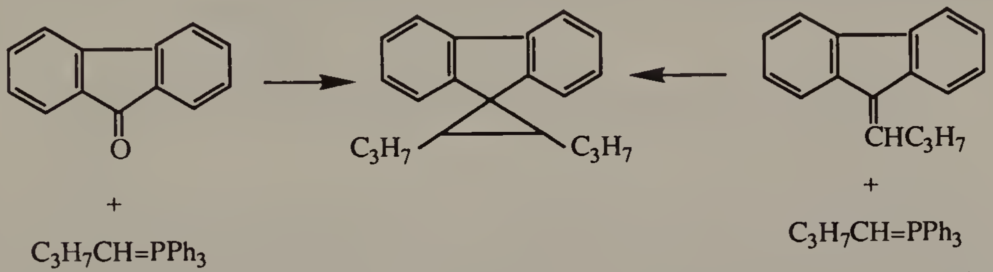
(7.8)



(7.9)

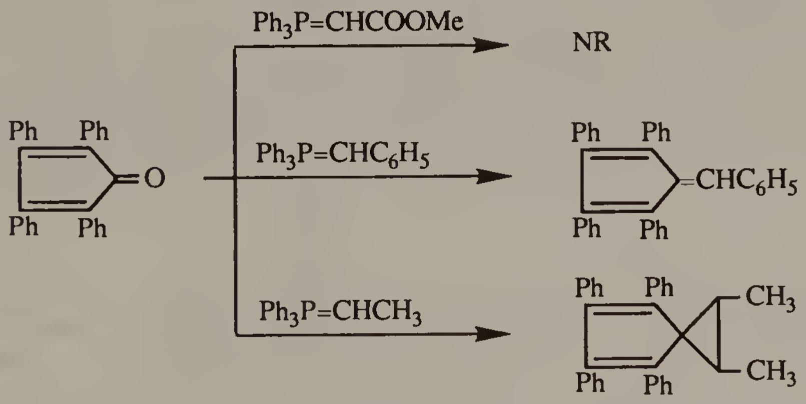
route **B** reaction, eventually including a Wittig cyclization, the product cyclohexadienecarboxylate being obtained in 60% yield (Eq. 7.9).

Ylides have been shown to react with certain hydrocarbon alkenes if sufficient delocalization is present for the intermediate carbanion, and the reactions invariably follow route **A**. Mechoulam and Sondheimer[17] found that the butylide reacted with fluorenone to afford the cyclopropane adduct, triphenylphosphine oxide, and triphenylphosphine (Eq. 7.10). They explained the result



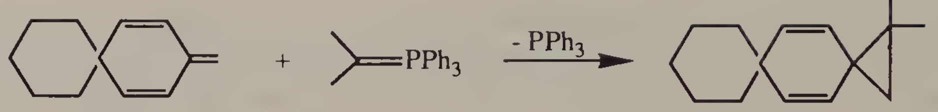
(7.10)

by proposing an initial Wittig reaction to form 9-butylidenefluorene, which then underwent a route **A** addition reaction. This latter step was demonstrated separately, and also again by Bestmann et al.[18] Reid et al.[19,20] found similar behavior in the cyclopentadienone series, with the stabilized ylides not reacting at all, semistabilized ylides effecting a Wittig reaction to afford fulvenes, and the reactive alkylides reacting twice, converting the fulvenes to cyclopropane adducts in moderate yields via route **A** (Eq. 7.11). Finally, the isopropylidene ylide



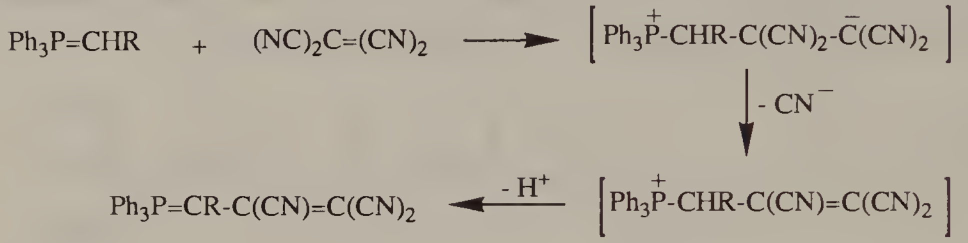
(7.11)

reacted via path **A** with a cross-conjugated triene to afford good yields of adduct (Eq. 7.12),[21] but less nucleophilic ylides gave only low yields.



(7.12)

Route **C** reactions of ylides with alkenes require the presence of a leaving group on the alkene. Trippett[22] reported two early examples with a cyano group or an ethoxy group leaving, but Zbiral[23] reported the addition of a variety of ylides, both reactive and stabilized, to tetracyanoethylene followed by expulsion of a cyano group to produce new ylides (Eq. 7.13). Similarly, bromine served as a leaving group when 9-bromomethylenefluorene reacted with methylenetriphenylphosphorane.[24]



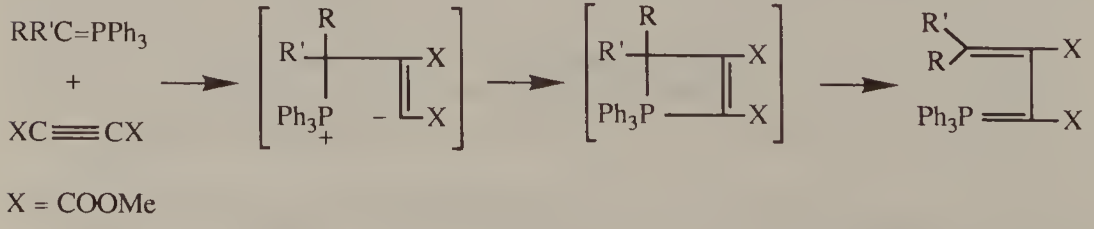
$$Ph_3P{=}CHR + (NC)_2C{=}(CN)_2 \longrightarrow \left[Ph_3\overset{+}{P}\text{-}CHR\text{-}C(CN)_2\text{-}\overset{-}{C}(CN)_2\right] \xrightarrow{-CN^-} \left[Ph_3\overset{+}{P}\text{-}CHR\text{-}C(CN){=}C(CN)_2\right] \xrightarrow{-H^+} Ph_3P{=}CR\text{-}C(CN){=}C(CN)_2$$

(7.13)

Finally, many years ago Inhoffen et al.[25] and Bohlmann[26] both reported unusual additions of allylidene ylides with α,β-unsaturated ketones and claimed products not accounted for by routes **A**, **B**, or **C**. They proposed six-membered oxaphosphacycle intermediates which, by rearrangement, were proposed to eliminate triphenylphosphine oxide, but compelling evidence for these unusual mechanisms is absent.

### 7.1.2 Alkynes

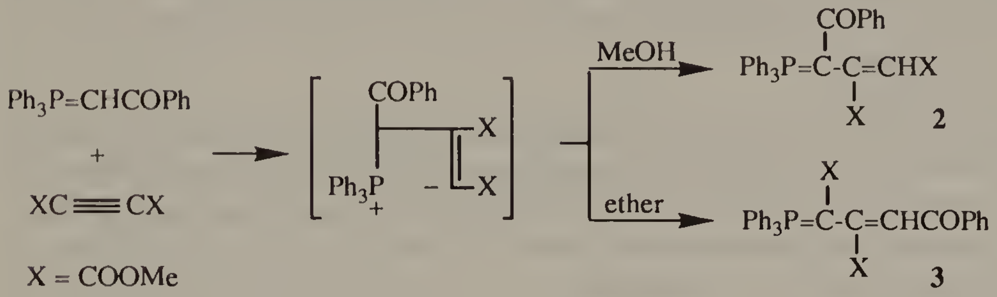
In the early days of ylide chemistry, dimethyl acetylenedicarboxylate (DMAD) was the alkyne substrate of choice for reaction with ylides. A variety of ylides were reacted with DMAD in aprotic solvents by initial addition across the triple bond, formation of a four-membered phosphacycle intermediate, and ring opening to afford a new ylide. The overall result was that DMAD had been inserted between the carbanion and the phosphonium group of the starting ylide (Eq. 7.14). It must be cautioned that there is no evidence demanding the finite existence of the phosphacyclobutene intermediate. In 1964 Brown et al.[27] used



(7.14)

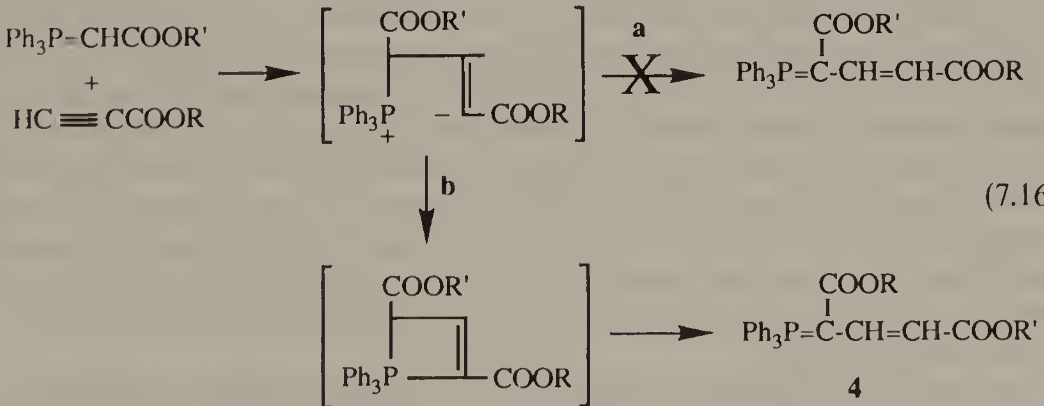
the benzhydrylidene (R = R′ = Ph) and fluorenylidene ylides; Bestmann and Rothe[28] used alkylides (R = H, R′ = alkyl), benzylides (R = Ph, R′ = H or alkyl), and a cinnamylide (R = ω-styryl; R′ = H) in such reactions. More recently Gilheany et al.[29] and Barluenga et al.[30] have applied this same reaction with unique ylides.

Hendrickson[31] was the first to report a reaction with DMAD in a protic solvent (methanol), in that instance using the phenacylide, and claimed a phosphorin hexacycle structure for the product. However, the product instead was suspected to be,[32,33] and later was shown to be,[34] a new ylide (**2**) which resulted from the initial addition of ylide to the triple bond, followed by proton transfer (Eq. 7.15). In the absence of a protic solvent the isomeric ylide (**3**) resulted, presumably via the general mechanism shown in Eq. 7.14. Trippett[22] also found that a stabilized ylide, cyanomethylenetriphenylphosphorane, reacted with DMAD in methanol solution by addition and subsequent proton transfer, rather than by the phosphacyclobutene intermediate.



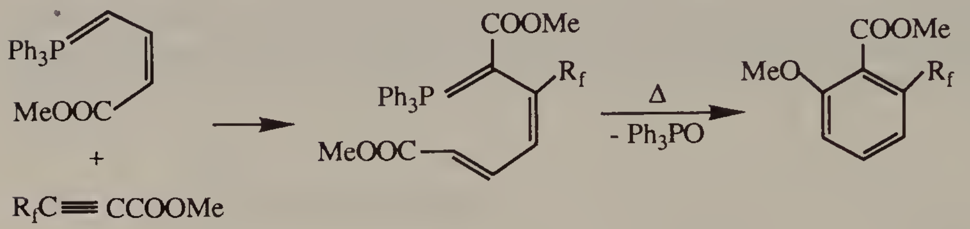
(7.15)

In 1967 Brown[35] reported that a variety of alkynes other than DMAD would *not* react with ylides. However, there have been several more recent reports of successful reactions. The most important seems that of Barluenga et al.,[36] which proved that even in instances where the overall reaction *appeared* to be a Michael-type addition followed by proton transfer (Eq. 7.16, path **a**), the phosphacyclobutene mechanism (Eq. 7.16, path **b**) actually was operating. Thus, the carbo*methoxy* ylide and *ethyl* propynoate afforded the new ylide (**4**,



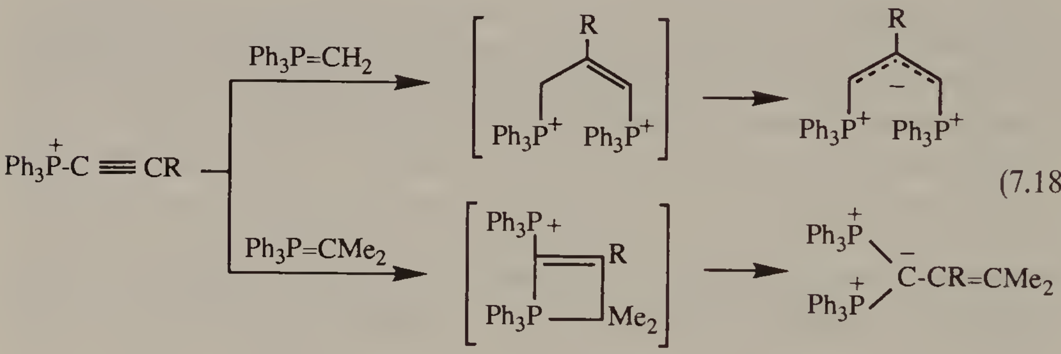
(7.16)

R′ = Me; R = Et), whereas the carb*ethoxy* ylide and *methyl* propynoate afforded the isomeric ylide (**4**, R′ = Et; R = Me), in both instances necessitating the path **b** mechanism. The same reaction had been used to prepare **4** with deuterium labelling specifically in the $\beta$- or $\gamma$-position.[37] Ding et al.[38] effected the addition of an allylidene ylide to a series of perfluoro alkynoates in high yields, the latter undergoing an intramolecular Wittig reaction upon heating to afford perfluoroalkyl methyl *o*-anisoates (Eq. 7.17).



(7.17)

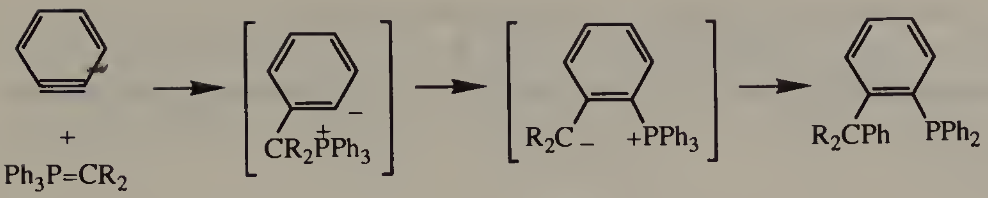
Recently Bestmann and Kisielowski[39] added triphenylphosphoniummethylide to the triple bond of alkynylphosphonium salts. Proton transfer followed to afford a symmetrical ylide (Eq. 7.18). Use of the isopropylidene ylide instead, which has no $\alpha$-protons for transfer, produced the allylidene ylide, undoubtedly via a phosphacyclobutene intermediate.



(7.18)

In summary, phosphonium ylides react by addition to a variety of alkynes carrying electron-withdrawing groups, with the reaction involving in most instances the formation of a phosphacyclobutene intermediate which opens in a new direction to afford a new ylide, the alkyne group effectively being inserted between the phosphonium group and the carbanion of the original ylide. This overall process will be called an "ylide interchange" process hereafter. The rare exceptions to this process occur when the original ylide carries a strong stabilizing group and only when the reaction is conducted in a protic solvent, in which case a proton transfer occurs in the first intermediate to afford an isomeric ylide adduct instead.

Brief mention should be made of Zbiral's[40] discovery that phosphonium ylides reacted with benzyne via an initial addition followed by transfer of the triphenylphosphorus group and retransfer of a phenyl group (Eq. 7.19). An allylidene ylide effected simple addition to benzyne through the $\gamma$-position.[41]

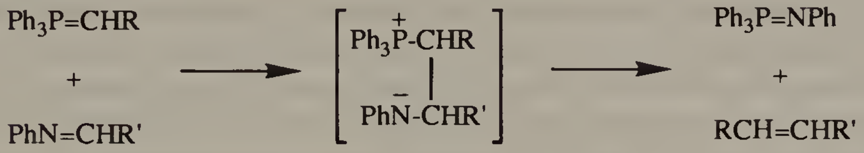


(7.19)

## 7.2 CARBON–HETEROATOM MULTIPLE-BONDED SYSTEMS

### 7.2.1 Carbon–Nitrogen Systems

*7.2.1.1* ***Imines.*** Phosphonium ylides are known to add to imines (Schiff bases) to form alkenes and iminophosphoranes in good yield (Eq. 7.20).[42] The reaction

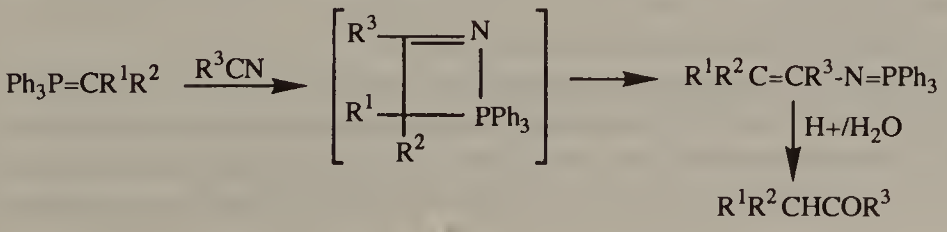


(7.20)

is of little practical value because the products are more readily obtained by other methods; the alkene by a direct Wittig reaction with the corresponding carbonyl compound and the iminophosphorane from an azide and triphenylphosphine. It was proposed that the reaction proceeded analogously to the Wittig reaction, but there is no evidence regarding the separate existence of the betaine and/or azaphosphetane intermediate.

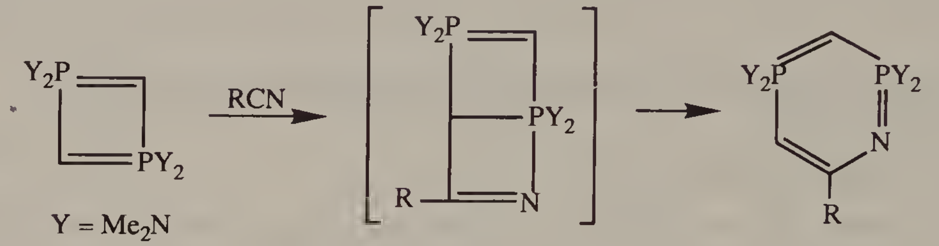
The same reaction, but using ylides with a $\beta$-proton, resulted in the formation of allenes, with amine and phosphine being byproducts.[42] In this instance the betaine intermediate was isolable.

*7.2.1.2* ***Nitriles.*** Phosphonium ylides add to nitriles in much the same manner as they do to alkynes, although the similarity was not realized initially. In the early work the initially formed adducts were not isolated and instead the reaction mixtures were hydrolyzed to afford phosphine oxides and ketones, and the method was claimed to be a useful synthesis of ketones.[43,44] Later Cianek[45] was able to isolate the iminophosphorane adduct, and separately hydrolyzed it to the ketone. The adduct structure also was confirmed by a separate synthesis, and he proposed that an azaphosphacyclobutene intermediate was involved in its formation (Eq. 7.21). In effect, the nitrile group was



(7.21)

inserted between the phosphorus group and the carbanion group of the starting ylide in an ylide interchange reaction. Fluck et al.[46] effected the same ylide interchange reaction with a four-membered cyclic bis-ylide and nitriles, producing a ring expansion to a six-membered cyclic ylide–iminophosphorane (Eq. 7.22).



(7.22)

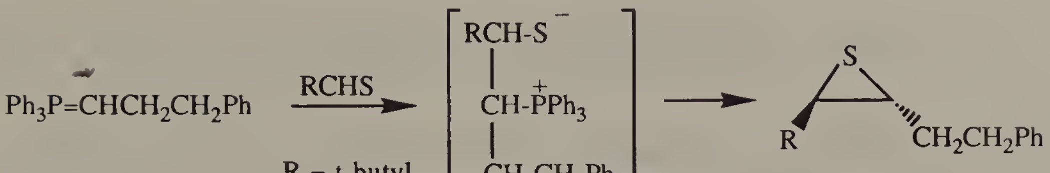
The overall result of the addition of ylides to nitriles followed by the hydrolytic reaction is the synthesis of a ketone in which one substituent came from the ylide and the other came from the nitrile. Accordingly, the ylide becomes a synthon for ketones, and the ready availability of disubstituted ylides makes this route practical. Recently Trabelsi et al.[47] applied this concept in reacting a series of ylides with a series of perfluoroalkylnitriles as a very high-yield route to perfluoroalkylketones.

Stabilized ylides only reacted with nitriles carrying strong electron-withdrawing groups, such as cyanogen and trifluoroacetonitrile.[45] However, Vicente et al.[48] recently effected a reaction of the ester ylide with benzonitrile when the latter was complexed with platinum dichloride, the complexation apparently making the nitrile more reactive.

### 7.2.2 Carbon–Sulfur Systems

*7.2.2.1* ***Thiones and Thials.*** Compounds with carbon–sulfur double bonds would be expected to react with phosphonium ylides in a manner analogous to that of carbonyl compounds (i.e., the Wittig reaction), with sulfur being transferred to phosphorus and an alkene resulting. The apparent first such reaction, in which triphenylphosphoniummethylide reacted with thiobenzophenone to afford 1,1-diphenylethylene and triphenylphosphine sulfide, never was published in the open literature.[49] However, Tewari et al.[50] reported that benzylidene ylides afforded good yields of alkenes in reactions with thiobenzophenone and 2,7-dibromofluorenthione. In 1970 it was shown that semistabilized and reactive ylides reacted with elemental sulfur to afford alkenes and triphenylphosphine sulfide, presumably via conversion of ylide first to thial which then reacted with more ylide to afford alkene,[51] and Okuma et al.[52] provided additional evidence for this proposition.

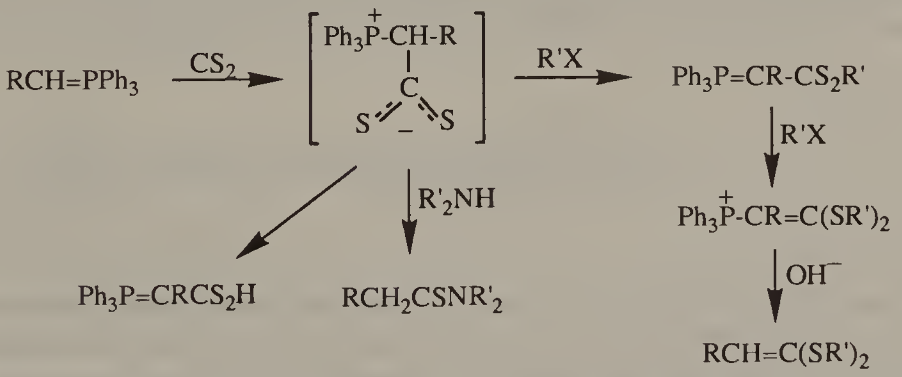
In the course of exploring the chemistry of the newly obtained thiopivaldehyde, Vedejs et al.[53] reported a quite different course for the reaction with ylides, with the products in this instance being a *trans*-thiirane and triphenylphosphine (Eq. 7.23). Two questions arise from this report. First, why did sulfur not transfer



(7.23)

to phosphorus as in the previously cited examples, but instead displace triphenylphosphine? Both oxygen (in the Wittig reaction) and nitrogen (see Section 7.2.1) in similar circumstances are known to be scavenged by phosphorus, as is sulfur, as documented in the preceding paragraphs. Second, why should the *trans*-thiirane be the product, rather than the *cis*, evolving as it must from the presumably higher-energy erythro form of the betaine and/or cis thiaphosphetane? The answer to both questions may be that the steric bulk of the *t*-butyl group forced the two reacting centers to approach each other orthogonally, and then rather than rotating 90° to close a four-membered thiaphosphetane ring, it rotated 90° in the opposite direction to form a more stable rotamer of the erythro form. In this conformation the sulfide group would be well positioned to effect an $S_N2$ displacement of triphenylphosphine. By this proposal the involvement of a thiaphosphetane intermediate is not necessary.

*7.2.2.2* ***Carbon Disulfide.*** Carbon disulfide reacts with some ylides in a Wittig-type reaction to afford triphenylphosphine sulfide and a thioketene, but with other ylides only an addition reaction takes place. Staudinger et al.[54] isolated only triphenylphosphine sulfide from reaction with diphenylmethylenetriphenylphosphorane, claiming that the other product was diphenylthioketene which polymerized, but with the similar ylide fluorenylidenetriphenylphosphorane the dimer of the thioketene was identified.[55] Two groups later found that from a variety of ylides 1:1 adducts were obtained[56,57] (Eq. 7.24). The initial betaine adduct could be mono- or dialkylated, the product of the latter being hydrolyzeable to a ketene mercaptal[58] (Eq. 7.24). The betaine adduct also could be

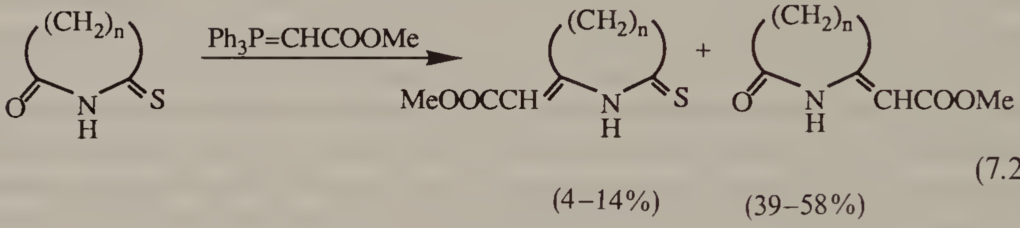


(7.24)

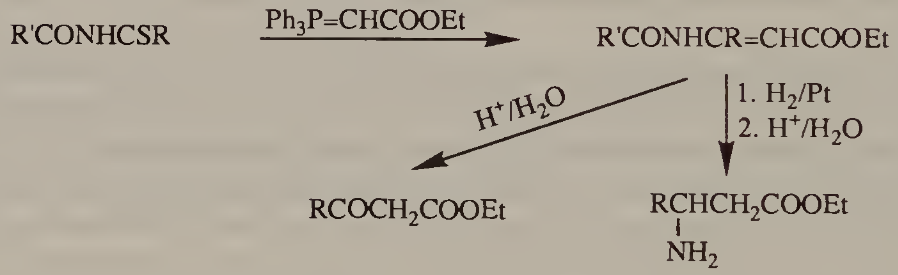
trapped by amines[59] and metal carbonyl.[60] A betaine adduct also was isolated from the reaction of $CS_2$ with carbodiphosphorane, but it could be made to thermally lose triphenylphosphine sulfide and produce triphenylphosphoranylidenethioketene (Eq. 7.25).[61]

$$Ph_3P{=}C{=}PPh_3 \xrightarrow{CS_2} (Ph_3\overset{+}{P})_2\overset{-}{C}\text{-}CS_2^{-} \xrightarrow[-\,Ph_3PS]{\Delta} Ph_3P{=}C{=}C{=}S \qquad (7.25)$$

*7.2.2.3* ***Thioimides and Thioamides.*** In 1977 Gossauer et al.[62] reported reaction of an ester ylide with cyclic monothioimides to produce mainly alkylidene lactams, taking advantage of the heightened reactivity of the C=S group over the C=O group (Eq. 7.26). This discrimination also was applied to the synthesis of phyçocyanobilin dimethyl ester.[63] Later work reported reaction with dithioimides.[64] The use of acylic monothioimides afforded routes to β-ketoesters and β-amino acids[64,65] (Eq. 7.27).

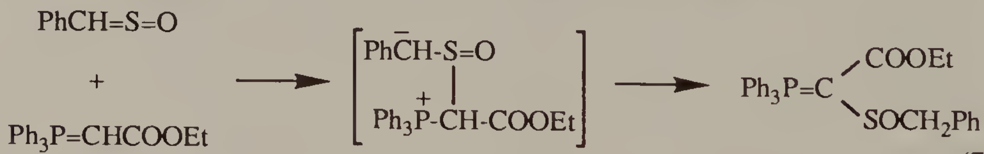


(7.26)



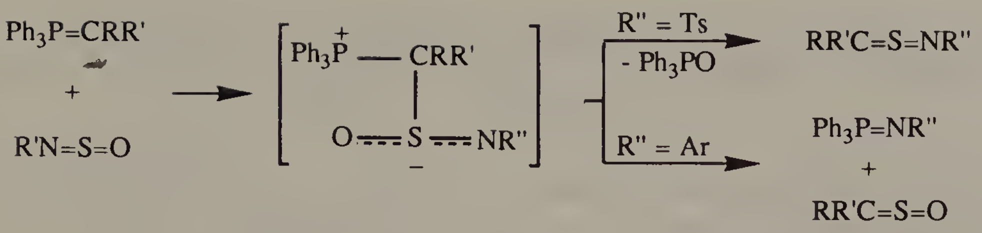
(7.27)

*7.2.2.4* ***Sulfines.*** Phenyl sulfine reacted with an ester ylide with apparent attack at sulfur, followed by proton transfer, to form a sulfinyl-substituted ester ylide[66] (Eq. 7.28). In spite of this reactivity, Zwanenburg et al.[67] found that fluorenylidenesulfine was unreactive enough that it could be prepared in good yield from triphenylphosphoniumfluorenylide and sulfur dioxide.



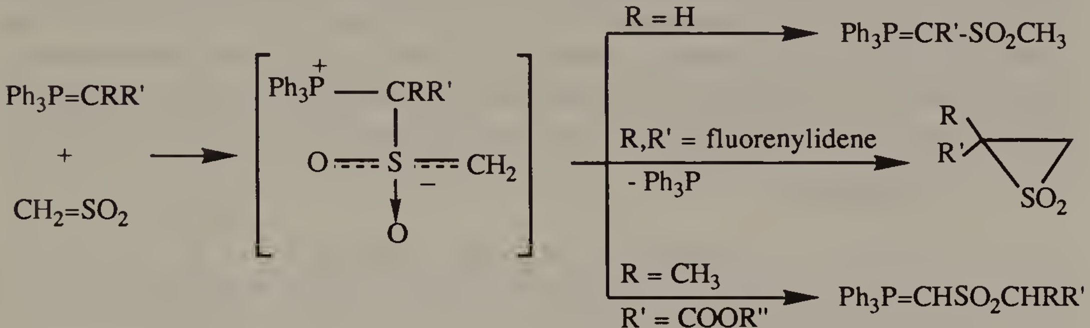
(7.28)

The closely related sulfinylamines also reacted with phosphonium ylides, and the ylidic carbon attached at sulfur in every case (Eq. 7.29). When the substrate was N-tosylsulfinyl-amine, the reaction proceeded with oxygen transfer in a Wittig-type reaction to afford thione-*S*-imides.[68,69] However, when the substrate was N-*p*-nitrophenylsulfinylamine, the nitrogen group transferred to phosphorus to form an iminophosphorane and a sulfine,[68] another ylide interchange reaction.



(7.29)

*7.2.2.5* ***Sulfenes.*** Since sulfenes undergo reaction with electron-rich species and initiate cycloadditions, they would be expected to be susceptible to reaction with phosphonium ylides. Ito et al.[70] studied the reaction of a variety of stabilized ylides with sulfene, prepared in solution from methanesulfonyl chloride and triethylamine, and explained the observations on the basis of initial attack by the ylidic carbanion at sulfur to form a betaine intermediate (Eq. 7.30). When the ylide had α-protons, proton transfer occurred to afford a sulfonyl ylide. In the absence of α-hydrogen in the ylide two other routes prevailed. With the fluorenylidene ylide, and with others in lower yield, displacement of triphenylphosphine occurred to afford an episulfone, which in most instances spontaneously evolved sulfur dioxide to produce an alkene. With ester ylides (R = $CH_3$; R′ = COOR″) the product was a new sulfonyl ylide in which the sulfene had inserted itself between the phosphorus and the carbanion of the original ylide, perhaps via an ylide interchange reaction similar to that proposed for reaction with imines (Eq. 7.20).

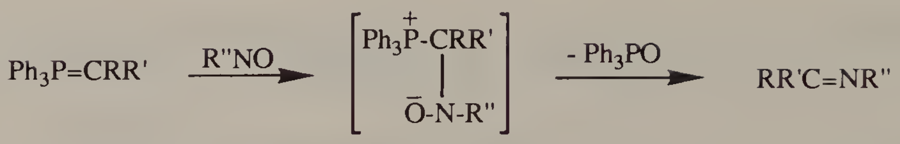


(7.30)

## 7.3 OTHER MULTIPLE-BONDED SYSTEMS

### 7.3.1 Nitrogen Systems

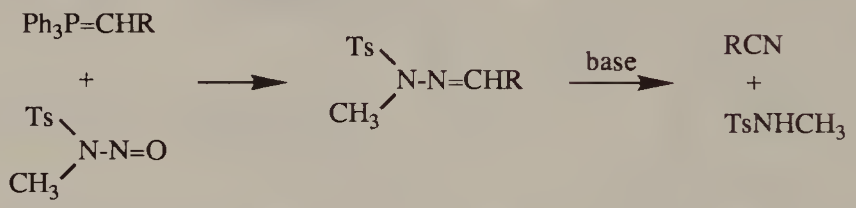
*7.3.1.1* ***Nitroso Compounds.*** It is not surprising that, in view of their electronic similarity to carbonyl compounds, nitroso compounds react with phosphorus ylides to eliminate triphenylphosphine oxide and form imines (Eq. 7.31). Apparently first conducted by Schollkopf,[71] but first published by others,[72] this reaction has been used to characterize ylides.[73] Schollkopf pointed out that this reaction, followed by hydrolysis of the imine, makes possible an overall oxidation route from alkyl halide → ylide → imine → carbonyl.



$$Ph_3P{=}CRR' \xrightarrow{R''NO} \left[\begin{array}{c} Ph_3\overset{+}{P}\text{-}CRR' \\ | \\ \overset{-}{O}\text{-}N\text{-}R'' \end{array}\right] \xrightarrow{-\,Ph_3PO} RR'C{=}NR'' \qquad (7.31)$$

Nurrenbach and Pommer[74] found that β-carotene could be prepared in a dimerization reaction by reacting the monomer phosphonium ylide with *p*-dimethylaminonitrosobenzene, the reaction presumably occurring via initial imine formation followed by reaction of additional ylide with the imine (see Section 7.2.1.1). The result was the same as obtained by oxidation of the monomer phosphonium ylide (see Section 5.2). Mahran et al.[75] recently applied the reaction to nitrosonaphthols and obtained ylide dimers, imines, and azo compounds, all explainable by known reactions.

Use of N-nitroso-N-methyltosylamide in reaction with phosphonium ylides carrying an α-hydrogen proceeded differently in the presence of an amine base. The initial reaction proceeded normally to afford imine, but the base effected an elimination reaction to produce a nitrile (Eq. 7.32).[74] Thus, benzylidenetriphenylphosphorane was converted to benzonitrile, and vitamin A triphenylphosphonium salt produced vitamin A nitrile in 78% yield.



$$Ph_3P{=}CHR + \begin{array}{l} Ts\diagdown \\ \quad N\text{-}N{=}O \\ CH_3\diagup \end{array} \longrightarrow \begin{array}{l} Ts\diagdown \\ \quad N\text{-}N{=}CHR \\ CH_3\diagup \end{array} \xrightarrow{base} RCN + TsNHCH_3 \qquad (7.32)$$

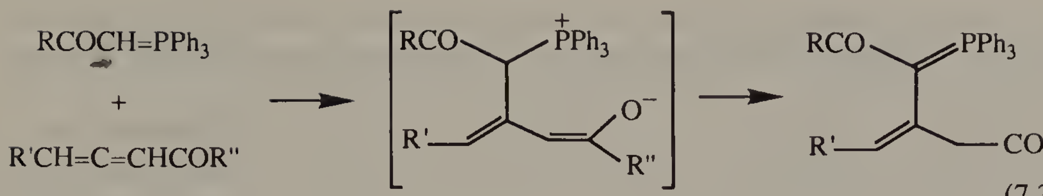
*7.3.1.2 Azo Compounds.* Stabilized phosphonium ylides added across the N=N bond of diethyl azodicarboxylate to afford, after proton transfer, new ylides (Eq. 7.33),[76] not fragmentation products as earlier reported.[77] It also was

$$Ph_3P{=}CHCO\overset{-}{O}Me + EtOOCN{=}NCOOEt \longrightarrow Ph_3P{=}\underset{}{\overset{\overset{COOMe}{|}}{C}}\text{-}\underset{\underset{COOEt}{|}}{N}\text{-}NHCOOEt \qquad (7.33)$$

reported that nonstabilized ylides initially added to give the same intermediate betaine, but in this instance it was claimed that triphenylphosphine was lost to form an azomethine which participated in 1,3-dipolar additions. However, details of this report have not been published.[76] More recently Attanasi et al.[78] reacted stabilized ylides with conjugated azoalkenes, but obtained new ylides resulting from addition to the C=C bond, rather than to the N=N bond.

### 7.3.2 Cumulenes

*7.3.2.1 Allenes.* Only two brief reports[79, 80] exist of the reaction of allenes with phosphonium ylides. Both groups used stabilized ylides with allenic alkyl

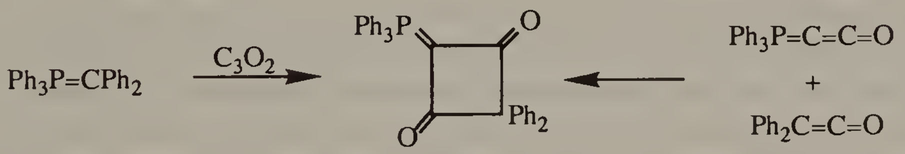


(7.34)

ketones and found ylide addition occurred as though to an α,β-unsaturated ketone and was followed by proton transfer to form allylidene ylides (Eq. 7.34).

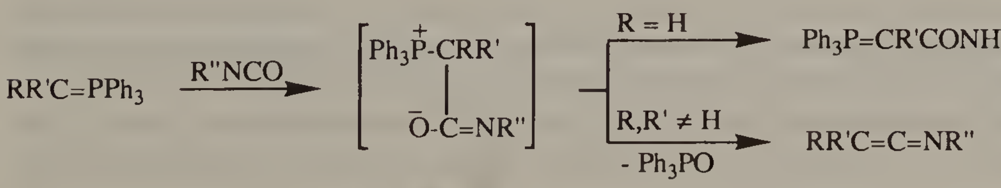
*7.3.2.2* ***Ketenes.*** Staudinger and Meyer[81] reacted diphenylmethylenetriphenylphosphorane with diphenylketene but were unable to isolate the products, even though they expected the products to be tetraphenylallene and triphenylphosphine oxide. Three years later Luscher[82] successfully repeated the reaction by heating in benzene at 140°C, and this was the first example of a Wittig reaction, one in which the carbanion attacked carbonyl carbon, and oxygen was transferred to phosphorus. It generally has been assumed since that the reaction between a phosphonium ylide and a ketene would proceed readily and normally to afford an allene and phosphine oxide. There have been many examples of this reaction which fail to attract special attention, with a recent example being that of Schweizer et al.[83]

A somewhat similar reaction is that with carbon suboxide, which probably proceeded by initial attack of ylide carbanion at the carbonyl carbon, but which may have continued via an oxaphosphetane intermediate, ring opening, and final ring reclosure to afford a phosphoranylidenecyclobutanedione (Eq. 7.35).[84] This same product was obtained by Birum and Matthews when they reacted triphenylphosphoranylideneketene with diphenylketene. A Wittig-type reaction did not occur and instead the reactants effected a cycloaddition, a well-known characteristic of ketenes.[85]



(7.35)

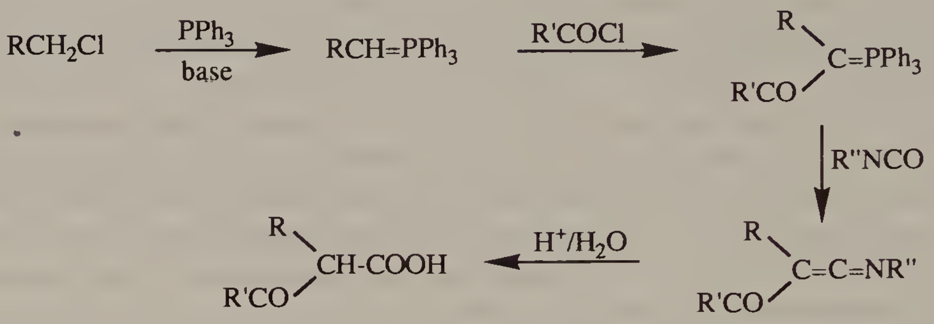
*7.3.2.3* ***Isocyanates.*** One of the earliest reactions of phosphonium ylides with compounds containing a carbonyl group was effected by Staudinger and Meyer[81] when they obtained a ketenimine from a Wittig-type reaction of diphenylmethylenetriphenylphosphorane with phenyl isocyanate (Eq. 7.36). Forty years later Trippett and Walker[86] found that using ylides with one or



(7.36)

more α-hydrogens led instead to amidation of the ylide, probably resulting from the same initially formed betaine, but via a subsequent proton transfer (Eq. 7.36).

Bestmann and Kumar[87] reported additional examples of ketenimine formation and their hydrolysis to amides. This reaction can be a useful part of an overall route to disubstituted carboxylic acids (Eq. 7.37). In their studies of the



(7.37)

reactions of allylidene ylides, Capuano and Willmes[88] found cases of carbanion activity at the α- and γ-positions of the ylide, and both sites were capable of adding to the carbonyl carbon of isocyanates, forming amides when there was α-hydrogen on the ylide and forming ketenimines when there was not. Cristau et al.[89] observed amidation of their diylides with isocyanates.

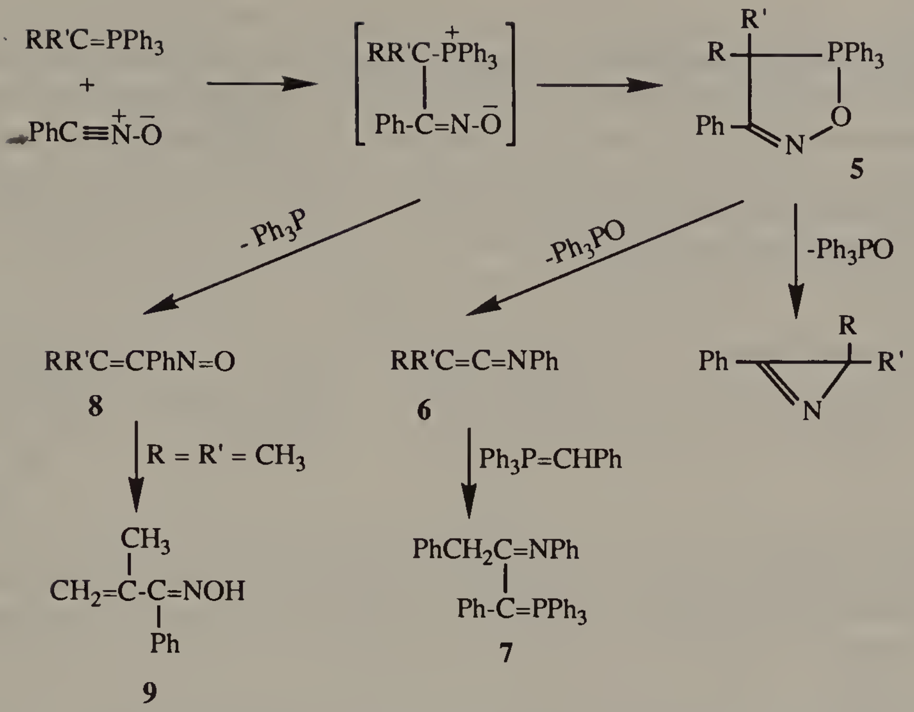
*7.3.2.4* ***Isothiocyanates.*** Isothiocyanates react with phosphonium ylides as do isocyanates, forming α-thioamide ylides by proton transfer when the starting ylide has an α-hydrogen[90,91] but eliminating triphenylphosphine sulfide and forming alkene in a Witting-type reaction when there is no α-hydrogen.[92]

### 7.3.3 1,3-Dipolar Compounds

Phosphonium ylides react with a variety of 1,3-dipolar compounds and provide effective synthesis routes to several heterocyclic systems. Although there are a large variety of 1,3-dipolar compounds, as recently discussed by Padwa and his coauthors in a two-volume work,[93] ylides have been reacted with only a few. Although 1,3-dipoles commonly react with normal multiple bonds (e.g., alkenes, alkynes, and carbonyls) the curiosity is whether they will react with the ylidic P–C bond. This section briefly reviews phosphonium ylide reactions with nitrile oxides, nitrilimines, nitrones, and azides. Diazo compounds also react with ylides, as discussed in Section 6.6, but they function as electrophiles rather than as 1,3-dipoles.

*7.3.3.1* ***Nitrile Oxides.*** The course of the reaction of phosphonium ylides with nitrile oxides depends significantly on the nature of the substituents on the ylide carbanion. The known reactions are represented by Eq. 7.38.

The unsubstituted ylide ($R = R' = H$),[94,95] monoalkylides ($R = H$, $R' = \text{alkyl}$),[94] and dialkylides (R and $R' = \text{alkyl}$)[94] reacted in nonpolar solvents



(7.38)

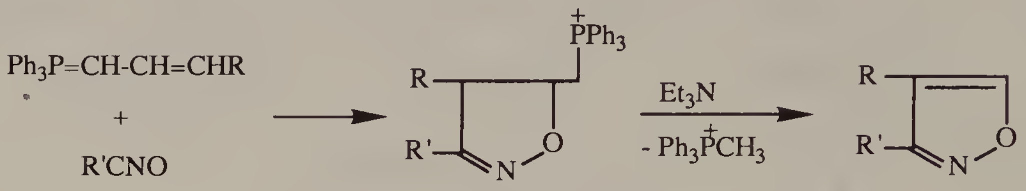
with benzonitrile oxide to afford good yields of the 3-phenyldihydro-1,2,5-$\lambda^5$-oxazaphosphol-2-ines (**5**). An azirine was isolated from some reactions, but it was formed from thermal elimination of triphenylphosphine oxide from the heterocycle (**5**) in a separate step. Italian workers[96] found that in DMSO solution the unsubstituted ylide or the ethylide and benzonitrile oxide afforded the oxime corresponding to protonation of the initial zwitterionic adduct, and the treatment of the oxime with aqueous base resulted in formation of the heterocycle (**5**) in good yield.

Use of a benzylide (R = H, R′ = phenyl) resulted in ketenimine (**6**) formation, but it was trapped by excess ylide adding across the C=N bond, followed by a prototrophic shift to afford a new ylide (**7**).[95] The α-methylbenzylide (R = $CH_3$, R′ = phenyl), in a one-of-a-kind reaction, afforded only the azirine directly, but in only 38% yield.[94] When the ylide carried an ester group (R = H, R′ = COOR″) the product was the ketenimine (**6**),[94, 95] and in some instances a second equivalent of ylide reacted to form a new ylide similar to **7**. Use of a β-keto ylide led to isoxazoles, probably via the same initial intermediate, as well as more complex ylides from reaction of ketimine (**6**) with the original ylide.[97]

Use of *p*-chlorobenzonitrile oxide[94] with most ylides led to formation of azirine only. However, with the isopropylide (R = R′ = $CH_3$) triphenylphosphine was formed by elimination, probably to form **8** which rearranged to the isolated oxime (**9**).[94]

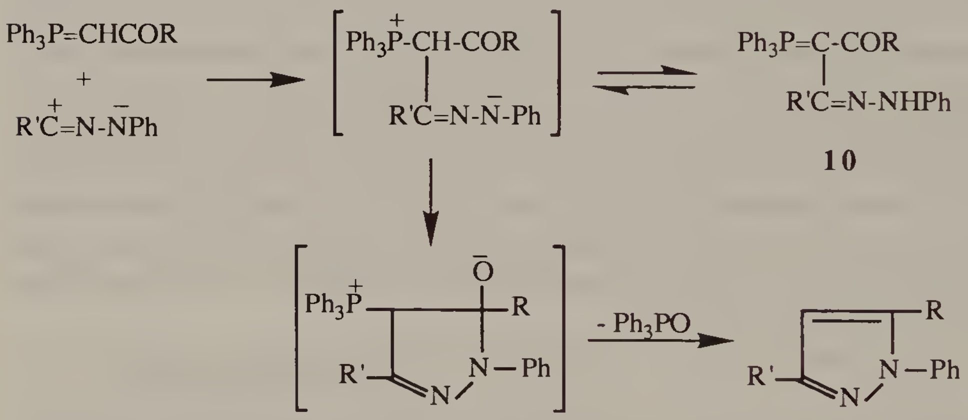
It appears that facilitating the migration of the substituent on the nitrile oxide facilitated elimination of triphenylphosphine oxide and formation of azirines to the point that the intermediate heterocycle (**5**) was not observed. On the other hand, the presence of electron-withdrawing groups on the starting ylide facilitated formation of the ketenimines (**6**), perhaps by weakening the C–P bond in **5**.

Finally, it should be noted that reaction of nitrile oxides with ylides containing other double bonds indicates a clear preference for reaction at other than the ylidic P–C bond to form isoxazole derivatives. Thus, allylides formed the normal dihydroisoxazoles which could be converted to isoxazoles by an unusual elimination of methyltriphenylphosphonium bromide (Eq. 7.39).[98] Similarly, phosphoranylidenecumulenes of various types reacted at other than the P–C bond to form isoxazoles directly.[99, 100]



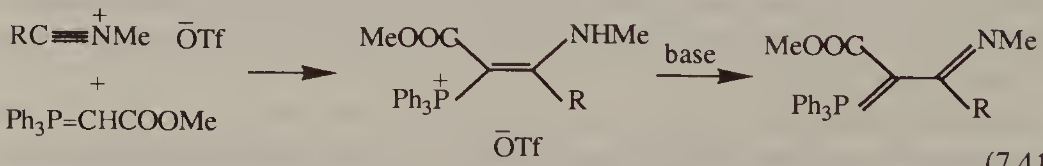
(7.39)

*7.3.3.2 Nitrilimines.* Carbonyl-stabilized ylides reacted with nitrilimines to afford initial adducts (**10**), which could be but need not be isolated, and which were readily thermally converted to pyrazoles (Eq. 7.40). Ester ylides (R = OEt)[101] and $\beta$-ketoylides (R = alkyl or aryl)[102, 103] have been reacted with a variety of nitrilimines in nonpolar solvents and at room temperature usually produced **10**, but under reflux conditions produced the pyrazoles. As with nitrile oxides, if an ylide also contained a normal carbon–carbon double bond, reaction occurred at that site in preference to the P–C ylide bond.[98]



(7.40)

The ester ylide also added to nitrilium salts at carbon, and proton removal afforded a new conjugated ylide[104] (Eq. 7.41).



(7.41)

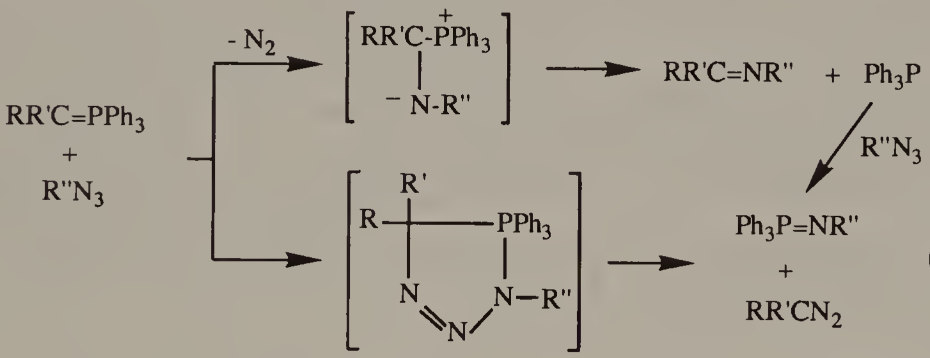
*7.3.3.3 Nitrones.* Methylenetriphenylphosphorane reacted with a variety of nitrones, including cyclic nitrones, in the same manner as with nitrile oxides to

(7.42)

form a heterocycle, specifically 1,2,5-$\lambda^5$-oxazaphospholidines (Eq. 7.42).[105] The same overall result was obtained with the isopropylide and the benzylide, but there seem to be no reports of reaction using stabilized ylides. Alemagna et al.[106] have reported extensively on reactions of stabilized ylides also containing an α-arylazo group with nitrones. No reaction occurred unless the two reactants were in the same molecule and even then the resulting intramolecular reaction usually did not involve the P–C ylide bond. The proposed mechanism called for unusual nucleophilicity by the α-nitrogen of the azo group.

*7.3.3.4 Azides.* Triphenylphosphonium ylides react with azides by two separate routes, depending on the availability of a C=C double bond with which to react.

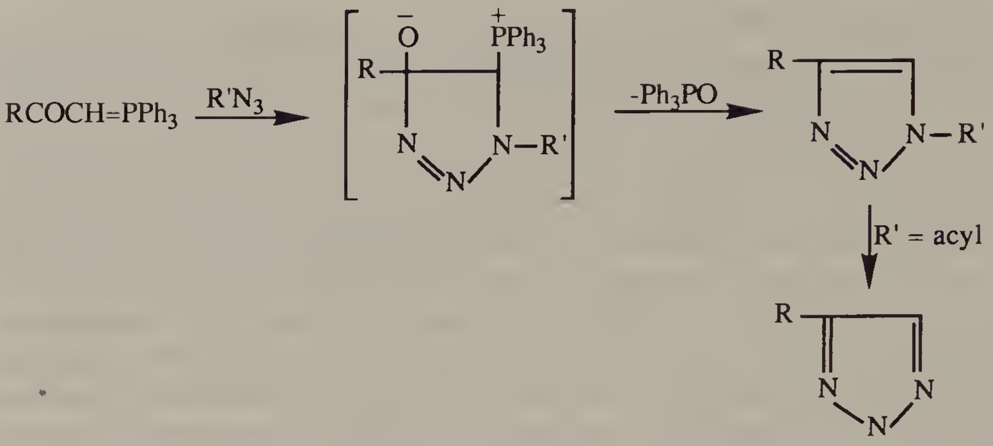
In the first report of this reaction Hoffmann[107] used the benzylide and ethylide, and found that the major product was phosphinimine, together with some Schiff base in some instances. He proposed the reaction proceeded by ylide displacement of nitrogen from the azide, followed by triphenylphosphine ejection and the latter being trapped by additional azide in the known reaction to form iminophosphorane (Eq. 7.43). Later Ykman et al.[108] assumed that when



(7.43)

iminophosphorane was formed as a byproduct of azide reactions with other ylides it came about by a cycloaddition of azide to the P=C bond, to form a 1,2,3,5-$\lambda^5$-triazaphospholidine, followed by dissociation to iminophosphorane and a diazo compound in a kind of ylide interchange reaction (Eq. 7.43). There is no compelling evidence for either proposal.

Most of the azide reactions studied have involved the use of α-ester or β-keto ylides, and in these instances the enolate carbon–carbon bond of the ylide was the site of the reaction, and it was regioselective. Reaction of a variety of azides, including aryl,[108–110], tosyl,[109] and alkyl azides,[109] with acylides or ester ylides afforded mainly 1-substituted-1,2,3-triazoles carrying substituents also on carbons 4 and 5, depending on the ylide structure (Eq. 7.44). Triphenylphosphine



(7.44)

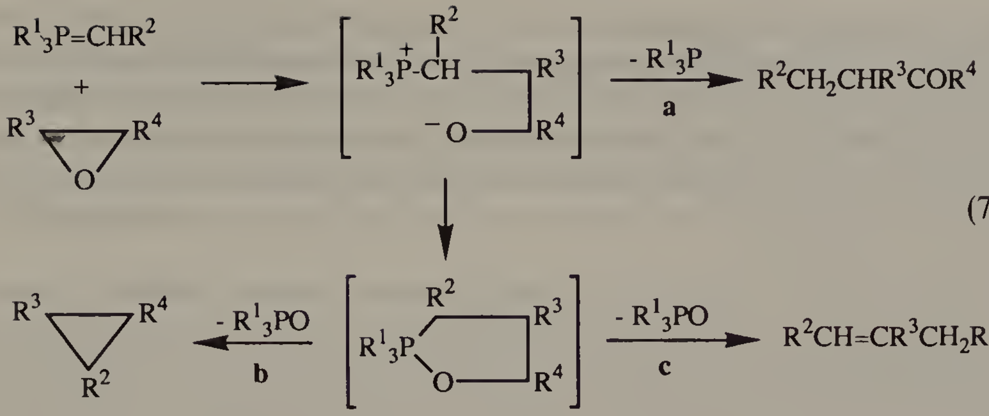
oxide was a byproduct, and in some instances phosphinimine was present. Based on kinetic studies, the reaction was proposed to occur by concerted cycloaddition of azide to the enolate form of the ylide followed by Wittig-type elimination of triphenylphosphine oxide.[93] Using ester ylides, the presence of an α-hydrogen on the ylide led to dominant formation of the phosphinimine (Eq. 7.43)[109, 111, 112] while in the absence of an α-hydrogen the triazole was the major product (Eq. 7.44).[108, 109, 111–114] The reaction for this pattern has not been explained.

Caution must be used in assuming the structure of the resulting triazole, because Ykman et al.[115] showed, using time series NMR, that when an acyl azide was used in the reaction, the initially formed 1-acyl triazole rearranged to a 2-acyltriazole (Eq. 7.44). Thus, a number of structures in the earlier literature are incorrect.[109, 111–113] In addition, the assumption of structure of the occasional diazo compounds reported isolated along with the phosphinimines must be questioned in view of subsequent results.[109, 114, 116] They probably are formed in all such instances, but often are converted to other products in the reaction. Finally, it must be noted that reaction of azides with phosphoranylidenecumulenes occurred at a carbon–carbon double bond rather than a P=C ylide bond, and afforded good yields of zwitterionic 1,4,5-trisubstituted triazoles.[99, 100]

## 7.4 THREE-MEMBERED RING SYSTEMS

### 7.4.1 Oxiranes

Over a relatively short span of time several research groups investigated the reaction of phosphonium ylides with oxiranes, usually styrene oxide or cyclohexene oxide. As a result of those efforts a relatively clear and consistent picture emerged of these reactions which was first summarized into three reaction paths (**a**, **b**, and **c**) by Trippett in his 1963 review (Eq. 7.45).[117] There is specific evidence for some of the proposed intermediates. McEwen and Wolf[118] were able to trap the LiI complex of the initially formed betaine and separately effect its thermal



(7.45)

decomposition. The oxaphospholidine intermediate, a species previously reported by Hands and Mercer[119] from another synthesis, has been isolated but only when using reactive ylides, the methylide,[101] the isopropylide,[101] or the cyclopropylide.[18] Bestmann et al.[120] recently isolated an oxaphospholidine, verified its structure by X-ray crystallographic analysis, and were able to monitor its equilibrium with the betaine by $^{31}$P NMR spectroscopy. Reaction of triphenylphosphoniummethylide with 1,3-butadiene monoxide resulted in the isolation of 5-vinyloxaphospholidine whose structure also has been determined[121]. In reactions using either styrene oxide[18,101] or cyclohexene oxide[18] the oxaphospholidine could be converted to triphenylphosphine and ketone (path **a**).[101]

When electron-donating groups were attached to phosphorus, formation of oxaphospholidine seemed hindered and 1,3 hydride transfer was favored, displacing phosphine and forming ketone (path **a**). Thus, while triphenylphosphoniumbenzylide with styrene oxide gave mainly 1,2-diphenylcyclopropane and triphenylphosphine oxide, methylethylphenylphosphoniumbenzylide afforded mainly phosphine and $\omega$-phenylpropiophenone.[118] This difference vanished with stabilized ylides, however.[122]

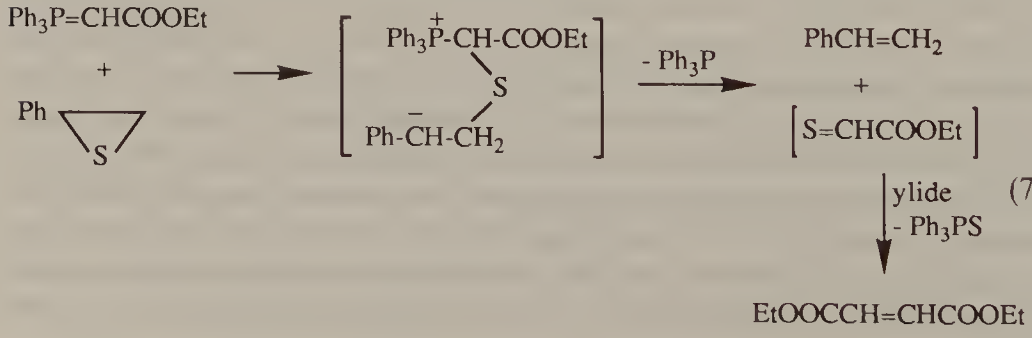
The nature of the substituents on the ylide carbanion greatly affected the course of the reaction. As mentioned above, use of nonstabilized ylides (e.g., alkylides, $R^2$ = alkyl) resulted in isolation of the oxaphospholidine intermediate, and with forcing it could be converted to ketone via path **a**. The highly stabilized phenacylide ($R^2$ = benzoyl) would not even react with oxiranes, presumably because of its low nucleophilicity.[123] However, ester ylides ($R^2$ = COOR″) resulted in path **b** reactions with moderate yields of cyclopropanes resulting. This route probably depends on the ability of the ester group to stabilize an incipient carbanion formed by breaking the P–C ring bond, that carbanion displacing phosphine oxide. Thus, the ester ylide ($R^1$ = phenyl, $R^2$ = COOEt) reacted with styrene oxide or cyclohexene oxide to afford ethyl 2-phenylcyclopropanecarboxylate or ethyl norcaranecarboxylate, respectively.[123] Interestingly, using the tri-*n*-butylphosphonium ester ylide, rather than the triphenylphosphonium ylide, caused a change in the reaction. Reaction with both styrene oxide and cyclohexene oxide afforded, along with some cyclopropane product (path **b**), dominant yields of alkene corresponding to path **c**.[122] In the case of styrene oxide this path probably resulted from hydride transfer in the triphenylphosphine oxide-ejection step. In the case of the cyclohexene oxide, the geometry of the transition state was such that hydride transfer was precluded, so ring contraction occurred to form ethyl $\beta$-cyclopentylacrylate. However, cyclopentene oxide produced no alkene, only the cyclopropane product (path **b**), albeit in low yield.[122]

Reaction of the semistabilized triphenylphosphoniumbenzylide ($R^1$ = phenyl, $R^2$ = phenyl) with styrene oxide and cyclohexane oxide afforded a mixture of products from paths **a**, **b**, and **c**.[124,125] McEwen et al.[126] proved the hydride transfer mechanism for path **a** by deuterium labelling, and ruled out a symmetrical oxetane intermediate through carbon-14 labelling.[118] They also showed that the presence of lithium in the solution, from preparation of the ylide in situ, stabilized the betaine intermediate, preventing ring closure, and thereby favoring path **a** elimination of phosphine. Using a sodium base for ylide formation resulted in virtually no phosphine formation and instead high yields of triphenylphosphine oxide was obtained accompanied by cyclopropane and alkene.

Evidence is available on the stereochemistry of the path **c** reaction, the one of most significance for synthesis purposes. Denney et al.[123] showed that optically active styrene oxide and an ester ylide ($R^1$ = phenyl, $R^2$ = COOEt) afforded optically active ethyl *trans*-2-phenylcyclopropanecarboxylate. Inouye et al.[127] and Tomoskozi[128] demonstrated that the reaction had occurred with inversion of configuration at the carbon carrying the phenyl group, although the optical yield was low. McEwen et al.[124] showed that the phosphine oxide resulting from such reactions was mainly of inverted configuration, indicating oxyanion attack on phosphorus at a basal position. Thus, cyclopropane formation from phosphonium ylides and oxiranes is a potentially useful stereoselective synthetic route.

## 7.4.2 Thiiranes

Okuma et al.[129] found that reaction of phosphonium ylides with episulfides led to desulfidation to produce alkenes, accompanied by dimers of the carbanion portion of the ylide. Thus, the ester ylide with styrene sulfide afforded triphenylphosphine, triphenylphosphine sulfide, styrene, and a mixture of maleate and

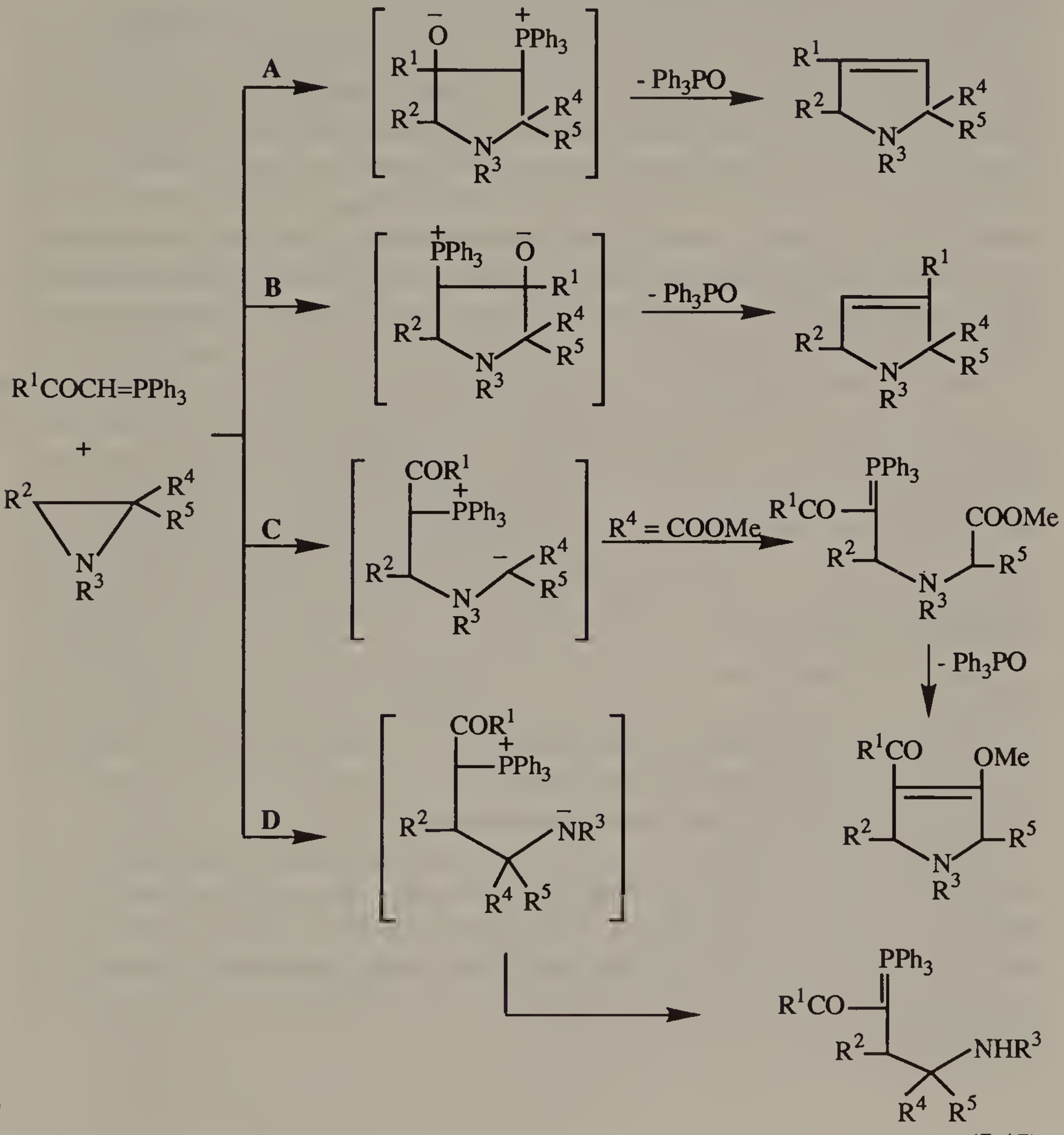


(7.46)

fumarate esters (Eq. 7.46). The reaction was proposed to occur by ylide attack on sulfur, followed by dissociation of the intermediate to triphenylphosphine, thial, and styrene. The thial was thought to be trapped by unchanged ylide in a known Wittig-type reaction (see Section 7.2.2.1) to afford a symmetrical alkene and triphenylphosphine sulfide[52]. Thus, the overall reaction is of no synthetic significance.

### 7.4.3 Aziridines

There have been no studies of the reaction of aziridines with nonstabilized or semistabilized phosphonium ylides, but several studies of their reaction with stabilized ylides, both ester ylides and acylides. Four different reaction routes have been proposed, which are summarized in Eq. 7.47.



(7.47)

Heine et al.[130] discovered that ester ylides with an α-hydrogen ($R^1$ = OEt) would open aziridine rings carrying nitrogen substituents, but only *alkyl* carbon substituents, by attack at unsubstituted carbon to cleave the C–N bond. Proton transfer followed to afford new ylides via path **D**. Recently Baldwin[131] used 1-aroyl-2(*S*)-carbomethoxy aziridines in this reaction for the synthesis of optically active amino acids, carrying out a Wittig reaction with the new ylide and hydrolyzing the ester and amide groups. When the starting ylide had an α-methyl group in place of the α-hydrogen to block formation of the new ylide, Heine reported conflicting results. In one paper[130] was claimed an intramolecular attack of the nitrogen anion on the ester group, followed by elimination of triphenylphosphine oxide, but in a second paper[132] was reported catalytic formation of a 3-oxa-1-pyrroline from the aziridine alone, but in neither of these reports were the substances absolutely identified.

Reaction of aziridines which carried *N*-phenyl or *N*-alkyl substituents, and which carried substituents on both of the carbons, at least one of which was an ester group, formed one or more of three possible 3-pyrrolines by paths **A**, **B**, and/or **C** (Eq. 7.47). With an ester ylide ($R^1$ = OMe) or a cyano ylide ($R^1$ = CN) the products were 4-methoxy-3-pyrrolines formed via path **C**.[133, 134] This reaction was proposed to involve nucleophilic cleavage of the carbon–carbon bond of the aziridine, or attack of the ylide carbanion at the positive end of the equilibrating azomethine 1,3-dipole, facilitated in both instances by stabilization of the resulting carbanion by the ester function on C-3. A Wittig reaction with the ester carbonyl was proposed to form the heterocycle and complete path **C**.

When the reacting ylide was a phenacylide ($R^1$ = phenyl) and the aziridine carried two ester groups on C-3 ($R^4$, $R^5$ = COOMe) paths **A** and **B** were followed. When $R^2$ was phenyl, path **A** was followed to produce only a 4-unsubstituted-3-pyrroline, whereas when $R^2$ was a carbomethoxy group, path **B** was followed to produce only a 3-unsubstituted-3-pyrroline. Both paths were proposed to occur by cycloaddition of the enolate form of the ylide to the azomethine ylide 1,3-dipole,[135] but the cause of the regioselectivity is unclear.

When the reacting ylide was the acetylide ($R^1$ = $CH_3$), and the aziridine carried two carbomethoxy groups on C-3, paths **A**, **B**, and **C** were followed. When $R^2$ was phenyl, path **A** produced a 4-unsubstituted-3-pyrroline and path **C** produced a fully substituted 3-pyrroline, in about a 2:1 ratio.[135] When $R^2$ was a carbomethoxy group, path **B** produced a 3-unsubstituted-3-pyrroline and path **C** produced a fully substituted 3-pyrroline.

The reasons for this pattern of ring formation are unclear at this time, but the balance clearly is very delicate, depending as it does on the difference between a phenacylide and an acetylide and the difference between a phenyl group or an ester group on C-2 of the aziridine ring. Thus, using this route for synthesis is risky, but the aziridine route is useful in less-substituted cases as demonstrated by Baldwin[131].

## REFERENCES

1 Johnson, A. Wm. *Ylid Chemistry*; Academic: New York, 1966; p. 120.

2 Freeman, J. P. *J. Org. Chem.* **1966**, *31*, 538.

3 Asunskis, J.; Shechter, H. *J. Org. Chem.* **1968**, *33*, 1164.

4 Connor, J. T.; von Strandtmann, M. *J. Org. Chem.* **1973**, *38*, 1047.

5 Bestmann, H. J.; Seng, F. *Angew. Chem.* **1962**, *1*, 116.

6 Grieco, P. A.; Finkelhor, R. S. *Tetrahedron Lett.* **1972**, 3781.

7 Devos, M. J.; Hevesi, L.; Bayet, P.; Krief, A. *Tetrahedron Lett.* **1976**, 3911.

8 Bernardi, A.; Scolastico, C.; Villa, R. *Tetrahedron Lett.* **1989**, *30*, 3733.

9 Mulzer, J.; Kappert, M. *Angew. Chem.* **1983**, *22*, 63.

10 Dauben, W. G.; Kozikowski, A. P. *Tetrahedron Lett.* **1973**, 3711.

11 Minami, T.; Yamanouchi, T.; Tokumasu, S.; Hirao, I., *Bull. Chem. Soc. Jpn.* **1984**, *57*, 2127.

12 Soliman, F.; Said, M. M. *Phosphorus Sulfur* **1991**, *61*, 335.

13 Abdou, W. M.; Gamoub, N. A. F.; Mahran, M. R. *Phosphorus Sulfur* **1992**, *66*, 79.

14 Wanner, M. J.; Koomen, G. J. *Tetrahedron Lett.* **1992**, *33*, 1513.

15 Potthoff, B.; Breitmaier. E. *Chem. Ber.* **1987**, *120*, 255.

16 Buchi, G.; Wuest, H. *Helv. Chim. Acta* **1971**, *54*, 1767.

17 Mechoulam, R.; Sondheimer, F. *J. Am. Chem. Soc.* **1958**, *80*, 4386.

18 Bestmann, H. J.; Denzel, T.; Kunstmann, R.; Lengyel, J. *Tetrahedron Lett.* **1968**, 2895.

19 Reid, W.; Hermann, H. J. *Liebigs Ann. Chem.* **1974**, 1239.

20 Reid, W.; Knorr, H.; Gurcan, H. *Liebigs Ann. Chem.* **1976**, 1415.

21 Murray, D. F. *J. Org. Chem.* **1983**, *48*, 4860.

22 Trippett, S. *J. Chem. Soc.* **1962**, 4733.

23 Zbiral, E. *Monatsh. Chem.* **1965**, *96*, 1967.

24 Fischer, H.; Fischer, H. *Chem. Ber.* **1966**, *99*, 658.

25 Inhoffen, H. H.; Bruckner, K.; Domagk, G. F.; Erdmann, H. M. *Chem. Ber.* **1955**, *88*, 1415.

26 Bohlmann, F. *Chem. Ber.* **1956**, *89*, 2191.

27 Brown, G. W.; Cookson, R. C.; Stevens, I. D. R. *Tetrahedron Lett.* **1964**, 1263.

28 Bestmann, H. J.; Rothe, O. *Angew. Chem.* **1964**, *3*, 512.

29 Gilheany, D. G.; Kennedy, D. A.; Malone, J. F.; Walker, B. J. *Tetrahedron Lett.* **1985**, *26*, 531.

30 Barluenga, J.; Lopez, F.; Palacios, F. *J. Chem. Soc. Chem. Commun.* **1986**, 1574.

31 Hendrickson, J. B. *J. Am. Chem. Soc.* **1961**, *83*, 2018.

32 Gough, S. T. D.; Trippett, S. *Proc. Chem. Soc.* **1961**, 302.

33 Ref. 1, pp. 42 and 124.

34 Hendrickson, J. B.; Hall, C.; Rees, R.; Templeton, J. F. *J. Org. Chem.* **1965**, *30*, 3312.

35 Brown, G. W. *J. Chem. Soc* (*C*) **1967**, 2018.

[36] Barluenga, J.; Lopez, F.; Palacios, F.; Sanchez-Ferrando, F. *Tetrahedron Lett.* **1988**, *29*, 381.

[37] Labuschagne, A. J. H.; Schneider, D. F. *Tetrahedron Lett.* **1983**, *24*, 743.

[38] Ding, W.; Zhang, P.; Cao, W. *Tetrahedron Lett.* **1987**, *28*, 81.

[39] Bestmann, H. J.; Kisielowski, L. *Tetrahedron Lett.* **1990**, *31*, 3301.

[40] Zbiral, E. *Monatsh Chem.* **1964**, *95*, 1759; *Tetrahedron Lett.* **1964**, 3963.

[41] Zbiral, E. *Monatsh. Chem.* **1967**, *98*, 916.

[42] Bestmann, H. J.; Seng, F. *Angew. Chem.* **1963**, *2*, 393; *Tetrahedron* **1965**, *21*, 1373.

[43] Blade-Font, A.; McEwen, W. E.; Vanderwerf, C. A. *J. Am. Chem. Soc.* **1960**, *82*, 2646.

[44] Barnhardt, R. G.; McEwen, W. E. *J. Am. Chem. Soc.* **1967**, *89*, 7009.

[45] Ciganek, E. *J. Org. Chem.* **1970**, *35*, 3631.

[46] Fluck, E.; Spahn, M.; Heckmann, G. *Z. Naturforsch.* **1991**, *46B*, 762.

[47] Trabelsi, H.; Bollens, E.; Cambon, A. *Synthesis* **1990**, 623.

[48] Vicente, J.; Chicote, M. T.; Fernandez-Baeza, J.; Lahoz, F. J.; Lopez, J. A. *Inorg. Chem.* **1991**, *30*, 3617.

[49] Duffner, P. Dissertation at Tubingen, 1957; cited in Schollkopf, U. *Angew. Chem.* **1959**, *71*, 260.

[50] Tewari, R. S.; Suri, S. K.; Gupta, K. C. *Z. Naturforsch.* **1979**, *34B*, 606.

[51] Magerlein, H.; Meyer, G. *Chem. Ber.* **1970**, *103*, 2995.

[52] Okuma, K.; Tachibana, Y.; Sakata, J. I.; Komiya, T.; Kaneko, I.; Komiya, Y.; Yamasaki, Y.; Yamamoto, S. I.; Ohta, H. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 4323.

[53] Vedejs, E.; Perry, D. A.; Wilde, R. G. *J. Am. Chem. Soc.* **1986**, *108*, 2985.

[54] Staudinger, H.; Rathsam, G.; Kjelsberg, F. *Helv. Chim. Acta* **1920**, *3*, 853.

[55] Schonberg, A.; Frese, E.; Brosowski, K. H. *Chem. Ber.* **1962**, *95*, 3022.

[56] Bestmann, H. J.; Engler, R.; Hartung, H. *Angew. Chem.* **1966**, *5*, 1040.

[57] Pappas, J. J.; Gancher, E. *J. Org. Chem.* **1966**, *31*, 3877.

[58] Bestmann, H. J.; Engler, R.; Hartung, H.; Roth, K. *Chem. Ber.* **1979**, *112*, 28.

[59] Schaumann, E.; Grabley, F. F. *Liebigs Ann. Chem.* **1979**, 1702.

[60] Kunze, U.; Merkel, R. *J. Organomet. Chem.* **1981**, *219*, 69.

[61] Matthews, C. N.; Birum, G. H. *Tetrahedron Lett.* **1966**, 5707.

[62] Gossauer, A.; Hinze, R. P.; Zilch, H. *Angew. Chem.* **1977**, *16*, 418.

[63] Gossauer, A.; Hinze, R. P. *J. Org. Chem.* **1978**, *43*, 283.

[64] Gossauer, A.; Roebler, F.; Zilch, H. *Liebigs Ann. Chem.* **1979**, 1309.

[65] Slopianka, M.; Gossauer, A. *Liebigs Ann. Chem.* **1981**, 2258.

[66] Hamid, A. M.; Trippett, S. *J. Chem. Soc.* (C) **1968**, 1612.

[67] Zwanenburg, B.; Venier, C. G.; Porskamp, P. A. T. W.; Vanderleij, M. *Tetrahedron Lett.* **1978**, 807.

[68] Saito, T.; Motoki, S. *J. Org. Chem.* **1977**, *42*, 3922.

[69] Saito, T.; Nakane, M.; Watanabe, T.; Motoki, S.; Kobayashi, K.; Sakurai, T. *Bull. Soc. Chem. Jpn.* **1985**, *58*, 2882.

[70] Ito, Y.; Okano, M.; Oda, R. *Tetrahedron* **1967**, *23*, 2137.

[71] Schollkopf, U. Dissertation at University of Tubingen, 1955; cited in *Angew. Chem.* **1959**, *71*, 260.

[72] Schonberg, A.; Brosowski, K. H. *Chem. Ber.* **1959**, *92*, 2602.

[73] Hedaya, E.; Theodoropulos, S. *Tetrahedron* **1968**, *24*, 2241.

[74] Nurrenbach, A.; Pommer, H. *Liebigs Ann. Chem.* **1969**, *721*, 34.

[75] Mahran, M. R.; Abdau, W. M.; Ganoub, N. A. F. *Phosphorus Sulfur* **1988**, *39*, 51.

[76] Bestmann, H. J. *In Organic Phosphorus Compounds*; Kosolapoff, G. M.; Maier, L., Eds.; Wiley-Interscience: New York, 1972; Vol. 3, Chapter 5A, p.47.

[77] Bestmann, H. J.; Zimmermann, R. *Chem. Ber.* **1968**, *101*, 2185.

[78] Attanasi, O.; Filippone, P.; Mei, A.; Borgini, A.; Foresti, E. *Tetrahedron* **1990**, *46*, 5685.

[79] Strzelecka, H.; Simalty-Siemiatycki, M.; Prevost, C. *C. R. Seances Acad. Sci.* **1963**, *257*, 926.

[80] Buono, G.; Pfeiffer, G.; Guillemonat, A. *C. R. Seances Acad. Sci.* **1970**, *271*, 937.

[81] Staudinger, H.; Meyer, J. *Helv. Chim. Acta* **1919**, *2*, 635.

[82] Luscher, G. Dissertation at ETH, Zurich, 1922; cited in Wittig, G. *Pure Appl. Chem.* **1964**, *9*, 247.

[83] Schweizer, E. E.; Hayes, J. E.; Rheingold, A.; Wei, X. *J. Org. Chem.* **1987**, *52*, 1810.

[84] Van Woerden, H.; Cerfontain, H.; Van Valkenburg, C. F. *Rec. Trav. Chim.* **1969**, *88*, 158.

[85] Birum, G. H.; Matthews, C. N. *J. Org. Chem.* **1968**, *90*, 3842.

[86] Trippett, S.; Walker, D. M. *J. Chem. Soc.* **1959**, 3874.

[87] Bestmann, H. J.; Kumar, K. *Chem. Ber.* **1983**, *116*, 2708.

[88] Capuana, L.; Willmes, A. *Liebigs Ann. Chem.* **1982**, 80.

[89] Cristau, H. J.; Perraud-Darcy, A.; Ribeill, Y. *Tetrahedron Lett.* **1992**, *33*, 2693.

[90] Bestmann, H. J.; Pfohl, S. *Angew. Chem.* **1969**, *8*, 762.

[91] Shevchuk, M. I.; Zabrodskaya, I. S.; Dombrovskii, A. V. *J. Gen. Chem.* **1969**, *39*, 1253.

[92] Birum, G. H.; Matthews, C. N. *Chem. Ind.* **1968**, 653.

[93] Padwa, A. *1,3-Dipolar Cycloaddition Chemistry*; Wiley-Interscience: New York, 1984.

[94] Bestmann, H. J.; Kunstmann, R. *Chem. Ber.* **1969**, *102*, 1816.

[95] Huisgen, R.; Wulff, J. *Chem. Ber.* **1969**, *102*, 1833.

[96] Gaudiano, G.; Mondelli, R.; Ponti, P. P.; Ticozzi, C.; Umani-Ronchi, A. *J. Org. Chem.* **1968**, *33*, 4431.

[97] L'Abbe, G.; Borsus, J. M.; Ykman, P.; Smets, G. *Chem. Ind.* **1971**, 1491.

[98] Dalla Croce, P.; Pocar, D. *J. Chem. Soc. Perkin Trans. (1)* **1976**, 619.

[99] Bestmann, H. J. *Angew. Chem.* **1977**, *16*, 349.

[100] Bestmann, H. J.; Schmid, G. *Tetrahedron Lett.* **1981**, 1679.

[101] Wulff, J.; Huisgen, R. *Chem. Ber.* **1969**, *102*, 1841.

[102] Fusco, R.; Dalla Croce, P. *Chim. Ind.* (*Milan*) **1970**, *52*, 45; *Chem. Abstr.* **1970**, *72*, 90361.

[103] Dalla Croce, P. *Ann. Chim.* (*Rome*) **1973**, *63*, 867; *Chem. Abstr.* **1976**, *84*, 58138.

[104] Amer, M. I. K.; Booth, B. L.; Bitrus, P. *J. Chem. Soc. Perkin Trans. (1)* **1991**, 1673.

[105] Huisgen, R.; Wulff, J. *Chem. Ber.* **1969**, *102*, 746.

[106] Alemagna, A.; Del Buttero, P.; Lícandro, E.; Papagni, A.; Ballabio, M. *Tetrahedron* **1985**, *41*, 2503.

[107] Hoffmann, H. *Chem. Ber.* **1962**, *95*, 2563.

[108] Ykman, P.; L'Abbe, G.; Smets, G. *Tetrahedron* **1973**, *29*, 195.

[109] Harvey, G. R. *J. Org. Chem.* **1966**, *31*, 1587.

[110] Ykman, P.; L'Abbe, G.; Smets, G. *Tetrahedron* **1971**, *27*, 845.

[111] L'Abbe, G.; Bestmann, H. J. *Tetrahedron Lett.* **1969**, 63.

[112] L'Abbe, G.; Ykman, P.; Smets, G. *Tetrahedron* **1969**, *25*, 5421.

[113] L'Abbe, G. *Bull. Soc. Chim. Belg.* **1969**, *78*, 147.

[114] Zbiral, E.; Stroh, J. *Monatsh. Chem.* **1969**, *100*, 1438.

[115] Ykman, P.; L'Abbe, G.; Smets, G. *Tetrahedron* **1971**, *27*, 5623.

[116] Sohn, M. B.; Jones, M.; Hendrick, M.; Rando, R. R.; Doering, W. von E. *Tetrahedron Lett.* **1972**, 53.

[117] Trippett, S. *Quart. Rev.* **1963**, *17*, 406.

[118] McEwen, W. E.; Wolf, A. P. *J. Am. Chem. Soc.* **1962**, *84*, 676.

[119] Hands, A. R.; Mercer, P. J. H. *J. Chem. Soc. C* **1967**, 1099.

[120] Bestmann, H. J.; Riemer, C.; Dotzer, R. *Chem. Ber.* **1992**, *125*, 225.

[121] Enholm, E. J.; Satici, H.; Prasad, G. *J. Org. Chem.* **1990**, *55*, 324.

[122] Gerkin, R. M.; Rickborn, B. *J. Am. Chem. Soc.* **1967**, *89*, 5850.

[123] Denney, D. B.; Vill, J. J.; Boskin, M. J. *J. Am. Chem. Soc.* **1962**, *84*, 3944.

[124] McEwen, W. E.; Blade-Font, A.; Vanderwerf, C. A. *J. Am. Chem. Soc.* **1962**, *84*, 677.

[125] Zbiral, E. *Monatsh. Chem.* **1963**, *94*, 78.

[126] McEwen, W. E.; Wolf, A. P.; Vanderwerf, C. A.; Blade-Font, A.; Wolfe, J. W. *J. Am. Chem. Soc.* **1967**, *89*, 6685.

[127] Inouye, Y.; Sugita, T.; Walborsky, H. M. *Tetrahedron* **1964**, *20*, 1695.

[128] Tomoskozi, I. *Tetrahedron* **1963**, *19*, 1969.

[129] Okuma, K.; Yamasaki, Y.; Kamiya, T.; Kodera, Y.; Ohta, H. *Chem. Lett.* **1987**, 357.

[130] Heine, H. W.; Lowrie, G. B.; Irving, K. C. *J. Org. Chem.* **1970**, *35*, 444.

[131] Baldwin, J. E.; Adlington, R.; Robinson, N. G. *J. Chem. Soc. Chem. Commun.* **1987**, 153.

[132] Heine, H. W.; Wachob, G. D. *J. Org. Chem.* **1972**, *37*, 1049.

[133] Texier, F.; Carrie, R. *Tetrahedron Lett.* **1971**, 4163.

[134] Vaultier, M.; Danion-Bougot, R.; Danion, D.; Hamelin, J.; Carrie, R. *Bull. Soc. Chim. Fr.* **1976**, 1537.

[135] Vaultier, M.; Danion-Bougot, R.; Tonnard, F.; Carrie, R. *Bull. Soc. Chem. Fr.* **1985**, 803.

# 8

# THE WITTIG REACTION I. SCOPE AND APPLICATIONS

The Wittig reaction, arguably the most important and useful of all the means of preparing alkenes, involves the condensation of a phosphonium ylide with a carbonyl compound to produce an alkene, eliminating triphenylphosphine oxide (Eq. 8.1). The significance of this reaction is attested to by its application to

$$\left.\begin{array}{l} Ph_3P{=}CR^1R^2 \quad + \quad R^3R^4C{=}O \\ \\ Ph_3P{=}CR^3R^4 \quad + \quad R^1R^2C{=}O \end{array}\right] \longrightarrow Ph_3PO \quad + \quad R^1R^2C{=}CR^3R^4 \tag{8.1}$$

almost every aspect of organic chemistry and by the award of the Nobel Prize for 1979 to George Wittig[1] (1897–1987). Although first discovered by Staudinger and his students in a single and fortunately chosen structural environment,[2, 3] the reaction was generalized and brought to wide attention by Wittig and his students in the early 1950s[4, 5] in what clearly was a serendipitous rediscovery. Wittig acknowledged his debt to Staudinger in an elegant 1964 lecture[6] entitled "Variationen zu Einem Thema Von Staudinger; Ein Beitrag Zur Geschichte der Phosphororganischen Carbonyl-Olefinierung." The history of the development of this reaction is described in Wittig's lecture[6] and in Johnson's monograph.[7]

The commercial significance of the reaction was quickly recognized and a patent was issued to BASF-AG in 1956 regarding its use in the synthesis of compounds in the vitamin A series.[8] The organic chemistry literature includes literally thousands of applications of the reaction both to relatively simple and very complex structures. The subsequent evolution of this reaction to permit both regioselectivity and stereoselectivity in the introduction of the alkene

---

*Ylides and Imines of Phosphorus*, Edited by A. William Johnson.
ISBN 0-471-52217-1

group has been a harbinger of the precision now available in much of organic synthesis.

The Wittig reaction has been reviewed many times (see the list of reviews at the end of this chapter), most thoroughly by Gosney and Rowley[9] in 1979 and most recently by Maryanoff and Reitz[10] in 1989. Since this new monograph treats *all* phosphorus ylides and imines and *all* of their chemistry, the following treatment of the Wittig reaction will not be encyclopedic or historical, but "state of the art" and exemplary. Earlier reviews should be consulted for further details on and additional examples of the reaction. This chapter provides an overview of the reaction, including its scope and exemplary application to a wide variety of classes of compounds, with the primary objective of serving those who use the reaction for synthesis purposes. The succeeding chapter discusses the mechanistic and stereochemical aspects of the reaction in detail.

The Wittig reaction has been a model of simplicity and convenience with specific advantages being severalfold:

1. The reaction is regiospecific in that there can be little doubt about where a new carbon–carbon double bond was introduced into a substrate. For example, reaction of cyclohexanone with methylmagnesium bromide, followed by acid-catalyzed dehydration, led to a mixture of methylenecyclohexane and methylcyclohexene, whereas reaction of the same ketone with methylenetriphenylphosphorane led to formation of *only* the exocyclic alkene.[5]

2. The reaction conditions usually are mild with reactions often performed at – 78°C and for short times. The milder conditions than for the Wadsworth–Emmons reaction frequently is an advantage,[11, 12] for example in the syntheses leading to calyculin.[13]

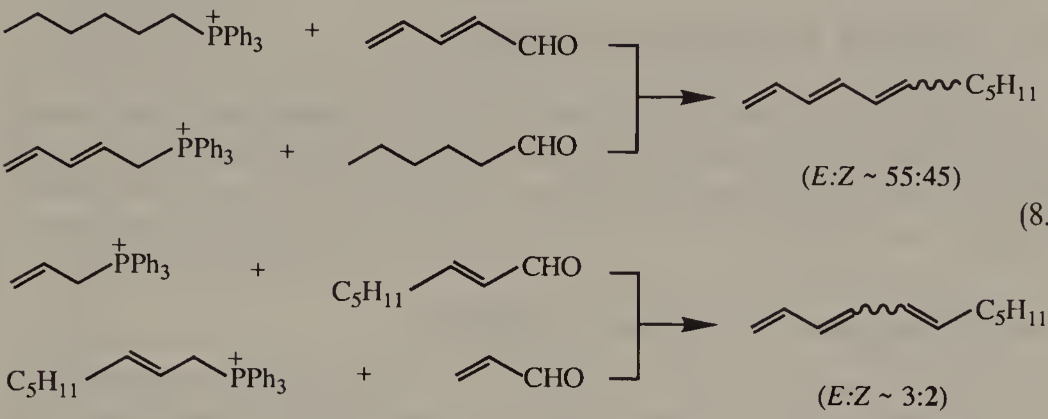
3. The starting materials often are readily accessible, with many syntheses of carbonyl reactants readily available and with several routes available for preparation of the necessary ylides (see Chapter 4). The ylide often is prepared *in situ.*

4. The reaction often can be performed in the presence of other functional groups, such as in the penicillin series[14] and with N-acetyl-2-hydroxyindolones.[15]

5. The "activating" group which permits the overall reaction, the phosphonium group, is ejected in the course of the reaction, not necessitating a separate cleavage step. The byproduct triphenylphosphine oxide usually, but not always, is readily separable from the desired alkene.

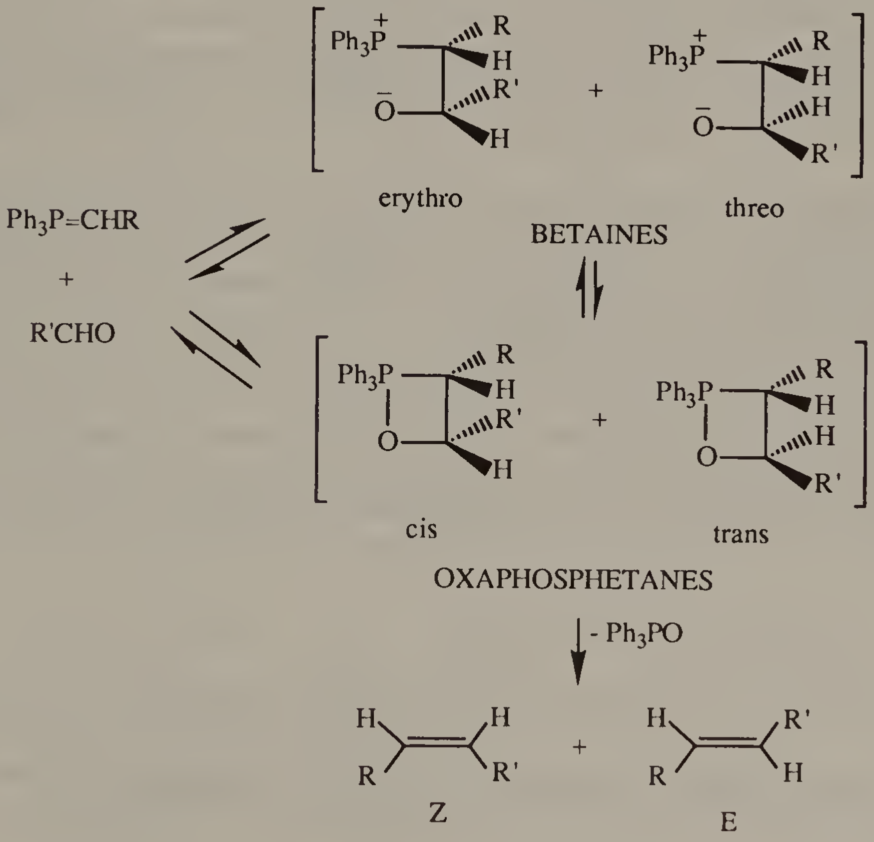
6. The reaction often is stereoselective, and ylide structure, carbonyl structure, and experimental conditions can be altered to influence the magnitude or even direction of such selectivity (This aspect will be illustrated in succeeding sections and will be discussed in detail in the next chapter). The alkene product can be obtained directly from the reaction, in contrast to the Peterson olefination in which separation of intermediate species often is necessary to effect overall stereoselectivity.[16]

7. A target alkene ($R^1R^2C{=}CR^3R^4$) often can be obtained by two routes (i.e., $R^1R^2C{=}$ could be derived from the ylide *or* the carbonyl reactant, see Eq. 8.1) and the choice may offer different stereoselectivities and/or reactivities. For example, Naf et al.[17] prepared mixtures of the four geometric isomers of 1,3,5-undecatriene using four different reactions (Eq. 8.2), and others recently have shown it is possible to exert even more stereochemical control on the products of such reactions.[18]



(8.2)

For about 30 years after its elaboration, the Wittig reaction generally was viewed as proceeding by nucleophilic attack of the ylide carbanion on a carbonyl carbon to reversibly form betaine intermediates in erythro and/or



(8.3)

threo configurations. These were proposed to cyclize to the respective transient oxaphosphetanes which, in turn, dissociated to phosphine oxide and *Z*- or *E*-alkene. In the 1980s, however, evidence accrued to indicate that the ylide and carbonyl reactants probably combined directly to form oxaphosphetanes (Eq. 8.3). Further discussion of the mechanism and the crucial stereochemical implications will be deferred to Chapter 9.

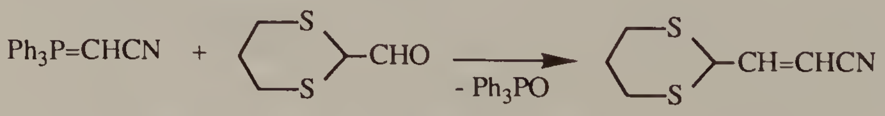
## 8.1 SCOPE OF THE WITTIG REACTION

In this section are presented the general characteristics of the Wittig reaction, including the effects of substitution on the ylide and the carbonyl reactants, the effects of various experimental conditions, useful modifications of the reaction, problems and limitations of the reaction, and stereochemical generalizations.

### 8.1.1 Stereochemistry of the Wittig Reaction

The Wittig reaction is known to involve a *syn*-elimination of the phosphine oxide by virtue of the observation that the configuration of phosphorus was retained throughout.[19,20] As shown in Eq. 8.3 the Wittig reaction can produce one or both geometric isomers of the alkene product, with the stereochemistry of the alkene being ordained by the stereochemistry of the precursor oxaphosphetane, and regardless of whether or not betaines are involved as discrete species. The stereochemical course of the reaction is most significantly affected by the nature of the ylide involved, with what follows being generalizations and with details deferred to Sections 8.1.2 and 8.1.3. Table 8.1 summarizes the effect of structure and reaction conditions on the stereochemical outcome of the Wittig reaction.

Stabilized phosphonium ylides, those carrying strong electron-withdrawing groups such as carbonyl on the ylide carbon, normally afford predominantly *E*-alkenes, with proportions of 95% not being unusual, but the reaction conditions to be discussed in Section 8.1.5 may influence the ratio. Thus, the cyanoylide reacted with an aldehyde to afford a 63% yield of substituted acrylonitrile which was 100% *E* (Eq. 8.4),[21] the ester ylide reacted with benzaldehyde to afford an 85:15 ratio of *E*:*Z* cinnamate (Eq. 8.5),[22] a 5′-aldehydoadenosine nucleoside reacted with the same ester ylide to afford exclusively *E*-alkenoate,[23] the α-methyl phenacylide reacted with *p*-nitrobenzaldehyde to afford exclusively the *E*-α-methyl cinnamate (Eq. 8.6);[24] and 2,2′-



(8.4)

$$Ph_3P{=}CHCOOEt + PhCHO \xrightarrow[-\,Ph_3PO]{} PhCH{=}CH\text{-}COOEt \tag{8.5}$$

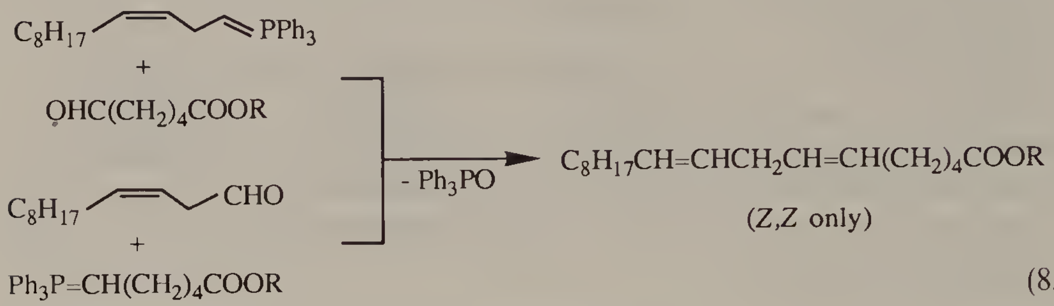
**TABLE 8.1** Effect of Structural and Reaction Variables on the Stereochemistry of the Wittig Reaction for Three Classes of Phosphonium Ylides

| Variable | Stabilized Ylides | Semistabilized Ylides | Nonstabilized Ylides |
|---|---|---|---|
| **A. Phosphorus Substituents** | | | |
| Triphenylphosphorus | *E* dominant | *E*:*Z* ~ 1:1 | *Z*-dominant |
| Alkyl group(s) on phosphorus | Increase *E* | Increase *E* | Increase *E* |
| Bulky group on phosphorus | Increase *E* | Increase *Z* | Increase *Z* |
| Dibenzophosphole group | Increase *Z* | Increase *E* | Increase *E* |
| Electron-donating group on phosphorus | | Increase *E* | |
| **B. Carbanion Substituents** | | | |
| Normal | *E* dominant | *E*:*Z* ~ 1:1 | *Z* dominant |
| COOH on carbanion side chain | | | Increase *E* |
| OH on carbanion chain | | | Increase *E* |
| $NH_2$ on carbanion chain | | | Increase *E* |
| **C. Carbonyl Substituents** | | | |
| Bulky Carbonyl | Increase *Z* | Increase *Z* | Increase *Z* |
| $\alpha,\beta$-Unsaturated carbonyl | Increase *E* | Increase *E* | Increase *E* |
| $\alpha$-Methoxy carbonyl | Increase *Z* | | |
| $\alpha$-Hydroxy carbonyl | Increase *E* | Increase *E* | Increase *E* |
| **D. Reaction conditions** | | | |
| Lithium present | Increase *Z* | Increase *Z* | Increase *E* |
| Protic polar solvent | Increase *Z* | No effect | Increase *E* |
| Dilution | | No effect | Increase *Z* |
| Anion | | $I^-$ increase *E* | $BF_4^-$ increase *E* |
| Acid catalyst | Increase *E* | | |
| Low temperature | No effect | No effect | Increase *Z* |
| High Pressure | Increase *E* | | |

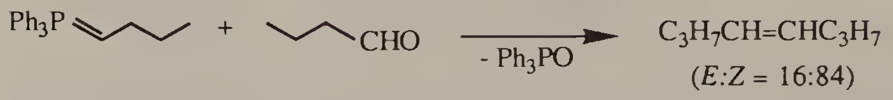
$$Ph_3P{=}C(CH_3)COPh + ArCHO \xrightarrow[-\,Ph_3PO]{} ArCH{=}C(CH_3)COPh \tag{8.6}$$

dipyridyl-6,6′-bisaldehyde was converted into a bipyridinophane using four simultaneous *E*-forming Wittig reactions.[25]

In contrast reactive (or nonstabilized) ylides, typically alkylides, normally produce predominantly *Z*-alkenes, although here too the conditions to be described in Section 8.1.5 can have a profound effect and be used to synthetic advantage. For example, Bergelson and Shemyakin[26] prepared linoleic esters, with two cis-double bonds, by two complementary routes (Eq. 8.7); the butylide and butyraldehyde produced an 82% yield of an 84:16 $Z:E$ ratio of 4-octene (Eq. 8.8)[27]; the propylide and benzaldehyde produced an 88% yield of a 96:4 $Z:E$ ratio of 1-phenylbutene (Eq. 8.9);[28] and numerous prostaglandin syntheses



(8.7)



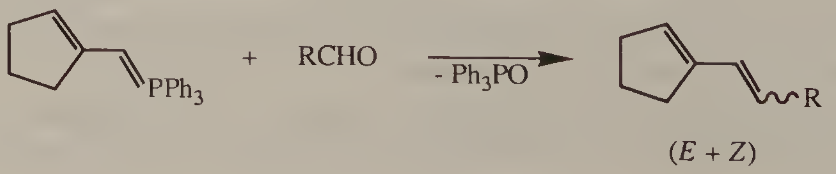
(8.8)

$$Ph_3P{=}CHEt + PhCHO \xrightarrow[- Ph_3PO]{} \underset{(E{:}Z = 4{:}96)}{PhCH{=}CHEt} \quad (8.9)$$

relied on the Wittig reaction for introduction of the 5,6-$Z$ double bond.[29] A recent synthesis of all *cis*-5,8,11,14,17-eicosapentaenoic ester relied on the Wittig reaction for coupling the two diene fragments.[30] However, there are many examples of $Z:E$ ratios approximating only 60:40 for alkylides.[9]

For ylides of intermediate stabilization (semistabilized or moderated ylides), typically benzylides or allylides, the stereochemical outcomes are less decisive, the ratio of isomers generally being in the 60/40 range in favor of either isomer. In such instances, the effect of experimental conditions and of substitution patterns can have major effects on the $Z:E$ ratio of the alkene products (see Sections 8.1.2–8.1.5). For example, Johnson and Kyllingstad[31] found a range of $Z:E$ ratios from 0.20 to 4.10 for reaction of a series of benzylides with a series of benzaldehydes; the allylide and benzaldehyde afforded a 48:52 $Z:E$ ratio of 1-phenyl-1,3-butadiene (Eq. 8.10);[5] the α-naphthylide reacted with α-naphthaldehyde to afford excellent yields of 1,2-di-α-naphthylethene with $Z:E$ ratios

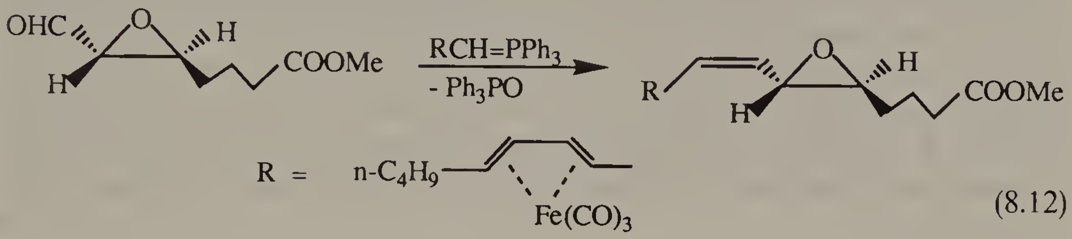
$$Ph_3P{=}CHCH{=}CH_2 + PHCHO \xrightarrow[- Ph_3PO]{} \underset{(E + Z)}{PhCH{=}CH{-}CH{=}CH_2} \quad (8.10)$$



(8.11)

ranging from 37:63 to 70:30;[32] reaction of a series of cyclopentenylmethylides with aldehydes produced a wide range of $Z$:$E$ ratios (Eq. 8.11).[33]

The Wittig reaction has been shown to transfer chirality from ylide or carbonyl to the alkene product, relying on chirality on phosphorus, in the carbanion substituent, or in the carbonyl component. An intramolecular Wittig reaction of an enantiomer afforded a cyclohexene derivative with 92% ee.[34] Bestmann et al.[35] found that the benzylide formed from optically active methylpropylphenylphosphine reacted with 4-substituted cyclohexanones to produce an enantiomeric excess of one alkene. Trost and Curran[36] obtained a similar result from an intramolecular Wittig reaction to form a bicyclo[3.3.0]-cyclooctenedione. Toda and Akai[37] found that incorporating cyclohexanone into an inclusion compound with an optically active host, followed by treatment with a nonchiral ylide, produced a 48–73% yield of alkene with up to 43% optical purity. Pinsard et al.[38] found that a racemic ylide produced an enantiomeric excess of $Z$-alkene when reacted with a chiral aldehyde, and that the individual enantiomeric ylides reacted separately to produce the separate enantiomeric alkenes (Eq. 8.12).



(8.12)

### 8.1.2 Phosphorus Substitution Effects

The original Wittig reaction was discovered[2,3] and developed[4,5] using triphenylphosphonium ylides, and most users of the reaction still rely on the readily accessible triphenylphosphorus group. It has been used as the reference standard for mechanistic and stereochemical studies. Further, with three phenyl groups on phosphorus there is no ambiguity regarding which proton is removed in ylide formation. Originally the use of trialkylphosphonium ylides in the Wittig reaction was thought impossible because of isolation of the betaine adduct hydrobromide rather than alkene from the reaction of methylenetrimethylphosphorane with benzophenone.[39] However, Johnson and LaCount[40,41] showed that trialkylphosphonium ylides were *more* reactive and produced good yields of alkene, and countless additional examples are now known.[42–44]

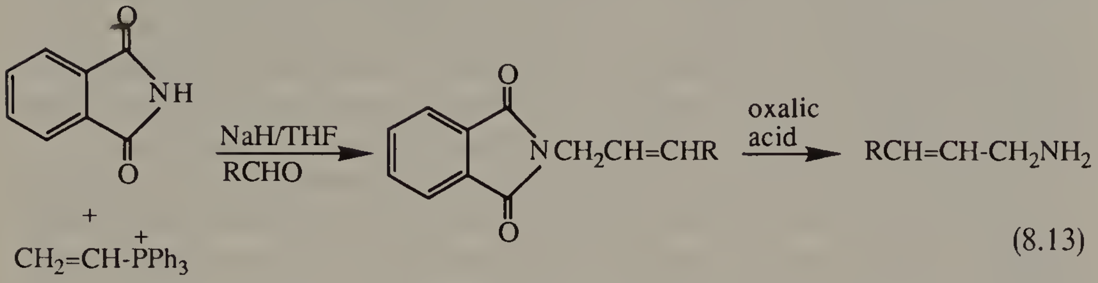
The placing of substituents on phosphorus which increase the electron density on phosphorus previously has been shown to increase the basicity of the ylides (see Section 3.3.2). This same electronic effect has the result of increasing the reactivity of ylides in the Wittig reaction, presumably through increased nucleophilicity of the ylide carbanion. Using kinetic studies on tri(substituted-phenyl)phosphonium ylides, two groups[45,46] have demonstrated that the rates of the Wittig reaction increased as the substituent was made more electron donating, and a $\rho$ value of $-1.7$ was calculated in one case.[45] Froyen[47] demonstrated the increased reactivity of fluorenylides when phenyl gradually was replaced by ethyl groups on phosphorus.

The use of bulky groups on phosphorus seems not to inhibit the reactivity of ylides although it does affect the stereochemistry (see below). Replacement of phenyl in the triphenylphosphonium group with *o*-tolyl, *o*-chlorophenyl, ferrocenyl, *o*-methoxymethoxyphenyl, or 2,6-difluorophenyl groups did not significantly affect yields of alkene with stabilized,[48] semistabilized,[49] or nonstabilized[50,51] ylides, although the 2,6-dimethoxyphenyl group did reduce yields with an alkylide.[52] The use of a phosphorus group which restricted pseudorotation in the transition state, such as a bridgehead bicyclic phosphorus group, prevented the Wittig reaction from occurring.[53]

The most interesting effect of changing phosphorus substituents is on the stereochemistry of the alkene product. For stabilized ylides, in which the normal stereochemical outcome is predominately the *E*-alkene, replacement of triphenylphosphorus with trialkylphosphorus resulted in increasing the $E$:$Z$ ratio from about 85:15 to as high as 99:1.[22,43] Replacement of one or more phenyl groups in the triphenylphosphonium group of an ester ylide with the ferrocenyl group increased the $E$:$Z$ ratio to 96:4,[48] while not significantly affecting the reaction rate, and replacement with *o*-tolyl groups raised the $E$:$Z$ ratio to 100:0.[54] Replacement with P-phenyldibenzophosphole, on the other hand, decreased the $E$ selectivity to as low as 28:72, while leaving the reaction rate very similar.[55]

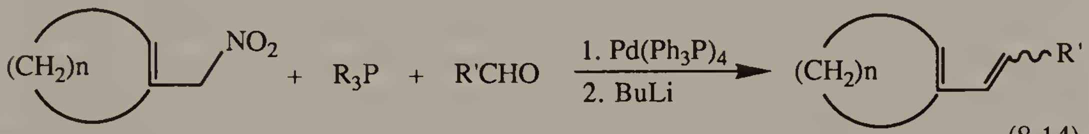
Nonstabilized ylides normally produce predominately the less thermodynamically stable *Z*-alkenes, and this has been a major mystery in the history of the reaction, materializing as they must from the most sterically crowded oxaphosphetanes. However, this fact has been of major importance in enabling introduction of cis stereochemistry into synthetic targets as illustrated by several prostaglandin syntheses.[29] The $Z$:$E$ ratios of 85:15 have been common,[9,56] but the Schlosser group have found that increasing the bulk of the phosphorus substituents, especially by using *o*-substituted phenyl groups, increased the ratio to as high as 99:1.[50,51] Surprisingly, McEwen and Cooney reported that a 2,6-dimethoxyphenyl group resulted in *reduction* of the $Z$:$E$ ratio to as low as 41:59 in reaction with benzaldehydes,[52] ascribing the result to "through space overlap between oxygen-2*p* and phosphorus-3*d* orbitals."

Although *Z*-alkenes often are readily isomerized to *E*-alkenes, means have been found to increase the proportion of *E*-alkene obtained directly from Wittig reactions of nonstabilized ylides. Two groups found that replacement of triphenylphosphorus with trialkylphosphorus produced a dramatic reversal of the $Z$:$E$ ratio in the ethylide from about 85:15 to as low as 1:9, depending on the aldehyde reactant.[56,57] Even more striking results were obtained when the triphenylphosphorus group was replaced by *P*-phenyldibenzophosphole, producing $Z$:$E$ ratios from 1:6 to 1:124.[58] Meyers et al.[59] used this phenomenon of stereoreversal in the synthesis of *E*-allyl amines by replacing vinyltriphenylphosphonium bromide with the tri-*n*-butyl analog as the starting material, thereby improving the $E$:$Z$ ratio of product from the original 27:73 to 90:10 (Eq. 8.13).



(8.13)

Semistabilized ylides with triphenylphosphonium groups usually are not significantly stereoselective. Tamura et al.[33, 60] found that geranyltriphenylphosphonium salt reacted with benzaldehyde to produce a 30:70 ratio of $E$:$Z$ triene, but with the tri-*n*-butylphosphonium salt a 85:15 ratio was obtained. From reaction of a series of cycloallyl nitrites with tri-*n*-butylphosphine, a variety of aldehydes, and in the presence of a palladium catalyst, could be obtained greater than 95% proportions of $E$-diene, whereas the use of triphenylphosphine afforded a 45% proportion of $E$-diene (Eq. 8.14).



(8.14)

In the benzylide series Johnson and Kyllingstad[27] showed that electron-donating groups, either substituted phenyl or alkyl, increased the $E$:$Z$ ratio, while electron-withdrawing groups decreased the ratio, all in reaction with benzaldehydes to form stilbenes. Zhao et al.[61] recently applied this capability to obtain a 99:1 $E$:$Z$ ratio of 4-alkenyloxazoles, the triphenylphosphonium counterpart providing only a 44:56 ratio. In contrast to these electronic influences, two groups have demonstrated that increasing the bulk of even one of the phosphorus substituents of a benzylide raised the proportion of $Z$-alkene significantly.[49, 51, 54] Allen's data[62] shows that all of the stereochemical effects of $P$-substituents for semistabilized ylides can be reconciled on the basis of steric bulk tending to increase the proportion of $Z$-alkene, and electron-donating effects increasing the proportion of $E$-alkene. Thus alkyl groups, the least sterically demanding and most electron-donating, increased the $E$-alkene, whereas bulky and relatively electron-withdrawing aromatic groups increased the $Z$-alkene.

### 8.1.3 Ylide Carbanion Substitution Effects

The effect of carbanion substituents on general ylide characteristics were described in Section 3.3.1. Such substituents affect the Wittig reaction of ylides by affecting ylide reactivity and alkene stereochemistry.

Ylides carrying strong carbanion-stabilizing groups simply do not undergo the Wittig reaction because of insufficient nucleophilicity. Triphenylphosphoniumcyclopentadienylide did not react with aldehydes or ketones,[63] while the more nucleophilic fluorenylides reacted with aldehydes but not with ketones.[41] When the ylide function was part of a napthalene ring system it would not react with carbonyls, but when it was part of an indenyl ring system it did react,[64] also reflecting a difference in delocalization of the electron pair on carbon.

Phenacylides react readily with aldehydes but only sluggishly or not all with ketones,[24,65] but replacement of the triphenylphosphonium group with the triethylphosphonium group enhances the reactivity.[44] Ylides with a formyl group[66] or with a cyano group[67] on the ylide carbanion also react well with aldehydes but not with ketones.

Ylides with an ester group on the ylide carbanion react readily with aldehydes,[22,24] although often requiring considerable time at room temperature or a few hours under mild reflux, but much more sluggishly with ketones.[68,69] Thioester ylides react similarly but are more stereoselective.[70]

Ylides with alkyl, cycloalkyl, vinyl, or aryl substituents on the ylide carbanion experience essentially no limitations in the Wittig reaction with respect to reactivity. Those with alkoxy and similar groups on the ylide carbanion also are quite reactive.[71]

Ylides carrying two substituents on the ylide carbanion seem equally effective in the Wittig reaction. For example, $\alpha$-halophenacylides,[24] $\alpha$-haloester ylides,[72] $\alpha$-methylester ylides,[73] and the $\alpha$-methyl-$\alpha$-cyanomethylide[74] all reacted effectively with aldehydes. Dialkyl-substituted ylides also experienced no limitations on their reactivity in the Wittig reaction. For example, the isopropylide,[75] the cyclopropylide,[76] other cycloalkylides,[77] and $\beta$-ionylidenetriphenylphosphorane (as used in the vitamin A synthesis)[78] all reacted effectively with carbonyl compounds. However, acetylferrocene did not react with dialkyl-substituted ylides.[78a]

Ylides with one or more halogens on the ylide carbanion, whose preparation was described in Section 4.1.3.2, effectively reacted with aldehydes and ketones to afford vinylic mono- and dihalides. Wittig reactions have been reported using $\alpha$-chloro-,[79,80] $\alpha$-bromo-,[81–86] $\alpha$-iodo-,[81,87] and $\alpha$-fluoroylides.[88–90] The $\alpha$,$\alpha$-dichloro-,[91] $\alpha$,$\alpha$-dibromo-,[92] and $\alpha$,$\alpha$-difluoroylides[93,94] all underwent Wittig reactions.

Ylides carrying reactive functional groups on an alkyl side chain also will react with aldehydes and ketones but the stereochemistry of the resulting alkenes may be reversed from the usual $Z$-predominance of an unsubstituted alkylide. Maryanoff et al.[95] concluded, on the basis of an exhaustive study, that when specific length (usually 2–4 carbons between phosphorus and the anionic center) side chains carrying anionic groups, such as carboxylate, oxido, and amido, were part of an ylide, the normal $Z$-dominant stereochemistry was inverted to as much as 90% $E$! Reaction of the carboxy phosphonium salts $[Ph_3P^+–(CH_2)_n–COOH\ Br^-]$ where $n = 2$ with aldehydes or ketones gave the $\beta,\gamma$-unsaturated acids in good yield using either dimsyl sodium ($Z$:$E$ ratio

= 20:80)[96] or 4 equivalents of butyllithium (100% *E* isomer).[97] When $n = 2$ or 3, *E* selectivity (2.5–6:1) was obtained using the carboxylate; *Z* selectivity (10:1) was obtained using the corresponding nitrile.[98] Where $n = 4$, an important case because of application to the synthesis of prostaglandins, dimsyl potassium was most effective.[99] The *Z*:*E* stereochemical outcomes have varied as follows: 100:0;[100] 80:20;[101] 60:40;[102] 25:75;[103] 10:90.[95] The *E*-stereochemical enhancement vanished with longer distances between the phosphonium and carboxylate groups, such as $n = 7$ where only the *Z*-isomer was obtained.[95,104]

A similar phenomenon has been observed when a hydroxy group was located in the alkyl side chain of an ylide.[95] For a series of hydroxyalkylides [$Ph_3P{=}CH{-}(CH_2)_n{-}OH$] the normally dominant *Z* stereochemistry was found to be changed to *Z*:*E* ratios as follows: $n = 1$ ($\sim$ 35:65);[105] $n = 2$ (mainly *E*,[106,107] 10:90[95]); $n = 3$ (42:58;[108] 15:85;[109] 4:96 to 73:27[95]); $n = 4$ (mainly *Z*;[110] 15:85 to 54:46[95]); $n = 5$ (26:74 to 71:29[95]). The *Z*-dominance returned for longer chain phosphonium alcohols used in the Wittig reaction. Use of the "instant ylide" technique with a variety of hydroxyalkylides also afforded alkenes with high *Z*:*E* ratios.[111]

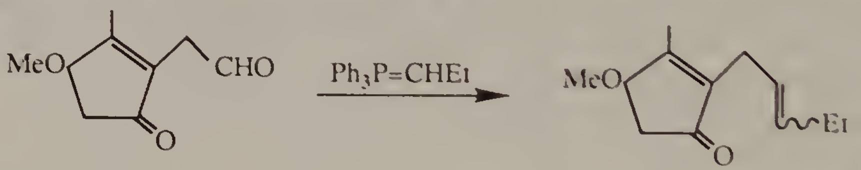
With aminoalkylides there also was some *E*-enhancement from the normal *Z*-dominance obtained with alkylides. For ylides of the type $Ph_3P{=}CH{-}CH_2NR^1R^2$ and no hydrogen on nitrogen, the *Z*:*E* ratios from Wittig reactions have been relatively nonstereoselective but quite variable with reaction conditions.[58,95,112,113] When the nitrogen carried at least one hydrogen atom, which could be removed by excess base in the course of the Wittig reaction, the enhancement of the proportion of *E*-alkene was apparent.[95,114]

### 8.1.4 Nature of The Carbonyl Reactant

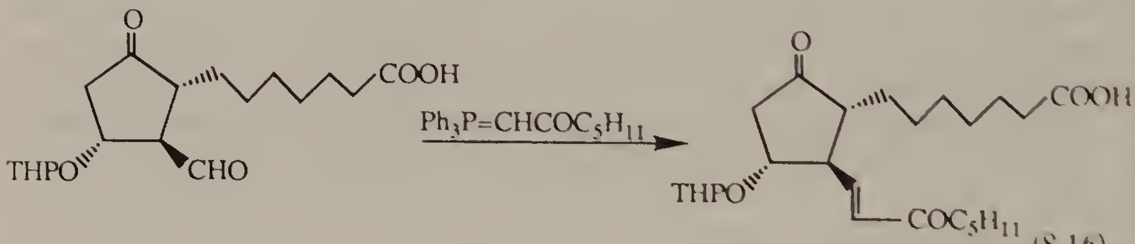
The nature of the carbonyl reactant also affects the outcome of the Wittig reaction in terms of reactivity and stereochemistry. This section is limited to reactions with aldehydes and ketones; those with carbonyl-containing carboxylic acid derivatives were discussed in Section 6.5 and will be summarized again in Section 8.2.2.7 of this chapter; those with cumulene-type carbonyl compounds were discussed in Section 7.3.2.

There is almost no limit to the kind of aldehyde or ketone which can be used in the Wittig reaction (but see Section 8.1.7.1). In their original work Wittig et al.[4,5] found that both benzaldehyde and benzophenone were effective reactants with methylenetriphenylphosphorane. However, it was soon discovered that with less reactive ylides, such as the phenacylide[63] and the fluorenylide,[115] there was a difference in the reactivity between aldehydes and ketones. It is clear that the Wittig reaction depends in part on the electrophilicity of the carbonyl group, with aldehydes being more susceptible to attack by the nucleophilic ylide than ketones. Hammett correlations have been reported for substituted benzaldehydes reacting with stabilized ylides and the $\rho$ values ranged from $+2.35$ to $+2.9$.[45,46,116] In the benzophenone series the $\rho$ value recently has been shown to be + 1.40[117] in reaction with triphenylphosphoniumisopropylide.

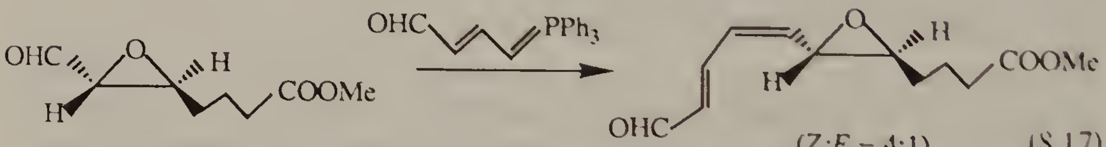
The selective susceptibility of carbonyl groups to ylide attack and Wittig reaction has been employed to advantage in syntheses. Thus, a rethrolone precursor reacted with the nonstabilized propylide only at the aldehyde group to produce mainly the *Z*-alkene (Eq. 8.15)[118] and a tetrafunctional acid reacted with a stabilized acylide only at the aldehyde group to afford exclusively the *E*-alkene (Eq. 8.16).[119] The selectivity also has been employed in leukotriene syntheses to effect a new $C_4$-extension, the formyl group on an oxirane being more susceptible to ylide attack than either the formyl group on the ylide (probably owing to carbanion delocalization through it), the oxirane group, or the ester group (Eq. 8.17).[120] Finally, Tamura et al.[33] reported that in the presence of benzaldehyde and acetophenone, an allylide reacted only with the former, although it would react separately with both carbonyl compounds.



(8.15)



(8.16)

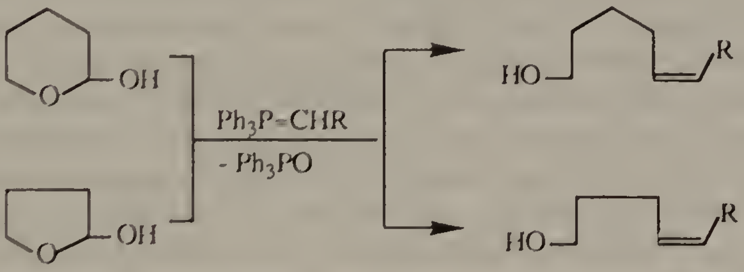


(*Z*:*E* = 4:1) (8.17)

There have been a few reports of the failure of the Wittig reaction with the cause being attributed to steric hindrance in the carbonyl group.[54,121–123] Far more frequent are reports of successful reactions with bulky (sterically hindered) aldehydes or ketones. In most instances what is observed is a significant *increase* in the proportion of the *Z*-alkene, which Vedejs and Snoble[124] attributed to the lowest energy orientation of the reactants in their orthogonal approach to each other as they eventually form the intermediate oxaphosphetane. Thus, high *Z*:*E* ratios have been obtained with pivaldehyde,[33,50,56,124] 17-ketosteroids,[125] benzaldehyde chromium tricarbonyl,[126] α-methylated-β-phenylpropionaldehyde,[57] and methylisopropyl ketone.[127] Di-*t*-butylketone even was found to react with the diylide from diphenyldimethylphosphonium bromide.[128]

There are only minor differences in the reactivity or steric orientation between aromatic aldehydes or aliphatic aldehydes as reflected in the Wittig reaction, with unsaturated aldehydes or ketones and aromatic aldehydes usually giving slightly more of the $E$-alkene.[10] Tables 4 and 11 in Gosney's 1979 review[9] illustrate this fact with nonstabilized and semistabilized ylides, and indicate no reluctance in reactions using unsaturated carbonyl compounds. Conjugate addition by the ylide as described in Section 7.1 must be guarded against, but its competitive occurrence is relatively rare. Thus, Battiste[129] was able to prepare a methylenecyclopropene by Wittig reaction with the precursor cyclopropenone.

The presence of $\alpha$-alkoxy groups in the carbonyl reactant can change the expected stereochemical outcome of a Wittig reaction. For example, with stabilized ylides the presence of such groups decreased the normal $E$ selectivity, often to the point of complete reversal.[10] However, the presence of hydroxyl groups in the carbonyl reactant usually does not invert the stereochemical selectivity, but tends to increase the $E$-component.[11, 109, 130] However, reactive ylides with methoxy acetone gave excellent yields of $Z$-alkenes with up to 99% stereoselectivity.[131] Maryanoff and Reitz reviewed these changes in detail.[10] Lactols have a special place in this brief discussion because of their use in the prostaglandin syntheses,[96, 99] in which they simply opened under Wittig reaction conditions and proceeded normally to form predominantly $Z$-alkenes.[132] 2-Hydroxytetrahydrofuran and 2-hydroxytetrahydropyran have served as effective precursors for alk-4Z-en-1-ols and alk-5Z-en-1-ols (Eq. 8.18).[133]



(8.18)

## 8.1.5 Effect of Experimental Conditions on the Wittig Reaction

The feasibility, the yields, and the stereochemistry of the Wittig reaction can be influenced by a variety of experimental conditions which may be applied to the reaction. These conditions are discussed separately in the following sections, which include (1) the choice of base to generate the ylide, (2) the solvent, (3) reactant ratios, (4) additives, (5) catalysts, (6) temperature, and (7) pressure.

*8.1.5.1 Effect of Base.* The nature of the base employed to generate the ylide does not affect the Wittig reaction of stabilized ylides because they usually are generated and purified separately and then introduced into the reaction with only the carbonyl component. Table 4.1 lists most of the different bases used to produce such ylides.

With semistabilized ylides, varying the base provides only small changes in stereochemical outcome. Drefahl et al.[32] were able to increase the $E$:$Z$ ratio of 1,2-di-$\alpha$-naphthylethene by 23 parts with a range of four bases from $n$-butyllithium to sodium amide. A reaction involving allylides was not affected by a change from butyllithium to potassium *t*-butoxide when the triphenylphosphonium group was attached, but was slightly affected (maximum 25 points) when the tri-*n*-butylphosphonium group was attached.[33]

With reactive ylides the avoidance of organolithium bases leads to the highest proportions of *Z*-isomers being produced. For example, reaction of triphenylphosphoniumpropylide with hexanal[134] afforded *Z*:*E* ratios of 3-nonene as follows using the various bases: $NaNH_2$, 97:3; $NaN(SiMe_3)_2$, 96:4; $NaCH_2SOMe$, 91:9; *n*-BuLi, 50:50. Anderson and Henrich[135] earlier had used the organolithium option to purposefully prepare a 1:1 mixture of a *Z* and *E* alkene which was converted to the naturally occurring 1:1 mixture comprising the sex pheromone of the pink bollworm moth (gossyplure). Others[95, 136] have noted the increased *Z*:*E* ratios obtainable when ω-hydroxy ylides or α-alkoxycarbonyls are involved in Wittig reactions and organolithium bases were avoided. With many alkylphosphonium salts, potassium *t*-butoxide afforded much better yields of alkenes in reactions with a variety of aldehydes and ketones than did organolithium bases.[137, 138] As discussed in Section 8.1.5.4, the presence or absence of the lithium ion is critical. Thus, lithium hexamethyldisilazide produced less *Z*-isomer than did the counterpart sodium or potassium base.[95]

A number of specialized Wittig reaction procedures have become available in recent years. Buddrus[139] used ethylene oxide as a base giving normal *Z*:*E* ratios with stabilized and semistabilized ylides, but abnormally low *Z*:*E* ratios with nonstabilized ylides. Mehta et al.[140] electrochemically generated a dianionic base to effect proton abstraction from the phosphonium salt, thereby avoiding base-catalyzed side reactions. Schlosser et al.[111, 141] prepared storable "instant ylides" by mixing paraffin-covered sodamide with solid phosphonium salt. Addition of this mixture to a carbonyl compound in diethyl ether or tetrahydrofuran produced excellent yields of alkene with high *Z*:*E* ratios in the case of alkylides and normal ratios in the case of benzylides. Le Bigot et al.[142–144] reported the use of biphasic conditions, such as slightly hydrated potassium carbonate or barium hydroxide with minimal amounts of protic or aprotic solvents, for reaction of alkyl phosphonium salts and carbonyl compounds to produce good yields of alkenes with high, though not outstanding, *Z*:*E* ratios. Tagaki et al.[145] used phase transfer catalysis of Wittig reactions (benzene and aqueous sodium hydroxide), but the process was seriously limited by being effective only with aldehydes, requiring a 2:1 ratio of phosphonium salt to aldehyde, and being nonstereoselective. Cesium fluoride served as a base for a nonstereoselective Wittig reaction of trifluoroethyltriphenylphosphonium triflate with benzaldehyde at room temperature.[146]

***8.1.5.2 Effect of Solvent.*** The choice of solvent can significantly affect the outcome of the Wittig reaction and Schlosser's early review[147] should be consulted for details. It usually is difficult to separately identify the effects of the solvent from those of the base and counterions.

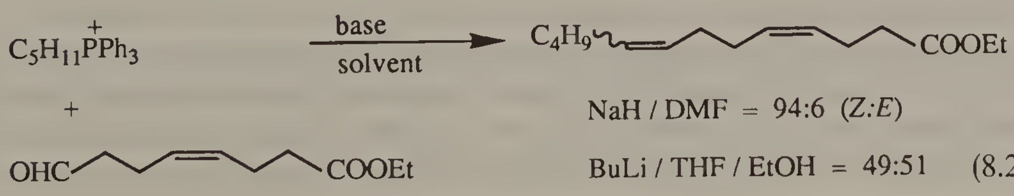
Stabilized ylides, which normally produce *E*-alkenes with high stereoselectivity, usually are reacted in nonpolar solvents such as benzene and methylene chloride. In their kinetic studies Speziale and Bissing[116] and Ruchardt et al.[45] both found that chloroform led to about a twofold increase in rate and methanol led to more than a hundredfold increase in rate. Although Bergelson and Shemyakin[26] claimed that there were no solvent stereoselectivity effects, others have since shown that increased solvent polarity, and especially use of a protic solvent such as methanol, leads to increasing proportions of the *Z*-alkene (i.e., a *decrease* in the selectivity of the reaction). House et al.[148] were able to drop the product mix from 96% *E* to 62% *E* by changing from methylene chloride to methanol in the reaction of carbomethoxymethylenetriphenylphosphorane with benzaldehyde. Tronchet and Gentile[149] obtained even more striking shifts with the ethyl ester ylide, moving from 86% *E* to 92% *Z*, although the surprising size of this effect may have been due mainly to the presence of an α-alkoxy group in the aldehyde (see Section 8.1.4). Prakash and Rao recently applied this same solvent effect to obtain higher proportions of *Z*-alkenes.[150]

Major solvent effects do not occur in the reaction of semistabilized ylides with carbonyl compounds. Under normal conditions (aprotic solvent, "salt-free" ylide) $Z:E$ ratios of 1:2–3 are typical for the alkene product. Increasing the polarity of the solvent, such as using dimethylformamide, usually leads to slight increases in the *Z*-component, and use of a protic solvent, such as methanol, usually leads to $Z:E$ ratios of about 1:1.[17, 26, 32, 148]

Nonstabilized ylides ("reactive ylides," usually alkylides) normally produce mainly *Z*-alkenes, and the highest stereoselectivity, often $>95\%$, can be achieved using polar aprotic solvents, most often tetrahydrofuran.[28, 147, 151] The use of protic solvents, such as DMSO or an alcohol, can reduce the *Z*-component to near 50%.[134, 135] The ability to vary solvents, and to choose between a phosphonium alkylide (**A**) and an allylide (**B**), has given considerable stereochemical flexibility to the recent synthesis of a series of dienols (Eq. 8.19).[18] Ethyl trideca-4,8-dienoate was prepared in nearly pure *Z,Z*-form and, in a separate reaction, in a desired 1:1 mixture of *Z,Z*- and *E,Z*-isomers, by judicious choice of solvent and base (Eq. 8.20),[135] eventually leading to the 1:1 mixture

$$\underset{}{Ph_3P{=}CH(CH_2)_8OH} + \underset{(E)}{C_2H_5CH{=}CHCHO} \xrightarrow{\textbf{A}} \underset{(E)\qquad (Z:E = 90:10)}{C_2H_5CH{=}CH\text{-}CH{=}CH\text{-}(CH_2)_8OH}$$

$$\underset{(E)}{Ph_3P{=}CH\text{-}CH{=}CH\text{-}C_2H_5} + HO(CH_2)_6CHO \xrightarrow{\textbf{B}} \underset{(E)\qquad (Z:E = 50:50)}{C_2H_5CH{=}CH\text{-}CH{=}CH\text{-}(CH_2)_6OH} \qquad (8.19)$$



NaH / DMF = 94:6 (*Z*:*E*)

BuLi / THF / EtOH = 49:51 (8.20)

known as gossyplure. Use of toluene solvent under reflux conditions led to dominant side reactions resulting from one-electron transfer from the isopropylide to ketone, leading to reduction of the latter.[152]

***8.1.5.3 Concentration Effects.*** Bergelson et al.[153] reported that doubling the concentration of either one of the reactants, triphenylphosphoniumpropylide and benzaldehyde, lead to an increase in the $Z$:$E$ ratio of 1-phenylbutene, but the effects were not dramatic. They attributed the effect to an inhibition of the reversibility of the reaction. Others[27, 32, 154] have reported on changing the ratio of reactants with no significant benefits resulting. The benzylide was reported to exhibit no dilution effects.[155]

Reitz et al.[156] reported that in the reaction of triphenylphosphoniumbutylide with aldehydes in tetrahydrofuran solvent and in the presence of lithium ion, at 0.015 M the $Z$:$E$ alkene ratio was 97:3, virtually the same as in the absence of lithium. However, increasing the concentration of the reactants resulted in an increasing proportion of $E$-alkene being produced, following a hyperbolic curve and approaching a limiting value of 36:64. Thus, highest selectivity in this reaction was obtained at highest dilutions, perhaps as a result of complexation of the lithium ion by solvent, making it less available to directly affect the stereoselectivity of the reaction.

***8.1.5.4 Effect of Additives.*** The presence of certain cations, anions, alcohols, and crown ethers have been shown to affect the stereoselectivity of the Wittig reaction. The literature is full of references to the misleading term "salt-free" ylides (see Section 4.1.3.1), and regrettably it continues to be used to mean "lithium-free" methods of ylide preparation and Wittig reaction (i.e., conversion of a phosphonium salt to ylide using other than an organolithium base, most often using sodium amide in benzene[28]). It is likely that *all* ylides prepared in solution from phosphonium salts, and not subsequently distilled or recrystallized, but instead used directly in the solution for a Wittig reaction, were not in fact salt-free.[157]

The effect of the presence of various cations, particularly lithium, has been the most visible and useful, as well as troubling on occasion. Little work has been done regarding cations influencing the reactions involving stabilized ylides because the latter usually are prepared separately, any extraneous materials removed, and the pure ylide then reacted with the carbonyl compound. House et al.[148] reported minor enhancements (e.g., a shift in the $Z$:$E$ ratio from the normal 6:94 to 22:78) in the proportion of $Z$-isomer obtained when reacting ester ylides with aliphatic or aromatic aldehydes in the presence of added lithium halides.

With semistabilized ylides the effect of lithium cation on the stereoselectivity also is modest. Although Bergelson and Shemyakin[26] originally reported major increases in the proportion of $Z$-isomer obtained from a benzylide, House et al.[148] revised this conclusion to show virtually no effect of lithium cation. Later, Mehta et al.[140] reported minor increases in the $Z$-isomer. However, McEwen and Ward[155] observed a reversal of $Z\!:\!E$ ratio from 27:73 to 66:34 in reacting a benzylide with aldehydes in the presence of lithium salts. With allylides, up to 27% increases in the $Z$-isomer were noted when lithium bases were replaced by potassium bases.[33]

The presence of lithium cation in the reaction of nonstabilized ylides with carbonyl compounds in nonpolar solvents leads to a significant *decrease* in the normal high $Z$-selectivity of the reaction. First noted by the Bergelson group[151] and the Schlosser group,[137] this conclusion has been confirmed many times since.[28, 95, 134] The effect gradually vanishes in more dilute solution, and the use of solvents which solvate the lithium cation also diminishes the effect.[156] Two groups[156,158] have shown that the stereochemical change occurs in the initial condensation step of the reaction, not as a result of reversibility as earlier hypothesized, but the details of how the lithium cation affects the condensation remain unknown. Thus, for high $Z$-selectivity, formation of alkylide with bases containing potassium or sodium cations provides the best route, but production of the maximum amount of $E$-isomer, usually 50%, is effected by purposeful addition of the lithium cation.

The effect of the anion present in a Wittig reaction is somewhat unclear. Hauser et al.[27] noted that better yields and faster reactions were observed from phosphonium chlorides than from bromides. Drefahl et al.[32] noted no effect of anion on the stereoselectivity of a benzylide, but later workers[159] noted an increase in the $E$-alkene when high concentrations of lithium iodide, but not chloride, were added. More recently, McEwen et al.[160] reported enhancement of $Z$-alkene production by the addition of sodium iodide. Finally, use of the tetrafluroborate anion along with the lithium cation and alkylides produced via the "salt free" method produced major shifts in $Z\!:\!E$ ratios from 96:4 to 52:48, this in a system where lithium halides produced only minor shifts toward the $E$-alkene (Eq. 8.21).[28, 161] On the other hand, sodium iodide or tetrafluoroborate reversed benzylide $Z\!:\!E$ alkene ratios from the normal 36:64 to 77:23 and 83:17 respectively.[162]

$$\mathrm{Ph_3P{=}CHEt} \;+\; \mathrm{PhCHO} \xrightarrow[-\,\mathrm{Ph_3PO}]{\mathrm{A}} \mathrm{PhCH{=}CHEt} \qquad (8.21)$$

| A (additive) | $Z\!:\!E$ ratio |
|---|---|
| None | 96:4 |
| LiCl | 90:10 |
| LiI | 83:17 |
| $\mathrm{LiBPh_4}$ | 52:48 |

The addition of small amounts of alcohols to organolithium-derived alkylide solutions led to a significant increase in the proportion of $E$-alkene (Eq. 8.20).[135] The use of a crown ether provided a dramatic change from $Z\!:\!E$ ratios normally about 95:5 to a ratio of 22:78 in methylene chloride solution, although in tetrahydrofuran solution the ratio was 85:15.[163] This may be a technique to consistently obtain high yields and proportions of *E*-alkenes from alkylides, an outcome seldom achieved by straightforward routes.

*8.1.5.5* ***Catalysis.*** Wittig reactions of stabilized ylides with aldehydes and ketones are facilitated by the presence of benzoic acid, with most applications being with the isolable ester ylides (carbomethoxy- or carboethoxymethylenetriphenylphosphorane) which otherwise reacted only sluggishly with ketones. Some *E*-alkene enhancement has been observed. The effect has been postulated to result from protonation of the carbonyl oxygen, making it more susceptible to attack by the weakly nucleophilic ylide.

Ruchardt et al.[164] first applied this approach to improve the yield in reaction with acetone from 6 to 80% and determined the maximum effect to be with 0.5–1.0 equivalents of acid.[45] The rate of such reactions was doubled by catalysis.[165a] Catalysis has been used to facilitate reaction with steroidal ketones,[166] to add the *E*-side chain in prostaglandin syntheses,[119] and in leukotriene syntheses[167–169] using from trace amounts up to 0.3 equivalent amounts of benzoic acid. The latter cases all produced high *E*-selectivity (~85%), and others[154] have noted enhancement of *E*-selectivity by catalysis, which makes mystifying the report by Bohlmann and Bax[170] of obtaining a $Z:E$ ratio of 2:1 in the catalyzed reaction of an ester ylide with 6-methyl-hepta-3,5-dien-2-one.

*8.1.5.6* ***Effect of Temperature.*** Wittig reactions using stabilized or semistabilized ylides usually are conducted at room temperature or under gentle reflux since they tend to be endothermic. Variation in the temperature involving stabilized[22] or semistabilized[32] ylides produced no significant effect on stereoselectivity. Hauser et al.[27] noted that using the lowest temperature possible tended to avoid aldol-type condensation of the carbonyl reactant, presumably catalyzed by the ylide.

In most cases Wittig reactions using the nonstabilized alkylides must be cooled, usually to about −78°C, and small temperature effects on the stereoselectivity have been observed.[17, 135, 171] Schlosser et al.[134] demonstrated that in the reaction of alkylides with aliphatic or aromatic aldehydes the $Z:E$ ratio of the alkene could be enhanced gradually from 87:13 obtained at room temperature to 96:4 obtained at −100°C. In a two-phase reaction higher temperatures increased the yields.[172]

High temperatures have been successfully used to effect Wittig reactions with hindered or unreactive ketones.[173, 174, 138] However, use of higher temperatures with alkylides and benzylides led to dominating side reactions involving one-electron transfers from ylide to carbonyl, resulting in reduction of the carbonyl compounds.[152]

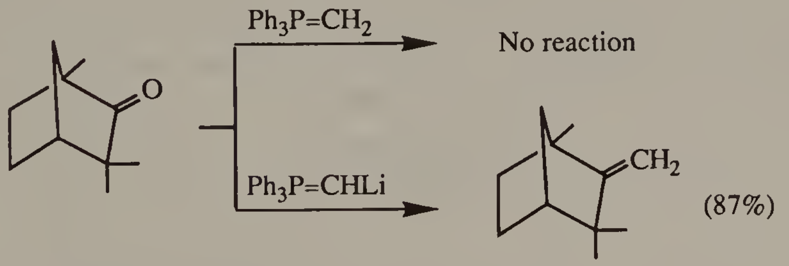
*8.1.5.7* ***Effects of Pressure.*** The use of pressure to enhance yields in Wittig reactions with less reactive carbonyl compounds is an attractive alternative to using higher temperatures or the more reactive ylide-anions.

Isaacs and Abed[175] determined that the volume of activation for a Wittig reaction was sufficiently negative for pressure to be useful in forcing reluctant reactions. They subsequently found that stabilized ylides, which reacted poorly with a number of ketones at atmospheric pressure,[42] produced good or excellent yields of alkenes at 9 kbar pressure.[176] Dauben and Takasugi[177] were able to improve yields and conversions in the reaction of a butylide with a series of hindered ketones using pressures up to 15 kbar. Previously Nonnenmacher et al.[178] had found that reaction of triphenylphosphoniumacetylide with aldehydes gave better yields and slightly higher $E$:$Z$ ratios of alkenes when conducted at 10 kbar. The yield of alkene from reaction of $Ph_3P{=}CHOMe$ with a 17-ketosteroid was increased from 10 to 70% under pressure conditions[179] and a $\beta$-keto ylide effected an intramolecular Wittig reaction with an ester in 60% yield under pressure.[180]

### 8.1.6 Modifications of the Wittig Reaction

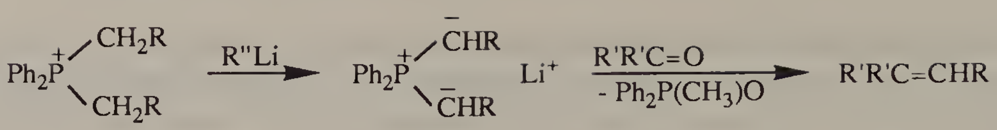
A number of modifications of the Wittig reaction have been reported. Since triphenylphosphine oxide occasionally is difficult to separate from the desired products, means of facilitating this separation have been explored. Trippett and Walker[181] formed ylides from *p*-dimethylaminophenyldiphenylphosphine, thereby permitting acid extraction to be used to remove the oxide, while Daniel and Le Corre[182] replaced one of the phenyl groups with the 2-carboxyethyl group, thereby permitting base extraction to remove the oxide. In the latter case the stereoselectivity of the Wittig reaction did not change significantly using stabilized ylides, but with semistabilized ylides the proportion of $E$-alkene increased, possibly due simply to alkyl substitution on phosphorus (see Section 8.1.2) or to the presence of the carboxylate anion (see Section 8.1.3).

Increasing the nucleophilicity of an unreactive ylide by its conversion to an ylide anion (see Section 3.4.2) was first successfully used by Broquet and Simalty,[183] enabling the reaction of a phenacylide with ketones. Corey et al.[184] applied this approach to the methylenation of hindered ketones such as fenchone, with which triphenylphosphoniummethylide does not react (Eq. 8.22), although others had difficulty repeating the work.[185]



(8.22)

Cristau et al.[128] accomplished the same result as Corey's work, and reported additional examples, by using the other kind of ylide anion (**1**, R = H), that prepared from diphenyldimethylphosphonium bromide (Eq. 8.23). The ylide

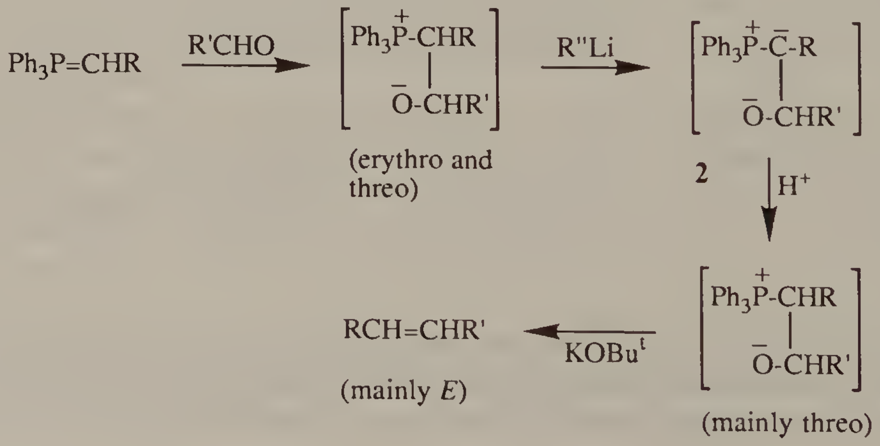


**1**

(8.23)

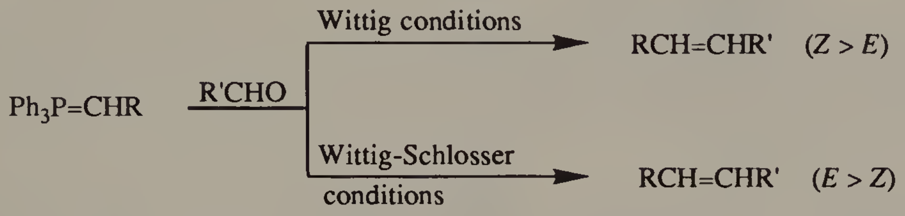
anion (**1**, R $=$ H) formed a sulfinoxy ylide with sulfinates, and subsequent Wittig reactions produced good yields of vinylic sulfoxides with high $E$ stereoselectivity and with substantial optical purity when using an optically active sulfinate.[186] It was claimed that enolizable ketones and stabilized ylides (**1**, R $=$ PhCO) both could not be used in this modification of the Wittig reaction.[128] However, McKenna and Walker[187] succeeded in using stabilized ylides (**1**, R $=$ CN or COOMe) and in using enolizable ketones such as cyclohexanone. Using the ester ylide anion there was no significant change in the already low $Z$:$E$ ratios of products (~2:98) formed using $Ph_3P{=}CHCOOMe$, but there was some decrease in the $E$ component (20:80 to 56:44) using the cyanoylide. Using the semistabilized benzylide (**1**, R $=$ $CH_2Ph$) they found a significant increase in the proportion of $E$-isomer produced compared to $Ph_3P{=}CHPh$,[188] perhaps due to analogy with the phosphoryl ylides (see Chapter 11) and/or simply due to the replacement of a phenyl group with an alkyl group (see Section 8.1.2).

***8.1.6.1 Schlosser Modification.*** Based on their analysis of the probable mechanism of the Wittig reaction involving reactive (nonstabilized) ylides, Schlosser and Christmann[28, 189] determined that interception of the erythro and threo betaines from the Wittig reaction and permitting them to equilibrate could result in dominance of the threo betaine and subsequent formation of alkenes of predominate $E$-stereochemistry, in contrast to the usual dominance of the $Z$-alkene. Equilibration of the supposed betaines was accomplished through treatment of the betaines with additional strong base, usually an organolithium such as $t$-butyllithium, resulting in formation of a betaine-ylide ($\beta$-oxidophosphonium ylide) (**2**). Completion of the reaction was obtained by providing a proton source to form a $\beta$-hydroxyphosphonium salt which then was treated with potassium $t$-butoxide to reform betaine and eliminate triphenylphosphine oxide (Eq. 8.24). Application of this method, now known as the



(8.24)

"Wittig–Schlosser method," resulted in $Z:E$ ratios of $< 5:95$, a complete reversal of the Wittig reaction stereoselectivity for reactive ylides (Eq. 8.25).[189, 190] However, it must be noted that lithium salts must be present to obtain this stereoselectivity.[191] The Wittig–Schlosser modification clearly provides outstanding stereochemical options for the synthesis of 1,2-disubstituted alkenes.

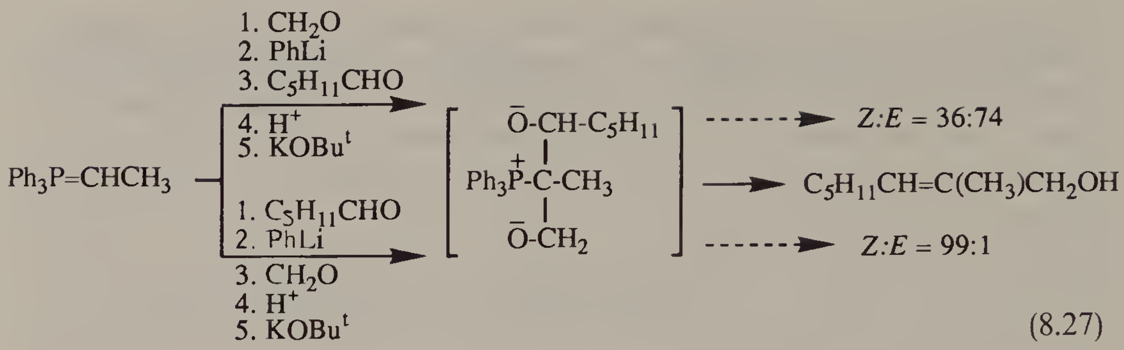


$$Ph_3P{=}CHR \xrightarrow{R'CHO} \begin{cases} \xrightarrow{\text{Wittig conditions}} RCH{=}CHR' \quad (Z > E) \\ \xrightarrow[\text{conditions}]{\text{Wittig-Schlosser}} RCH{=}CHR' \quad (E > Z) \end{cases} \qquad (8.25)$$

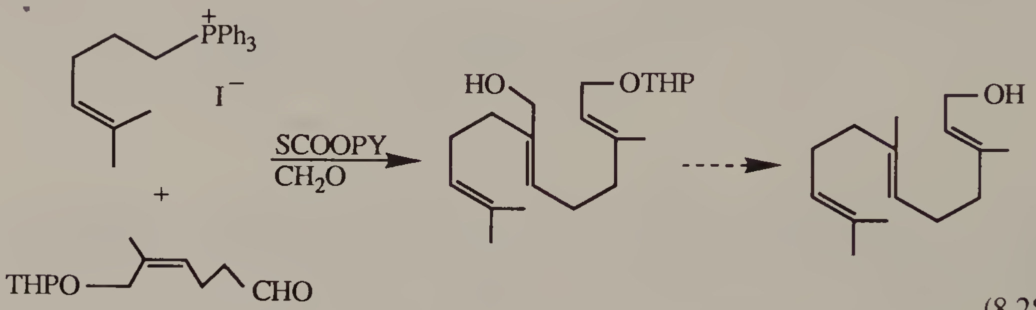
***8.1.6.2 The SCOOPY Modification.*** First the Schlosser group[192] and then the Corey group[193] found that the betaine-ylide (**2**) could be intercepted by electrophiles other than the proton, with the overall result that the reaction produced a trisubstituted alkene with a new electrophile located on what was the ylide (α-) carbon, the overall process being "α-substitution plus carbonyl olefination via β-oxidophosphorus ylides (SCOOPY)." Successful reactions but with varying stereoselectivities included methylation[194, 195] (although other alkylations were not successful), fluorination,[192] bromination,[192] chlorination,[193] iodination,[193] and deuteration.[191] The added electrophile usually, but not always,[193] resided cis to the former aldehyde substituent in the resulting alkene (Eq. 8.26). In this manner the trisubstituted alkene 1-phenyl-2-methylpentene was obtained with an $E:Z$ ratio of 78:22, whereas a direct Wittig reaction afforded a ratio of 46:54,[194] while the haloalkenes were obtained in $E:Z$ ratios greater than 95:5.[193]

$$Ph_3P{=}CHR \quad + \quad R'CHO \xrightarrow[X^+]{\text{SCOOPY}} RCX{=}CHR' \qquad (8.26)$$

Probably the most important SCOOPY reaction employed formaldehyde as the electrophile, resulting in the addition of a carbinol group to the normal alkene which would result from the Wittig reaction. First reported by Corey and Yamamoto,[195] and later by Schlosser and Coffinet,[196] this reaction usually results in the loss of the oxyanion from the *original* aldehyde group.[195, 197] Later it was shown that regardless of the sequence of addition of the two aldehydes used in the reaction, the carbinol group invariably remained, but the stereochemistry varied depending on the order of aldehyde addition. Thus, the ethylide could be converted into oct-2-en-1-ol using formaldehyde and hexanal in either order (Eq. 8.27).[195] Application of this method to the synthesis of α-santalol strikingly exhibited its usefulness,[195] and this was followed shortly by a high-yield elegant synthesis of *trans,trans*-farnesol (Eq. 8.28).[198]



(8.27)



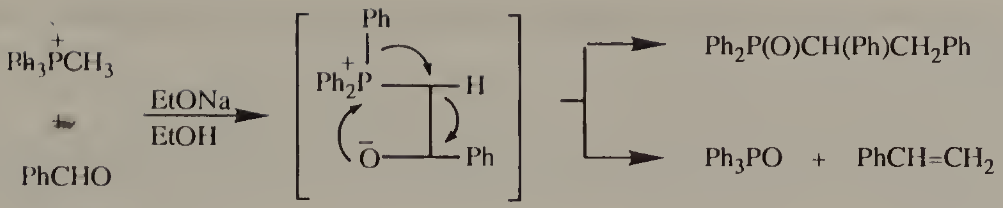
(8.28)

When aldehydes other than formaldehyde were used as electrophiles, the oxyanion from the *second* aldehyde was invariably lost as phosphine oxide. Thus, using acetaldehyde and heptanal in two sequences permitted two positional isomers to be obtained, the *E* stereoisomer dominating in both instances.[195] This modification of the Wittig reaction has evolved into an important general synthesis of *E*-allylic alcohols [$R^1CH{=}CR{-}CH(OH)R^2$] and trisubstituted alkenes from ylides ($RCH{=}PPh_3$) and two aldehydes ($R^1CHO$ and $R^2CHO$), as described in detail by Gosney.[9]

### 8.1.7 Limitations of the Wittig Reaction

Although few in number, there have been some limitations and/or problems discovered with use of the Wittig reaction. Some have claimed that the major problems are lack of stereoselectivity in the reaction, the inability to react stabilized ylides with ketones, the inability to produce highly substituted alkenes, and the difficulty of removing triphenylphosphine oxide from the products. The experimental techniques discussed in the previous section conquer each of these limitations.

The limitations are discussed as problems originating with either the carbonyl reactant or the ylide reactant. First, however, mention must be made of a problem noted with the choice of sodium ethoxide in ethanol as the ylide-forming base in reactions of methylides, a choice which clearly is avoidable and was not reasonable for synthetic purposes when made. Methyltriphenylphosphonium bromide, when treated with sodium ethoxide in ethanol solvent and benzaldehyde, afforded only an 11% yield of the expected styrene, with the major product being an adduct phosphine oxide (Eq. 8.29).[199] Later, Allen



(8.29)

et al.[200] found that the same conditions with methylides carrying bulky groups on phosphorus led to formation of vinylphosphine oxides rather than the expected alkenes. Avoidance of oxygenated bases probably would have resulted in effective Wittig reactions in both cases.

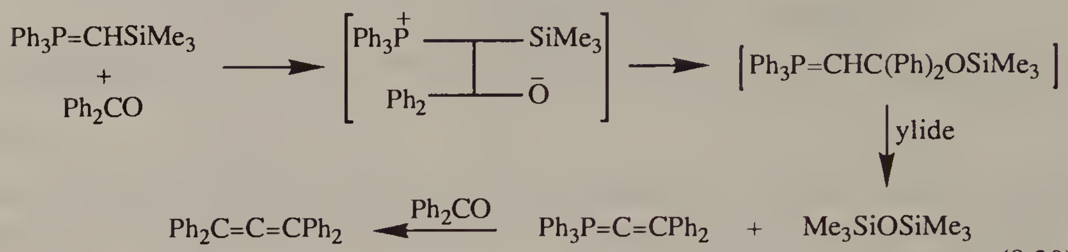
*8.1.7.1* ***Problems with Carbonyl Reactants.*** Side reactions of the carbonyl reactant triggered by the ylide occasionally have been observed. Wittig et al.[201] (with cyclopentanone) and Witschard and Griffin[202] (with 1-tetralone) found that the ylides were sufficiently basic to catalyze aldol condensations, and this tendency was enhanced with stronger conditions.[27] The migration of the double bond in cholest-5-en-3-one during reaction with the methylide, resulting in the conjugated methylenecholest-4-ene, also was effected by the ylide.[203] Reaction with the methylide also served to open the cyclobutane-1,3-dione ring, rather than form a 1-methylene-3-cyclobutanone.[204] With some ylides enolizability of the carbonyl reactant inhibited the Wittig reaction.[205]

Epimerization of adjacent assymetric centers by ylides has been a problem in only a few instances. Three groups reported the conversion of *cis*-1-decalone carbon skeletons to *trans*-1-methylenedecalin systems using methylenetriphenylphosphorane.[206] However, Corey et al.,[207] in the synthesis of caryophyllene, and Kende et al.,[69] in the recent synthesis of gelsedine, both effected Wittig reactions without epimerizing especially sensitive adjacent carbons.

Steric hindrance in some ketones,[208] especially bicyclic ketones such as fenchone[209] and admantanone,[152] has been noted. However, the use of (a) more reactive ylides such as the ylide-anions[184, 128] (see Section 8.1.6), (b) high-temperature conditions (see Section 8.1.5.6), or (c) high-pressure conditions (see Section 8.1.5.7) has facilitated such reactions. Cyclopropanone was simply too unstable to survive usual Wittig reaction conditions, but its ethyl hemiketal had limited replacement use.[205]

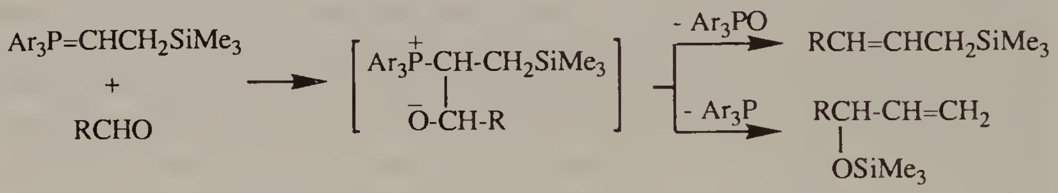
*8.1.7.2* ***Problems with Ylide Reactants.*** Few problems have been created by the ylide reactant itself in a Wittig reaction, although there are limitations regarding the preparation and stability of some ylides (see Chapters 4 and 5, respectively).

Ylides with an $\alpha$-trimethylsilyl group are unpredictable. Triphenylphosphoniumtrimethylsilylmethylide reacted normally with benzaldehyde to afford $\beta$-trimethylsilylstyrene,[210] but a similar reaction with benzophenone[211, 212] and acetone[212] proceeded abnormally. Benzophenone afforded low yields of tetraphenylallene as the major product, with silyl group migration from carbon to oxygen and formation of hexamethyldisiloxane being proposed as driving forces (Eq. 8.30).



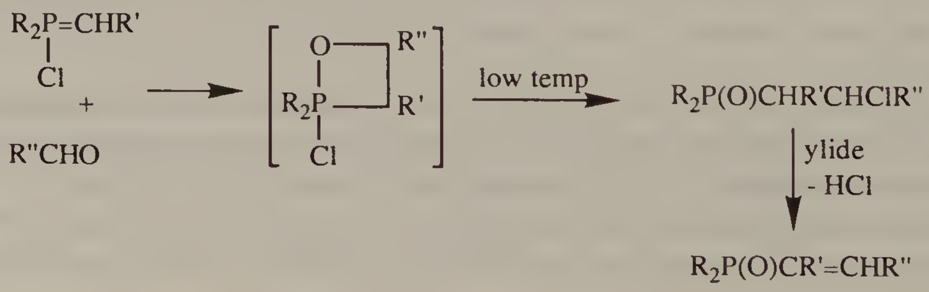
(8.30)

Abnormal Wittig reactions recently have been discovered when using $\beta$-trimethylsilyl ylides, again the result of oxyanion attack at silicon rather than at phosphorus, as required for the Wittig reaction. Reaction of triphenylphosphonium-$\beta$-trimethylsilylethylide with aldehydes produced a mixture of the expected allylic silane and a vinylsiloxane with the latter usually dominating, especially if the aldehyde was $\alpha$-substituted (Eq. 8.31).[213,214] When the ylide was $\alpha$-substituted almost no allylsilane was obtained and the siloxane was obtained mainly in the *E*-configuration. However, excellent yields of the *Z*-allylsilane (as expected for a nonstabilized ylide in the Wittig reaction) could be obtained by using tri-*p*-tolylphosphine to prepare the ylides and low-temperature Wittig reaction conditions.[215]



(8.31)

P-Chlorophosphonium ylides were found to react in situ with aldehydes and ketones to produce phosphinoxy derivatives of the expected alkenes or precursors thereof, both in good yield. Thus with one equivalent of ylide at low temperature the $\beta$-chlorophosphine oxide, resulting from Wittig adduct formation followed by chlorine migration, resulted and could be isolated.[216] With two equivalents of ylide and at a higher temperature dehydrohalogenation ensued, resulting in the phosphinoxyalkene (Eq. 8.32).[217] More recently a P-fluoro ylide has been found to produce some normal Wittig reaction product as well.[218,219]



(8.32)

## 8.2 APPLICATIONS OF THE WITTIG REACTION

This section provides examples of a variety of organic syntheses that have employed Wittig reactions as key steps. The treatment is not encyclopedic, but is exemplary both as to examples and references cited, and includes reference to available compendia.

Wittig reactions normally are conducted with aldehydes or ketones to produce alkenes, but the fact that the carbonyl group is found also in derivatives of carboxylic acids raises the possibility of Wittig reactions at those sites. The reader is referred to Sections 6.5 and 8.2.2.7, and to Murphy and Brennan's recent review,[220] for detailed discussions of the reactions of ylides with such derivatives in which there is a possibility of a Wittig reaction at the carbonyl group or an acylation of the ylide, the initial step being nucleophilic attack of the ylide at the carbonyl carbon in both instances. In this section are described only Wittig reactions using aldehydes and ketones.

Prior to discussing the synthesis of individual classes of compounds, it should be pointed out that the Wittig reaction has been used for general homologation purposes. One-carbon homologation has been achieved by reaction of the methoxymethylide with a carbonyl compound, followed by hydrolysis of the enol ether (Eq. 8.33).[71,201,221,221a] Two-carbon homologations have been effected by using (1) the formylmethylide as its acetal to produce excellent yields of the unsaturated homolog with high *Z*-stereoselectivity (Eq. 8.34),[222] (2) an ester ylide which produced a variable mixture of *Z*- and *E*-unsaturated esters (Eq. 8.35),[223] (3) a thiazolylmethylide as a surrogate for the formylmethylide,[224] and (4) a hydrazonyl derivative of the formylmethylide.[225] Three-carbon homologations have been effected by the methoxyallylide, which produced good yields of the *E*-unsaturated aldehyde (Eq. 8.36).[226]

$$\mathrm{R'R''C{=}O} \xrightarrow[\mathrm{-\ Ph_3PO}]{\mathrm{Ph_3P{=}CHOMe}} \mathrm{R'R''C{=}CHOMe} \xrightarrow{\mathrm{H^+}} \mathrm{R'R''CH\text{-}CHO} \qquad (8.33)$$

$$\mathrm{RCHO} \xrightarrow[\mathrm{-\ Ph_3PO}]{\mathrm{Ph_3P{=}CHCH(OEt)_2}} \mathrm{RCH{=}CHCH(OEt)_2} \xrightarrow{\mathrm{H^+}} \mathrm{RCH{=}CHCHO} \qquad (8.34)$$

$$\mathrm{RCHO} \xrightarrow[\mathrm{-\ Ph_3PO}]{\mathrm{Ph_3P{=}CHCOOMe}} \mathrm{RCH{=}CHCOOMe} \qquad (8.35)$$

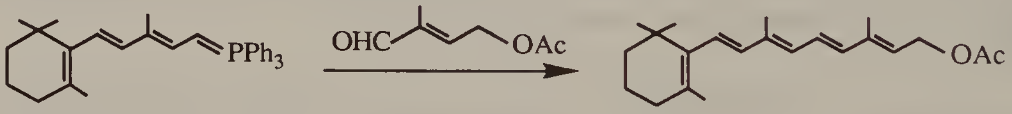
$$\begin{array}{l}\mathrm{R'R''C{=}O}\\ \quad +\\ \mathrm{Ph_3P{=}CH\text{-}CH{=}CHOMe}\end{array} \xrightarrow{\mathrm{-\ Ph_3PO}} \mathrm{R'R''C{=}CH\text{-}CH{=}CHOMe} \xrightarrow{\mathrm{H^+}} \mathrm{R'R''CH\text{-}CH{=}CH\text{-}CHO} \qquad (8.36)$$

All possible combinations of substituted alkenes are now accessible via the Wittig reactions and an example of each follows. 1,1-Disubstituted alkenes were among the earliest available, such as the reaction of benzophenone with a methylide to produce 1,1-diphenylethylene[4] and the more recent formation of methyleneadamantane.[152] 1,2-Disubstituted alkenes also have long been prepared by the Wittig reaction, such as the series of cinnamates from benzaldehyde and carboethoxymethylenetriphenylphosphorane.[22] Trisubstituted alkenes have been readily available from alkylides and aldehydes[85] or ketones[102] and, more recently, from application of the SCOOPY modification (see Section 8.1.6.2). Finally, although more difficult to obtain in some cases, 1,1,2,2-tetrasubstituted alkenes, from the reaction of disubstituted ylides with ketones, also are available using the Wittig reaction.[117, 153, 176, 227, 228]

As indicated throughout this chapter, the presence of other functional groups on the carbonyl reactant seldom precludes a successful Wittig reaction (see Section 8.1.4). Advantage has been taken of reactivity differences (e.g., ester versus carbonyl, ketone versus aldehyde) and the ability to neutralize proton sites with excess base. The presence even of a hydroperoxy group recently has been tolerated![229]

### 8.2.1 Syntheses Employing the Wittig Reaction

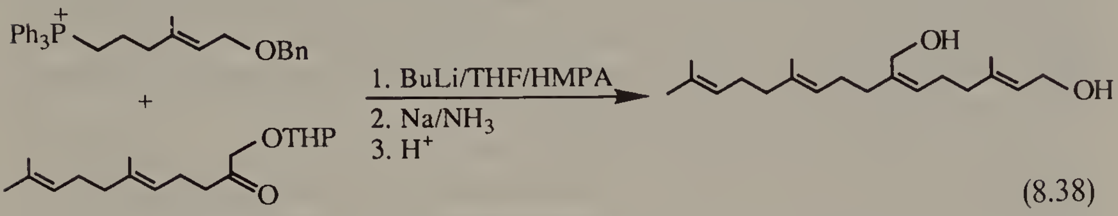
*8.2.1.1* ***Carotenoids.*** The first commercial application of the Wittig reaction seems to have been the synthesis of vitamin A by the BASF group. The readily available $\beta$-ionone was converted to an allylide which was condensed with 2-methyl-4-acetoxy-2-butenal to afford a 70:30 mixture of the *trans*- and *cis*-vitamin A acetates with the cis form being converted into the trans form in a subsequent isomerization step (Eq. 8.37).[230] Recent attempts to prepare cis isomers of vitamin A have been even more nonstereoselective.[231]



(8.37)

Several different $\beta$-carotene syntheses have relied on the Wittig reaction to form the $C_{40}$ molecule. Oxidative dimerization of the phosphonium ylide derived from vitamin A produced $\beta$-carotene.[232] A $C_{20} + C_{20}$ coupling was effected by Wittig reaction of an ylide and an aldehyde, both of which were readily derived from vitamin A. Additional coupling sequences involving Wittig reactions of diylides or dialdehydes (e.g., 2 $C_{10} + C_{20}$; 2 $C_{15} + C_{10}$) were discovered. Full descriptions are available in reviews by Gosney,[9] Bestmann and Vostrowsky,[29] or Pommer,[230] the latter detailing the flexible "building block" approach which has been applied to many carotenoids.

*8.2.1.2* ***Terpenoids.*** The first synthesis of a terpene using the Wittig reaction was that of squalene with two syntheses being reported the same year.[233, 234] The better one, affording squalene in 35% yield, involved reacting the bis-ylide from 1,4-di(triphenylphosphonio)butane with two equivalents of geranyl acetone. Corey and Yamamoto[198] effected an elegant synthesis of the sesquiterpene farnesol using the SCOOPY modification (Eq. 8.28). Methylenetriphenylphosphorane has been effective in numerous terpene syntheses for introduction of the frequently appearing methylene group, for example, that of ε-cadinene.[206b] Inoue et al.[235] prepared the diterpene diol plaunotol in excellent yield by a stereoselective reaction (Z-isomer only!) between a β-benzyloxy ketone and an alkylide, followed by removal of the protecting groups (Eq. 8.38).



(8.38)

Many examples of the use of the Wittig reaction in terpene syntheses are described by Gosney[9] and in the lengthy review by Bestmann and Vostrowsky.[29]

*8.2.1.3* ***Steroids.*** The Wittig reaction has been employed extensively in the synthesis of polyenes used as precursors in the cyclization processes leading to steroids.[9] Particular use has been made of ylides in the elaboration of steroidal side chains through reaction with carbonyl groups at C-3,[125, 166] C-6,[125] C-17,[125, 179, 236] and on the side chain,[109] some of the latter producing Z-stereochemistry[237] and some producing E-stereochemistry.[130, 238]

*8.2.1.4* ***Fatty Acids.*** The Wittig reaction has been widely employed for the synthesis of mono- and polyunsaturated fatty acids, and stereoselective techniques have permitted obtaining very high (>95%) proportions of the naturally occurring Z-isomers. Readers are referred to the early review by Bergelson and Shemyakin[239] and to the more recent reviews by Gosney[9] and Bestmann and Vostrovsky[29] for details and many examples of this application.

Bergelson et al.[239] reacted many ω-formylesters with alkylides to obtain Z-alkenoates, and Bestmann et al.[240] improved the Z proportion with a large series of 9-alkenoates. E,Z-dienoates were prepared by reaction of ω-formylesters first with formylmethylenetriphenylphosphorane (to form the E bond) and then with the appropriate triphenylphosphoniumalkylide to form the Z bond (Eq. 8.39).[241] "Skipped" Z,Z-dienoates (i.e., n,n + 3-dienoates) have been a more

$$\mathrm{OHC(CH_2)nCOOMe} \;+\; \mathrm{Ph_3P{=}CHCHO} \longrightarrow \underset{(E)}{\mathrm{OHCCH{=}CH(CH_2)_nCOOMe}}$$

$$\Big\downarrow\, \mathrm{Ph_3P{=}CH(CH_2)_mCH_3}$$

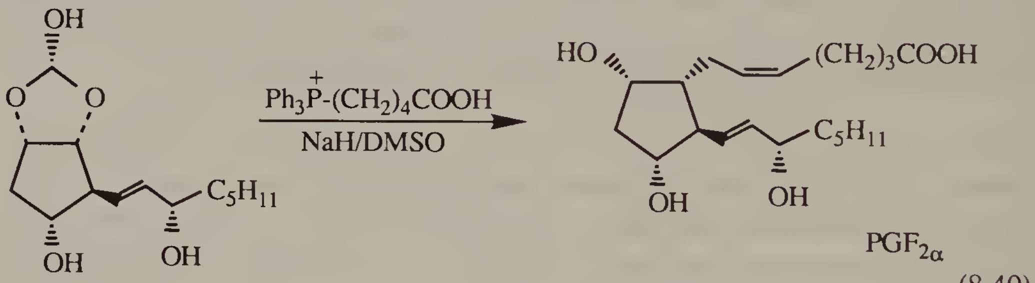
$$\mathrm{CH_3(CH_2)_m}\underset{(Z)}{\mathrm{CH{=}CH}}\mathrm{\text{-}}\underset{(E)}{\mathrm{CH{=}CH}}\mathrm{(CH_2)_nCOOMe}$$

(8.39)

difficult synthesis challenge because use of a $\gamma,\delta$-unsaturated ylide leads to byproducts resulting from prior isomerization of the ylide to the $\beta,\gamma$-unsaturated isomer. Viala et al.[242] recently solved this problem by using a masked $\beta$-formylethylide to form the first (*Z*)-alkene bond.

*8.2.1.5* ***Prostaglandins.*** From the first published synthesis[243] of this important class of compounds in 1967 to Corey's 1969 generic approach,[100] synthesis of prostaglandins A, E, and F have relied on the Wittig reaction for introduction of alkene groups. The reviews by Gosney[9] and Bestmann and Vostrowsky[29] report many examples of this application and reviews of prostaglandin chemistry should be consulted for even more details.

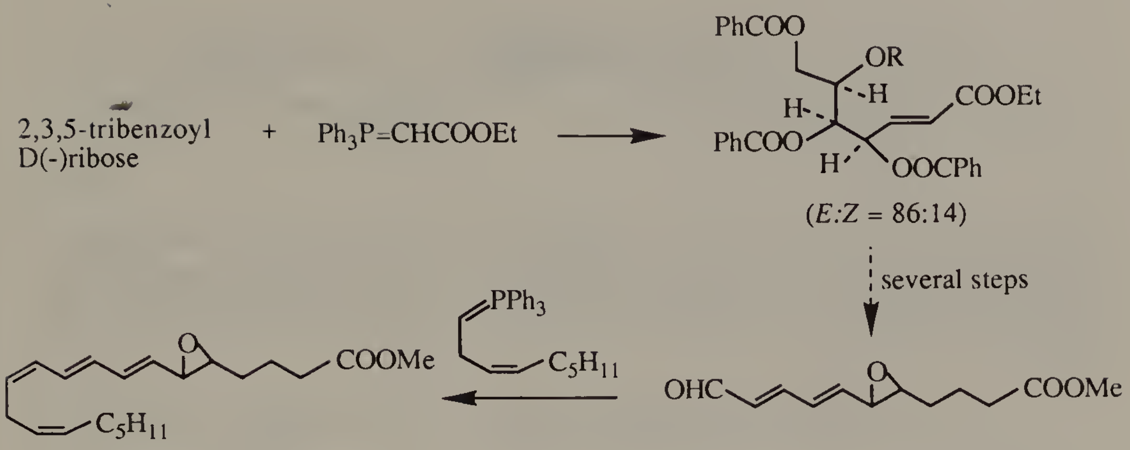
In the original Corey synthesis,[100] and in most new modifications thereof,[244] the upper ($\alpha$) side chain with its *Z* double bond was introduced by reaction of the ylide from $\omega$-carboxybutyltriphenylphosphonium bromide with a lactol (Eq. 8.40). The double bond in the lower ($\beta$) side chain often has been introduced using a $\beta$-ketophosphonate ylide (Wadsworth–Emmons reaction) because of its usual *E* stereoselectivity, but frequently a stabilized phosphonium ylide such as $Ph_3P{=}CH{-}CO{-}C_5H_{11}$ has been employed to afford the *E* stereochemistry,[119] with the carbonyl group then being reduced to an alcohol. Corey et al.[245] later employed a $\beta$-hydroxyylide to produce the lower chain alkene and the adjacent hydroxyl function in a single step, both with the correct stereochemistry!



(8.40)

*8.2.1.6* ***Leukotrienes.*** Wittig reactions have been prominent in the various syntheses of the biologically important leukotriene family of unsaturated carboxylic acids, and such chemistry has been summarized by Bestmann and Vostrowsky.[29]

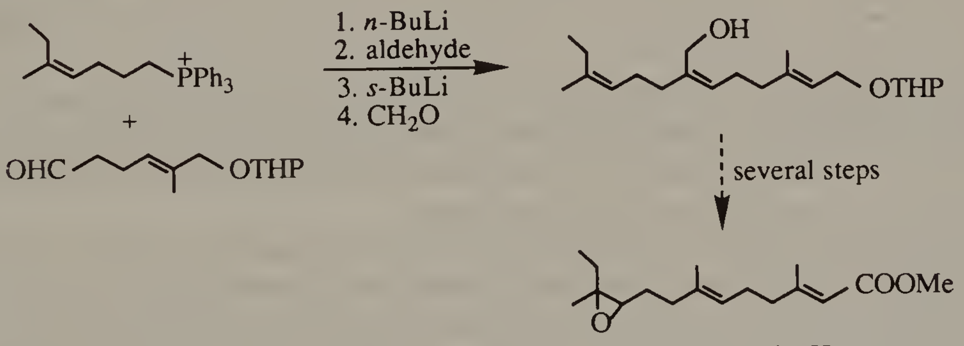
The Gleason synthesis[246] employed three Wittig reactions in the synthesis of $LTA_4$, introducing two *E*-alkene groups and a *Z*-alkene (though the latter with low stereoselectivity). The Corey synthesis[169] from 2,3,5-tribenzoyl-D(−)ribose involved two Wittig reactions to introduce an *E*- and a *Z*-alkene (Eq. 8.41), but later Ernest et al.[120] replaced the four-carbon "Wallenburg extension" for generating the *E*,*E*-dienal group with a third highly stereoselective Wittig reaction using $\gamma$-triphenylphosphoranylcrotonaldehyde. Recent syntheses of $LTB_4$[247] and substituted derivatives[248] have continued to employ Wittig reactions although some stereoselectivities could be better to avoid difficult separations.



LTA$_4$ ester

(8.41)

*8.2.1.7* ***Juvenile Hormones.*** The isolation of these substances from silkworm moths and the hope that they could serve as agricultural chemicals to control moth populations led to numerous syntheses involving Wittig reactions which generally produced poor stereoselectivities in the trisubstituted alkene groups[9, 29] and therefore required complex separations. The Corey synthesis (Eq. 8.42),[249] in contrast, elegantly assembled the carbon skeleton of the juvenile hormones in a single reaction with the correct stereochemistry employing the SCOOPY modification of the Wittig reaction. Modifications of this synthesis provided access to a variety of naturally occurring and synthetic analogs. Other syntheses also employed the Wittig reaction to assemble somewhat different fragments.[250]



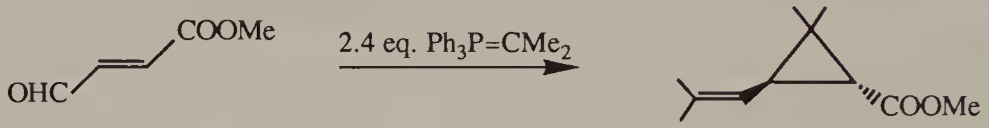
*dl*-$C_{17}$ Juvenile Hormone

(8.42)

*8.2.1.8* ***Chrysanthemum Derivatives.*** Condensation of the α-methyl ester ylide with a formylcyclopropane derivative afforded only the *E*-alkene diester (Eq. 8.43)[251] which could be hydrolyzed to pyrethric acid, whereas the phosphono ylide route was less stereoselective.[252] Methyl *trans*-chrysanthemate was prepared in a single step with the correct *E*-stereochemistry via reaction of

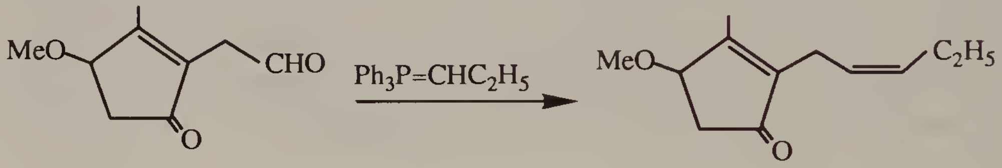
(8.43)

methyl $\beta$-formylacrylate with 2.4 equivalents of isopropylidenetriphenylphosphorane, the result of a Wittig reaction with the formyl group followed by conjugate addition of a second equivalent of ylide to the dienoate ester (Eq. 8.44).[75]



(8.44)

The rethrolones, alchoholic components of the naturally occurring pyrethrin ester mixtures, also have been prepared by Wittig reactions. For example, a multifunctional intermediate was converted into $O$-methyljasmolone with dominant ($Z$:$E$ = 88 : 12) desired stereochemistry, and without competing reactions at the alkene or ketone groups, using the propylide (Eq. 8.45).[118] Gosney[9] has reviewed this chemistry.



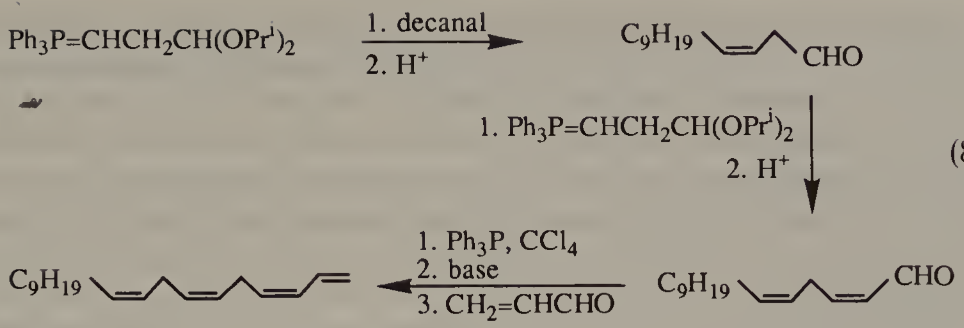
($Z$:$E$ = 88:12)

(8.45)

*8.2.1.9* ***Pheromones.*** The Wittig reaction has been a significant component of the synthetic approaches which have made these important substances available in reasonable quantities. Gosney[9] and Bestmann and Vostrowsky[29] both have published extensive reviews of such syntheses.

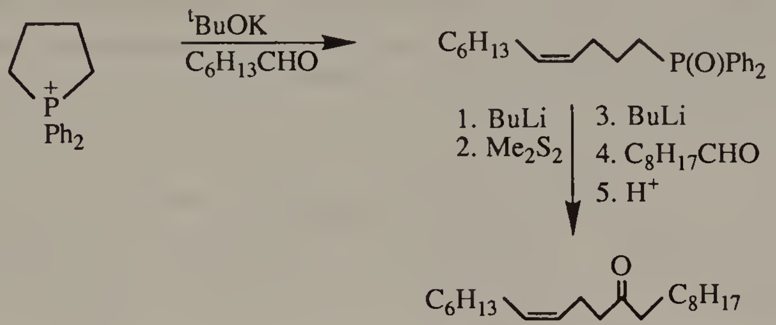
The sex pheromone of the female gypsy moth, a serious pest of the northern hemispheres, was synthesized by $Z$-stereoselective reaction of undecanal with an alkylide followed by stereospecific epoxidation (Eq. 8.46).[253] An elegant synthesis of 1,3,6,9-nonadecatetraene, the sex attractant of the winter moth incorporating a "skipped triene" system, involved double use of a masked $\gamma$-formylethylide and produced excellent $Z$-stereoselectivity (Eq. 8.47).[247] Use of a cyclic phosphonium salt as an ylide precursor permitted the execution of two

(8.46)



(8.47)

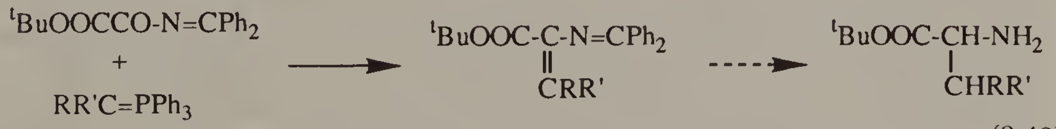
Wittig reactions (a "tandem Wittig reaction") in the synthesis of the sex pheromone of the Japanese peach fruit moth (Eq. 8.48).[254]



(8.48)

*8.2.1.10* ***Fragrances.*** Many fragrances are aliphatic long-chain 1-functionalized-2-alkenes with *E* stereochemistry. Thus, synthesis is facile involving stabilized ylides. For those fragrances with *Z*-alkene groups further along the chain, once again the use of nonstabilized ylides has proven effective for synthesis. For example, synthesis of the pear ester, ethyl 2*E*,4*Z*-decadienoate, involved reaction of 2,2-diethoxyethylidenetriphenylphosphorane with hexanal, removal of the ethoxy protecting groups, and reaction of the resulting 2*Z*-octenal with carbethoxymethylidenetriphenylphosphorane to introduce the 2*E*-double bond.[255] Bestmann and Vostrowsky have reviewed these syntheses.[29]

*8.2.1.11* ***Amino Acids, Carbohydrates, Nucleotides.*** The Wittig reaction has been used to prepare unique α-amino acids. Reaction of phosphonium ylides with readily obtainable oxalamides produced azadienes which were reduced to amino acids. By this approach, any potential side chain which can be assembled into an ylide form can be coupled to a glycine synthon (Eq. 8.49).[256, 257] Serine esters have been converted into higher amino acids using the Wittig reaction while maintaining optical purity.[258]

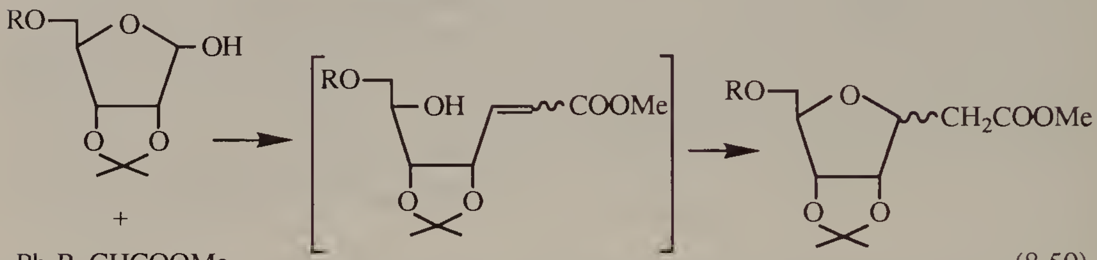


$$\begin{array}{c} {}^tBuOOCCO\text{-}N{=}CPh_2 \\ + \\ RR'C{=}PPh_3 \end{array} \longrightarrow \begin{array}{c} {}^tBuOOC\text{-}C\text{-}N{=}CPh_2 \\ \| \\ CRR' \end{array} \dashrightarrow \begin{array}{c} {}^tBuOOC\text{-}CH\text{-}NH_2 \\ | \\ CHRR' \end{array}$$

(8.49)

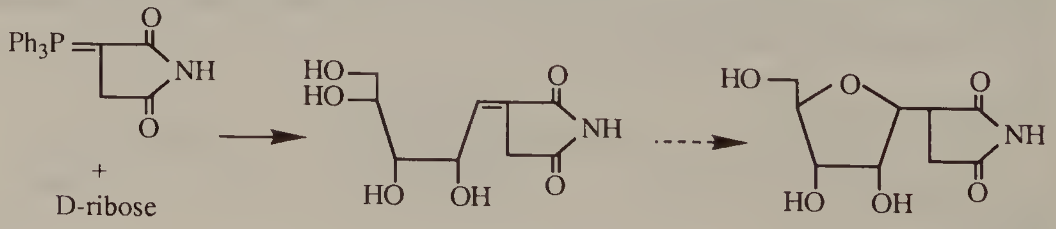
Exploration of the biological properties of nucleotide analogs requires their synthesis, and the Wittig reaction has been used to alter the ribose component thereof. A protected adenosine-5′-aldehyde reacted with carbobenzyloxymethylenetriphenylphosphorane to produce eventually the *E*-two carbon homolog, called adenosine acetic acid, which could be incorporated into several oligonucleotides.[23] Methylenation of analogous aldehydes[259] and ketoribonucleosides[260] has been effected by $CH_2{=}PPh_3$. The tosylmethylene could be added similarly.[259]

Zhdanov et al.[261] were among the early workers to explore the reaction of phosphonium ylides with carbohydrates and found that glucose pentaacetate would react with stabilized ylides to produce the expected alkene, apparently in the *E* configuration.[262] Moffatt and co-workers[263] reacted 2,3-isopropylidene-5-tritylribofuranose with carbomethoxymethylenetriphenylphosphorane in acetonitrile but could not isolate the expected alkene, obtaining instead both anomeric recyclized *C*-glycosides (Eq. 8.50). Recently Herrera et al.[223] duplicated the reaction but in different solvents and were able to isolate the unsaturated glycosides presumed to be intermediates by Moffatt, mainly the *Z*-isomer in methylene chloride and mainly the *E*-isomer in hexane. Use of 2,3,5,6-diisopropylideneribofuranose produced only the *E*-isomer in benzene or methylene chloride. Use of tetrabenzylglucopyranose with the same ester ylide produced another side reaction in that the initially formed alkene suffered an elimination reaction to produce a conjugated ester–diene,[264] although other hexopyranoses did not eliminate. Reitz et al.[265] observed recyclization following the Wittig reaction using cyanomethylenetriphenylphosphorane with 2,3,5-tri-*O*-benzylarabinose, but they separately effected elimination to the dienenitrile using added base.



$Ph_3P{=}CHCOOMe$ (8.50)

Although Harmon et al.[266] reported that ylides would not react directly with unprotected ribose, Barrett et al.[267] succeeded in such a reaction with a stabilized ylide to form only the *E*-alkene, one more step providing a simple synthesis of showdomycin (Eq. 8.51). Giannis et al.[268] recently reported alkene

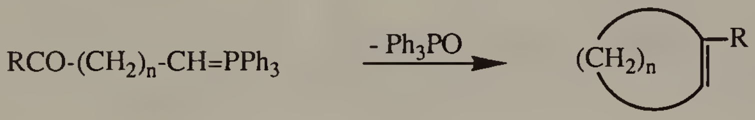


(8.51)

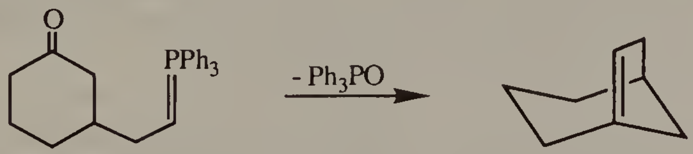
formation from several unprotected carbohydrates, including acetamido derivatives, by reaction with benzylidenetriphenylphosphorane.

*8.2.1.12 Cycloalkenes.* The formation of cycloalkenes using the Wittig reaction was discovered early in the evolution of the reaction and continues to be one of its most important applications. Five fundamental approaches have been used: (1) the intramolecular reaction of an ylide carrying a carbonyl group with appropriate separation between the two functional groups; (2) formation of an adduct between an ylide and another reactant, the product of which then undergoes an intramolecular Wittig reaction as described in (1); (3) formation of an adduct between a $\beta$-ketoylide and another nucleophile, the product of which has an oxido group adjacent to a phosphonium group in a position to eliminate triphenylphosphine oxide and produce an alkene; (4) double condensation between a bis-ylide and a bis-carbonyl reactant; (5) oxidation of a bis-ylide. The formation of cycloalkenes by the Wittig reaction has been quite effective, even in forming strained ring systems, because the initial ring closure forms only a C–C single bond, the strain-inducing double bond being formed in a second but exothermic step eliminating triphenylphosphine oxide.

Bieber and Eisman[269] and Griffin and Witschard[270] were the first of many to follow the first approach and close cycloalkene rings using an intramolecular Wittig reaction to form cyclopentenes and cyclohexenes (Eq. 8.52). They[270, 271] were unable to obtain three- or four-membered rings by this process. Cyclododec-2-enone was produced from the appropriate $\beta$-keto-$\omega$-formyl ylide.[272] Halmos et al.[273] recently used the same approach to prepare a series of unsaturated cyclic ethers. Johnson et al.[34] cyclized one enatiomer of an $\varepsilon$-keto ylide to a cyclohexene in 92% ee. Becker[274] has reviewed this type of cyclization, including its use to form annulated bridgehead cycloalkenes from cycloalkanones with ylide side chains attached at the $\alpha$-position. Cyclization of cycloalkanones with the ylide tethered to the $\beta$-position afforded trappable quantities of strained bridgehead bicycloalkenes (Eq. 8.53).[275] Formation of the five-membered ring of the penemic acid skeleton also has been effected by a Wittig reaction, but using the carbonyl group of a thiolester.[276] Bestmann and Schobert[277] prepared the $C_{14}$ cyclic dilactone precursor to grahamimycin through a Wittig reaction cyclization and others[278] developed a generic cyclization for $C_{14}$ to $C_{16}$ dilactones starting with readily available diols. Yvergnaux

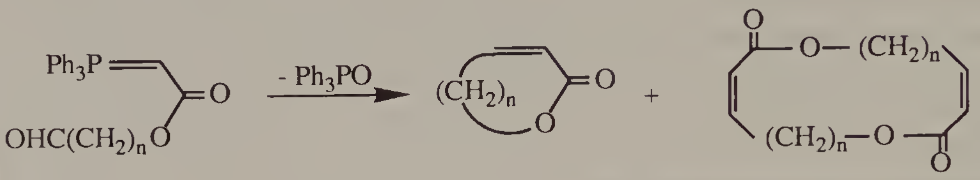


(8.52)



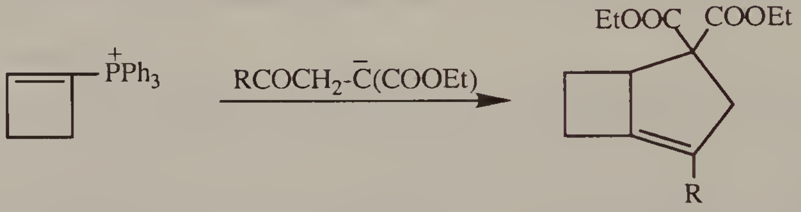
(8.53)

et al.[279] cyclized ω-formyl ester ylides and obtained good yields of the *E*-lactones when n = 3, and of the *Z*-lactones when n = 8 or 9, but for n = 4–7 the major products were the intermolecular dimers and higher oligomers (Eq. 8.54). This method has been used to synthesize patulolides A and C.

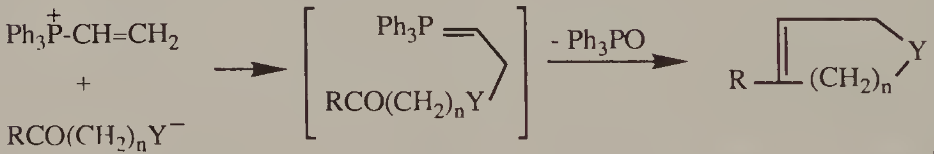


(8.54)

The second approach, formation of an adduct which produces an ylide and/or carbonyl group which are in proximity for a Wittig reaction, also has become common.[274] Schweizer et al.[280] discovered and developed the addition of anions to vinylphosphonium salts to form ylides which then cyclized to alkenes, a technique recently applied by Okada et al.[281] to prepare [2.3.0]-bicycloheptenes from 1-triphenylphosphoniocyclobutene (Eq. 8.55). Zbiral[282] has reviewed the application of this approach using heteroatom anions to the synthesis of heterocyclic compounds, including pyrrolizines, dihydrofurans, chromenes, and dihydroquinolines (Eq. 8.56) and Becker[274] has reviewed the use of carbanions



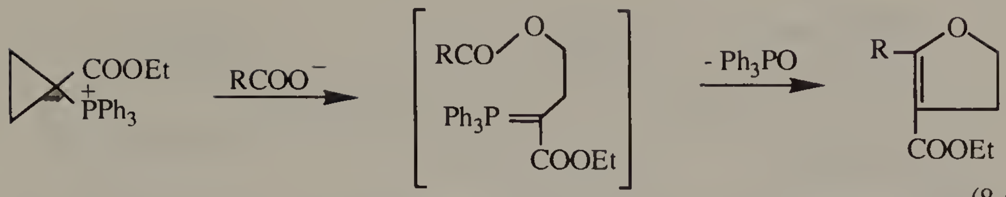
(8.55)



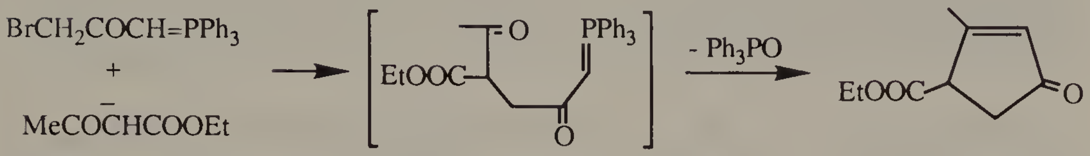
(8.56)

in a similar manner. The use of such carbanions with butadienylphosphonium salts, a vinylog of the vinylphosphonium salts, provided a means for incorporating four carbons from the ylide into a cycloalkene, the first step being addition of a carbanion to the terminus of the diene system.[283]

Cyclopropylphosphonium salts similarly serve as a means to incorporate three carbons from an ylide into a cycloalkene. For example, Dauben and Hart[284] opened a three-membered ring with a carboxylate anion, the resulting ylide then cyclizing with ejection of triphenylphosphine oxide (Eq. 8.57). Altenbach[285] used a β-keto-γ-bromoylide as an alternate source of three carbons for incorporation into a cyclopentenone system (Eq. 8.58). Bestmann's additions of β- and γ-carboxyketones to phosphacumulenes such as $Ph_3P=C=C=O$ and $Ph_3P=C=C=NPh$ similarly afforded cyclopentenones and cyclohexenones.[286]

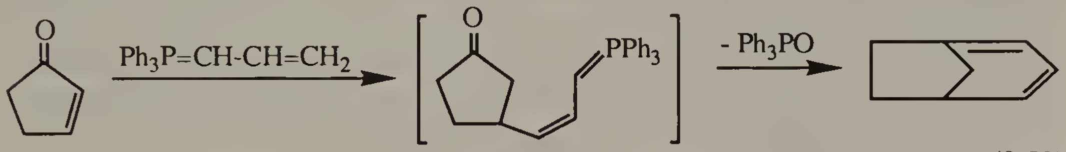


(8.57)



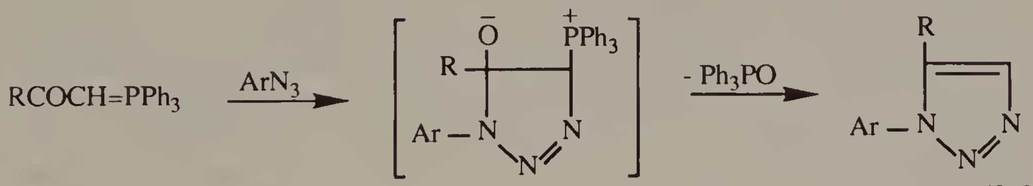
(8.58)

The addition of allylides, using the γ-position as the nucleophile, to the β-position of α,β-unsaturated carbonyls has been exploited to produce cyclic dienes.[274] Dauben and Ipaktschi[287] applied this approach to the synthesis of several annulated bridgehead dienes, including the highly strained bicyclo-[3.2.1]octa-1,3-diene which was isolated as its dimer (Eq. 8.59). The analogous reaction, but applied to conjugated alkynones, afforded substituted benzenes.[288] Similarly, reaction of allylides with α-bromoketones recently has afforded cyclopentenones.[289]



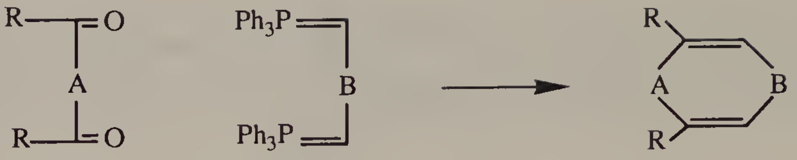
(8.59)

The third approach to cycloalkene synthesis using the Wittig reaction involves the addition of a nucleophile, usually a 1,3-dipolar compound, to the carbonyl group of a β-ketoylide, with the resulting oxidoylide then eliminating triphenylphosphine oxide as in the second step of a Wittig reaction. For example, reaction of aryl azides with β-keto ylide afforded 1,5-disubstituted triazoles (Eq. 8.60).[290] Zbiral[282] has reviewed these reactions.

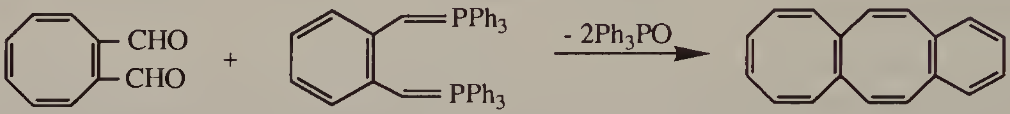


(8.60)

The fourth approach to the use of Wittig reactions to form cycloalkenes has a lengthy history, that being the double reaction of a bis-ylide with a bis-carbonyl compound to form a cyclodiene. This reaction, which has been reviewed in detail by Vollhardt[291] and by Becker,[274] has been applied to the synthesis of an amazing variety of cyclic compounds, ranging from 5 to at least 36 members, and including both carbocycles and heterocycles (Eq. 8.61)! Wittig et al.[292] were


(8.61)

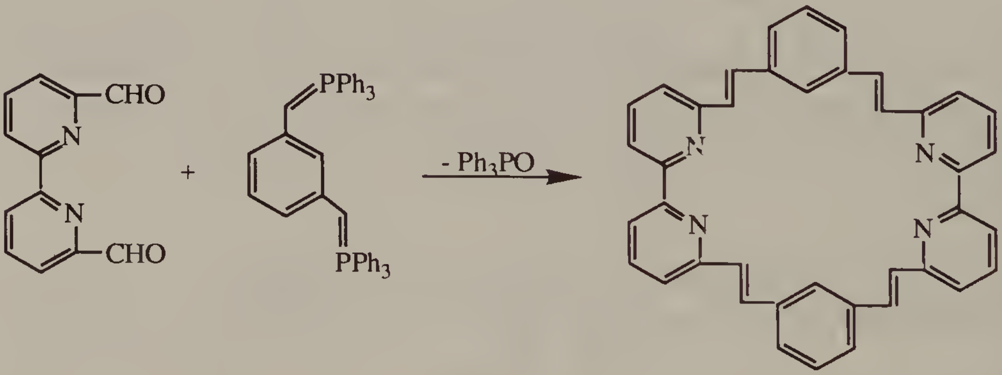
the first to employ the reaction using *o*-phthalaldehyde with the ylide from 1,3-bis(triphenylphosphonio)propane to produce 3,4-benzocycloheptene. Breslow et al.[293] obtained the first example of an octalene using this approach (Eq. 8.62).



(8.62)

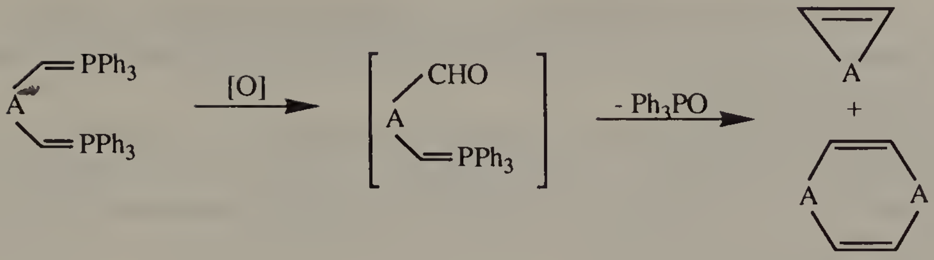
Tetrabenzo[16]-annulene was prepared in 1962 by a lengthy route involving the bis-ylide + bis-aldehyde reaction in the final step,[294] but tetrabenzo[12]-annulene was prepared from 2,2′-diformylbiphenyl and 2,2′-bis(methylidene-triphenyl-phosphoranyl)biphenyl in a single step in 1972.[295] The list of applicable ylides is almost endless, except that the 1,2- and 1,4-bis-ylides are only difficultly available because of competing elimination reactions (see Section 4.1.2.3).

Cyclophanes also have been prepared using this approach.[274] Terephthalaldehyde reacted with the ylide from bis-*p*-xylylidenetriphenylphosphorane to form the paracyclophane in a single step,[296] and Vogtle et al.[25] recently prepared bipyridinophane by a similar route (Eq. 8.63).



(8.63)

The final approach to formation of cycloalkenes from ylides relies on the oxidation of ylides, a process discussed in Section 5.2. Under appropriate conditions, including limiting the amount of oxidant, one ylide group is converted to a carbonyl compound which then undergoes a Witting reaction with the other ylide, but as the prospective ring size increases, competition from intermolecular reactions prevails (Eq. 8.64).



(8.64)

## 8.2.2 Miscellaneous Wittig Reactions

*8.2.2.1* ***Isotopic Labelling.*** The regiospecificity and stereospecificity of the Wittig reaction makes it ideally suited for the placement of isotopic labels. Treatment of a benzylphosphonium salt with tritiated ethanol and sodium ethoxide produced the α-tritiobenzylide which reacted with benzaldehyde to afford monotritiated stilbene.[297] Corey and Yamamoto[195] applied the SCOOPY reaction (see Section 8.1.6.2) of a phosphonium ethylide to benzaldehyde and deuterobenzaldehyde in both possible sequences and obtained both possible deuterated allylic alcohols. They also used trideuteriomethyl iodide as the electrophile in a similar reaction with heptanal to produce $C_6H_{13}CH{=}C(CH_3)\ (CD_3)$. Recently Goerger and Hudson[298] used the Wittig reaction to prepare all-*trans*-parinaric ester with the four alkene groups fully deuterated (Eq. 8.65).

$$\begin{array}{c}C_2H_5\text{-}(CD{=}CD)_2\text{-}CD_2\text{-}\overset{+}{P}Ph_3\\ + \\ ODC\text{-}CD{=}CD\text{-}(CH_2)_7\text{-}COOMe\end{array} \xrightarrow[\text{THF}]{\text{BuLi}} C_2H_5\text{-}(CD{=}CD)_4\text{-}(CH_2)_7\text{-}COOMe \qquad (8.65)$$

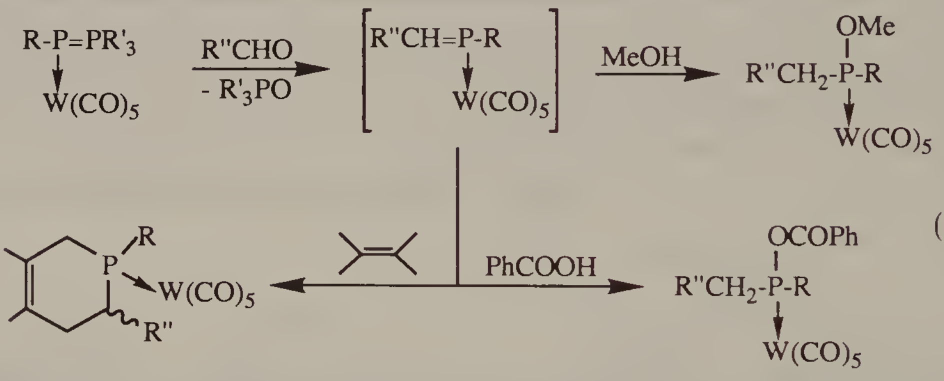
*8.2.2.2* ***Polyenes.*** Cumulenes have been prepared using the Wittig reaction from its earliest days when Wittig and Haag[299] prepared an allene from diphenylketene and triphenylphosphonium isopropylide. Ratts and Partos[300] reacted $Ph_3P{=}C{=}C{=}CPh_2$ with aldehydes to obtain butatrienes and with diphenylketene to produce tetraphenylpentatetraene. Van Woerden et al.[301] did not obtain a pentatetraene when they reacted ylides with carbon suboxide, but Nader and Brecht[302] were successful 17 years later in obtaining symmetrical pentatetraenes. Ylides were reported to react with allenic acid chlorides in the presence of triethylamine to produce pentatetraene diesters,[303] probably by initial dehydrohalogenation of the acid chloride to a ketene,[304] rather than by Wittig reaction with the acid chloride carbonyl group as proposed.

Interest in preparing conjugated polyenes via the Wittig reaction arose quite early, with Campbell and McDonald[305] preparing $Ph{-}(CH{=}CH)_2{-}Ph$ and $Ph{-}(CH{=}CH)_2{-}C_6H_4\ (p){-}(CH{=}CH)_2{-}Ph$ and with Drefahl and Plottner[306] preparing $Ph{-}(CH{=}CH)_6{-}Ph$, the latter in a laborious stepwise manner starting with *p*-chloromethylbenzaldehyde and benzylidenetriphenylphosphorane. Later, Manecke and Luttke[307] prepared a similar series of oligomers containing all trans double bonds.

With the current interest in polyacetylene derivatives [i.e., $-(CH{=}CH)_n-$] as electroactive polymers which show nonlinear optical activity, Spangler and Rathunde[308] have employed the Wittig reaction of polyenealdehydes with polyene bis-ylides to obtain air-sensitive long chain polyenes (n = 7–10) with an all-*E* configuration (Eq. 8.66).

$$Bu_3P{=}CH(CH{=}CH)_yCH{=}PBu_3 \xrightarrow[\text{- }Bu_3PO]{2\ R(CH{=}CH)_xCHO} \underset{(n = 2x + y+2)}{R(CH{=}CH)_nR} \tag{8.66}$$

***8.2.2.3 Phospha-Wittig Reactions.*** Phosphaylides ($R'P{=}PR_3$) have been observed but not isolated.[309–313] However, Le Floch and Mathey recently have prepared and isolated phosphaylides ($RP{=}PPh_3$) as complexes with $W(CO)_5$,[314, 315] $Fe(CO)_4$,[316] or $Cr(CO)_5$,[316] and among the properties of the more reactive examples was their ability to effect a phospha-Wittig reaction, sluggishly with ketones, but easily with aldehydes (Eq. 8.67). The complexed phosphaalkenes have not been isolated, but have been trapped for identification. Application of the technique to the preparation of phosphacyclopentene and phosphacyclohexene complexes, through use of δ- and ε-ketophosphaylides, recently has been reported.[317] These authors have reviewed progress in their interesting adaptation of the Wittig reaction to the study of second row alkenes.[318]



(8.67)

***8.2.2.4 Use of Cyclic Phosphonium Ylides.*** The use of an ylide prepared from a cyclic phosphonium salt means the phosphorus atom will be retained in the product for possible future use. Lednicer[319] was the first to take advantage of this approach, but the yields were very low. Application of the approach to the synthesis of gossyplure, the sex pheromone of the bollworm moth, was effective[320] and a similar approach, involving a Wittig reaction followed by a Wittig–Horner reaction, gave good yields of other sex pheromones

(Eq. 8.48).[254, 321] Minami and Yamamoto recently have reviewed the use of cyclic phosphonium salts in Wittig reactions.[322]

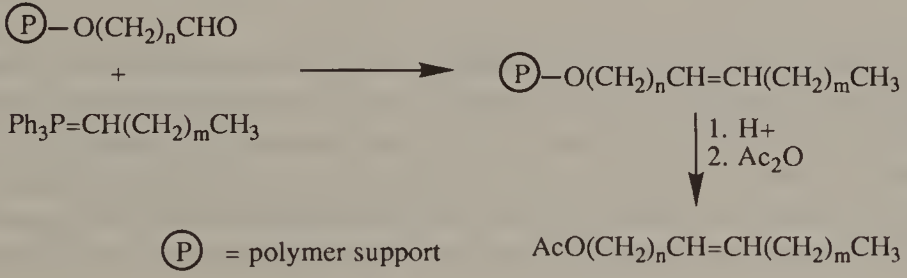
*8.2.2.5* ***Polymer-Based Wittig Reactions.*** Wittig reactions have produced excellent yields when conducted on polymer supports, and Ford[323] has provided an excellent review, including exhaustive tables of results.

Although several approaches have been employed,[323] the best involved brominating a commercially available cross-linked (1–2%) polystyrene resin then displacing the bromine with lithium diphenylphosphide. Alkylation of the resulting diphenylpolystyrylphosphine, generation of the ylides using normal bases, and reaction with a carbonyl compound afforded an alkene in solution and the phosphine oxide as part of the resin, thereby facilitating separations. The phosphine oxide could be reduced to phosphine and recycled.

Three groups pioneered this work in the early 1970s using benzylides,[324–326] allylides,[325] alkylides,[324,325] and the methylide[324] and obtained excellent yields with stereochemical results similar to those obtained under normal conditions. In fact, it was shown that alkylides could be reacted in a *Z*- or *E*-stereoselective manner using the salt-free or Schlosser modifications, respectively.[327] Reactions were successful with both aldehydes and ketones. More recently the methoxymethylide and the carbomethoxymethylide have been similarly employed.[328]

Higher degrees of cross linking of the resin did not lead to better yields of alkene,[329] and there was relatively little variation in stereoselectivity. Phase transfer catalysis has been employed, leading to excellent yields and normal stereoselectivity, but with considerable reduction in the reactivity of some ylides and carbonyl compounds.[330] It is clear that a number of factors affecting the access of the carbonyl compound to the active sites affected the course of the reaction.[323]

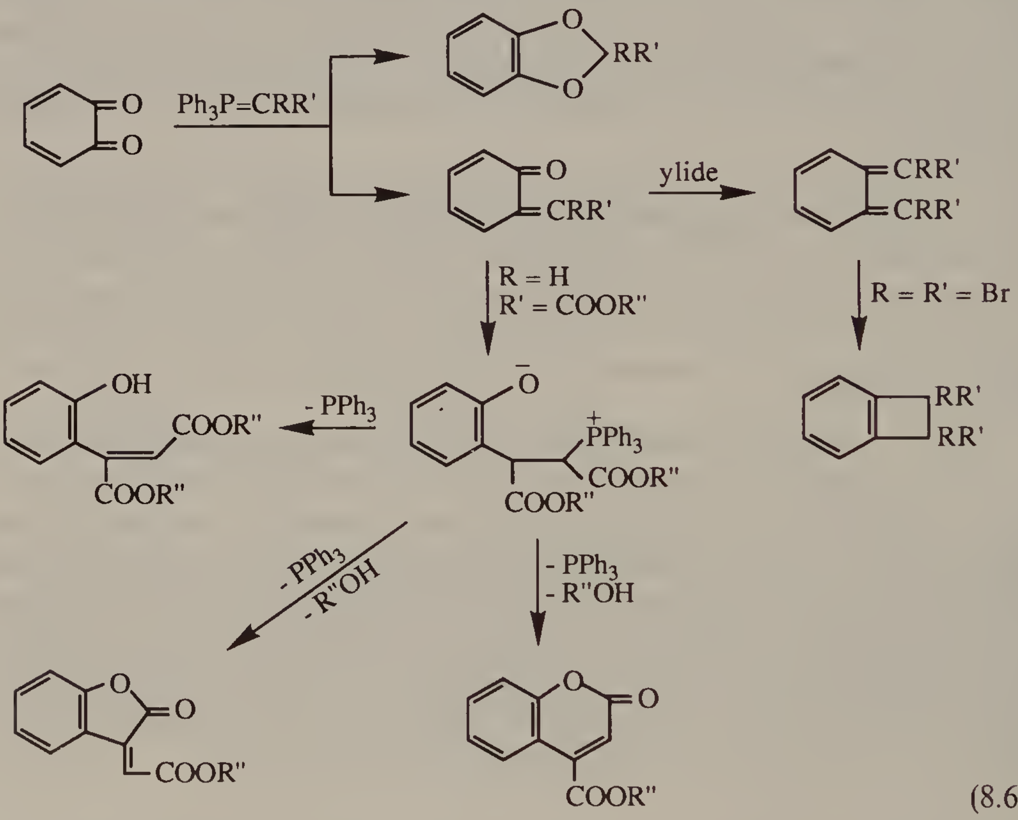
Polymer with chloromethyl groups attached has been converted into a phosphonium group and the ylide therefrom has been reacted with chloroacetaldehyde to produce the $-CH{=}CH-CH_2Cl$ group attached to the resin.[331] Long-chain alken-1-ols, of the type which are sex pheromones of Lepidoptera, have been synthesized on a polymer with the aldehyde group attached to the resin (Eq. 8.68) or with the ylide group attached to the resin, followed by cleaving the product from the resin.[332, 333] The reverse process also was effective with the ylide group on the long chain attached to the resin, and the aldehyde supplied externally. Yields were good and stereoselectivity was high.



(8.68)

*8.2.2.6* ***Reaction with Vicinal Diketones and Quinones.*** The presence of two carbonyl groups adjacent to one another provides some potential for complications in the Wittig reaction. Benzil reacted normally with a benzylide, but only at one carbonyl group,[334] but using a bis-ylide the second ylide group effected a conjugate addition to the monoolefinated product.[335] Acenaphthenedione reacted normally with a bis-ylide to afford the expected diene,[336] its monoxime reacted at both the carbonyl and oxime sites with a bis-ylide,[337] and benzothiophanedione reacted normally with an ester ylide, but only at one carbonyl group.[338] The Garratt group[339] and Cava et al.[340] reacted cyclobutenedione derivatives with several bis-ylides and obtained the expected cyclobutadienes. Cyclobutenedione reacted with the ester ylide to produce mono- or diolefinated product, depending on the amount of reagent used.[341]

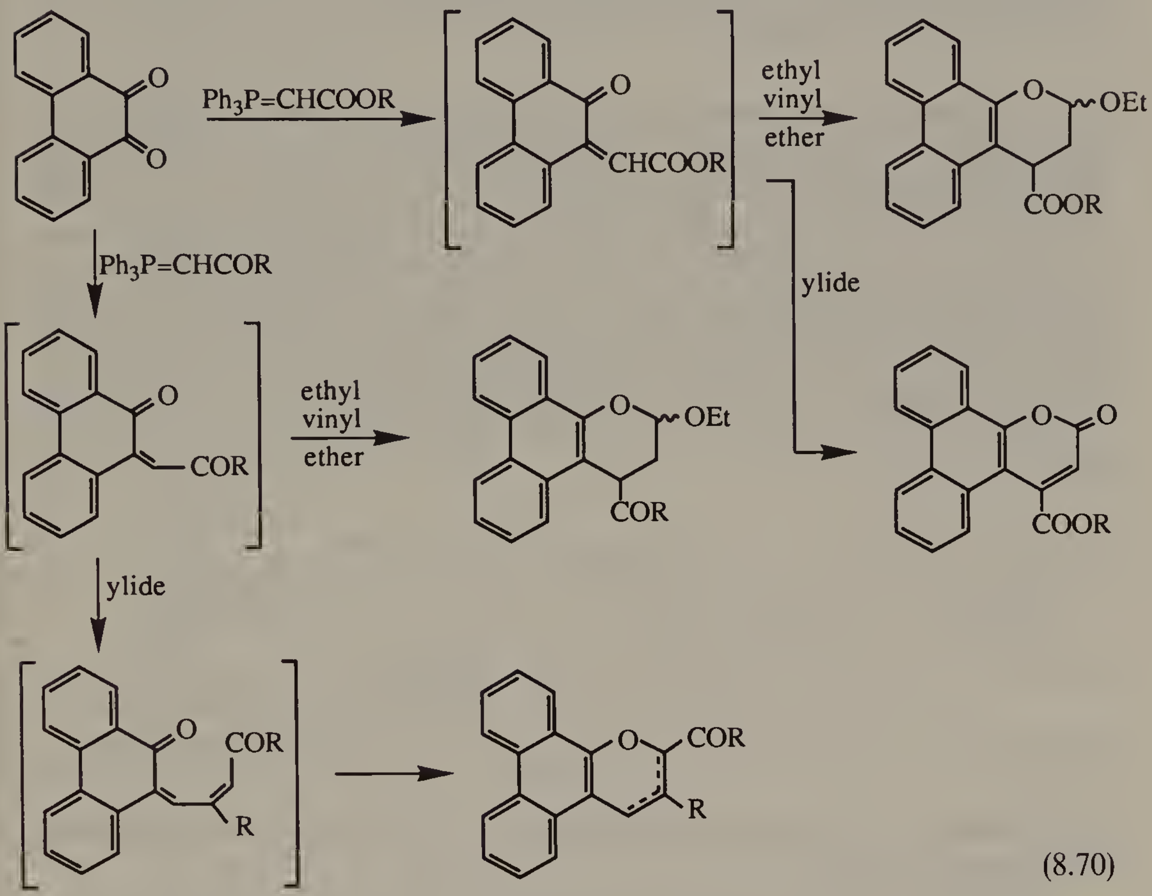
When a vicinal diketone is placed in a setting such that it is an *o*-quinone, complexities abound. *o*-Benzoquinone and its substituted derivatives (3,4,5,6-tetrachloro-, 3,5-di-*t*-butyl-) have produced major products in accord with Eq. 8.69, with reaction conditions and the ratio of reactants being major



(8.69)

determining factors. Most have concluded than the monoolefinated product, the *o*-quinonemethanide,[342] was more reactive than the original quinone in that it underwent conjugate addition by a second equivalent of ylide,[343, 344] the dimethanide only being observed when reacted with a *β*-ketoylide.[342] The benzocyclobutene adduct only was observed with $Ph_3P{=}CBr_2$ as the ylide[342, 345] and the dioxaindane showed up only rarely.[336, 343, 346] Diimide analogs of *o*-quinones underwent conjugate addition on the ring with ylides, resulting in eventual aromatization and the formation of phenyl-substituted ylides.[347]

Phenanthroquinones reacted with ylides in a manner similar to *o*-benzoquinone (Eq. 8.70). Parrick[334] and Sullivan[345] observed low yields of mono-olefination with a benzylide, and with two equivalents of ylide a dihydrofuran derivative was obtained from conjugate addition.[343,345] Isolation of a monoolefination product from reaction with an ester ylide first reported by the latter authors proved to be incorrect. Instead, the initial monoolefination product had undergone a conjugate addition to produce chromene-type products,[348] and recently the monoolefination product has been trapped with ethyl vinyl ether[344] and other reagents.[349] Use of an acylide rather than the ester ylide led to similar but slightly different behavior, with the initial monoolefinated product being trappable (Eq. 8.70).[348] Minsky and Rabinowitz[350] succeeded in obtaining normal cyclization reactions from phenanthroquinone and bis-ylides using phase-transfer catalysis, but Litinas and Nicolaides[351] were unsuccessful with different bis-ylides, but using a less than ideal base. Instead, monoolefin-derived rearrangement products were obtained.

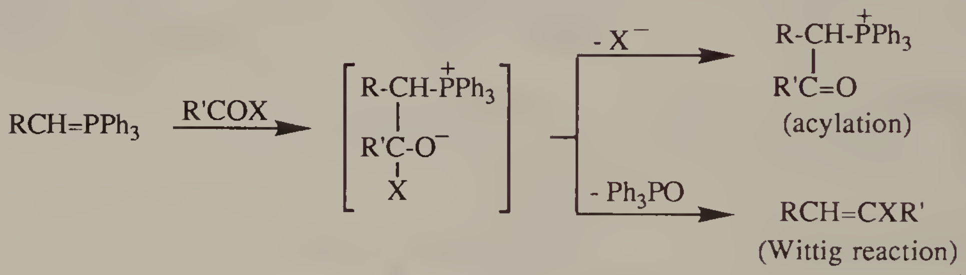


(8.70)

*p*-Benzoquinones reacted normally and in good yield with ylides, in the case of a benzylide and an ester ylide reacting only at one carbonyl group.[301]

However, the monoolefinated product of the ester ylide reaction underwent a conjugate addition with a second equivalent of ylide with concomitant aromatization. The dimethylacetal of *p*-benzoquinone reacted normally at the remaining carbonyl group.[352] Imide analogs of *p*-benzoquinone reacted with ester ylides or acylides via 1,4-addition at a ring carbon site in the case of bis-N-benzoyl-imides,[353] or by 1,2-addition to one of the C=N bonds followed by transylidation in the case of bis-N-sulfonimides.[354]

***8.2.2.7 Reaction with Derivatives of Carboxylic Acids (Esters, Anhydrides, Acyl Halides, Amides, Imides).*** Reaction of a phosphonium ylide with a carboxylic acid derivative probably proceeds initially by attack of the ylide carbanion at the carbonyl carbon to produce an oxyanion intermediate which can, in principle, either expel an anion to produce an acylated phosphonium salt or can eliminate triphenylphosphine oxide to produce an alkene in a Wittig reaction (Eq. 8.71). Whether those that follow the Wittig reaction route involve a discrete betaine and/or a discrete oxaphosphetane intermediate is not known. The course of these reactions was discussed in detail in Section 6.5, to which the reader is referred.



(8.71)

The usual course of the reactions of ylides with the various derivatives can be summarized as follows:

1. Acyl halides and linear anhydrides effect acylation of ylides while $C_4$ and $C_5$ cyclic anhydrides produce enol lactones via Wittig reactions.
2. Esters can be acylating agents or can be alkenylated to enol ethers, depending on the "ketonicity" of the carbonyl group, and variation in experimental conditions often provides considerable choice.
3. Thiolesters have been used as acylating agents frequently, but they also have undergone Wittig reactions to form enol thioethers in the right structural circumstance.
4. Lactones have effected acylation, often followed by an intramolecular Wittig reaction, and there is one report of a direct Wittig reaction to produce an enol ether.
5. Amides most frequently undergo Wittig reactions at the carbonyl group to produce enamines, but in some circumstances they acylate ylides.
6. Imides invariably undergo Wittig reactions.

## REVIEWS

**1965** Maercker, A. *Organic Reactions 14*, 270–490. A full review of the Wittig reaction.

**1966** Johnson, A. Wm. *Ylid Chemistry*; Academic: New York. A full review of the Wittig reaction.

**1970** Schlosser, M. In *Topics in Stereochemistry*; Eliel, E. L. and Allinger, N. L., Eds.; Wiley-Interscience: New York; Vol. 5, pp. 1–30. A review of the stereochemistry of the Wittig reaction.

**1975** Vollhardt, K. P. C. *Synthesis* 765–780. A review of the bis-Wittig reaction to form nonbenzenoid aromatic ring systems.

**1979** Gosney I.; Rowley, A. G. In *Organophosphorus Reagents in Organic Synthesis*; Cadogan, J. I. G., Ed.; Academic: London; Chapter 2, pp. 17–153. A review of the applications and stereochemistry of the Wittig reaction.

**1979** Zbiral, E. In *Organophosphorus Reagents in Organic Synthesis*; Cadogan, J. I. G., Ed.; Academic: London; Chapter 5. A review of the application of the Wittig reaction to the synthesis of heterocyclic compounds.

**1980** Becker, K. B. *Tetrahedron 36*, 1717–1745. A review of the synthesis of cycloalkenes by intramolecular Wittig reactions.

**1980** Warren, S. *Chem. Ind.* 824–828. A review of the synthetic applications of the Wittig reaction.

**1983** Morris, D. G. *Recent Advances in the Chemistry of Ylides* in *Survey of Progress in Chemistry*; Wubbels, G. G., Ed.; Butterworths: London; Vol. 10, pp. 200–215. A review of the Wittig reaction.

**1983** Bestmann, H. J.; Vostrowsky, O. *Topics In Curr. Chem. 109*, 85–163. A review of the use of the Wittig reaction in natural products syntheses.

**1983** Pommer, H.; Thieme, P. C. *Topics Curr. Chem. 109*, 165–188. A review of the industrial applications of the Wittig reaction.

**1986** Ford, W. T. In *Polymeric Reagents and Catalysts*; Ford, W. T., Ed.; American Chemical Society: Washington, DC; Chapter 8, pp. 155–185. A report on a symposium of the conduct of the Wittig reaction on polymeric supports.

**1988** Murphy, P. J.; Brennan, J. *Chem. Soc. Rev. 17,* 1–30. A review of the Wittig reaction with the carbonyl group of derivatives of carboxylic acids.

**1989** Maryanoff, B. E.; Reitz, A. B. *Chem. Revs. 89*, 863–927. A review of the mechanism, stereochemistry, and some applications of the Wittig reaction.

**1991** Minami, T.; Yamamoto, I., *Revs. Heteroatom Chem. 5*, 270–311. Review of the chemistry of phosphonium salts carrying cyclic systems, including their use in the Wittig reaction.

## REFERENCES

[1] See Vedejs, E. *Science* **1980**, *207*, January 4, pp. 42–44 for a review of Wittig's prize-winning work. Wittig's own Nobel lecture was reprinted in *Science* **1980**, *210*, November 7, pp. 600–604.

[2] Staudinger, H.; Meyer, J. *Helv. Chim. Acta* **1919,** *2*, 635.

[3] Luscher, G. Dissertation at ETH, Zurich, **1922**.

[4] Wittig, G.; Geissler, G. *Liebigs Ann. Chem.* **1953**, *580*, 44.

[5] Wittig, G.; Schollkopf, U. *Chem. Ber.* **1954,** *87*, 1318.

[6] Wittig, G. *Pure Appl. Chem.* **1964**, *9*, 245.

[7] Johnson, A. Wm. *Ylid Chemistry*; Academic: New York, 1966.

[8] Wittig, G.; Pommer, H. *Chem. Abstr.* **1959**, *53*, 436.

[9] Gosney, I.; Rowley, A. G. In *Organophosphorus Reagents in Organic Synthesis*; Cadogan, J. I. G., Ed.; Academic: London, 1979; Chapter 2.

[10] Maryanoff, B. E.; Reitz, A. B. *Chem. Rev.* **1989**, *89*, 863.

[11] Garner, P.; Ramakanth, S. *J. Org. Chem.* **1987**, *52*, 2629.

[12] Kawasaki, T.; Nonaka, Y.; Uemura, M.; Sakamoto, M. *Synthesis* **1991**, 701.

[13] Evans, D. A.; Gage, J. R.; Leighton, J. L. *J. Org. Chem.* **1992**, *57*, 1964.

[14] Gilpin, M.; Harbridge, J. B.; Hawarth, T. T. *J. Chem. Soc. Chem. Commun.* **1981**, 929.

[15] Kawasaki, T.; Nonaka, Y.; Ohtsuka, H.; Sato, H.; Sakamoto, M. *J. Chem. Soc. Perkin Trans. (1)* **1990**, 1101.

[16] Ager, D. J. In *Organic Reactions*, Paquette, L. A., Ed.; Wiley: New York, 1990; Chapter 1, pp. 83–85.

[17] Naf, F.; Decorzant, R.; Thommen, W.; Willhalm, B.; Ohloff, G. *Helv. Chim. Acta* **1975**, *58*, 1016.

[18] Ideses, R.; Shani, A. *Tetrahedron* **1989**, *45*, 3523.

[19] Blade-Font, A.; Vanderwerf, C. A.; McEwen, W. E. *J. Am. Chem. Soc.* **1960**, *82*, 2396.

[20] Horner, L.; Winkler, H. *Tetrahedron Lett.* **1964**, 3265.

[21] Meyers, A. I.; Strickland, R. C. *J. Org. Chem.* **1972**, *37*, 2579.

[22] Bissing, D. E. *J. Org. Chem.* **1965**, *30*, 1296.

[23] Dong, Z. J.; He, Z. L. *Synthesis* **1990**, 909.

[24] Speziale, A. J.; Ratts, K. W. *J. Am. Chem. Soc.* **1963**, *85*, 2790.

[25] Vogtle, F.; Hochberg, R.; Kochendorfer, F.; Windscheif, P. M.; Volkmann, M.; Jansen, M. *Chem. Ber.* **1990**, *123*, 2181.

[26] Bergelson, L. D.; Shemyakin, M. M. *Tetrahedron* **1963**, *19*, 149.

[27] Hauser, C. F.; Brooks, T. W.; Miles, M. L.; Raymond, M. A.; Butler, G. B. *J. Org. Chem.* **1963**, *28*, 372.

[28] Schlosser, M.; Christmann, K. F. *Liebigs Ann. Chem.* **1967**, *708*, 1.

[29] Bestmann, H. J.; Vostrowsky, O. *Topics Curr. Chem.* **1983**, *109*, 85.

[30] Viala, J.; Sandri, J. *Tetrahedron Lett.* **1992**, *33*, 4897.

[31] Johnson, A. Wm.; Kyllingstad, V. L. *J. Org. Chem* **1966**, *31*, 334.

[32] Drefahl, G.; Lorenz, D.; Schnitt, G. *J. Prakt. Chem.* **1964**, *23*, 143.

[33] Tamura, R.; Saegusa, K.; Kakihana, M; Oda, D. *J. Org. Chem.* **1988**, *53*, 2723.

[34] Johnson, S. J.; Kesten, S. R.; Wise, L. D. *J. Org. Chem.* **1992**, *57*, 4746.

[35] Bestmann, H. J.; Heid, E.; Ryschka, W.; Lienert, J. *Liebigs Ann. Chem.* **1974**, 1684.

[36] Trost, B. M.; Curran, D. P. *J. Am. Chem. Soc.* **1980**, *102*, 5699.

[37] Toda, F.; Akai, H. *J. Org. Chem.* **1990**, *55*, 3446.

[38] Pinsard, P.; Lellouche, J. P.; Beaucourt, J. P.; Gree, R. *Tetrahedron Lett.* **1990**, *31*, 1137.

[39] Wittig, G.; Rieber, M. *Liebigs Ann. Chem.* **1949**, *562*, 177.

[40] Johnson, A. Wm.; LaCount, R. B. *Chem. Ind.* **1959**, 52.

[41] Johnson, A. Wm.; LaCount, R. B. *Tetrahedron* **1960**, *9*, 130.

[42] Trippett, S.; Walker, D. M. *J. Chem. Soc.* **1961**, 1266.

[43] Bestmann, H. J.; Kratzer, O. *Chem. Ber.* **1962**, *95*, 1894.

[44] Heathcock, C. H.; Blumenkopf, T. A.; Smith, K. M. *J. Org. Chem.* **1989**, *54*, 1548.

[45] Ruchardt, C.; Panse, P.; Eichler, S. *Chem. Ber.* **1967**, *100*, 1144.

[46] Giese, B.; Schoch, J.; Ruchardt, C. *Chem. Ber.* **1978**, *111*, 1395.

[47] Froyen, P. *Acta Chem. Scand.* **1972**, *26*, 2163.

[48] McEwen, W. E.; Sullivan, C. E.; Day, R. O. *Organometallics* **1983**, *2*, 420.

[49] Allen, D. W.; Ward, H. *Tetrahedron Lett.* **1979**, 2707.

[50] Schaub, B.; Jeganathan, S.; Schlosser, M. *Chimia* **1986**, *40*, 246.

[51] Jeganathan, S.; Tsukamoto, M.; Schlosser, M. *Synthesis* **1990**, 109.

[52] McEwen, W. E.; Cooney, J. V. *J. Org. Chem.* **1983**, *48*, 983.

[53] Quin, L. D.; Spence, S. C. *Tetrahedron Lett.* **1982,** *23*, 2529.

[54] Allen, D. W. *Z. Naturforsch.* **1980**, *35B*, 1455.

[55] Wilson, I. F.; Tebby, J. C. *J. Chem. Soc. Perkin Trans. (1)* **1972**, 2713.

[56] Schlosser, M.; Schaub, B. *J. Am. Chem. Soc.* **1982**, *104*, 5821.

[57] Vedejs, E.; Marth, C. F.; Ruggeri, R. *J. Am. Chem. Soc.* **1988**, *110*, 3940.

[58] Vedejs, E.; Marth, C. *Tetrahedron Lett.* **1987**, *28*, 3445.

[59] Meyers, A. I.; Lawson, J. P.; Carver, D. R. *J. Org. Chem.* **1981**, *46*, 3119.

[60] Tamura, R.; Kato, M.; Saegusa, K.; Kakihana, M.; Oda, D. *J. Org. Chem.* **1987**, *52*, 4121.

[61] Zhao, Z.; Scarlato, G. R.; Armstrong, R. W. *Tetrahedron Lett.* **1991**, *32*, 1609.

[62] Allen, D. W. *Z. Naturforsch.* **1980**, *35B*, 981.

[63] Ramirez, F.; Levy, S. *J. Am. Chem. Soc.* **1957**, *79*, 67.

[64] Markl, G. *Angew. Chem.* **1963**, *2*, 153; *Z. Naturforsch.* **1963**, *18B*, 84.

[65] Ramirez, F.; Dershowitz, S. *J. Org. Chem.* **1957**, *22*, 41.

[66] Trippett, S.; Walker, D. M. *Chem. Ind.* **1960**, 202.

[67] Schiemenz, G. P.; Engelhard, H. *Chem. Ber.* **1961**, *94*, 578.

[68] Sugasawa, S.; Matsuo, H. *Chem. Pharm. Bull.* **1960**, *8*, 819.

[69] Kende, A. S.; Luzio, M. J.; Mendoza, J. S. *J. Org. Chem.* **1990**, *55*, 918.

[70] Keck, G. E.; Boden, E. P.; Mabury, S. A. *J. Org. Chem.* **1985**, *50*, 709.

[71] Levine, S. G. *J. Am. Chem. Soc.* **1958**, *80*, 6150.

[72] Elliot, M.; Janes, N. F.; Pulman, D. A. *J. Chem. Soc. Perkin Trans. (1)* **1974**, 2470.

[73] House, H. O.; Rasmussen, G. H. *J. Org. Chem.* **1961**, *26*, 4278.

[74] Plieninger, H.; Meyer, E.; Nassirian, F. S.; Weidmann, E. *Liebigs Ann. Chem.* **1976**, 1475.

[75] Devos, M. J.; Hevesi, L.; Bayet, P.; Krief, A. *Tetrahedron Lett.* **1976**, 3911.

[76] Schweizer, E. E.; Berninger, C. J.; Thompson, J. G. *J. Org. Chem.* **1968**, *33*, 336.

[77] Bestmann, H. J.; Kranz, E. *Angew. Chem.* **1967**, *6*, 81.

[78] Pommer, H. *Angew. Chem.* **1960**, *72*, 811.

[78a] Miller, E. J.; Weigelt, C. A.; Serth, J. A.; Rusyid, R.; Brenner, J.; Luck, L. A.; Godlewski, M. *J. Organomet. Chem.* **1992**, *440*, 91.

[79] Seyferth, D.; Grim, S. O.; Read, T. O. *J. Am. Chem. Soc.* **1961**, *83*, 1617.

[80] Miyano, S.; Izumi, Y.; Fujii, K.; Ohno, Y.; Hashimoto, H. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 1197.

[81] Seyferth, D.; Heeren, J. K.; Singh G.; Grim, S. O.; Hughes, W. B. *J. Organomet. Chem.* **1966**, *5*, 267.

[82] Kobrich, G.; Trapp, H.; Flory, K.; Drischel, W. *Chem. Ber.* **1966**, *99*, 689.

[83] Smithers, R. H. *J. Org. Chem.* **1978**, *43*, 2833.

[84] Pattenden, G.; Robson, D. C. *Tetrahedron Lett.* **1987**, *28*, 5751.

[85] Bestmann, H. J.; Bomhard, A. *Angew. Chem.* **1982**, *21*, 545.

[86] Bestmann, H. J.; Arenz, T. *Tetrahedron Lett.* **1986**, *27*, 1995.

[87] Bestmann, H. J.; Rippel, H. C.; Dostalek, R. *Tetrahedron Lett.* **1989**, *30*, 5261.

[88] Burton, D. J.; Greenlimb, P. E. *J. Org. Chem.* **1975**, *40*, 2796.

[89] Schlosser, M.; Zimmerman, M. *Synthesis* **1969**, *1*, 75.

[90] Thenappan, A.; Burton, D. J. *J. Org. Chem.* **1990**, *66*, 2311.

[91] Gadreau, C.; Foucaud, A. *Bull Soc. Chim. Fr.* **1976**, 2068.

[92] Olah, G. H.; Wu, A. H. *Synthesis* **1990**, 885.

[93] Bessard, Y.; Muller, U.; Schlosser, M. *Tetrahedron* **1990**, *46*, 5213.

[94] Riesel, L.; Vogt, H.; Kolleck, V. *Z. Anorg. Allg. Chem.* **1989**, *574*, 143.

[95] Maryanoff, B. E.; Reitz, A. B.; Duhl-Emswiler, B. A. *J. Am. Chem. Soc.* **1985**, *107*, 217.

[96] Corey, H. S.; McCormick, J. R. D.; Swenson, W. E. *J. Am. Chem. Soc.* **1964**, *86*, 1884.

[97] Baker, S. R.; Clissold, D. W.; McKillop, A. M. *Tetrahedron Lett.* **1988**, *29*, 991.

[98] Gapinski, D. M.; Roman, C. R.; Rinkema, L. E.; Fleisch, J. H. *J. Med. Chem.* **1988**, *31*, 172.

[99] Greene, A. E.; Depres, J. P.; Meana, M. C.; Crabbe, P. *Tetrahedron Lett.* **1976**, 3755.

[100] Corey, E. J.; Weinschenker, N. M.; Schaaf, T. K.; Huber, W. *J. Am. Chem. Soc.* **1969**, *91*, 5675.

[101] Morris, J.; Wishka, D. *Tetrahedron Lett.* **1988**, *29*, 143.

[102] Bhalerao, U. T.; Plattner, J. J.; Rapoport, H. *J. Am. Chem. Soc.* **1970**, *92*, 3429.

[103] Bremmer, M. L.; Khatri, N. A.; Weinreb, S. M. *J. Org. Chem.* **1983**, *48*, 3661.

[104] Dawson, M. I.; Vasser, M. *J. Org. Chem.* **1977**, *42*, 2783.

[105] Kubota, T.; Yamamoto, M. *Tetrahedron Lett.* **1992**, *33*, 2603.

[106] Cheik-Rouhou, F.; Le Bigot, Y.; El Gharbi, R.; Delmas, M.; Gaset, A. *Synth. Comm.* **1986**, *16*, 1617.

[107] Kitahara, T.; Horiguchi, A.; Mori, K. *Tetrahedron* **1988**, *44*, 4713.

[108] Hands, A. R.; Mercer, A. J. H. *J. Chem. Soc. (C)* **1968**, 2448.

[109] Salmond, W. G.; Barta, M. A.; Havens, J. L. *J. Org. Chem.* **1978**, *43*, 790.

[110] Meyers, A. I.; Collington, E. W. *Tetrahedron* **1971**, *27*, 5979.

[111] Schaub, B.; Blaser, G.; Schlosser, M. *Tetrahedron Lett.* **1985**, *26*, 307.

112 Marxer, A.; Leutert, T. *Helv. Chim. Acta* **1978**, *61*, 1708.

113 DeCastro Dantas, T. N.; Laval, J.; Lattes, A. *Tetrahedron* **1983**, *39*, 3337.

114 Linderman, R. J.; Meyers, A. I. *Tetrahedron Lett.* **1983**, *24*, 3043.

115 Johnson, A. Wm. *J. Org. Chem.* **1959**, *24*, 282.

116 Speziale, A. J.; Bissing, D. E. *J. Am. Chem. Soc.* **1963**, *85*, 3878.

117 Yamataka, H.; Nagareda, K.; Takai, Y.; Sawada, M.; Hanafusa, T. *J. Org. Chem.* **1988**, *53*, 3877.

118 Pattenden, G.; Storer, R. *J. Chem. Soc. Perkin Trans. (1)* **1974**, 1603.

119 Miyano, M.; Stealey, M. A. *J. Org. Chem.* **1975**, *40*, 1748.

120 Ernest, I.; Main, A. J.; Menasse, R. *Tetrahedron Lett.* **1982**, *23*, 167.

121 Boeckman, R. K.; Silver, S. M. *Tetrahedron Lett.* **1973**, 3497.

122 McMurry, J. E.; Choy, W. *Tetrahedron Lett.* **1980**, *21*, 2477.

123 Pine, S. H.; Shen, G. S.; Hoang, H. *Synthesis* **1991**, 165.

124 Vedejs, E.; Snoble K. A. J. *J. Am. Chem. Soc.* **1973**, *95*, 5778.

125 Drefahl, G.; Ponsold, K.; Schick, H. *Chem. Ber.* **1965**, *98*, 604.

126 Drefahl, G.; Horhold, H. H.; Kuhne, K. *Chem. Ber.* **1965**, *98*, 1826.

127 Dusza, J. P. *J. Org. Chem.* **1960**, *25*, 93.

128 Cristau, H. J.; Ribeill, Y.; Chiche, L.; Plenat, F. *J. Organomet. Chem.* **1988**, *352*, C47.

129 Battiste, M. A. *J. Am. Chem. Soc.* **1964**, *86*, 942.

130 Hanenkamp, J. C.; Rookhuizen, R. B.; Heuvel, H. L. A.; Bos, H. J. T.; Brandsma, L. *Tetrahedron Lett.* **1991**, *32*, 5397; *Tetrahedron* **1992**, *48*, 5151.

131 Sreekumar, C.; Darst, K. P.; Still, W. C. *J. Org. Chem.* **1980**, *45*, 4260.

132 Webb, T. H.; Thomasco, L. M.; Schlachter, S. T.; Gaudino, J. J. *Tetrahedron Lett.* **1988**, *30*, 6823.

133 Ohloff, G.; Vial, C.; Naf, F.; Pawlak, M. *Helv. Chim. Acta* **1977**, *60*, 1161.

134 Schlosser, M.; Schaub, B.; De Oliveira-Neto, J.; Jeganathan, S. *Chimia* **1986**, *40*, 244.

135 Anderson, R. J.; Henrick, C. A. *J. Am. Chem. Soc.* **1975**, *97*, 4327.

136 Kareeda, M.; Patel, P. D.; Brown, L. *J. Org. Chem.* **1985**, *50*, 5910.

137 Schlosser, M.; Christmann, K. F. *Angew. Chem.* **1964**, *3*, 636.

138 Fitjer, L.; Quabeck, *U. Synth. Comm.* **1985**, *15*, 855.

139 Buddrus, J. *Angew. Chem.* **1968**, *7*, 536.

140 Mehta, R. R.; Pardini, V. L.; Utley, J. H. *J. Chem. Soc. Perkin Trans. (1)*, **1982**, 2921.

141 Schlosser, M.; Schaub, B. *Chimia* **1982**, *36*, 396.

142 Le Bigot, Y.; Delmas, M.; Gaset, A. *Tetrahedron* **1986**, *42*, 339.

143 Le Bigot, Y.; Gharbi, R. E.; Delmas, M.; Gaset, A. *Tetrahedron* **1986**, *42*, 3813.

144 Clement, M. S.; Marinas, J. M.; Mouloungui, Z.; Le Bigot, Y.; Delmas, M.; Gaset, A.; Sinisterra, J. V. *J. Org. Chem.* **1989**, *54*, 3695.

145 Tagaki, W.; Inoue, I.; Yano, Y.; Okonogi, T. *Tetrahedron Lett.* **1974**, 2587.

146 Unemoto, T.; Gotoh, Y. *Bull Chem. Soc. Jpn.* **1991**, *64*, 2008.

147 Schlosser, M. In *Topics in Stereochemistry*; Eliel, E. L. and Allinger, N. L., Eds.; Wiley-Interscience: New York, 1970; Chapter 1.

148 House, H. O.; Jones, V. K.; Frank, G. A. *J. Org. Chem.* **1964**, *29*, 3327.

[149] Tronchet, J. M.; Gentile, B. *Helv. Chim. Acta* **1979**, *62*, 2091.

[150] Prakash, K. R. C.; Rao, S. P. *Tetrahedron Lett.* **1991**, *32*, 7473.

[151] Bergelson, L. D.; Shemyakin, M. M. *Pure Appl. Chem.* **1964**, *9*, 271.

[152] Olah, G. A.; Krishnamurthy, V. V. *J. Am. Chem. Soc.* **1982**, *104*, 3987.

[153] Bergelson, L. D.; Vaver, V. A.; Barsukov, L. I.; Shemyakin, M. M. *Tetrahedron Lett.* **1964**, 2669.

[154] Tronchet, J. M. J.; Baehler, B.; Eder, H.; Le-Hong, N.; Perret, F.; Poncet, J.; Zumwald, J. B. *Helv. Chim. Acta* **1973**, *56*, 1310.

[155] McEwen, W. E.; Ward, W. J. *Phosphorus Sulfur* **1989**, *41*, 393.

[156] Reitz, A. B.; Nortey, S. O.; Jordan, A. J.; Mutter, M. S.; Maryanoff, B. E. *J. Org. Chem.* **1986**, *51*, 3302.

[157] Albright, T. A.; Schweizer, E. E. *J. Org. Chem.* **1976**, *41*, 1168.

[158] Vedejs, E.; Meier, G. P.; Snoble, K. A. J. *J. Am. Chem. Soc.* **1981**, *103*, 2823.

[159] Bottin-Strzalko, T.; Seyden-Penne, J.; Tchoubar, B. *C. R. Seances Acad. Sci. (C)* **1971**, *272*, 778.

[160] McEwen, W. E.; Chia, W. L.; Baughman, L.; Mari, F. *Abstracts of Papers*, 198th National Meeting of the American Chemical Society, Miami Beach, Fl, 1989; ORGN 223.

[161] Schlosser, M.; Muller, G.; Christmann, K. F. *Angew. Chem.* **1966**, *5*, 667.

[162] McEwen, W. E.; Mari, F.; Lahti, P. M.; Baugham, L. L.; Ward, W. J. In *Phosphorus Chemistry: Developments in American Science*; ACS Symposium Series No. 486, Walsh, E. N.; Griffith, E. J.; Quin, L. D.; Parry, R. W., Eds.; American Chemical Society: Washington, DC, 1992; Chapter 12.

[163] Boden, R. M. *Synthesis* **1975**, 784.

[164] Ruchardt, C.; Eichler, S.; Panse, P. *Angew. Chem.* **1963**, *2*, 619.

[165] Fliszar, S.; Hudson, R. F.; Salvadori, G. *Helv. Chim Acta* **1964**, *47*, 159.

[165a] Kayser, M. M.; Hatt, K. L.; Hooper, D. L. *Can. J. Chem.* **1991**, *69*, 1929; **1992**, *70*, 1985.

[166] Bose, A. K.; Manhas, M. S.; Ramer, R. M. *J. Chem. Soc. (C)* **1969**, 2728.

[167] Marriott, D. P.; Bantick, J. R. *Tetrahedron Lett.* **1981**, *22*, 3657.

[168] Corey, E. J.; Goto, G. *Tetrahedron Lett.* **1980**, *21*, 3463.

[169] Corey, E. J.; Clark, D. A.; Goto, G.; Marfat, A.; Mioskowski, C.; Samuelsson, B.; Hammarstrom, S. *J. Am. Chem. Soc.* **1980**, *102*, 1436.

[170] Bohlmann, F.; Bax, H. J. *Chem. Ber.* **1974**, *107*, 1773.

[171] Bestmann, H. J.; Stransky, W.; Vostrowsky, O. *Chem. Ber.* **1976**, *109*, 1694.

[172] Bettach, N.; Le Bigot, Y.; Mouloungui, Z.; Delmas, M.; Gaset, A. *Synth. Comm.* **1992**, *22*, 513.

[173] Openshaw, H. T.; Whittaker, N. *Proc. Chem. Soc.* **1961**, 454.

[174] Fodor, G.; Tomoskozi, I. *Tetrahedron Lett.* **1961**, 579.

[175] Isaacs, N. S.; Abed, O. H. *Tetrahedron Lett.* **1986**, *27*, 995.

[176] Isaacs, N. S.; El-Din, G. N. *Tetrahedron Lett.* **1987**, *28*, 2191.

[177] Dauben, W. G.; Takasugi, J. J. *Tetrahedron Lett.* **1987**, *28*, 4377.

[178] Nonnenmacher, A.; Mayer, R.; Plieninger, H. *Liebigs Ann. Chem.* **1983**, 2135.

[179] Galakhova, T. N.; Stashina, G. A.; Zhulin, V. M.; Kamernitskii, A. V.; Levina, I. S. *Bull. Acad. Sci. USSR* **1990**, 2613.

[180] Bestmann, H. J.; Roth, D. *Angew. Chem.* **1990**, *29*, 99.

[181] Trippett, S.; Walker, D. M. *J. Chem. Soc.* **1961**, 2130.

[182] Daniel, H.; Le Corre, M. *Tetrahedron Lett.* **1987**, *28*, 1165.

[183] Broquet, C.; Simalty, M. *Tetrahedron Lett.* **1972**, 933.

[184] Corey, E. J.; Kang, J. J.; Kyler, K. *Tetrahedron Lett.* **1985**, *26*, 555.

[185] Schaub, B.; Jenny, T.; Schlosser, M. *Tetrahedron Lett.* **1984**, *25*, 4097.

[186] Mikolajczyk, M.; Perlikowska, W.; Omelanczuk, J.; Cristau, H. J.; Perraud-Darcy, A. *Synlett.* **1991**, 913.

[187] McKenna, E. G.; Walker, B. M. *J. Chem. Soc. Chem. Commun.* **1989**, 568.

[188] McKenna, E. G.; Walker, B. M. *Tetrahedron Lett.* **1988**, *29*, 485; *Phosphorus Sulfur* **1990**, *49/50*, 445.

[189] Schlosser, M.; Christmann, K. F. *Angew. Chem.* **1966**, *5*, 126.

[190] Schlosser, M.; Tuang, H. B.; Schaub, B. *Tetrahedron Lett.* **1985**, *26*, 311.

[191] Schlosser, M.; Christmann, K. F.; Piskala, A. *Chem. Ber.* **1970**, *103*, 2814.

[192] Schlosser, M.; Christmann, K. F. *Synthesis* **1969**, 38.

[193] Corey, E. J.; Shulman, J. I.; Yamamoto, H. *Tetrahedron Lett.* **1970**, 447.

[194] Schlosser, M.; Christmann, K. F.; Piskala, A.; Coffinet, D. *Synthesis* **1971**, 29.

[195] Corey, E. J.; Yamamoto, H. *J. Am. Chem. Soc.* **1970**, *92*, 226.

[196] Schlosser, M.; Coffinet, D. *Synthesis* **1971**, 380.

[197] Schlosser, M.; Coffinet, D. *Synthesis* **1972**, 575.

[198] Corey, E. J.; Yamamoto, H. *J. Am. Chem. Soc.* **1970**, *92*, 6637.

[199] Trippett, S.; Walker, B. J. *J. Chem. Soc.* **1966**, 887.

[200] Allen, D. W.; Heatley, P.; Hutley, B. G.; Mellor, M. T. J. *Tetrahedron Lett.* **1974**, 1787.

[201] Wittig, G.; Boll, W.; Kruck, K. H. *Chem Ber.* **1962**, *95*, 2514.

[202] Witschard, G.; Griffin, C. E. *J. Org. Chem.* **1964**, *29*, 2335.

[203] McMurry, J. E.; Von Beroldingen, L. A. *Tetrahedron* **1974**, *30*, 2027.

[204] LaLancette, E. A. *J. Org. Chem.* **1964**, *29*, 2957.

[205] Salaun, J.; Bennani, F.; Compain, J. C.; Fadel, A.; Oliver, J. *J. Org. Chem.* **1980**, *45*, 4129.

[206] (a) Marshall, J. A.; Pike, M. T.; Carroll, R. D. *J. Org. Chem.* **1966**, *31*, 2932. (b) Soffer, M. D.; Burk, L. A. *Tetrahedron Lett.* **1970**, 211. (c) Heathcock, C. H.; Ratcliff, R. *J. Am. Chem. Soc.* **1971**, *93*, 1746.

[207] Corey, E. J.; Mitra, R. B.; Uda, H. *J. Am. Chem. Soc.* **1964**, *86*, 485.

[208] McMurry, J. E. *J. Am. Chem. Soc.* **1988**, *90*, 6821.

[209] Corey, E. J.; Kang, J. J. *J. Am. Chem. Soc.* **1982**, *104*, 4724.

[210] Schmidbaur, H.; Tronich, W. *Chem. Ber.* **1967**, *100*, 1032.

[211] Gilman, H.; Tomasi, R. A. *J. Org. Chem.* **1962**, *27*, 3647.

[212] Schmidbaur, H.; Stuhler, H. *Angew. Chem.* **1973**, *12*, 321.

[213] Tsukamoto, M.; Iio, H.; Tokoroyama, T. *Tetrahedron Lett.* **1985**, *26*, 4471; *ibid.* **1987**, *28*, 4561.

[214] Iio, H.; Fujii, A.; Ishii, M.; Tokoroyama, T. *J. Chem. Soc. Chem. Commun.* **1991**, 1390.

[215] Iio, H.; Tsukamoto, M.; Tokoroyama, T. *Tetrahedron Lett.* **1988**, *29*, 5965.

[216] Kolodiazhnyi, O. I. *Tetrahedron Lett.* **1981**, *22*, 1231.

[217] Kolodiazhnyi, O. I. *Tetrahedron Lett.* **1985**, *26*, 439.

[218] Kolodiazhnyi, O. I.; Golokhov, D. B. *J. Gen. Chem. USSR* **1988**, *58*, 426.

[219] Kolodiazhnyi, O. I.; Golokhov, D. B. *J. Gen. Chem. USSR* **1989**, *59*, 252.

[220] Murphy, P. J.; Brennan, J. *Chem. Soc. Rev.* **1988**, *17*, 1.

[221] Campa, C.; Sanchez-Ferrando, F.; Tristan-Polo, M. *New. J. Chem.* **1985**, *9*, 493.

[221a] Anderson, C. L.; Soderquist, J. A.; Kabalka, G. W. *Tetrahedron Lett.* **1992**, *33*, 6915.

[222] Bestmann, H. J.; Roth, K.; Ettlinger, M. *Chem. Ber.* **1982**, *115*, 161.

[223] Herrera, F. J. L.; Gonzalez, M. S. P.; Sampedro, M. N.; Aciego, R. M. D. *Tetrahedron* **1989**, *45*, 269.

[224] Dondini, A.; Fantin, G.; Fogagnolo, M.; Medici, A.; Pedrini, P. *Tetrahedron* **1988**, *44*, 2021.

[225] Cristau, H. J.; Gasc, M. B. *Tetrahedron Lett.* **1990**, *31*, 341.

[226] Martin, S. F.; Garrison, P. J. *Tetrahedron Lett.* **1977**, 3875.

[227] Shen, Y.; Qui, W. *Tetrahedron Lett.* **1987**, *28*, 449.

[228] Eitel, M.; Pindur, U. *Synthesis* **1989**, 364.

[229] Dussault, P.; Sahli, A. *Tetrahedron Lett.* **1990**, *31*, 5117.

[230] Pommer, H.; Thieme, P. C. *Topics Curr. Chem.* **1983**, *109*, 165.

[231] Soukop, M.; Widmer, E. *Tetrahedron Lett.* **1991**, *32*, 4117.

[232] Bestmann, H. J.; Kratzer, O. *Chem. Ber.* **1963**, *96*, 1899.

[233] Trippett, S. *Chem. Ind.* **1956**, 80.

[234] Dicker, D. W.; Whiting, M. C. *Chem. Ind.* **1956**, 351; *J. Chem. Soc.* **1958**, 1994.

[235] Inoue, S.; Honda, K.; Iwase, N.; Sato, K. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 1629.

[236] Kubriner, A. M.; Oliveto, E. P. *J. Org. Chem.* **1966**, *31*, 24.

[237] Wyllie, S. G.; Djerassi, C. *J. Org. Chem.* **1968**, *33*, 305.

[238] Barton, D. H. R.; Davies, P. J.; Kempe, U. M.; McGarrity, J. F.; Widdowson, D. A. *J. Chem. Soc. Perkin Trans. (1)* **1972**, 1231.

[239] Bergelson, L. D.; Shemyakin, M. M. *Angew. Chem.* **1964**, *3*, 250.

[240] Bestmann, H. J.; Stransky, W.; Vostrowsky, O.; Range, P. *Chem. Ber.* **1975**, *108*, 3582.

[241] Bestmann, H. J.; Sub, J.; Vostrowsky, O. *Liebigs Ann. Chem.* **1981**, 2117.

[242] Viala, J.; Munier, P.; Santelli, M. *Tetrahedron* **1991**, *47*, 3347.

[243] Just, G.; Simonovitch, C. *Tetrahedron Lett.* **1967**, 2093.

[244] Danishefsky, S.; Cabal, M. P.; Chow, K. *J. Am. Chem. Soc.* **1989**, *111*, 3456.

[245] Corey, E. J.; Shirahama, H.; Yamamoto, H.; Terashima, S.; Venkateswarlu, A.; Schaaf, T. K. *J. Am. Chem. Soc.* **1971**, *93*, 1490.

[246] Gleason, J. G.; Bryan, D. B.; Kinzig, C. M. *Tetrahedron Lett.* **1980**, *21*, 1129.

[247] LeMerrer, Y.; Gravier-Pelletier, C.; Micas-Languin, D.; Mestre, F.; Dureault, A.; Depezay, J. C. *J. Org. Chem.* **1989**, *54*, 2409.

[248] Hanzawa, Y.; Kawagoe, K. I.; Inazawa, K.; Kobayashi, Y. *Tetrahedron Lett.* **1988**, *29*, 5665.

[249] Corey, E. J.; Yamamoto, H.; Herron, D. K.; Achiwa, K. *J. Am. Chem. Soc.* **1970**, *92*, 6636.

[250] Henrick, C. A.; Schaub, F.; Siddall, J. B. *J. Am. Chem. Soc.* **1972**, *94*, 5374.

[251] Crombie, L.; Doherty, C. F.; Pattenden, G. *J. Chem. Soc.* (*C*) **1970**, 1076.

[252] Ueda, K.; Matsui, M. *Agric. Biol. Chem.* **1970**, *34*, 1119.

[253] Bestmann, H. J.; Vostrowsky, O. *Tetrahedron Lett.* **1974**, 207.

[254] Yamamoto, I.; Tanaka, S.; Fujimoto, T.; Ohta, K. *J. Org. Chem.* **1989**, *54*, 747.

[255] Bestmann H. J.; Sub, J. *Liebigs Ann. Chem.* **1982**, 363.

[256] Bazureau, J. P.; Person, D.; Le Corre, M. *Tetrahedron Lett.* **1989**, *30*, 3065.

[257] O'Donnell, M. J.; Arasappan, A.; Hornback, W. J.; Huffmann, J. C. *Tetrahedron Lett.* **1990**, *31*, 157.

[258] Sibi, M. P.; Renhowe, P. A. *Tetrahedron Lett.* **1990**, *31*, 7407.

[259] Wnuk, S. F.; Robins, M. J. *Can. J. Chem.* **1991**, *69*, 334.

[260] Samano, V.; Robbins, M. J. *Synthesis* **1991**, 283.

[261] Zhdanov, Y. A.; Alexeev, Y. E.; Alexeeva, V. G. *Adv. Carbohydr. Chem. Biochem.* **1972**, *27*, 227.

[262] Zhdanov, Y. A.; Dorofeenko, G. N.; Uzlova, L. A. *Dokl. Akad. Nauk. SSSR* **1965**, *160*, 47.

[263] Ohrui, H.; Jones, G. H.; Moffatt, J. C.; Maddox, M. L.; Christensen, A. T.; Byram, S. K. *J. Am. Chem. Soc.* **1975**, *97*, 4602.

[264] Nicotra, F.; Ronchette, F.; Russo, G.; Toma, L. *Tetrahedron Lett.* **1984**, *25*, 5697.

[265] Reitz, A. B.; Jordan, A. D.; Maryanoff, B. E. *J. Org. Chem.* **1987**, *52*, 4800.

[266] Harmon, R. E.; Wellman, G.; Gupta, S. R. *Carbohydr. Res.* **1970**, *14*, 123.

[267] Barrett, A. G. M.; Broughton, H. B.; Attwood, S. V.; Gunatilaka, A. A. L. *J. Org. Chem.* **1986**, *51*, 1986.

[268] Henk, T.; Giannis, A.; Sandhoff, K. *Liebigs Ann. Chem.* **1992**, 167.

[269] Bieber, T. I.; Eisman, E. H. *J. Org. Chem.* **1962**, *27*, 678.

[270] Griffin, C. E.; Witschard, G. *J. Org. Chem.* **1964**, *29*, 1001.

[271] Griffin, C. E.; Witschard, G. *J. Org. Chem.* **1962**, *27*, 3334.

[272] Masamune, S.; Bates, G. S.; Corcoran, J. W. *Angew. Chem.* **1977**, *16*, 585.

[273] Halmos, T.; Anderson, P. C.; Kheang, T. Y.; Guindon, Y. *Abstracts of Papers*, 195th National Meeting of the American Chemical Society, Toronto: Canada; American Chemical Society; Washington, DC, 1988; ORGN 107.

[274] Becker, K. B. *Tetrahedron* **1980**, *36*, 1717.

[275] Dauben, W. H.; Robbins, J. D. *Tetrahedron Lett.* **1975**, 151.

[276] Ernest, I.; Gosteli, J.; Greengrass, C. W.; Holick, W.; Jackman, D. E.; Pfaendler, H. R.; Woodward, R. B. *J. Am. Chem. Soc.* **1978**, *100*, 8214.

[277] Bestmann, H. J.; Schobert, R. *Tetrahedron Lett.* **1987**, *28*, 6587.

[278] Yvergnaux, F.; Le Floch, Y.; Gree, R. *Tetrahedron Lett.* **1989**, *30*, 7397.

[279] Yvergnaux, F.; Le Floch, Y.; Gree, R.; Toupet, L. *Tetrahedron Lett.* **1989**, *30*, 7393; *Bull Soc. Chim. Fr.* **1991**, 724.

[280] Schweizer, E. E.; Schepers, R. *Tetrahedron Lett.* **1963**, 979.

[281] Okada, Y.; Minami, T.; Yahiro, S.; Akinaga, K. *J. Org. Chem.* **1989**, *54*, 974.

[282] Zbiral, E. In *Organophosphorus Reagents in Organic Synthesis*; Cadogan, J. I. G., Ed.; Academic: NY, 1979; Chapter 5, p. 250.

[283] Fuchs, P. L. *Tetrahedron Lett.* **1974**, 4055.

[284] Dauben, W. G.; Hart, D. J. *Tetrahedron Lett.* **1975**, 4353.

[285] Altenbach, H. J. *Angew. Chem.* **1979**, *18*, 940.

[286] (a) Bestmann, H. J.; Schmid, G.; Sandmeier, D. *Angew. Chem.* **1976**, *15*, 115; (b) Bestmann, H. J.; Schade, G.; Lutke, H.; Monius, T. *Chem. Ber.* **1985**, *118*, 2640.

[287] Dauben, W. G.; Ipaktschi, J. *J. Am. Chem. Soc.* **1973**, *95*, 5088.

[288] Ding, W.; Zhang, P.; Cao, W. *Tetrahedron Lett.* **1987**, *28*, 81.

[289] Hatanaka, M.; Himeda, Y.; Ueda, I. *Tetrahedron Lett.* **1991**, *32*, 4521.

[290] Ykman, P.; L'Abbe, G.; Smets, G. *Tetrahedron* **1971**, *27*, 845.

[291] Vollhardt, K. P. C. *Synthesis* **1975**, *765.*

[292] Wittig, G.; Eggers, H.; Duffner, P. *Liebigs Ann. Chem.* **1958**, *619*, 10.

[293] Breslow, R.; Horspool, W.; Sugiyama, H.; Vitale, W. *J. Am. Chem. Soc.* **1966**, *88*, 3677.

[294] Griffin, C. E.; Martin, K. R.; Douglas, B. E. *J. Org. Chem.* **1962**, *27*, 1627.

[295] Staab, H. A.; Wehinger, E.; Thorwart, W. *Chem Ber.* **1972**, *107*, 2290.

[296] Thulin, B.; Wennerstrom, O.; Hoberg, H. E. *Acta Chem. Scand.* **1975**, *29B*, 138.

[297] Bestmann, H. J.; Kratzer, O.; Simon, H. *Chem. Ber.* **1962**, *95*, 2750.

[298] Goerger, M. M.; Hudson, B. S. *J. Org. Chem.* **1988**, *53*, 3148.

[299] Wittig, G.; Haag, A. *Chem. Ber.* **1963**, *96*, 1535.

[300] Ratts, K. W.; Partos, R. D. *J. Am. Chem. Soc.* **1969**, *91*. 6112.

[301] Van Woerden, H. F.; Cerfontain, H.; Van Valkenburg, C. F. *Rec. Trav. Chim.* **1969**, *88*, 158.

[302] Nader, F. W.; Brecht, A. *Angew. Chem* **1986**, *25*, 93.

[303] Nader, F. W.; Brecht, A.; Kreiz, S. *Chem. Ber.* **1986**, *119*, 1208.

[304] Lang, R. W.; Bestmann, H. J. *Helv. Chim. Acta* **1980**, *63*, 438.

[305] Campbell, T. W.; McDonald, R. N. *J. Org. Chem.* **1959**, *24*, 1969.

[306] Drefahl, G.; Plotner, G. *Chem. Ber.* **1961**, *94*, 907.

[307] Manecke, G.; Luttke, S. *Chem. Ber.* **1970**, *103*, 700.

[308] Spangler, C. W.; Rathunde, R. A. *J. Chem. Soc. Chem. Commun.* **1989**, 26.

[309] Burg, A. B.; Mahler, W. *J. Am. Chem. Soc.* **1961**, *83*, 2388.

[310] Weber, D.; Fluck, E. *Z. Anorg. Allg. Chem.* **1976**, *424*, 103.

[311] Cowley, A. H.; Cushner, M. C. *Inorg. Chem.* **1980**, *19*, 515.

[312] Zurmuhlen, F.; Regitz, M. *Angew. Chem.* **1987**, *26*, 83.

[313] Fritz, G.; Mayer, B.; Matern, E. *Z. Anorg. Allg. Chem.* **1992**, *607*, 19.

[314] Le Floch, P.; Marinetti, A.; Ricard, L.; Mathey, F. *J. Am. Chem. Soc.* **1990**, *112*, 2407.

[315] Le Floch, P.; Mathey, F. *Synlett.* **1991**, 743.

[316] Le Floch, P.; Mathey, F. *Synlett.* **1990**, 171.

[317] Marinetti, A.; Le Floch, P.; Mathey, F. *Organometallics* **1991**, *10*, 1190.

[318] Mathey, F.; Marinetti, A.; Bauer, S.; Le Floch, P. *Pure Appl. Chem.* **1991**, *63*, 855.

319 Lednicer, D. *J. Org. Chem.* **1970**, *35*, 2307; *ibid.* **1971**, *36*, 3473.

320 Muchowski, J.; Venuti, M. C. *J. Org. Chem.* **1981**, *46*, 459.

321 Fujimoto, T.; Hotei, Y.; Takeuchi, H.; Tanaka, S.; Ohta, K.; Yamamoto, I. *J. Org. Chem.* **1991**, *56*, 4799.

322 Minami, T.; Yamamoto, I. *Revs. Heteroatom. Chem.* **1991**, *5*, 270.

323 Ford, W. T. In *Polymeric Reagents and Catalysts*; Ford, W. T., Ed.; American Chemical Society: Washington, DC, 1986; Chapter 8.

324 Camps, F.; Castells, J.; Font, J.; Vela, F. *Tetrahedron Lett.* **1971**, 1715.

325 McKinley, S. V.; Rakshys, J. W. *J. Chem. Soc. Chem. Commun.* **1972**, 134.

326 Heitz, W.; Michels, R. *Angew. Chem.* **1972**, *11*, 298.

327 Heitz, W.; Michels, R. *Liebigs Ann. Chem.* **1973**, 227.

328 Campa, C.; Font, J.; Sanchez-Ferrando, F.; Virgili, A. *An. Quim.* **1986**, *82*, 46; *Chem. Abstr.* **1986**, *106*, 138024.

329 Bernard, M.; Ford, W. T. *J. Org. Chem.* **1983**, *48*, 326.

330 Clarke, S. D.; Harrison, C. R.; Hodge, P. *Tetrahedron Lett.* **1980**, *21*, 1375.

331 Frechet, J. M.; Schuerch, C. *J. Am. Chem. Soc.* **1971**, *93*, 492.

332 Leznoff, C. C.; Fyles, T. M.; Weatherstone, J. *Can. J. Chem.* **1977**, *55*, 1143.

333 Fyles, T. M.; Leznoff, C. C.; Weatherstone, J. *Can. J. Chem.* **1978**, *56*, 1031.

334 Parrick, J. *Can. J. Chem.* **1964**, *42*, 190.

335 Bestmann, H. J.; Morper, H. *Angew. Chem.* **1967**, *6*, 561.

336 Nicolaides, D. N.; Litinas, K.; Argyropoulos, N. G. *J. Chem. Soc. Perkin Trans. (1)* **1986**, 415.

337 Papageorgiou, G.; Nicolaides, D.; Stephanidon-Stephanatou, J. *Liebigs Ann. Chem.* **1989**, 397.

338 Soliman, F. M.; Khalil, K. M.; Naim, G. A. E. *Phosphorus Sulfur* **1988**, *35*, 41.

339 Garratt, P. J.; Nicolaides, D. N. *J. Org. Chem.* **1974**, *39*, 2222.

340 Cava, M. P.; Firouzabadi, H.; Krieger, M. *J. Org. Chem.* **1974**, *39*, 480.

341 Cava, M. P.; Pohl, R. J. *J. Am. Chem. Soc.* **1960**, *82*, 5242.

342 Abdou, W. M.; Ganoub, N. A. F.; Rahman, N. M. A. *Phosphorus Sulfur* **1991**, *61*, 91.

343 Bestmann, H. J.; Lang, H. J. *Tetrahedron Lett.* **1969**, 2101.

344 Nicolaides, D. N.; Adamopoulos, S. G.; Lefkaditis, D. A.; Litinas, K. E. *J. Chem. Soc. Perkin Trans. (1)* **1990**, 2127.

345 Sullivan, W. W.; Ullmann, D.; Schechter, H. *Tetrahedron Lett.* **1969**, 457.

346 Abdou, W. A. *Phosphorus Sulfur* **1992**, *66*, 285.

347 Boulos, L. S.; Arsanious, M. H. N. *Phosphorus Sulfur* **1988**, *36*, 23.

348 Nicolaides, D. N.; Lefkaditis, D. A.; Lianis, P. S.; Litinas, K. E. *J. Chem. Soc. Perkin Trans. (1)* **1989**, 2329.

349 Nicolaides, D. N.; Adamopoulos, S. G.; Lefkaditis, D. A.; Litinas, K. E.; Tarantili, P. V. *J. Chem. Soc. Perkin Trans. (1)* **1992**, 283.

350 Minsky, A.; Rabinowitz, M. *Synthesis* **1983**, 497.

351 Litinas, K. E.; Nicolaides, D. N. *J. Chem. Soc. Perkin Trans. (1)* **1985**, 429.

352 Hart, D. J.; Cain, P. A.; Evans, D. A. *J. Am. Chem. Soc.* **1978**, *100*, 1548.

353 Boulos, L. S.; Arsanious, M. H. N. *Phosphorus Sulfur* **1989**, *42*, 47.

354 Boulos, L. S.; Khoshnieh, Y. O. E.; Arsanious, M. H. N. *Phosphorus Sulfur* **1990**, *47*, 199.

## 9

# THE WITTIG REACTION II. MECHANISM AND STEREOCHEMISTRY

The mechanism of the Wittig reaction has been a topic of study for almost 40 years, and while much has changed by way of evidence, experimental techniques, understandings, and conclusions, the intermediates and transition states being discussed most actively at present are almost the same as those first described by Wittig in the 1950s! It is still a topic of active research and debate with the subtleties of reactant structure and reaction conditions becoming even more evident, and the capability to use the reaction for synthetic purposes even more precise.

The complexity of the mechanistic problem associated with the Wittig reaction did not become obvious until the stereochemical intricacies of the reaction, especially obtaining *Z*-alkenes in some stereoselective reactions, appeared in the early 1960s. In his 1964 lecture Trippett[1] concluded that "the unravelling of the features which control the competing reactions leading to isomeric olefins is far from uncomplicated." Two years later Johnson[2] commented that "the mechanistic details of the reaction, in their intricate relationships, more than balance the synthetic simplicities of the reaction and make for most interesting study." Thirteen years later, and 26 years after the discovery of the reaction, in their excellent 1979 compendium, Gosney and Rowley[3] commented that "Any attempt to rationalize the stereochemistry of the alkene formed in the Wittig reaction hinges on a full understanding of the mechanism of the reaction. Unfortunately, some of the mechanistic aspects are still something of a puzzle, . . . ." In their exhaustive 1989 review Maryanoff and Reitz[4] noted that even then "a certain mystique has persisted with respect to (the) high preference for contra-thermodynamic *Z*-alkenes in . . . reactions of triphenylphosphorus non-stabilized ylides with aldehydes." Finally, in 1990 Seebach,[5] in

---

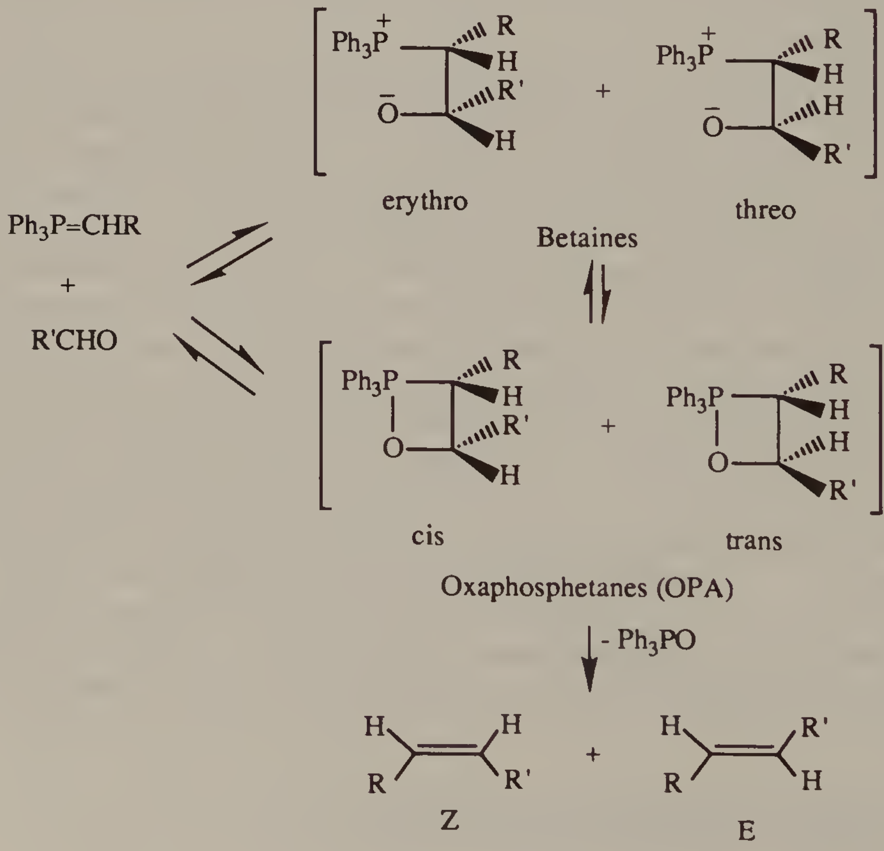
*Ylides and Imines of Phosphorus*, Edited by A. William Johnson.
ISBN 0-471-52217-1

his lengthy review and prognostication entitled "Organic Chemistry—Where Now?" perhaps overconfidently noted that "It appears that the mechanism (of the Wittig reaction) has now been clarified once and for all." Whether this is the case still remains to be seen!

This chapter presents the mechanistic interpretations for the reaction which seem to be most acceptable as of 1992. The salient experimental facts on which these mechanisms rest will be presented. The prior mechanistic proposals are briefly described and reasons for discarding them are summarized.

## 9.1 THE EVOLUTION OF MECHANISTIC PROPOSALS

Wittig's mechanism proposed for "his" reaction between phosphonium ylides and carbonyl compounds underwent evolution from (a) an initially proposed[6] direct 2 + 2 combination of reactants to form *only* an oxaphosphetane (OPA) which then dissociated directly to products, copied from Staudinger's 34-year-old proposal,[7] to (b) a revised proposal involving *only a* betaine intermediate,[8] to (c) his final proposal[9] involving initial nucleophilic attack of ylide carbanion on carbonyl carbon to form a betaine, closure of the betaine to an oxaphosphetane (OPA), and decomposition of the latter to products (Eq. 9.1 illustrates these



(9.1)

intermediates and incorporates the elements of several proposals, but is not meant to imply any single mechanism). The mechanistic issues were quite straightforward until it was observed that the reaction could produce alkene geometric isomers, and that various ylides and aldehydes produced widely disparate isomeric ratios. However, the betaine and OPA intermediates have remained the focus of most proposals, with the latter being at the heart of current proposals.

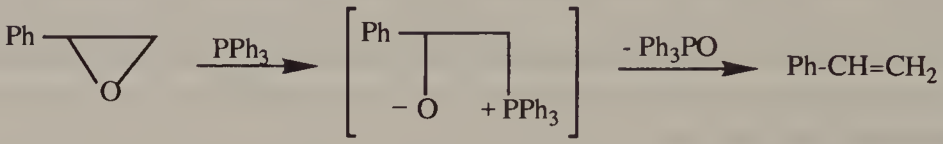
Some basic experimental evidence is relevant in consideration of virtually all mechanisms. First, it was shown by two groups that the overall reaction using a chiral phosphorus in the starting ylide resulted in phosphine oxide produced with retention of configuration.[10, 11] Thus a *syn*-elimination process involving a cyclic intermediate or transition state was envisaged, and included a trigonal bipyramidal phosphorus. It was surmised that the geometry of the alkene was determined by the geometry of its precursor OPA or betaine, the *cis*-OPA and/or erythro betaine producing the *Z*-alkene. Second, speculation regarding intermediates was based initially on the isolation of a protonated betaine [i.e., $\beta$-hydroxyphosphonium salt (HPS), usually obtained by quenching Wittig reactions with hydrogen bromide] from only a certain few reactions.[8] It was not until 1973 that oxaphosphetanes (OPA) were observed spectroscopically in Wittig reactions.[12] Further, no betaine has been observed in a Wittig reaction to this date. Third and finally, in the 1960s much mechanistic information was deduced from the ratio of *Z*- and *E*-isomers produced in Wittig reactions and it was assumed that such a ratio reflected a stable state of affairs in the reaction. However, it since has been shown that the ratio of alkenes identified in or isolated from a reaction does not necessarily reflect the ratio of stereoisomeric OPAs in a reaction, this phenomenon being labelled “stereochemical drift”.[13]

The following section presents the various mechanisms proposed for the Wittig reaction and briefly provides evidence of their acceptance or refutation. Section 9.1.2 presents the specific evidence regarding various proposed intermediates.

### 9.1.1 Proposed Mechanisms

A total of eight mechanisms have been proposed for the Wittig reaction since 1953. Each of these is described briefly using the name of the major proposer for identification purposes.

*9.1.1.1* ***Wittig.*** The first of the many mechanistic proposals was formulated by the developer of the reaction and involved initial formation of a betaine, ring closure to an OPA, and dissociation to products (Eq. 9.1).[9] The major impetus for this proposal was the isolation of $\beta$-hydroxy-$\beta$-phenylethyltriphenylphosphonium bromide (an HPS), obtained upon adding hydrogen bromide to a solution in which triphenylphosphoniummethylide and benzaldehyde had been reacted.[8] The fact that styrene could be obtained from the reaction of styrene oxide with triphenylphosphine,[9] presumably via the same betaine intermediate as proposed for the Wittig reaction, added credibility to this mechanism (Eq. 9.2). Others soon verified this alternate route and used it to address



(9.2)

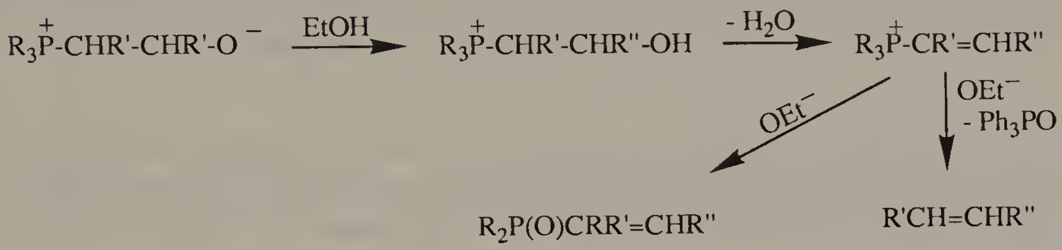
stereochemical issues.[14, 15] This latter reaction also was used to demonstrate a "crossover" reaction in which the addition of a more electrophilic aldehyde, often *m*-chlorobenzaldehyde, resulted in two alkene products, the aldehyde component coming from the original aldehyde and from the added aldehyde.[15] Therefore, betaine formation was determined to be reversible in some instances, and this made rationalization of the stereochemical outcomes of the Wittig reaction feasible in terms other than just the geometry of the original ylide–carbonyl adduct.[2]

Wittig's mechanism did not even address the issue of stereochemistry because at that time most of the products were the expected thermodynamically favored *E*-alkenes. The formal Wittig mechanism seldom is referred to now because of that fact, but also because it has so far been impossible to detect an uncomplexed betaine in solution, or to isolate one. However, the essence of this mechanism is retained to this day, as will be apparent in the discussion to follow.

House et al.[16] used the Wittig mechanism in a proposal to explain some of the stereochemical results then available in terms of betaine solvation and lithium cation complexation. They proposed differences in the relative stability of threo and erythro betaines and their syn and anti rotamers. Speziale and Bissing[17] more fully developed the possible interconversion of betaines, and the relative rates of their formation, decomposition to products, and dissociation to starting materials, all as a basis for rationalizing the stereochemical outcomes of the reactions using different ylides and carbonyls.

***9.1.1.2 Bergelson.*** In 1963 the Moscow group[18] proposed that the initial combination between ylide and carbonyl should result from carbonyl oxygen attack on the phosphorus atom, affording a new betaine intermediate (e.g., $R'CH^{+}–O–PR_3–CHR''^{-}$) and leading mainly to *E*-alkenes. By 1967[19] they had abandoned this proposal, being unable to substantiate it, being unable to account for the stereoselective formation of *Z*-alkenes in systems they were studying, and in view of the fact that Hammett correlations for the reaction of ylides with substituted benzaldehydes produced positive $\rho$-values,[17] whereas negative values were required for the Bergelson mechanism. Several years later Schneider[20] revived the original Bergelson mechanism proposal with refinements as a means of accounting for the newly accumulating evidence for predominant *Z*-alkene formation from nonstabilized ylides. The known Hammett correlations still argued against the proposal for initial P–O bonding, but two elements of his proposal were viable enough to influence subsequent research. Schneider presented a new stereochemical perspective on OPA formation which later workers incorporated to account for the $Z$-stereoselectivity, and he raised serious doubts about the necessity of considering a betaine as a necessary part of the Wittig reaction mechanism.

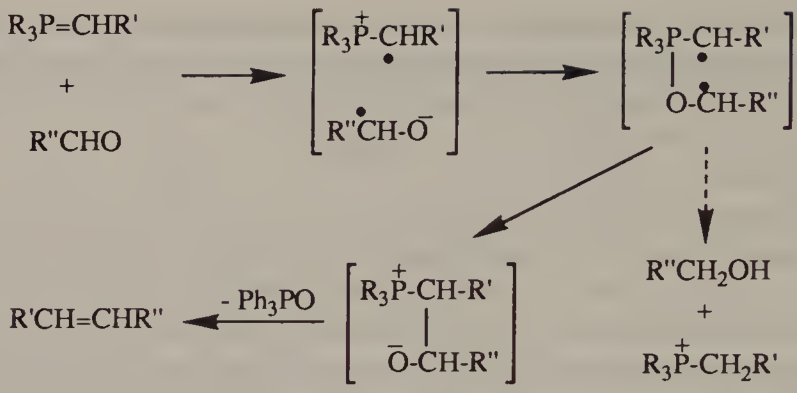
*9.1.1.3* ***Schweizer.*** In 1971 Schweizer et al.[21] proposed that in alcoholic media certain phosphonium ylides and carbonyl compounds underwent Wittig reactions by an alternate route, involving initial formation of a betaine, its protonation, loss of water to form a vinylphosphonium salt, and cleavage of the latter in an alcoholysis reaction to form olefin and phosphine oxide. The basis for this proposal was the observation that some ylides reacted with carbonyl compounds to form rearranged phosphine oxides rather than alkenes (Eq. 9.3). It



(9.3)

was subsequently shown by Smith and Trippett[22] and by Allen et al.[23] that while the rearrangement does occur in that media, there was no evidence for the Wittig reaction portion proceeding via a vinylphosphine oxide. Trippett[22] suggested that the reaction route shown in Eq. 9.3 for production of rearranged phosphine oxide was operating in competition with the normal Wittig mechanism (Eq. 9.1) in alcoholic media.

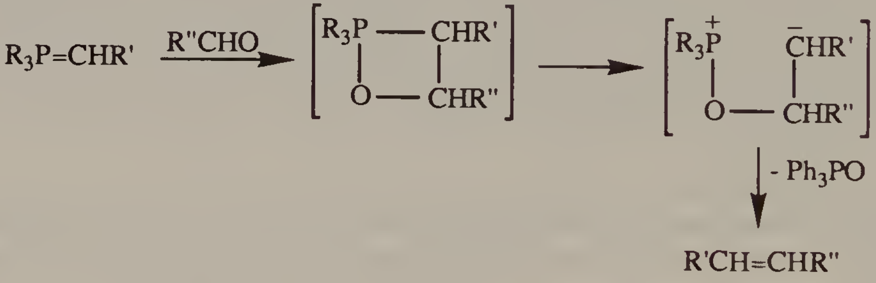
*9.1.1.4* ***Olah.*** Based on the observation that reaction of triphenylphosphoniumalkylides or benzylides with adamantanone or benzophenone at high temperatures resulted in the formation of the alcohol corresponding to reduction of the ketone, occasionally accompanied by some of the expected alkene product, Olah and Krishnamurthy[24] suggested that the Wittig reaction was occurring by a one-electron transfer from ylide to ketone, formation of a tight radical ion pair, coupling through P–O bond formation to a diradical, and its collapse to a betaine which then proceeded normally to alkene (Eq. 9.4). In those cases where steric hindrance was a factor, it was proposed that the diradical would not collapse to betaine, but instead would abstract hydrogen from the solvent, the reduction leading to the corresponding alcohol and regenerated phosphonium salt. No evidence was provided for this mechanism of alkene formation, and the authors were unable to obtain CIDNP spectra. Recently Yamataka et al.[25] have resurrected this single electron transfer (SET) mechanism, but mainly on the basis of negative evidence: (a) the absence of a significant kinetic isotope effect in the reaction of isopropylide with benzaldehyde, and (b) the low $\rho$ value ($+0.59$) for the reaction of the ylide with



(9.4)

substituted benzaldehydes. More recently the same group proved the occurrence of radicals in selected Wittig reactions, but it appears such reactions are competitive with the normal ionic Wittig reaction mechanism.[25a]

*9.1.1.5* **Bestmann.** Initial direct formation of an OPA, with an apical oxygen and with aldehyde and ylide substituents cis to one another, via a four-centered reaction between ylide and carbonyl, followed by pseudorotation of the OPA to make the oxygen equatorial, then bond breaking to a new betaine (C–C–O–P) formed the heart of the Bestmann mechanism.[26, 27] Completion of the reaction was proposed to occur by elimination of phosphine oxide (Eq. 9.5). If the ylide

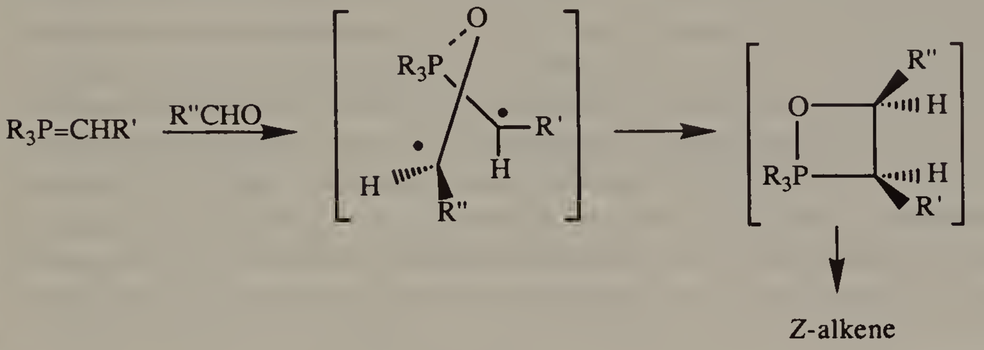


(9.5)

substituent R′ was electron withdrawing, the betaine would have sufficient lifetime to undergo a bond rotation such that R′ and R″ could be trans, and subsequent phosphine oxide elimination would result in mainly *E*-alkene, as is observed with stabilized ylides. Thus, thermodynamic control of the reaction would prevail. However, if R′ was not carbanion stabilizing, the betaine would have a short lifetime, undergo little bond rotation, and fast elimination would result in mainly *Z*-alkenes.

The Bestmann mechanism generally has been discarded because of several problems.[28] First, no positive evidence has been provided by the authors or others which demands this mechanism, and especially the unusual $^{-}C\text{–}C\text{–}O\text{–}P^{+}$ betaine. Second, it did not explain the mainly cis orientation of the substituents in the initially formed OPA, an essential aspect of the proposal. Third, demonstration of stereospecific kinetic control in the formation of *E*-alkene from betaine generated from HPS[29] removed the necessity for an equilibration route such as proposed by Bestmann. However, the issue regarding pseudorotation raised by Bestmann is one that needed to be incorporated into any satisfactory overall mechanism.

***9.1.1.6 McEwen.*** In 1985 McEwen et al.[28] proposed that an ylide and carbonyl compound initially formed a spin-paired diradical intermediate containing a C–C bond which eventually closed stereospecifically to an OPA which in turn dissociated to products. Normal geometry for the intermediate was proposed to arise from orthogonal approach of ylide and carbonyl, an idea first proposed by Vedejs,[12] resulting in the most stable configuration which, when closed to a ring, would produce a *cis*-OPA and eventually a *Z*-alkene. More recently the proposal has been revised to involve initial P–O bond formation and the existence of two carbon radicals (Eq. 9.6).[30] The presence of a stabilizing group on the ylide was proposed to extend the radical lifetime, thereby permitting bond rotation before closing to the thermodynamically favored *trans*-OPA. This entire mechanism was proposed to prevail *only* in those instances where lithium cation or sodium iodide were *absent*, and to result in enhancement of *E*-alkene formation with semistabilized or stabilized ylides.

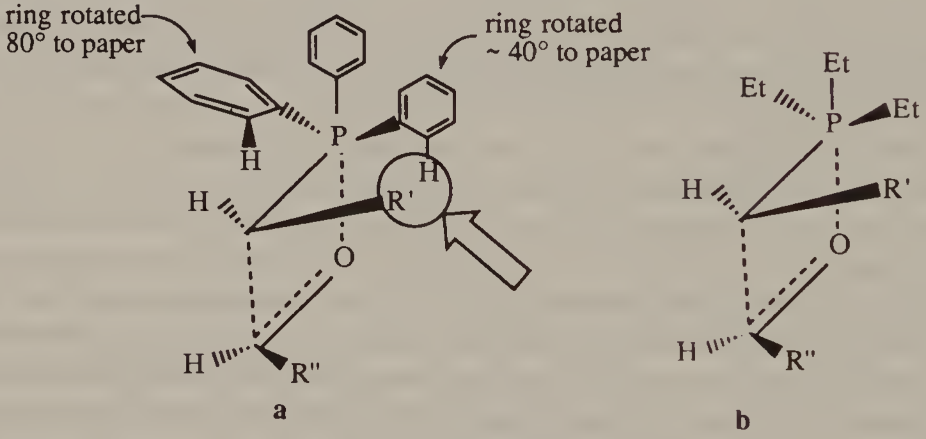


(9.6)

Although this mechanism has been described numerous times in the literature, no significant evidence has been provided which demands its consideration, and structural situations conducive to radical side reactions reacted normally, failing to provide evidence for radicals.[31] Also, the proposal involved initial P–O bond formation, as did the Bergelson–Schneider mechanism (Section 9.1.1.2), and the counter arguments apply equally well to the McEwen proposal.

Recently, the McEwen group[32] studied the Wittig half-reaction (i.e., the first step formation of intermediate) using the MNDO–PM3 semiempirical molecular orbital method, relying on geometries calculated using the MMX8 force field. They have concluded that the half reaction involves a "very asynchronous cycloaddition (borderline two-step mechanism)" involving a transition state with the C–C bond 30–50% formed but with no P–O bonding! The models did not predict *Z*-stereoselectivity and the authors could not explain the *Z*-stereoselectivity of nonstabilized ylides other than by reverting to the previously discarded House[16] proposal for an "anti" erythro betaine-like transition state.

***9.1.1.7 Schlosser.*** Schlosser[33] has long maintained the involvement of betaines in the Wittig reaction, even if only as precursors to detectable OPAs in the form of "betaine-like transition states." The involvement of betaines in the SCOOPY modification of the Wittig reaction seems essential on the basis of the reaction between salt-free triphenylphosphoniumethylide and both $CH_2O$ and $CD_2O$.[33] The two related 2-methylpropenols contained deuterium only on the methylene groups and the ratio of the two products was identical regardless of the order of addition of the aldehydes, arguing for a mobile equilibrium between two betaines, perhaps prior to OPA formation. The most recent Schlosser mechanism was advanced in 1982,[34] after it was generally recognized that OPAs, rather than betaines, were the key intermediates in the Wittig reaction. It was proposed that a 1,3-interaction in the transition state leading to the OPA was key to the cis geometry of the OPA. The ylide β-carbon (R′) forced rotation of an equatorial P-phenyl group, thereby providing space for the aldehyde substituent (R″) on the same side of the OPA ring, resulting in cis geometry (Eq. 9.7a). The R′---H interaction would be less in Eq. 9.7a than it would be if the R′ group were trans to the R″ group. If the aldehyde substituent were to approach from the other side of the incipient OPA ring, it would be hindered by the other (equatorial) P-phenyl ring which had rotated only 10°. This difference was suggested to account for normal *Z* dominance in the Wittig reaction of triphenylphosphoniumalkylides. By this argument, a decrease in the spatial demands of *P* substituents (e.g., replacement of phenyl with alkyl) should permit formation of more *trans*-OPA, leading to more *E*-alkene formation (Eq. 9.7b). In fact tri*ethyl*phosphoniumethylide reacted with aliphatic and aromatic aldehydes to produce *Z*:*E* ratios of 33:67 to 4:96 while tri*phenyl*phosphoniumethylide produced *Z*:*E* ratios of 86:14 to 98:2. Previous data indicating that bulky groups on phosphorus or on the carbonyl both led to enhancement of *Z*-alkene production (Sections 8.1.2 and 8.1.4) also were cited as supporting the proposal. The proposal does require a planar OPA ring with C–C and P–O bond formation equally advanced.

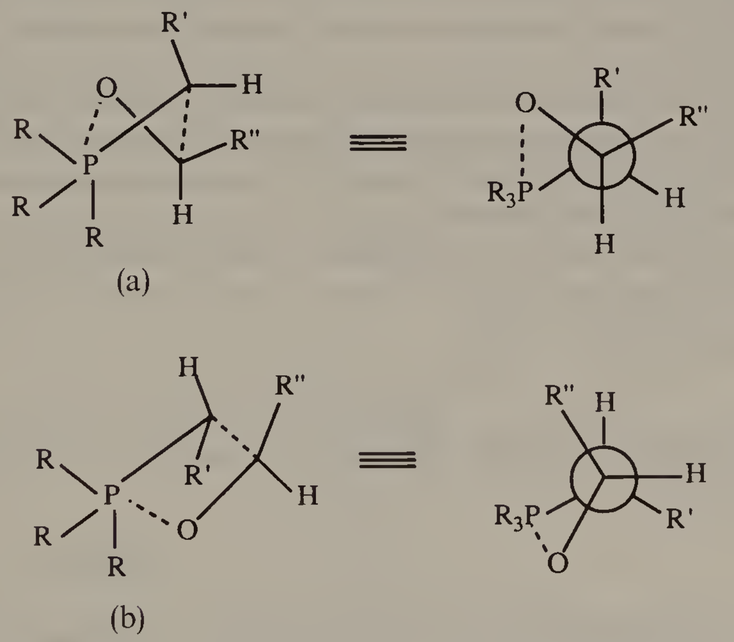


(9.7)

The Schlosser proposal,[35] relying on the propeller-like orientation of the phenyl groups about phosphorus, has been described as involving a "leeward" approach of the carbonyl reactant, and reflects an interesting change in concept from 20 years earlier. At that time the production of *E*-alkenes was seen as the normal course of events, with abnormal features (and explanations) required to account for *Z*-alkene selectivity. The Schlosser proposal, and others since then, propose that *Z*-alkene formation is the normal outcome of a Wittig reaction, with abnormal features usually producing the more stable *E*-alkenes.

Contrary to Schlosser's assumption,[34] it appears that *trans*-OPAs are more stable than the cis isomers,[36, 37] implying that the cis transition state must not be product-like. This latter observation also implies that the phosphorus geometry must be closer to tetrahedral than to trigonal bipyramidal, as required by the Schlosser geometry, the result of asynchronous addition (i.e., C–C bond formation is ahead of P–O bond formation). It also implies that the OPA ring is not necessarily planar.

*9.1.1.8* ***Vedejs.*** The most recent proposal, advanced by Vedejs in 1988,[36] included a four-center asynchronously formed transition state leading to the OPA, with the geometry of the latter being the result of a delicate balance of 1,2- and 1,3-interactions. Nonstabilized ylides were proposed to have an early transition state, and therefore tetrahedral phosphorus atom, involving a nonplanar or "puckered" geometry, with 1,3-interactions dominating and leading to lower energy for the *cis*-OPA and dominance of *Z*-alkene product (Eq. 9.8a).



(9.8)

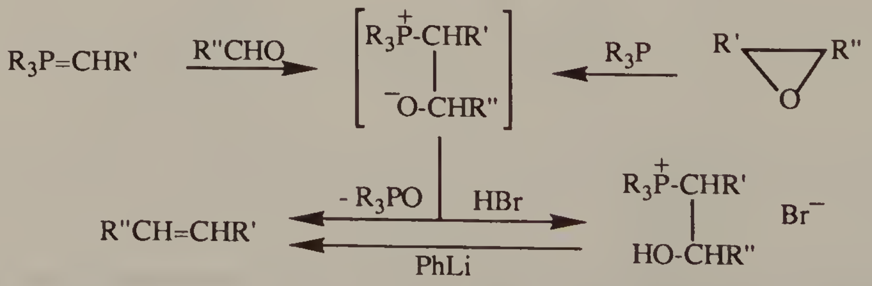
The aldehyde substituent (R″) and the ylide carbanion substituent (R′) were proposed to have quasi-equatorial and quasi-axial orientations, respectively, to diminish 1,2-interactions. Factors which reduced the 1,3-steric interactions, such as a single smaller substituent on phosphorus (e.g., in $EtPh_2P{=}CHR'$) or an aldehyde with at least one α-hydrogen, would relatively diminish 1,3-interactions and increase the importance of 1,2-interactions, resulting in a shift toward *trans*-OPA and *E*-alkene. Stabilized ylides, whose transition states would be product-like, and therefore would include a nearly trigonal bipyramidal phosphorus atom, were proposed to form relatively planar OPAs where 1,2-interactions would dominate, leading mainly to *trans*-OPA and *E*-alkene (Eq. 9.8b). All reactions were proposed to operate under kinetic control.

To date, serious objections have not been raised to this proposal and it appears to be the most useful for explaining both *E*- and *Z*-stereoselectivities.[4]

### 9.1.2 Evidence Regarding Proposed Intermediates

During the history of the study of the Wittig reaction, various reactive intermediates have been proposed. The evidence regarding intermediates is presented in this section. Although there have been a few proposals for mechanisms that involve radicals (Sections 9.1.1.4 and 9.1.1.6), there has been little concrete evidence supplied regarding their existence. As various geometries are considered for transition states to explain the stereochemical outcome of the Wittig reaction, many could apply to radicals as well as to the ions considered.

***9.1.2.1 Betaines.*** Wittig and Schollkopf[8] quenched the reaction of triphenylphosphoniummethylide and benzaldehyde with hydrogen bromide and isolated β-hydroxy-β-phenylethyltriphenylphosphonium bromide, the HPS proposed to arise from protonation of a betaine. Treatment of the HPS with phenyllithium at higher temperatures produced styrene and triphenylphosphine oxide, the expected end products of a Wittig reaction. Trippett[1] found that producing the HPS via another route, followed by its treatment with base, afforded the same result and others showed that the *threo*-HPS afforded *E*-alkene and the *erythro*-HPS afforded mainly *Z*-alkene.[38] Others[14, 17] found that reaction of a tertiary phosphine with an oxirane would result in overall deoxygenation, producing triphenylphosphine oxide and an alkene. It was proposed that this reaction proceeded via the same P–C–C–O betaine, with *cis*-oxirane affording threo betaine and *E*-alkene (Eq. 9.9).



(9.9)

Only one betaine seems to have been isolated, and that in the unusual case from reaction of triphenylphosphoniumisopropylide and diphenylketene, its stability presumably due to its enolate character.[39] Kozminykh et al.[40] recently reported the isolation of a β-hydroxy ylide, presumably from proton transfer within the betaine with which it was in equilibrium, and which was converted to phosphine oxide and alkene after 24 h at room temperature. Lithium halide adducts of betaines also have been isolated.[41] However, there has been no report of the observation of a free betaine in solution, in spite of numerous attempts, especially using $^{13}$P NMR spectroscopy. In addition, several groups have reported calculations which indicate that betaines are about 20 kcal/mol higher in energy than OPAs.[26,42–44]

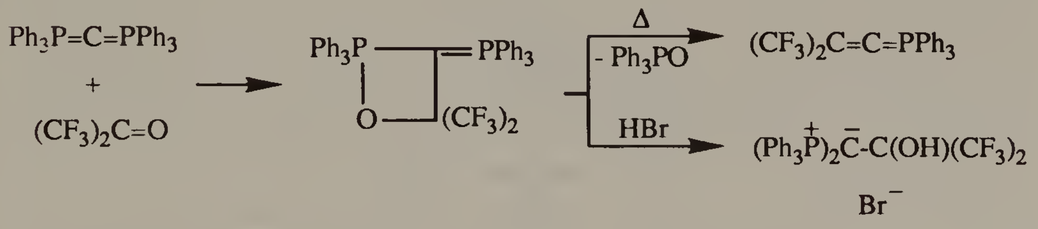
Vedejs and Marth[31] recently have reported a significant experiment in which OPAs have been produced both from precursor HPSs and from a Wittig reaction. The fact that different ratios of OPA rotamers were produced, both ratios being different than the equilibrium ratio, was the basis for claiming that "no evidence remains to support the conventional betaine pathway that is featured in virtually all textbooks." It has been separately demonstrated that the isolation of HPSs by acidification of Wittig reactions can be explained by cleavage of OPAs[45] and that LiBr adducts of betaines also can be obtained from OPAs.[46] Thus, the need for betaine intermediates in reactions of nonstabilized ylides seems to have vanished.

Although some have proposed that two other kinds of betaines (i.e., C–P–O–C and P–O–C–C) should be considered as intermediates (see Sections 9.1.1.2 and 9.1.1.5), no evidence has been provided for their existence, however fleeting, so they will not be considered further herein.

It may be concluded that P–C–C–O betaines have no mandatory role in the Wittig reaction, although a four-center transition state with a sufficient degree of asynchroneity to its formation would seem to acquire betaine character![32]

### *9.1.2.2 Oxaphosphetanes (OPAs).*

The Staudinger[7] and initial Wittig proposals[6] of an OPA intermediate were unprecedented, since none had ever been observed. Birum and Matthews[47] were the first to isolate an OPA and did so from the Wittig reaction of hexaphenylcarbodiphosphorane and hexafluoroacetone (Eq. 9.10). It could be converted to its HPS with acid, and simply upon heating the OPA the Wittig reaction continued with production of triphenylphosphine oxide and the allenic ylide. As have all OPAs, it showed a characteristic $^{31}$P NMR peak at high field, this one at − 54 ppm. Similar oxaphospholanes showed $^{31}$P absorption in the same region.[48] The oxaphosphetane structure was verified by X-ray crystallography,[49] which showed a trigonal bipyramidal phosphorus, a very long apical P–O bond (with ionic character?), a slightly off-square planar ring, and one apical P-phenyl bond.



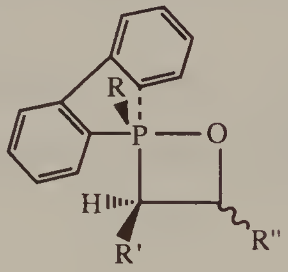
(9.10)

Subsequently a few other, but more complex, OPAs have been isolated[50–52] and have had their structures determined by X-ray crystallography.[53–55].

In 1973 the first observation of an OPA in an *n*-butyllithium-initiated Wittig reaction was made at −70°C in a $^{31}$P NMR spectrometer tube,[12] and shortly thereafter an OPA produced from a salt-free ylide was identified,[56] both using nonstabilized alkylides. The high-field $^{31}$P NMR absorption, usually about −60 ppm, has become a clear-cut indicator for the presence of OPAs. In a significant advance, in 1984 Reitz et al.[57] were able to identify both *cis*- (−61.4 ppm) and *trans*-oxaphosphetanes (−63.8 ppm) from the reaction of *n*-butylidenetriphenylphosphorane with benzaldehyde at −78°C, and could monitor their disappearance to form alkenes and triphenylphosphine oxide, this at a temperature of −25°C. Using a second preparative route, the same OPAs were observed when formed from the corresponding HPS upon treatment with base.[38] A third route to OPAs involved the opening of an oxirane with a phosphide, quaternization of the hydroxyphosphine into an HPS, and treatment of the latter with base.[58] The OPAs could be observed when prepared from ylides in a lithium environment, in a lithium-free (i.e., sodium or potassium present) environment, and in a totally salt-free environment.[13]

As a sidelight, it should be noted that the ratio of *cis*- to *trans*-OPAs in a Wittig reaction also could be determined by quenching the reaction at −78°C with HBr and the results were the same as those determined by $^{31}$P NMR techniques.[45]

Although most ordinary OPAs are thermally unstable, necessitating working at −70 to −100°C, a few are relatively stable, such as those with a half-life of 30 min at −8°C obtained from $Ph_3P{=}CHMe$ and PhCHO, and those from alkylides (**1**) incorporating dibenzophosphole (DBP) in the phosphonium group, some of which had to be heated to 70°C over several hours to effect alkene formation.[59]



**1**

The question of the influence of pseudorotation of OPAs on the Wittig reaction needed to be settled, since some mechanistic proposals provided for initial apical P–O bonding as the ylide coupled to the carbonyl compound, followed by pseudorotation to put the former ylide carbanionic carbon in an apical position preparatory to bond breaking and alkene formation. All four OPAs for which structures have been determined have the P–O bond in the apical position.[49, 53–55] Bestmann et al.[60] calculated that there was a "surprisingly small (~4.7 kcal/mol) apicophilicity" associated with hypothetical OPAs, a conclusion reached by six other groups as well.[42,43–44,61–63] In 1989 Vedejs and Marth,[64] using the stable OPAs incorporating the DBP group on phosphorus (**1**), were able to determine by $^{13}$C NMR spectroscopy that the oxygen atom in OPAs obtained from three different ylides were all in the apical position. Further, they determined that the rate of pseudorotation (*O*-apical to *O*-equatorial) was about $10^8$ times faster than the rate of decomposition to alkene and phosphine oxide.[31] Thus, the rate of Wittig reactions should not be limited by the rate of OPA pseudorotation.

The OPAs have been observed using nonstabilized ylides in reactions with straight-chain aliphatic aldehydes,[65, 33] fully branched aldehydes such as pivaldehyde,[46] aromatic aldehydes,[46] and ketones.[46] They also have been observed using triphenylphosphonium ylides,[12] trialkylphosphonium ylides,[34] and mixed ylides.[58]

Generally speaking OPAs have not been detectable for semistabilized ylides or for stabilized ylides, whether sought in a Wittig reaction[66] or by deprotonation of an HPS.[37] However, by using DBP ylides, Vedejs and Fleck[58] have been the first to detect OPAs from benzylides and allylides. This success takes advantage of the reluctance of the OPA, containing a 94° C–P–C angle in the five membered ring and a trigonal bipyramidal phosphorus (90° C–P–C angle) (**1**), to decompose to products which included a tetrahedral phosphorus (109° C–P–C angle). However, even in the favorable DBP ylide case no OPAs could be detected from stabilized ylides.

No matter how they are generated, OPAs are known to decompose into alkenes and phosphine oxides as the final step of the Wittig reaction. The rate of disappearance of OPA has been shown in several instances to be equal to the rate of appearance of phosphine oxide and alkene.[37, 57, 67] Further, the decomposition is known to be a syn elimination, affording phosphine oxides and alkenes with retention of configuration.[29] Thus, *cis*-OPAs afford *Z*-alkenes and *trans*-OPAs afford *E*-alkenes in the absence of reversal (see discussion below).

The OPAs generally do not revert to the starting ylide and aldehyde once formed.[67a] Thus, the stereochemical composition of the alkenes obtained from a Wittig reaction generally reflected the stereochemical mix of the OPAs.[36] However, there are a few known instances of reversal,[17, 41] but only in the case of *cis*-oxaphosphetanes, thereby enhancing the proportion of *E*-alkene obtained. These reversals, mainly detected through $^{31}$P NMR detection of OPAs and alkene product analysis, occurred in the following cases:

1. *Aromatic aldehydes* with triphenylphosphonium nonstabilized ylides showed reversals. Reitz et al.[57] found that in the presence of Li salts $Ph_3P{=}CHC_3H_7$ and benzaldehyde afforded a cis:trans OPA ratio of 3.8:1 which, however, resulted in a final *Z*:*E* alkene ratio of 1.5:1. Thus, *cis*-OPA disappeared relative to trans. This "stereochemical drift" did not occur when the reaction was free of lithium salts, only the *cis*-OPA being detected and the final

$Z:E$ ratio being 96:4. Further, when the threo and erythro HPSs were converted to OPAs in the absence of Li the erythro HPS afforded a 97:3 $Z:E$ ratio of alkenes and the threo HPS afforded a 2:98 $Z:E$ ratio of alkenes, indicating virtually no drift. Piskala et al.[68] were able to trap both reactants resulting from reversal of OPA formation, the released benzaldehyde by adding a new ylide, and the released ylide by the addition of a new aldehyde.

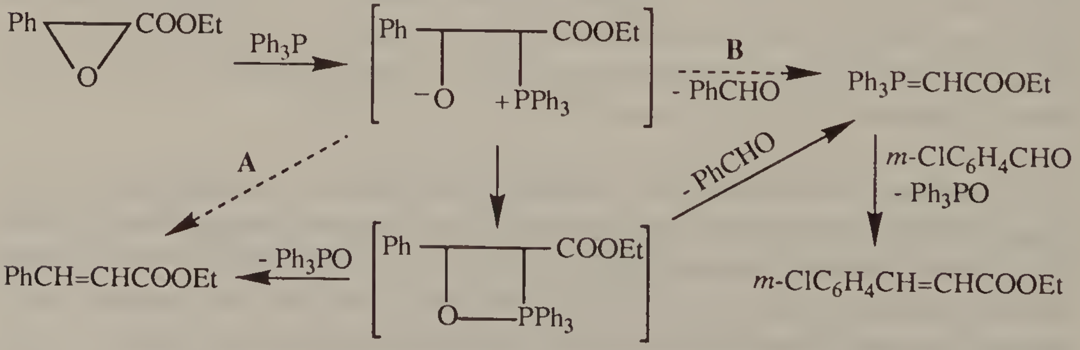
2. Stereochemical drift occurred when *trialkylphosphoniumalkylides* (the ethylide and the butylide) were reacted with tertiary aldehydes.[57,67,69] Drift did not occur with diphenylalkylphosphonium ylides,[59,67] with but one known exception.[65]

3. Stereochemical drift occurred in reactions with *tertiary aldehydes* ($R_3CCHO$),[69] but it did not occur with aliphatic aldehydes of the type $RCH_2CHO$ or $R_2CHCHO$, nor with ketones.[46] One instance of drift with an aliphatic aldehyde was proven in a reaction with a triphenylphosphonium $\gamma$-oxidoalkylide.[70]

4. Reversal occurred in a reaction which must have involved carbethoxymethylenetriphenylphosphorane with aromatic aldehydes.[17,58] However, an erythro HPS corresponding to an ester-stabilized ylide and carrying a deuterium label alpha to phosphorus was converted to mixture of $Z$ and $E$ alkene in which *all* of the $E$ alkene was devoid of deuterium, indicating that Wittig reaction reversal probably did not occur in order to produce the "wrong" $E$-stereoisomer.[29]

Reversibility of OPA formation in those special instances listed above and involving nonstabilized ylides has been demonstrated to occur only in the presence of lithium cation or when *both* stereoisomeric OPAs were present.[37] When only one OPA was present or when a nonlithium base was used, there was essentially no drift from cis to trans.[37]

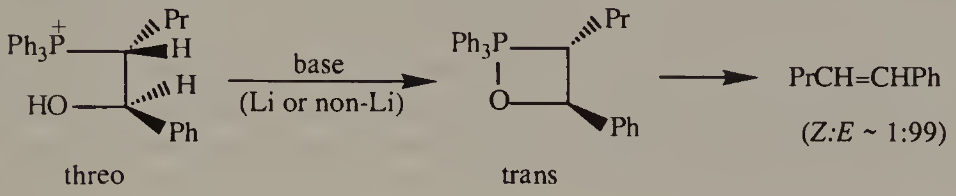
Reversibility of OPA formation also has been demonstrated through the use of "crossover" experiments, although the OPAs usually were not generated in a Wittig reaction. Early work by Speziale and Bissing[17] showed that reaction of ethyl phenylglycidates with tributyl or triphenylphosphine in the presence of *m*-chlorobenzaldehyde afforded both ethyl cinnamate and ethyl *m*-chlorocinnamate (Eq. 9.11). They proposed that the reaction proceeded to a betaine which



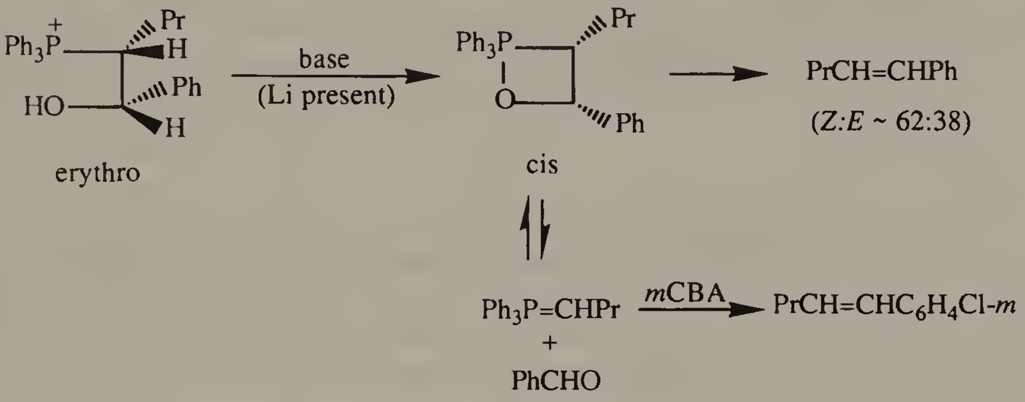
(9.11)

could decompose directly to cinnamate (path A) or could dissociate to ylide and benzaldehyde (path B) (via dotted arrow routes). To the extent that path B occurred, some of the resulting ylide would be trapped by the more electrophilic *m*-chlorobenzaldehyde to produce *m*-chlorocinnamate. This interpretation is still valid if the OPA also is incorporated into the process (solid arrow routes).

Reversal of OPA formation also has been demonstrated for nonstabilized ylides by deprotonation of the corresponding HPS as shown in Eqs. 9.12 and 9.13.[37, 38, 68] Thus, the threo isomer with either a lithium or nonlithium base



(9.12)

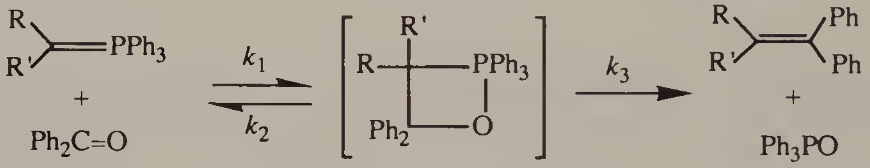


(9.13)

afforded almost exclusively *E*-alkene, and in the presence of *p*-chlorobenzaldehyde no crossover product was obtained (Eq. 9.12). In the presence of a lithium base the erythro isomer gave a $Z$:$E$ ratio of 62:38, plus crossover product (Eq. 9.13). The erythro isomer, in the presence of a nonlithium base, afforded almost exclusively *Z*-alkene and little crossover product (there should have been no crossover product in this experiment!). A $\gamma$-oxidoalkyltriphenylphosphonium also produced crossover products.[70] In summary, the reversibility of OPA formation (stereochemical drift) generally occurred for *cis*-OPAs and only in the presence of lithium cation or the *trans*-OPA, and was detectable by a change in the $Z$:$E$ alkene mix or by the obtaining of crossover product.

Finally, the question of the relative stability of *cis*- and *trans*-OPAs must be addressed. Although there is no evidence available regarding the OPAs for stabilized or semistabilized ylides, due to the general inability to detect them in a reaction, the evidence regarding OPAs from nonstabilized ylides is that the trans is more stable than the cis,[4, 36, 37] contrary to Schlosser's earlier conclusions.[34] In view of the stereochemical drift previously demonstrated, this implies that some thermodynamic control may be exerted within certain Wittig reactions. It also has been demonstrated that *cis*-OPAs decompose to alkenes and phosphine oxides faster than do *trans*-OPAs.[36, 37]

***9.1.2.3 Kinetics of the Wittig Reaction.*** Kinetic studies first were accomplished for the Wittig reaction using stabilized ylides (ester ylides and fluorenylides) in reaction with substituted benzaldehydes.[17, 71–75] Reactions were second order, first order in each reactant, and ylide disappeared at the same rate as alkene appeared. Hammett correlations indicated $\rho$ values for the benzaldehyde substituents ranging from $+2.5$ to 2.9, indicating that the carbonyl group was undergoing a nucleophilic attack by ylide carbanion in the slow step. Substituent effects exerted by phosphorus substituents were consistent with this same description. Based mainly on crossover experimental results for the reaction of ester ylides with benzaldehyde,[17] which now must be viewed with caution,[58] the rate sequence was $k_3 > k_2 > k_1$ (Eq. 9.14, R = H; R′ = COOEt; betaine in place of OPA). More recent interpretations place $k_2 \sim 0$.[58] The early work[17] indicated a modest solvent effect with faster rates in more polar solvents, consistent with a betaine intermediate. However, later work[72] showed rate decreases in polar solvents, and entropy calculations indicated highly ordered transition states, consistent with an oxaphosphetane intermediate. In all cases use of alcohol solvents resulted in major rate increases.



(9.14)

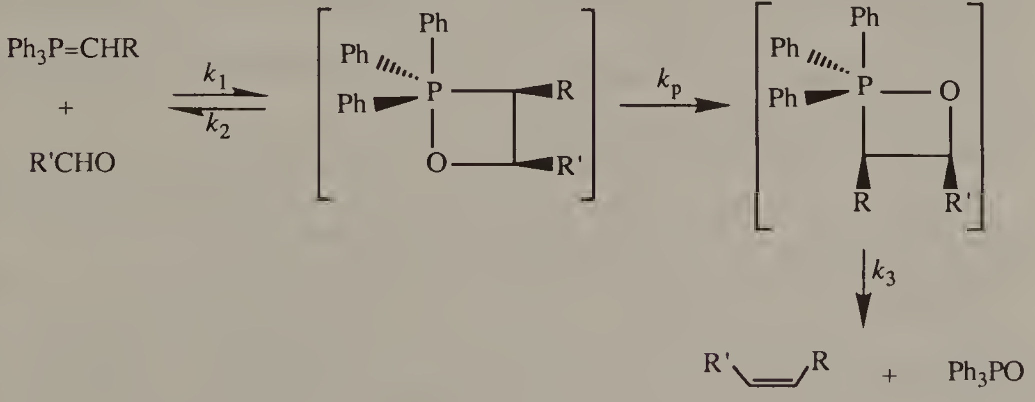
For nonstabilized ylides the Hammett correlations have revealed $\rho$ values from $+0.59$ to 1.40 for reactions with benzaldehydes or benzophenones.[25, 56, 68, 76] The Yamataka group[76] also determined a 1.053 kinetic isotope effect using benzophenone-$C^{14}$, leading them to verify that the bonding at the carbonyl carbon was changing in the rate-determining step. They suggested that the rate sequence for the reaction of benzophenone with triphenylphosphonium-isopropylide was $k_1 > k_2 \sim k_3$, a conclusion reached earlier by Fliszar et al.[77] using the methylide [Eq. 9.14, R = R′ = H]. Piskala et al.[68] demonstrated that carbonyl reactant disappeared faster than alkene appeared, and therefore an intermediate must be accumulating. The Maryanoff group reported several kinetic studies using benzaldehyde or pivaldehyde with nonstabilized ylides,[4] and although they could not determine $k_1$ for the formation of both stereoisomeric OPAs, they were able to determine that $k_2$ was faster for the *cis*-OPA than for the trans, and that the $k_3$ ratio for *cis*- and *trans*-OPA decomposition was close to 1.0. Interestingly, no large differences were observed in reversal or decomposition rates between trialkylphosphonium and triphenylphosphonium ylides.

In recent reports Soderquist and Anderson[78] and Kawashima et al.[55] provided kinetic evidence on the decomposition of OPA to alkene. The decomposition was first order, for carbonyl substituents the $\rho$ value was negative, there was a small solvent effect, and $\Delta S^\dagger$ values were small and negative, all indicating a slightly polar transition state for OPA opening. In the OPA for alkyl trimethylsilyl ketones, the geometry is consistent with the Vedejs model leading to $>96\%$ $Z$-alkene formation.[78]

There have been three recent determinations of the kinetics of the reaction of semistabilized ylides (benzylides), and those with benzaldehydes[79-81] showed the reaction to be second order, first order in each component. Electron-withdrawing substituents on the aldehyde were found to enhance the reaction rate ($\rho = +1.38$ to $+2.77$), consistent with the carbonyl group undergoing nucleophilic attack, and consistent with the results for stabilized and nonstabilized ylides. However, the first group reported that the $\rho$ value for the Wittig reaction of substituted benzylidenetriphenylphosphoranes was $+3.31$, contrary to expectations for a reaction involving nucleophilic attack of ylide carbanion on carbonyl carbon. It is difficult to imagine how $\rho$ values could be positive for both the carbonyl and ylide reactants, especially in view of the characteristics of nonstabilized and stabilized ylides, and the authors offered no rational mechanistic explanation. Use of benzaldehydes revealed a kinetic isotope effect at the carbonyl carbon, indicating that the carbonyl bonding was changing in the slow step of the reaction.[81]

## 9.2 CURRENT MECHANISMS FOR THE WITTIG REACTION

Almost 40 years of research has been invested in the effort to elucidate the mechanism of the Wittig reaction, with the underlying hope on the part of many that a single mechanism could account for the tremendous wealth of experimental observations. However, by now it seems clear that no single mechanism, with all its transition state and stereochemical intricacies, will suffice.[36] However, a single "general mechanism" such as represented by Eq. 9.15 does encompass the behavior of the three classes of ylides, with differences between them lying in two major aspects—a difference in rate-determining step and detailed structure of the transition state to the OPA. The details of these two



(9.15)

aspects seem to account for the various stereochemical outcomes for the three classes. This section describes mechanisms which seem to account for the known information (as of the date of writing this book) separately for nonstabilized ylides, stabilized ylides, and semistabilized ylides. Readers should refer to Table 8.1 (page 225) for a tabulation of the known stereochemical effects of structural changes made in reactants mentioned in the following sections.

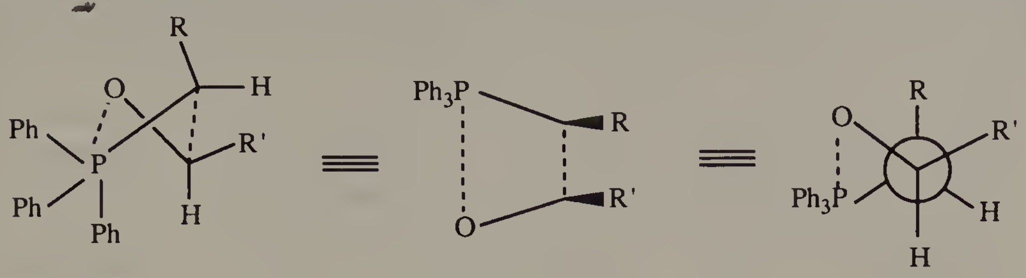
### 9.2.1 Nonstabilized Ylides

The normal reaction of nonstabilized triphenylphosphonium ylides with aldehydes in a salt-free medium, and often just lithium-free, presently is best described (i.e., best explains the experimental observations) as a two-step reaction involving the formation of oxaphosphetanes with apical P–O bonds in an asynchronous four-centered reaction, with the carbanion–carbonyl carbon bond formation sufficiently ahead of the P–O bond formation in the transition state to maintain approximately tetrahedral geometry about the phosphorus atom, but not so far ahead as to create significant betaine character for the transition state. Thus, the transition state is reactant-like, occurring early along the reaction coordinate. Kinetic control normally prevails, leading in a stereoselective reaction to *dominant* formation of *cis*-OPAs ($k_{1\,\mathrm{cis}} > k_{1\,\mathrm{trans}}$), and normally there is no reversal of OPA formation ($k_2 \sim 0$), resulting in *dominant* (but not exclusive) production of *Z*-alkenes (Eq. 9.15).[34] The OPA probably undergoes a pseudorotation ($k_p$) before decomposition to phosphine oxide and alkene in the final step, but the rotation is not rate controlling ($k_p > k_3$). The rate of the decomposition ($k_3$) may be similar for the two isomeric OPAs. The decomposition of the OPAs to products probably is slightly asynchronous.

This mechanism is consistent with the major facts surrounding this particular reaction:

1. The carbonyl group is acting as an electrophile.[25, 56, 75]
2. The ylide is acting as a nucleophile.
3. There is no indication of radical involvement on this pathway.
4. The bonding at the carbonyl carbon is changing in the rate-determining step.[76]
5. An intermediate is accumulating in the reaction.[68] OPAs can be observed during the course of the reaction.[12, 37, 56, 78]
6. Product compositions correspond to the ratio of OPAs present in the reactions (i.e., the reaction is under kinetic control) so the stereochemistry is determined during initial carbon–carbon bond formation.[36, 57]
7. For the reaction of a disubstituted ylide with a symmetrical ketone (i.e., only one OPA can be formed) $k_1 > k_3$, $k_1 > k_2$, $k_3 \geq k_2$ (Eq. 9.15).[76]
8. From a kinetic study for a reaction that was reversible, $k_3$ is similar for *cis*- and *trans*-OPAs, $k_2$ is larger for *cis*- than *trans*-OPAs, $k_2 \geq k_3$ for *cis*-OPAs, and $k_3 > k_2$ for *trans*-OPAs (Eq. 9.15).[4]

The transition state for OPA formation probably has a slightly nonplanar shape (**2**) with the major potential steric repulsion being between an "axial" R′



**2**

group and a P-phenyl group (a 1,3-interaction), repulsion between R and R′ (a 1,2-interaction) being less significant in this shape, especially in that they are oriented axially and equatorially, respectively, about the forming oxaphosphetane ring.[36] The rotational angles of the three phenyl groups may be a factor in the precise geometry of the transition state.[35] This transition state proposal also accommodates the major stereochemical facts:

1. Triphenylphosphoniumalkylides normally react stereoselectively with aliphatic aldehydes to produce high $Z:E$ ratios of alkenes, approaching 99 : 1.[34, 36, 67, 82]

2. The use of low temperatures enhances the kinetic selectivity in formation of the transition state, leading to very high $Z:E$ ratios.[83]

3. Replacement of a single P-phenyl group with a nontertiary alkyl group (a *t*-butyl group gave about the same high degree of *Z*-stereoselectivity as did the phenyl group[67]) results in removing the dominant phenyl———R′ 1,3-interaction, thus allowing the recessive R———R′ 1,2-interaction to become important and thereby favoring the more stable *trans*-OPA.[36] In that instance, the reaction is not stereoselective, producing a considerable proportion of *E*-alkene. A similar result can be achieved by replacing two or three of the phenyl groups with alkyl groups.[67]

4. The use of bulky groups on phosphorus[82, 84, 85] increases the importance of 1,3-interactions, leading to very high *Z*-stereoselectivities.

5. The use of bulky aldehydes (e.g., pivaldehyde and other tertiary aldehydes) increases the importance of 1,3-interactions, and therefore produces high $Z:E$ selectivities.[67]

6. The use of unsymmetrical ketones leads to trisubstituted alkenes with the bulky groups oriented *Z*.[78]

7. The use of ketones with similar-sized substituents on the carbonyl is a much closer call, but for those with disparate-sized substituents, and especially with different numbers of α-hydrogens, the balance between the 1,2- and 1,3-interactions is controlling.[86]

There are several exceptions to the general mechanistic and transition state considerations described above.

1. Reactions with aromatic aldehydes and tertiary aliphatic aldehydes occasionally operate under thermodynamic control, with reversible formation of OPAs.[46,68,87] Thus, *trans*-OPAs dominate and high *E*-stereoselectivities have been achieved. The same result was achieved with ylides containing anionic groups on their aliphatic chains, probably also due to reversibility of the OPA formation step.[70] The cause for the reversibility in reactions with aromatic and tertiary aliphatic aldehydes is unknown, but may be the result of simply too much steric congestion. In the case of the anionic ylides, it may be due to competing complexation of the anionic group with phosphorus, especially since there clearly is a distance factor. The exact mechanism(s) of OPA interconversion have not been proven, although in some instances retro-Wittig reactions have been documented through crossover experiments. But in others there is no direct evidence.

2. Although it is clear that the presence of lithium cation decreases *Z*-stereoselectivity,[37,86] it is not clear how. Dilution of reactions containing lithium, or otherwise complexing the lithium cations, can significantly reverse the "lithium effect"[86] and restore *Z*-stereoselectivity. It has been argued that the lithium effect is on initial OPA formation, not on OPA equilibration,[4] but the nature thereof is unclear. Lithium bromide is known to react with OPAs under certain conditions to afford betaine-LiBr complexes.[46]

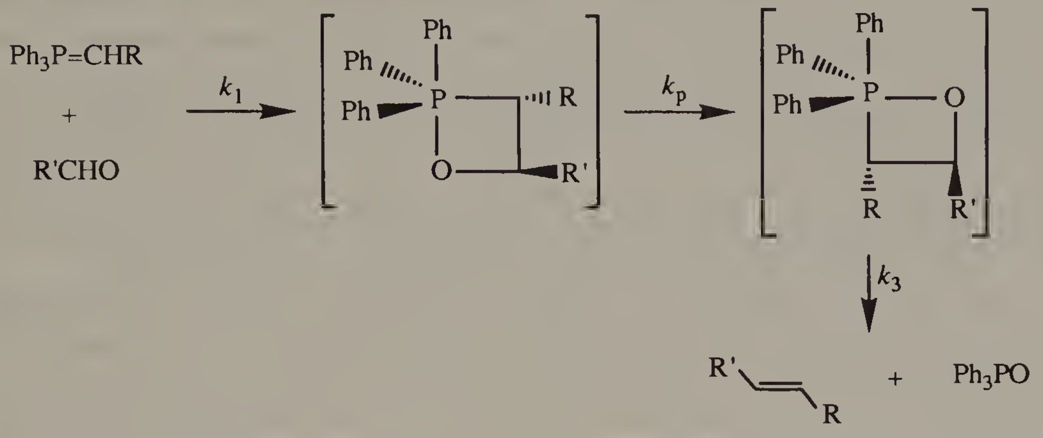
3. The incorporation of the DBP group on the phosphorus of a nonstabilized ylide structure results in increasingly *E*-stereoselective reactions, which are not the result of OPA reversal (i.e., the reactions remain under kinetic control).[59,88] The 94° C–P–C bond angle in DBP produces a significant ring strain advantage to the OPA structure over the ylide reactant, and reduction of 1,3-interactions in the transition state makes the latter more OPA-like, thus favoring formation of the *trans*-OPA. With the third phosphorus substituent being phenyl, the normally high $Z:E$ ratio dropped to $1:1$ with primary aldehydes, and with the substituent being ethyl removal of additional 1,3-interactions resulted in a complete reversal of *Z*-stereoselectivity, to a $Z:E$ ratio of $1:18$.[67].

4. Protic polar solvents decrease the *Z*-stereoselectivity, perhaps via the same unknown mechanism as do lithium cations, both acting as Lewis acids.[83,89]

In a thoughtful statement Vedejs[36] stated that "due to the highly congested environment of the four-center Wittig transition state, all of the steric effects are interdependent. The relative bond angles and the shape, rather than the bulk, of substituents can be critical, . . . ." The data and conclusions cited above testify to the appropriateness of that statement.

### 9.2.2 Stabilized Ylides

The normal reaction of stabilized triphenylphosphonium ylides with aldehydes, invariably in the absence of extraneous ions, normally produces mainly *E*-alkenes. It is best portrayed as involving nucleophilic attack of the ylide carbanion on the carbonyl carbon in a slow step to produce an oxaphosphetane (OPA) for which the transition state is late, product-like in structure (i.e., nearly planar), with a trigonal bipyramidal phosphorus. The reaction is completed by rapid decomposition of the OPA to a phosphine oxide and an alkene (Eq. 9.16).



(9.16)

This mechanism is consistent with the following experimental facts:

1. The reactions are second order, first order in each reactant, with alkene appearing at the same rate as ylide disappeared.[17]
2. The $\rho$ values for carbonyl reactants are positive[17,71,73,74] and for the ylides are negative.[71]
3. The rates of reaction are larger for trialkylphosphonium ylides than for triphenylphosphonium ylides in accord with the increased basicity and nucleophilicity of the former.[17,77,90]
4. Solvent effects are not strong, indicating the absence of a highly polar transition state,[71,75] and the entropy of activation is large,[72] indicating a highly ordered transition state.
5. The reactions generally are under kinetic control,[29] with the stereochemistry of the intermediate OPA being determined during initial C–C bond formation.
6. The *trans*-OPA is expected, but not proved, to be the most stable, leading to dominant *E*-stereoselectivity.
7. There has been no detection of OPAs or betaines in these reactions[29,45,58] consistent with the first step of the Wittig reaction being the slow step ($k_3 > k_1$). It seems that once formed OPAs from the slower Wittig reactions of stabilized ylides proceed exceedingly rapidly to alkenes, even at − 78°C![29]

The products from Wittig reactions with stabilized ylides, alkenes and phosphine oxides, also have been produced from the reaction of oxiranes and phosphines[17] and the deprotonation of HPSs.[29,67] In both instances the reactions presumably first afforded betaines which proceeded rapidly to alkene products. Although the involvement of betaines is mandatory in these two alternate routes, there has been no evidence whether the betaines proceeded directly to products, or whether they proceeded to the proposed but undetectable OPA intermediates. These two alternate routes have been used to detect reaction reversibility by performing crossover experiments with chlorobenzaldehydes. When primary or secondary aliphatic aldehyde structural elements were incorporated in the betaine structure, about 2% crossover products were detected.[67] Those cases incorporating benzaldehyde or tertiary aliphatic aldehyde elements exhibited about 5%[67] crossover reactions and these are the same and only carbonyl compounds that exhibited reversal of OPA formation using nonstabilized ylides (see Section 9.2.1). It seems safe to conclude that reversibility is not a significant factor in the Wittig reaction of stabilized ylides.

Previously it was claimed,[91, 17] mainly on the basis of crossover results, that the *E*-stereoselectivity of stabilized ylides was due to faster rates of formation of threo betaines, slower rates of reversal of threo betaines, and faster rates of decomposition of threo betaines to products. If the words "threo betaine" are replaced by "*trans*-oxaphosphetane (OPA)" the first and second conclusion still seem reasonable, but with reversal being virtually nonexistent. Many of the early studies on reversibility of the Wittig reaction of stabilized ylides were conducted in alcoholic solvents and at much higher temperatures, which clearly are atypical of usual Wittig reaction conditions (often at − 78°C and in aprotic nonpolar solvents) and atypical in their influence on Wittig reactions (see Section 8.1.5.2).[17, 29, 58, 67] In addition, isomerization of alkene products renders some of the conclusions drawn from the crossover results questionable.[17]

There are not drastic changes in the alkene $E:Z$ ratios when alkyl groups gradually replace phenyl groups in stabilized ylides, and even though the results in the literature are somewhat mixed, the direction of change generally is to increase the *E*-stereoselectivity by such substitution,[17, 58, 92, 93] perhaps by a steric effect.[94]

### 9.2.3 Semistabilized Ylides

The normal reaction of semistabilized triphenylphosphonium ylides (i.e., benzylides and allylides) with aldehydes produces mixtures of *Z*- and *E*-alkenes nonstereoselectively. The reaction is best portrayed as involving nucleophilic attack of the ylide carbanion on the carbonyl carbon, probably in the slow step of the reaction, to form OPA intermediates (cis and trans) which then decompose to alkenes and triphenylphosphine oxide.

This mechanism is consistent with the following facts:

1. No betaines have been detected in such reactions,[37, 49, 66] nor in alternate routes such as reaction of oxiranes with phosphines[84] or in deprotonation of HPSs.[58]

2. OPAs normally are not detectable in this Wittig reaction,[37, 65] even when electron-donating groups are substituted on phosphorus,[45] nor in HPS altern-

ate routes,[58] but recently have been detected only in the case of a DBP-substituted ylide, in which case they are especially stabilized by the 94° C–P–C ring angle.[58] Further, attempts to chemically trap OPAs with hydrogen chloride, which were successful with OPAs from nonstablilized ylides, were unsuccessful.[45]

3. OPAs are known to stereospecifically decompose to alkenes, *cis*-OPAs affording *Z*-alkenes and *trans*-OPAs affording *E*-alkenes.[58]

4. OPAs do not undergo interconversion,[58] so the reaction is under kinetic control.[36, 66]

5. There is little or no reversal of the Wittig reaction, as demonstrated by $^{31}P$ NMR analyses,[58] by stereospecific conversion of erythro and threo HPSs to *Z*- and *E*-alkenes,[30, 58] respectively, and by the absence of crossover reactions.[30, 66]

6. In the three kinetic studies which have been reported[79–81] the reaction was shown to be second order, and a positive $\rho$ value was obtained for the carbonyl reactant as expected.

7. OPAs normally disappear too fast to be detected,[58] similar to OPAs from the stabilized ylides, indicating that OPA decomposition is faster than OPA formation.

8. Benzaldehydes show a kinetic isotope effect at the carbonyl carbon.[81]

In earlier work[95] it was shown that in alcoholic media deprotonation of HPSs in the presence of chlorobenzaldehydes produced crossover products. However, these all involved benzaldehyde as the actual or incipient carbonyl compound, and it is known that such reactions are atypical in exhibiting reversibility.[36, 37] In these instances, the reactions exhibited expected stereospecificity with *erythro*-HPS affording noncrossover *Z*-alkene, crossover *Z*- and *E*-alkene, but no noncrossover *E*-alkene.[95] In the presence of lithium salts crossover products have been obtained with allylides, and $Z:E$ ratios were increased slightly from lithium-free reactions.[30, 65, 66] However, in the absence of lithium salts, no crossover products were formed.[65] Thus, lithium cation again is observed to encourage/permit reversibility of OPA formation as with nonstabilized ylides. Iodide ion also increased the proportion of *Z*-alkene.[30] However, the source of the lithium and iodide effects are unknown.

There is considerable uncertainty about the structure of the transition state to the OPA for semistabilized ylides, but it is clear that effects governing its structure are very delicately balanced. In addition there is no evidence regarding the relative timing of C–C and P–O bond formation. The stereochemical outcomes can be accounted for, however. A puckered (nonplanar) transition state with phenyl or vinyl carbanion substituents (R), such as proposed for nonstabilized ylides (**2**), (page 293) and occurring early along the reaction coordinate, would be expected to have fewer 1,3-interactions between the substituent (R) and *P*-phenyl groups because of the planarity of the trigonal carbon in R compared to the tetrahedral carbon in nonstabilized ylides. Thus, there should be less preference for cis geometry in the OPA, and higher proportions of *E*-alkenes would be expected than for nonstabilized ylides, as is observed. Alternatively, the transition state could be much later than for nonstabilized ylides, more like that for stabilized ylides, leading to increased planarity and enhanced 1,2-interactions, thereby producing enhanced proportions of *trans*-OPA and *E*-alkene, as is observed.

Phosphorus substituent effects on the stereoselectivity of the reaction of semistabilized ylides, mainly benzylides, with aliphatic and aromatic aldehydes are in accord with the mechanism described above. Further, these effects permit great flexibility in the stereochemical outcome of a Wittig reaction ranging from normal nonselectivity to dominant *Z*- or dominant *E*-alkenes. Increasing the steric requirements about phosphorus, usually by placing *o*-substituents on one or more of the phenyl groups, favors the production of *Z*-alkenes, regardless of the electronic effects.[82, 84, 85] Lowering the temperature increases the *Z*:*E* ratio even more in this kinetically controlled reaction to the point of *Z*-stereoselectivity.[82, 83] Increased steric requirements favor an early and/or nonplanar transition state because of increased 1,3-interactions. Decreasing the steric requirements of the P-substituents by using DBP as two of the P-substituents results in the opposite effect, nearly exclusive *E*-alkene production.[59] This too is the result of kinetic control in OPA formation, resulting from the stability added to the OPA by the 94° C–P–C angle of the DBP group.[58] Replacement of a phenyl group on phosphorus with a nontertiary alkyl group apparently reduces the steric requirements of the OPA as well because somewhat enhanced *E*-alkene proportions result.[58, 65]

Electronic effects also can be used to influence the stereochemistry of the Wittig reaction of semistabilized ylides. Electron-donating substituents on phosphorus, such as *p*-methoxyphenyl groups and alkyl groups, increase the proportion of *E*-alkenes, whereas electron-withdrawing groups, such as *p*-chlorophenyl, increase the proportion of *Z*-alkenes.[96] Increasing the electron density on phosphorus probably has the effect of making the transition state later (i.e., raising the energy of OPA formation), thus increasing the influence of 1,2 interactions and favoring the *trans*-OPA and *E*-alkene. Using the most nucleophilic of two possible ylides carrying the same *P*-substituents results in the larger proportions of *Z*-alkenes (Eq. 9.17).[82, 96] Making the ylide more nucleophilic and facilitating P–O bond formation by lowering the electron

$$R_3P{=}CHC_6H_4\text{-}X(p) \;+\; (p)Y\text{-}C_6H_4CHO \longrightarrow Y\text{-}C_6H_4CH{=}CHC_6H_4\text{-}X \qquad (9.17)$$

| R | X | Y | *Z*:*E* ratio |
|---|---|---|---|
| H | OMe | $NO_2$ | 0.79 |
| H | $NO_2$ | OMe | 0.35 |
| Cl | OMe | $NO_2$ | 4.10 |
| Cl | $NO_2$ | OMe | 1.10 |

density on phosphorus both probably make the transition state earlier, increasing the importance of 1,3 interactions and favoring the *cis*-OPA and *Z*-alkene. Increasing the electrophilicity of the carbonyl reactant has the same effect.[81, 96]

### 9.2.4 Unanswered Questions About the Mechanism of the Wittig Reaction

Although a great deal of information has been acquired regarding the mechanism of the Wittig reaction of the three classes of ylides (nonstabilized, stabilized, semistabilized), it has been acquired in the face of two major problems. First, the extensive variety of reaction conditions employed had made it difficult to apply what has been learned in one experimental circumstance to others. In the future, additional data should be acquired in nonpolar aprotic solvents, initially at least in the absence of lithium ions, and preferably in the absence of all ions. Second, there have been two eras of mechanistic studies, the first was when virtually all researchers assumed that betaines were the key and perhaps only intermediates, even though none had been detected! The second era dawned when it was discovered that oxaphosphetanes could be detected in the Wittig reaction and their appearance and disappearance could be monitored. In addition, the question of normal reaction reversibility was clarified. It has been difficult to compare data obtained during the first era with that of the second.

A number of unanswered questions regarding the Wittig reaction remain:

1. Although it is clear that lithium affects the stereochemical outcome of some Wittig reactions, perhaps via betaine·LiX complexes, there is no definitive information about how this occurs.

2. The specific reason for the reversibility of the reactions of all ylides with benzaldehydes and some ylides with tertiary aliphatic aldehydes is unknown.

3. The mechanism of "stereochemical drift" (i.e., OPA interconversion) needs additional attention. Some or all may occur via a "retro-Wittig" reaction, but this has not been proven to be the only route. Do phosphine oxides have an effect on this process?

4. Information needs to be obtained regarding the values for $k_1$ and $k_2$ for the reaction of nonstabilized ylides (Eq. 9.15).

5. Evidence should be acquired regarding the nature of the transition state for OPA formation with semistabilized ylides.

6. Theoretical studies on the possible geometries of transition states for OPA formation from "real" nonstabilized ylides in solvents would be helpful in view of extant proposals.

7. Evidence should be acquired to prove whether betaines generated from oxiranes and phosphines, or from HPSs and base, proceed through OPAs in the production of alkenes and in the regeneration of ylides (i.e., in the crossover experiments), or whether the betaines proceed directly to products or to ylides.

In view of these, and perhaps other, open questions, it may have been premature for Seebach to have stated that "It appears that the mechanism has now been clarified once and for all".[5] However, it does appear that a rather stable platform of mechanisms has been achieved which offer reasonable explanations for the course of the various Wittig reactions.

## 9.3 CALCULATIONS ON THE MECHANISM OF THE WITTIG REACTION

There have been 11 different calculations reported regarding various aspects of the Wittig reaction, starting in 1973 and most recently in 1992. A considerable measure of agreement has materialized from these reports, and the results will be described in terms of separate issues surrounding the mechanism proposals. These calculations, both semiempirical and ab initio, usually have been performed on the mythical reaction $H_3P{=}CH_2 + H_2CO \rightarrow CH_2{=}CH_2 + H_3PO$,[42,43,60,62,63,97] but a few have used larger molecules.[32,44,61,98,99] The normal reaction can be adequately represented by the free energy profile shown in Figure 9.1, which interestingly is almost identical to that proposed by this author in 1966,[100] but with the important substitution of oxaphosphetane for betaine! The initial step in the reaction has a very low energy of activation, with the overall driving force for the reaction being the exothermic production[62] of the highly stabilized phosphine oxide.

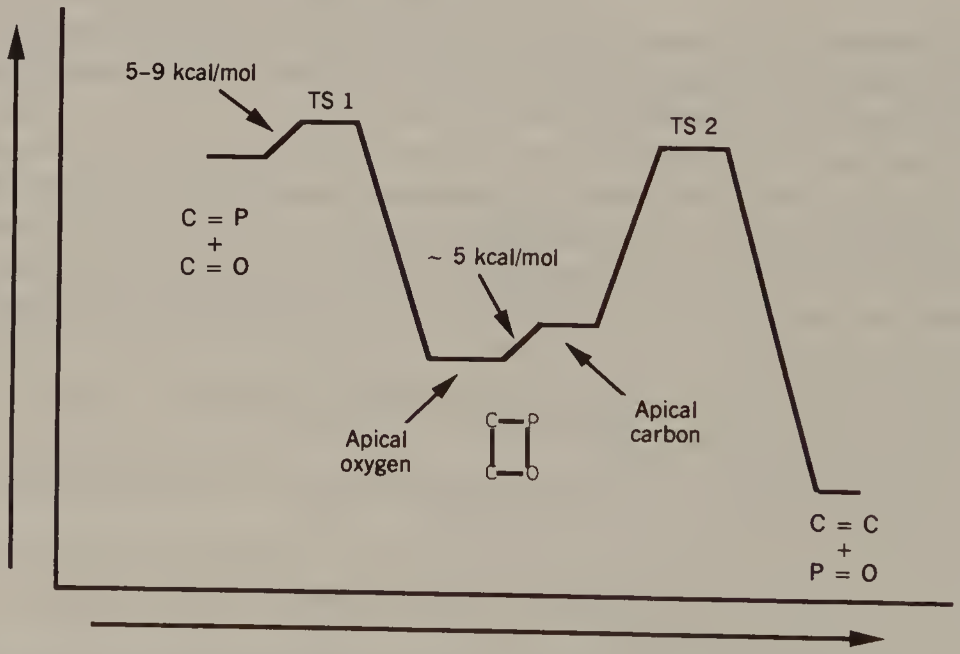


**Figure 9.1** Theoretical free-energy profile for a Wittig reaction of a nonstabilized ylide with an aldehyde.

Vertical scale: energy. Horizontal scale: reaction coordinate.

Other than the first calculation which assumed that the betaine was an intermediate and described the reaction from that point forward,[97] even then reporting that the OPA was 66–89 kcal/mol more stable than the betaine, calculations unanimously indicated that the betaine was not an intermediate in the reaction,[32, 42–44, 62, 63, 85, 98] in agreement with experiment. The energy of activation for the first step was uniformly found to be small, 5–9 kcal/mol,[42–44, 63, 98] consistent with the observation that many Wittig reactions occur extremely rapidly at very low temperatures. An oxaphosphetane (OPA) was found to be the intermediate in the reaction with a deep energy well (30–40 kcal/mol).[43, 63] The OPA has been determined to be close to planar[43, 44, 61, 63, 98] with its formation viewed as synchronous by some[42, 43] but slightly asynchronous by others.[32, 98, 99] Rzepa concluded that the mythical OPA transition state was planar, but that as substituents were added to phosphorus it became nonplanar and its formation less synchronous,[44] but Mari et al.[32, 98] concluded that the transition state was planar and its formation was asynchronous. Further, the inductive effect of phosphorus substituents was proposed to stabilize the positive phosphorus center, although the conclusion that phenyl groups should be more effective than methyl groups in that regard is in error (see Section 8.1.2).

The structure of the OPA has been of interest. All have concluded that an initial OPA is formed with an apical P–O bond, and that a rotation is required to place the former ylidic carbon in the apical position prior to decomposition, the P–C bond lengthening in the process.[62] The energy difference between the two OPA rotamers has been calculated to lie over a small range (4.2–10 kcal/mol,[42–44, 60, 63]), with the apical P–O rotamer being of lower energy. Mari et al.[98] have calculated the energy difference between two stereoisomeric OPAs (cis and trans) to be 4–6 kcal/mol, with the trans being of lower energy consistent with experimental observations.

The energy requirement for decomposition of the OPA to products has been calculated to be 15–26 kcal/mol,[42, 43, 63] considerably less than that for the reverse reaction to starting materials. No clue has been provided as to why benzaldehydes and tertiary aliphatic aldehydes frequently undergo reversible formation of OPAs. Trindle et al.[97] proposed that in OPA decomposition P–C cleavage was ahead of C–O cleavage, contrary to the more recent proposal of Kawashima et al.[55]

Interestingly, Trindle et al.[97] calculated that the OPA was far more stable than the usual betaine (P–C–C–O) considered to be the intermediate at that time, but that this betaine also was more stable than that (P–O–C–C) proposed by Bestmann[26] to account for stereoselectivities of the various classes of ylides, and more stable than an O–P–C–C betaine.

The McEwen group[32, 99] resurrected the earlier proposal for an antiperiplanar orientation for solvated betaine transition states to OPAs (in polar solvents), with the erythro configuration being of lower energy than the threo configuration, thereby favoring the dominant formation of *Z*-alkene.

## REVIEWS

**1966** Johnson, A. Wm., *Ylid Chemistry*, Academic: New York; Chapter 4, pp. 152–192. A full review of the Wittig reaction mechanism and stereochemistry.

**1983** Morris, D. G. In *Survey of Progress in Chemistry*, Wubbels G. G., Ed.; Butterworths: London; Vol. 10, pp. 200–215. A review of the Wittig reaction, including a discussion of mechanism and stereochemistry.

**1989** Maryanoff, B. E.; Reitz, A. B. *Chem. Revs. 89*, 863–927. A review of the mechanism and stereochemistry of the Wittig reaction.

## REFERENCES

[1] Trippett, S. *Pure and Appl. Chem.* **1964**, *9*, 268.

[2] Johnson, A. Wm. *Ylid Chemistry*; Academic: New York, 1966; p. 187.

[3] Gosney, I.; Rowley, A. G. In *Organophosphorus Reagents in Organic Synthesis*; Cadogan, J. I. G.; Ed.; Academic: London, 1979, p. 26.

[4] Maryanoff, B. E.; Reitz, A. B., *Chem. Revs.* **1989**, *89*, 864.

[5] Seebach, D. *Angew. Chem.* **1990**, *29*, 1320; ref. 338(a).

[6] Wittig, G.; Geissler, G. *Liebigs Ann. Chem.* **1953**, *580*, 44.

[7] Staudinger, H.; Meyer, J. *Helv. Chim. Acta* **1919**, *2*, 635.

[8] Wittig, G.; Schollkopf, U. *Chem. Ber.* **1954**, *87*, 1318.

[9] Wittig, G.; Haag, W. *Chem. Ber.* **1955**, *88*, 1654.

[10] Blade-Font, A.; Vanderwerf, C. A.; McEwen, W. E. *J. Am. Chem. Soc.* **1960**, *82*, 2396.

[11] Horner, L.; Winkler, H. *Tetrahedron Lett.* **1964**, 3265.

[12] Vedejs, E.; Snoble, K. A. J. *J. Am. Chem. Soc.* **1973**, *95*, 5778.

[13] Maryanoff, B. E.; Reitz, A. B.; Mutter, M. S.; Inners, R. R.; Alinand, H. R. *J. Am. Chem. Soc.* **1985**, *107*, 1068.

[14] Denney, D. B.; Boskin, M. J. *Chem. Ind.* **1959**, 330.

[15] Bissing, D. B.; Speziale, A. J. *J. Am. Chem. Soc.* **1965**, *87*, 2683.

[16] House, H. O.; Jones, V. K.; Frank, G. A. *J. Org. Chem.* **1964**, *29*, 3327.

[17] Speziale, A. J.; Bissing, D. E. *J. Am. Chem. Soc.* **1963**, *85*, 3878.

[18] Bergelson, L. D.; Shemyakin, M. M. *Tetrahedron* **1963**, *19*, 149.

[19] Bergelson, L. D.; Barsukov, L. I.; Shemyakin, M. M. *Tetrahedron* **1967**, *23*, 2709.

[20] Schneider, W. P. *J. Chem. Soc. Chem. Commun.* **1969**, 785.

[21] Schweizer, E. E.; Crouse, D. M.; Minami, T.; Wehman, A. *J. Chem. Soc. Chem. Commun.* **1971**, 1000.

[22] Smith, D. H.; Trippett, S. *J. Chem. Soc. Chem. Commun.* **1972**, 191.

[23] Allen, D. W.; Hutley, B. G.; Rich, T. C. *J. Chem. Soc. Perkin Trans. (2)* **1973**, 820.

[24] Olah, G. A.; Krishnamurthy, V. V. *J. Am. Chem. Soc.* **1982**, *104*, 3987.

[25] Yamataka, H.; Nagareda, K.; Hanafusa, T.; Nagase, S., *Tetrahedron Lett.* **1989**, *30*, 7187.

[25a] Yamataka, H.; Ando, K.; Takatsuka, T.; Hanafusa, T. *Chem. Lett.* **1992**, 1531.

26 Bestmann, H. J. *Pure Appl. Chem.* **1980**, *52*, 771.

27 Bestmann, H. J.; Vostrowsky, O. *Topics Curr. Chem.* **1983**, *109*, 85.

28 McEwen, W. E.; Beaver, B. D.; Cooney, J. V. *Phosphorus Sulfur* **1985**, *25*, 255.

29 Vedejs, E.; Fleck, T.; Hara, S. *J. Org. Chem.* **1987**, *52*, 4637.

30 Ward, W. J.; McEwen, W. E. *J. Org. Chem.* **1990**, *55*, 493.

31 Vedejs, E.; Marth, C. F. *J. Am. Chem. Soc.* **1990**, *112*, 3905.

32 Mari, F.; Lahti, P. M.; McEwen, W. E. *J. Am. Chem. Soc.* **1992**, *114*, 813.

33 Schlosser, M.; Tuong, H. B. *Angew. Chem.* **1979**, *18*, 633.

34 Schlosser, M.; Schaub, B. *J. Am. Chem. Soc.* **1982**, *104*, 5821.

35 Schlosser, M.; Oi, R.; Schaub, B. *Phosphorus Sulfur* **1983**, *18*, 171.

36 Vedejs, E.; Marth, C. F. *J. Am. Chem. Soc.* **1988**, *110*, 3948.

37 Maryanoff, B. E.; Reitz, A. B.; Mutter, M. S.; Whittle, R. R.; Olofson, R. A. *J. Am. Chem. Soc.* **1986**, *108*, 7664.

38 Maryanoff, B. E.; Reitz, A. B. *Tetrahedron Lett.* **1985**, *26*, 4587.

39 Wittig, G.; Haag, A. *Chem. Ber.* **1963**, *96*, 1535.

40 Kozminykh, V. O.; Igidov, N. M.; Kozminykh, E. N.; Andreichikov, Y. S.; Ustenko, S. N.; Kolodiazhnyi, O. I. *J. Gen. Chem.* **1991**, *61*, 1963.

41 Schlosser, M.; Christmann, K. F. *Liebigs Ann. Chem.* **1967**, *708*, 1.

42 Holler, R.; Lischka, H. *J. Am. Chem. Soc.* **1980**, *102*, 4632.

43 Volatron, F.; Eisenstein, O. *J. Am. Chem. Soc.* **1987**, *109*, 1.

44 Rzepa, H. Z. *J. Chem. Soc. Perkin Trans. (2)* **1989**, 2115.

45 Maryanoff, B. E.; Reitz, A. B. *Phosphorus Sulfur* **1986**, *27*, 167.

46 Vedejs, E.; Meier, G. P.; Snoble, K. A. J. *J. Am. Chem. Soc.* **1981**, *103*, 2823.

47 Birum, G. H.; Matthews, C. N. *J. Org. Chem.* **1967**, *32*, 3554.

48 Bestmann, H. J.; Riemer, C.; Dotzer, R. *Chem. Ber.* **1992**, *125*, 225.

49 Chioccola, G.; Daly, J. J. *J. Chem. Soc.* (*A*) **1968**, 568.

50 Kolodiazhnyi, O. I. *Tetrahedron Lett.* **1985**, *26*, 439.

51 Kolodiazhnyi, O. I.; Golokhov, D. B. *J. Gen. Chem.* **1988**, *58*, 426.

52 Kolodiazhnyi, O. I.; Ustenko, S. N. *Phosphorus Sulfur* **1991**, *62*, 111.

53 Haque, M. U.; Caughlan, C. N.; Ramirez, F.; Pilot, J. F.; Smith, C. P. *J. Am. Chem. Soc.* **1971**, *93*, 5229.

54 Bestmann, H. J.; Roth, K.; Wilhelm, E.; Bohme, R.; Burzlaff, H. *Angew. Chem.* **1979**, *18*, 876.

55 Kawashima, T.; Kato, K.; Okazaki, R. *J. Am. Chem. Soc.* **1992**, *114*, 4008.

56 Schlosser, M.; Piskala, A.; Tarchini, C.; Tuong, H. B. *Chimia* **1975**, *29*, 341.

57 Reitz, A. B.; Mutter, M. S.; Maryanoff, B. E. *J. Am. Chem. Soc.* **1984**, *106*, 1873.

58 Vedejs, E.; Fleck, T. J. *J. Am. Chem. Soc.* **1989**, *111*, 5861.

59 Vedejs, E.; Marth, C. F. *Tetrahedron Lett.* **1987**, *28*, 3445.

60 Bestmann, H. J.; Chandrasekhar, J.; Downey, W. G.; Schleyer, P. von R. *J. Chem. Soc. Chem. Commun.* **1980**, 978.

61 Mari, F.; Lahti, P.; McEwen, W. E. *Heteroatom Chem.* **1990**, *1*, 255.

62 Streitwesier, A.; McDowell, R. S. *Theochem.* **1986**, *31*, 89.

[63] Bishop, J. E.; O'Connell, J. F.; Rapoport, H. *J. Org. Chem.* **1991**, *56*, 5079.

[64] Vedejs, E.; Marth, C. F. *J. Am. Chem. Soc.* **1989**, *111*, 1519.

[65] Vedejs, E.; Fang, H. W. *J. Org. Chem.* **1984**, *49*, 210.

[66] (a) Cairns, S. M.; McEwen, W. E. *Tetrahedron Lett.* **1986**, *27*, 1541. (b) McEwen, W. E.; Ward, W. J. *Phosphorus Sulfur* **1989**, *41*, 393.

[67] Vedejs, E.; Marth, C. F; Ruggeri, R. *J. Am. Chem. Soc.* **1988**, *110*, 3940.

[67a] Anderson, C. L.; Soderquist, J. A.; Kabalka, G. W. *Tetrahedron Lett.* **1992**, *33*, 6915.

[68] Piskala, A.; Rehan, A. H.; Schlosser, M. *Coll. Czech. Chem. Commun.* **1983**, *48*, 3539.

[69] Maryanoff, B. E.; Reitz, A. B.; Graden, D. W.; Almond, H. R. *Tetrahedron Lett.* **1989**, *30*, 1361.

[70] Reitz, A. B.; Maryanoff, B. E. *J. Chem. Soc. Chem. Commun.* **1984**, 1548.

[71] Ruchardt, C.; Panse, P.; Eichler, S. *Chem. Ber.* **1967**, *100*, 1144.

[72] Froyen, P. *Acta Chem. Scand.* **1972**, *26*, 2163.

[73] Kuchar, M.; Kabac, B.; Nemecek, O.; Kraus, E.; Holubek, J. *Coll. Czech. Chem. Commun.* **1973**, *38*, 447.

[74] Giese, B.; Schoch, J.; Ruchardt, C. *Chem. Ber.* **1978**, *111*, 1395.

[75] Fliszar, S.; Hudson, R. F.; Salvadori, G. *Helv. Chim. Acta* **1964**, *47*, 159.

[76] Yamataka, H.; Nagareda, K.; Takai, Y.; Sawada, M.; Hanafusa, T. *J. Org. Chem.* **1988**, *53*, 3877.

[77] Fliszar S.; Hudson, R. F.; Salvadori, G. *Helv. Chim. Acta* **1963**, *46*, 1580.

[78] Soderquist, J. A.; Anderson, C. L. *Abstracts of Papers*, 203rd National Meeting of the American Chemical Society, San Francisco, CA; American Chemical Society: Washington, DC, 1992, ORGN 245.

[79] Donxia, L.; Dexian, W.; Yaozhong, L.; Huaming, Z. *Tetrahedron* **1986**, *42*, 4161.

[80] Isaacs, N. S.; Abed, O. H. *Tetrahedron Lett.* **1986**, *27*, 995.

[81] Yamataka, H.; Nagareda, K.; Ando, K.; Hanafusa, T. *J. Org. Chem.* **1992**, *57*, 2865.

[82] Tsukamoto, M.; Schlosser, M. *Synlett.* **1990**, 605.

[83] Schlosser, M.; Schaub, B.; De Oliveira-Neto, J.; Jeganathan, S. *Chimia* **1986**, *40*, 244.

[84] McEwen, W. E.; Beaver, B. D. *Phosphorus Sulfur* **1985**, *24*, 259.

[85] Allen, D. W.; Ward, H. *Tetrahedron Lett.* **1979**, 2707.

[86] Dusza, J. P. *J. Org. Chem.* **1960**, *25*, 93.

[87] Reitz, A. B.; Nortey, S. O.; Jordan, A. D.; Mutter, M. S.; Maryanoff, B. E. *J. Org. Chem.* **1986**, *51*, 3302.

[88] Allen, D. W.; Hutley, B. G.; Polasik, K. *J. Chem. Soc. Perkin Trans. (1)* **1975**, 619.

[89] Anderson, R. J.; Henrick, C. A. *J. Am. Chem. Soc.* **1975**, *97*, 4327.

[90] Johnson, A. Wm.; LaCount, R. B. *Tetrahedron* **1960**, *9*, 130.

[91] Johnson, A. Wm. *Ylid Chemistry*; Academic: New York, 1966; p. 180.

[92] Bestmann, H. J.; Kratzer, O. *Chem. Ber.* **1962**, *95*, 1894.

[93] Bissing, D. E. *J. Org. Chem.* **1965**, *30*, 1296.

[94] Allen, D. W. *Z. Naturforsch.* **1980**, *35B*, 1455.

[95] Jones, M. E.; Trippett, S. *J. Chem. Soc.* (*C*) **1966**, 1090.

[96] Johnson, A. Wm.; Kyllingstad, V. L. *J. Org. Chem.* **1966**, *31*, 334.

[97] Trindle, C.; Hwang, J. T.; Carey, F. A. *J. Org. Chem.* **1973**, *38*, 2664.

[98] Mari, F.; Lahti, P.; McEwen, W. E. *Heteroatom. Chem.* **1991**, *2*, 265.

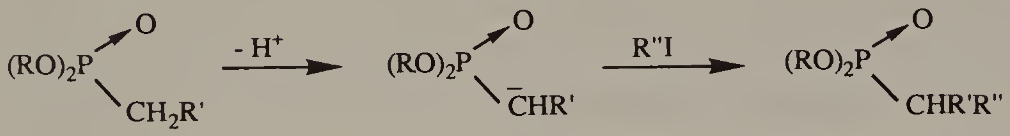
[99] McEwen, W. E.; Mari, F.; Lahti, P. M.; Baugham, L. L.; Ward, W. J. In *Phosphorus Chemistry: Developements in American Science*; ACS Symposium Series No. 486; Walsh, E. N.; Griffith, E. J.; Quin, L. D.; Parry, R. W., Eds.; American Chemical Society: Washington, DC 1992; Chapter 12.

[100] Johnson, A. Wm. *Ylid Chemistry*; Academic: New York, **1966**; p. 152.

# 10

# PHOSPHONATE CARBANIONS (PHOSPHONO YLIDES)

Phosphonate carbanions (**1**), which also might be called phosphono ylides by analogy with phosphonium ylides, have been known since at least 1927 when Arbuzov and Dunin[1] deprotonated triethyl phosphonoacetate (Eq. 10.1, R = Et, R′ = COOEt) and alkylated the resulting anion with alkyl iodides. These carbanions have been employed as nucleophiles in numerous reactions, but interest in their chemistry heightened when it was discovered in 1958 that they would effect olefinations of aldehydes and ketones in a reaction similar to that of phosphonium ylides (the Wittig reaction). Phosphono ylides have evolved to the point where now they are effective complementary, and even competitive, olefinating reagents. This chapter describes their preparation, their physical properties, their reaction with carbonyl compounds, including comparison with the use of phosphonium ylides in the Wittig reaction, and their general nucleophilic behavior. It has become clear that the phosphono group is just another of a family of heteroatom groups which can provide stabilization of an adjacent carbanion, and that in certain reactions the heteroatom group can be eliminated.



(10.1)

**1**

---

*Ylides and Imines of Phosphorus*, Edited by A. William Johnson.
ISBN 0-471-52217-1

## 10.1 PREPARATION AND PROPERTIES

Phosphonate carbanions are most often prepared by the straightforward deprotonation of phosphonates (Eq. 10.1), the preparation of which is described in Section 10.1.1. A few reactions have evolved which allow for direct preparation of the carbanion without isolation of the phosphonate, and these are described in Section 10.1.1.4. In most instances the carbanion can be prepared in advance of adding the second reactant, but in some instances the carbanion cannot be preformed[2].

Although Arbuzov used sodium[1] or potassium[3] metal in his early experiments, a variety of modern bases such as sodium hydride, sodium ethoxide, sodium amide, sodium hexamethyldisilazide (NaHMDS), lithium diethylamide (LDA), and organolithium reagents now are routinely employed. These are the same bases that have often been employed to deprotonate phosphonium salts (Section 4.1.2), but for a given phosphonate a stronger base must be employed than for the analogous phosphonium salt owing to the lower acidity of the former (details are provided in Section 10.2.1.1). The solvents employed are typical of those used with the various bases listed above and include aromatics, ethers [especially dimethoxyethane (DME) and tetrahydrofuran (THF)], dimethylformamide (DMF), and alcohols as well as more exotic solvents such as hexamethylphosphoramide (HMPA).

### 10.1.1 Preparation of Phosphonates

***10.1.1.1 Michaelis–Arbuzov Rearrangement.*** The reaction of alkyl halides with trialkylphosphites, usually triethylphosphite (Eq. 10.2), was discovered in

$$(EtO)_3P \; + \; RCH_2X \longrightarrow \left[(EtO)_3\overset{+}{P}\text{-}CH_2R\right] \xrightarrow{-\,EtX} (EtO)_2P(O)CH_2R \qquad (10.2)$$

1898[4] to produce phosphonates, and it has been widely employed since because of its simplicity and good yields. The reaction, which has been reviewed several times,[5–8] is most effective with primary alkyl halides, but of limited use with secondary halides. The mechanism involves the nucleophilic attack of phosphorus on the alkyl halide in a $S_N2$ reaction and the displaced halide ion then attacks an *O*-alkyl group to form alkyl halide and expel phosphonate. Triethyl phosphite, readily and economically available from $PCl_3$ and ethanol, is the reagent of choice. In most uses of phosphonate carbanions the phosphorus entity is eliminated eventually, so the particular phosphite used often is of little subsequent consequence. However, a popular method for directing the stereoselectivity of the reaction of phosphono ylides with carbonyl compounds necessitates the use of another phosphite, $(CF_3CH_2O)_3P$, which is of marginal nucleophilicity, to effect the Michaelis-Arbuzov reaction.

Although used to prepare the important phosphonate $(EtO)_2P(O)\,CH_2COOEt$ from ethyl α-bromoacetate, the reaction is of very limited use with α-haloaldehydes or ketones because of competition from the Perkow reaction,[6,9] which involves phosphite attack at halogen and eventual formation of enolphosphates. Although some control over the course of such a reaction is possible,[2,8] mixtures of products usually result. Reaction of triethylphosphite with α-chloro-N-methyl-N-methoxyacetamide proceeded normally.[10] Alternative approaches to β-ketophosphonates are available (Section 10.1.1.3).

***10.1.1.2 Michaelis–Becker Reaction.*** Discovered in 1892,[11] the nucleophilic displacement reaction by alkali phosphites [e.g., $(RO)_2P(O)^- Na^+$] on alkyl halides also affords phosphonates.[12] For example, the use of propargyl halide followed by a Wadsworth–Emmons (W–E) reaction provided ready access to enynes.[13] However, elimination reactions often compete when using other than primary halides, and α-halocarbonyl compounds produce mainly oxiranes through initial phosphite addition to the carbonyl group.[14] Protection of the carbonyl group as an enol ether prior to reaction with the phosphite anion, followed by ether cleavage, has provided an effective route to β-ketophosphonates.[15]

Britelli[16] effected the Michaelis–Becker synthesis with bromoacetic acid in the presence of aldehydes in a one-pot reaction to produce cinnamic and acrylic acids via subsequent W–E reactions. In a variant of the Michaelis–Becker synthesis, Zimmer et al. have added phosphite to aldehyde to produce α-hydroxyphosphonates in solution, which have been transformed to α-chlorophosphonates with phosphorus oxychloride[17] and to α-aminophosphonates with amines.[18,19]

***10.1.1.3 Preparation of β-Carbonylphosphonates.*** Since β-carbonylphosphonates are not normally accessible via the Michaelis–Arbuzov reaction (see Section 10.1.1.1), and because of the importance of such compounds in the olefination reaction, alternate syntheses have been evolved (see also Section 10.3.1.4). Corey and Kwaitkowski mentioned, but only in a footnote,[20] the reaction of lithium dimethylphosphonomethylide with esters in an acylation reaction, but two groups[21,22] recently published a detailed procedure for this reaction using a variety of esters (Eq. 10.3). Savignac and Mathey[23] converted the same lithium methylide to a cuprate, which then reacted with acyl halides to effect acylation and produce β-ketophosphonates.

$$(MeO)_2P(O)CH_3 \xrightarrow[THF]{BuLi} \left[(MeO)_2P(O)\overset{-}{C}H_2\right] \xrightarrow[-\,R'O^-]{RCOOR'} (MeO)_2P(O)CH_2COR \qquad (10.3)$$

Alkynylphosphonates [$(EtO)_2P(O)CCR$] have been converted to β-ketophosphonates by amine addition followed by hydrolysis of the formed enamine.[24] Grieco et al.[25] prepared a variety of β-ketophosphonates by γ-alkylation of the dianion of dimethyl(β-oxopropyl)phosphonate. Recently it has become possible to phosphonylate cyclic ketones with chlorodiethylphosphate when the enolate was formed using LDA at low temperatures, the intermediate enolphosphate being rearranged with LDA to the β-ketophosphonate.[26] Better yields recently have been obtained using chlorodiethylphosphite followed by air oxidation.[27]

***10.1.1.4 Miscellaneous Methods.*** A considerable variety of other methods for the synthesis of phosphonates have been employed in special circumstances, many of which are described in a review;[7] only a few are mentioned here because of recent application.

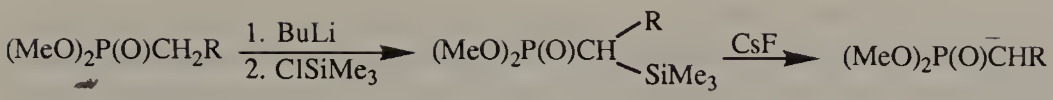
As with vinylphosphonium salts (Section 4.2), nucleophiles will add to vinylphosphonates to produce phosphonate carbanions which can be protonated, acylated, or alkylated to phosphonates, but which also are capable of reacting directly with other electrophiles or with carbonyl compounds in an olefination reaction.[28–35] The necessary vinylphosphonates often are available from the reaction of tetraethylmethylenebisphosphonate carbanion with carbonyl compounds[35–37] (see Section 10.2.4.1) or from α-selenation then oxidation of phosphonates.[31, 38]

Reaction of chlorodiethylphosphate [$ClP(O)(OEt)_2$] with various nucleophiles also affords phosphonates. Two equivalents of triphenylphosphoniummethylide afforded [$Ph_3P{=}CH{-}P(O)(OEt)_2$],[39] a mixed phosphonium–phosphono carbanion, and the use of α-carbanions from nitriles, nitroalkanes, and esters afforded the corresponding phosphonates.[40] Reference was made earlier to the use of enolate anions followed by isomerization of the enolphosphate to afford β-ketophosphonates.[26] The use of Grignard or organolithium reagents as the nucleophiles often is not straightforward.[7]

Cyclic phosphonates have been prepared by transesterification of trimethylphosphite with a vicinal diol followed by a Michaelis–Arbuzov rearrangement,[41,42] by reaction of phosphorus oxychloride with a vicinal diol followed by reaction with another nucleophile,[43] or by reaction of a dichlorophosphonate with a diol.[39]

Hatakeyama et al.[44] have found that 4-dimethylaminopyridine was an effective catalyst for ester interchange with alcohols, replacing the methyl group of $(RO)_2P(O)CH_2COOMe$ with a wide variety of other alkyl groups, including optically active groups. Hensel and Fuchs[45] reported a modified method of converting diethyl phosphonates to di-(2,2,2-trifluorethyl)phosphonates, important in the formation of Z-alkenes from phosphonate carbanions, by reaction first with trimethylsilyl iodide, then phosphorus pentachloride, and finally 2,2,2-trifluoroethanol.

Other phosphonate syntheses meriting mention include reaction of dialkylphosphites with stabilized diazo compounds,[46] addition of dimethylphosphonate to α, β-unsaturated compounds,[47] reaction of organolithium compounds with triethylphosphate, resulting in the displacement of ethoxy by alkyl groups,[43,48] and displacement of the trimethylsilyl group from the α-carbon of a phosphonate using cesium fluoride.[49, 50] The latter reaction provides a means of generating a phosphonate carbanion in the absence of strong base for reaction with base-sensitive compounds (Eq. 10.4).



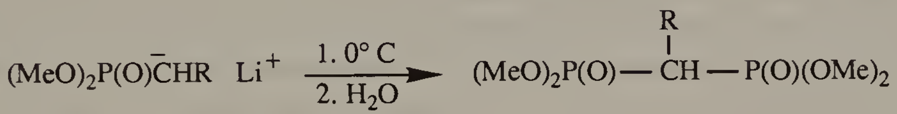
$$(MeO)_2P(O)CH_2R \xrightarrow[2.\ ClSiMe_3]{1.\ BuLi} (MeO)_2P(O)CH\begin{matrix} R \\ SiMe_3 \end{matrix} \xrightarrow{CsF} (MeO)_2P(O)\bar{C}HR$$

(10.4)

### 10.1.2 Properties of Phosphonate Carbanions

In contrast to phosphonium ylides, of which numerous nonstabilized and stabilized ylides have been isolated for physical study, phosphono ylides (phosphonate carbanions) seldom have been isolated. Instead, they usually have been formed by deprotonation either in the presence of another reactant or immediately prior to its addition, and the reaction occurred immediately.

Although essentially all phosphonate carbanions carrying electron-withdrawing groups on the carbanion are stable enough to persist in solution indefinitely in the absence of a proton source, the unsubstituted carbanion or those carrying alkyl substituents usually are quite unstable, even at low temperatures, normally producing dimeric products upon workup (Eq. 10.5).[51] The



$$(MeO)_2P(O)\bar{C}HR\ \ Li^+ \xrightarrow[2.\ H_2O]{1.\ 0°\ C} (MeO)_2P(O)—\overset{\displaystyle R}{\overset{|}{C}}H—P(O)(OMe)_2$$

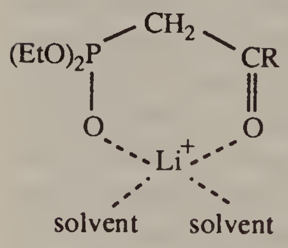
(10.5)

anion stability varied with the nature of the alkoxy groups attached to phosphorus, decreasing in the order $i$-PrO > EtO > MeO > $OCH_2C(CH_3)_2CH_2O$, the latter being unstable at $-50°C$, but the isopropoxy being stable for several hours at 0°C. It has been noted more recently that when the methylide (Eq. 10.5, $R' = H$) was formed using lithium diisopropylamide rather than butyllithium, it was stable in solution and did not dimerize.[52]

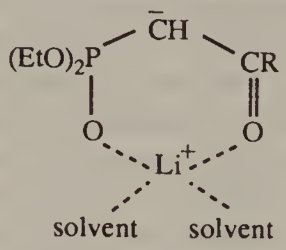
The acidity of phosphonates varies with the nature of the carbon substituents and the alkoxy groups, and in all cases is less than the corresponding phosphonium salt. When the common keto, ester, phenyl, or cyano groups are attached to the α-carbon to stabilize the carbanion to be formed, sodium hydride and sodium ethoxide seem to be the bases of choice. However, in the absence of such groups, stronger bases are necessary, usually organolithium or alkali amide reagents. Bordwell reported the $pK_a$ of only a few phosphonates, diethoxybenzylphosphonate being 27.55 in DMSO.[53] Burton and Yang recently have reviewed the chemistry of metal difluoromethylphosphonate carbanions with ZnBr, CdBr, and Cu cations.[54] Teulade et al.[48] used organolithium exchange to determine acidity differences among a series of phosphonates $[(RO)_2P(O)CH_2R']$ with the acidity decreasing in the order $R = OCH_2C(CH_3)_2CH_2O$ > MeO > EtO > $i$-PrO and $R' = Ph > Cl > Me > Et > i\text{-}Pr$.

A French group has published extensively on NMR studies ($^1H$, $^{13}C$, $^{31}P$) of phosphonate carbanions, and this work has been summarized.[55, 56] Studies on cyano-, phenyl-, carbomethoxy-, and acetyl-substituted phosphonates and their anions [$(EtO)_2P(O)CHR^-M^+$], usually with lithium or potassium cations, permitted the following conclusions:[57] (1) the phosphorus was deshielded about 15–20 ppm when converted to the carbanion, in contrast to phosphonium ylides which were more shielded than the precursor phosphonium salt (however, in diphenyl α-aryl-α-arylaminomethylphosphonates the phosphorus was reported to be more shielded in the carbanion than in the neutral form[58]); (2) the shielding of phosphorus decreased in the order R = COMe > COOMe > CN, with the major effect of the CN group being electrostatic rather than conjugative;[59] (3) the carbanionic shielding decreased in the order CN > Ph > COOMe > COMe; (4) the carbanion was $sp^2$ hybridized and planar, as reflected by the $J_{PC}$ values of 194–235 ppm and the $J_{CH}$ values of 143–161 ppm, both larger than for the neutral phosphonate. In THF solution and with the potassium ion complexed to 2.2.2-cryptand, the ester carbanion could be detected in both the *Z* (most stable) and *E* configurations and reversible coalescence could be observed with a free energy of activation of 17.7 kcal/m.[60] The acetyl carbanion showed similar behavior with a free energy of activation of 22 kcal/m, but in an "associating" solvent (pyridine) the carbanion existed only as the *Z*-chelate.[61]

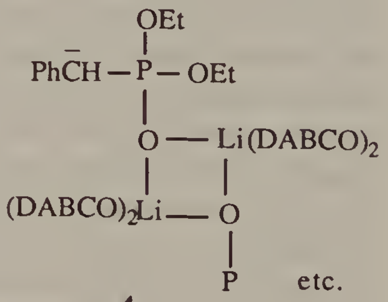
Light has been shed on the stepwise process of conversion of a neutral phosphonate to its carbanion. Earlier it had become clear that with a potassium base, the phosphonate carbanion was a relatively free anion, but with a lithium base a less reactive tight chelate was formed.[60] Subsequently, it has been shown that in the presence of less than an equivalent of organolithium reagent, an initial phosphonate–lithium bidentate intermediate (**2**) was formed ($^{31}P = 16–32$ ppm; $J_{PC} = 132–134$ ppm). In the presence of excess organolithium reagent a planar bidentate chelate (**3**) was formed ($^{31}P = 32–40$ ppm; $J_{PC} = 195–224$ ppm).[56, 62] The carbonyl and phosphoryl frequencies in the infrared spectra of the anion both were lowered as expected.[62] The lithium carbanions existed as a mixture of free anions or solvated ion pairs and as aggregates, depending on the solvent.



**2**



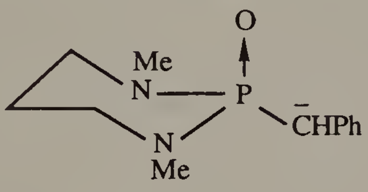
**3**



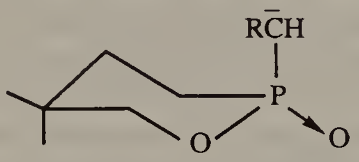
**4**

Several phosphonate carbanion salts recently have had their structure determined by X-ray crystallography. Zarges et al.[63] isolated the diethylbenzylphosphonate anion as its lithium salt when complexed to two molecules of diazabicyclooctane (DABCO). The P–C distance was 1.64 Å, similar to those of phosphonium ylides, and the carbanion was very slightly pyramidalized. The dimeric unit was as shown in **4** and the $J_{PC}$ value was 225.2 Hz, indicating an approximately planar carbanion. Earlier Macicek et al.[64] and Weiss et al.[65] had determined the structures of copper and magnesium $\beta$-keto-phosphonate anions, respectively, and reported hexacyclic chelates with planar O–C–C–P–O groups with lengthened P–O and C–O bonds and shortened P–C and C–C bonds, all relative to the normal single bond lengths. These observations are consistent with describing a phosphonate carbanion as an $sp^2$-hybridized, delocalized, and approximately planar carbanion, perhaps with $p\pi$–$d\pi$ overlap between the carbanion and phosphorus.

The structure of the related diazaphosphorinane carbanion (**5**) has recently been reported and it showed a planar carbanion with a P–C distance of 1.689 Å.[66] Several groups[43,66–69] have reported NMR studies on cyclic phosphonates and their carbanions (**6**), revealing facile conversion of conformation dependent on solvent, temperature, and cation. The P–O bond normally is equatorial in the phosphonate, and two groups[43,67] reported that it remained so when coordinated with lithium, but became axial with the potassium cation, all at low temperature. The third group[66] claimed that the lithium benzyl carbanion had a dominant (65:35 at 20°) axial P–O bond.



**5**



**6**

## 10.2 REACTION OF PHOSPHONATE CARBANIONS WITH ALDEHYDES AND KETONES (THE WADSWORTH–EMMONS REACTION)

It was not until 1953,[70] the same year as the discovery of the Wittig reaction and 26 years after their use as carbanions for other purposes, that phosphonate carbanions were reacted with carbonyl compounds. However, the result was proposed to be a Knoevenagel reaction, and a 1960 report[71] mistakenly concluded that product had to be dephosphonylated to produce what is now recognized as the directly produced olefination product. Horner et al.,[72, 73] from a single reaction in a study otherwise devoted to phosphinoxy carbanions, were the first to recognize that a phosphonate carbanion would react with a carbonyl compound to produce an alkene and phosphate. Wadsworth and Emmons were the first to study this reaction in detail and they developed it into a useful and important synthetic tool applicable to a range of phosphonates and carbonyl compounds (Eq. 10.6).[74] The alkene usually is formed stereoselectively, often

$$(EtO)_2P(O)CH_2R \xrightarrow{\text{Base}} \left[(EtO)_2P(O)\bar{C}HR\right] \xrightarrow[-\,(EtO)_2PO_2^-]{R'R''CO} R'R''C{=}CHR \tag{10.6}$$

with ratios of $> 90{:}10$, and usually with predominant *E* stereochemistry. However means have been developed to produce predominantly *Z*-alkenes from this reaction (see Section 10.2.3).

Nomenclature for the reaction of phosphonate carbanions with carbonyls to afford alkenes has been very confused, with almost every possible combination and single use of the names *Wittig*, *Horner*, *Wadsworth*, and *Emmons* having appeared in the literature in the past decade and in *Chemical Abstracts*, making literature searches for this reaction difficult. It is proposed that hereafter the following terms be rigorously applied by all concerned, and especially journal and indexing editors, to the major reactions of phosphorus-stabilized carbanions with carbonyl compounds; the **Wittig reaction** for phosphonium ylides with carbonyls (this has been well accepted and applied, see Chapter 8); the **Wadsworth–Emmons (W–E) reaction** for phosphonate carbanions with carbonyls; the **Horner reaction** for phosphinoxy carbanions with carbonyls (see Chapter 11). These terms are mutually exclusive and precise. The case for the W–E name arises by direct analogy with the name for the Wittig reaction, which was named not for the discoverer (who was Staudinger), but for the developer of the reaction. Likewise, Pudovik (unknowingly), Patai (unknowingly), and Horner each can lay some claim to the discovery of a single example of the reaction of phosphonate carbanions with carbonyls, but it was Wadsworth and Emmons who demonstrated the potential for the reaction, in a manner similar to Wittig, and who developed it as a major synthesis tool. Pommer[75] and Trippett and Walker[76] also reported early examples of the W–E reaction.

### 10.2.1 Introduction

Interest in the W–E reaction as an important tool in the preparation of alkenes stems from a number of advantages over the Wittig reaction, both reactions using carbonyl compounds in reaction with phosphorus-substituted carbanions:

1. Upon completion of the W–E reaction the phosphorus entity appears as a phosphate which is water soluble and therefore readily separable from most organic products, whereas phosphine oxide separation occasionally has been troublesome in the Wittig reaction.
2. The phosphorus-containing starting material for the W–E reaction, usually triethyl phosphite, is about one third as costly as triphenylphosphine. On the other hand, the product phosphine oxide from the Wittig reaction can be recycled by reduction, thereby reducing its net cost for large-scale reactions. Some phosphonates, such as triethylphosphonoacetate [$(EtO)_2P(O)CH_2COOEt$], are available for purchase from specialty chemical manufacturers.

3. Phosphonate carbanions are more nucleophilic than the identically substituted phosphonium carbanions, presumably because of decreased stabilization of the carbanion by phosphorus. The practical implications of this fact are that while stabilized phosphonium ylides are relatively unreactive with ketones, the corresponding phosphonate carbanions are sufficiently reactive to afford alkenes in the W–E reaction. Thus, for the carbethoxy-stabilized carbanions, R–CH$^-$–COOEt reaction with some ketones failed to produce alkenes when R = $Ph_3P^+$ but proceeded when R = $(EtO)_2P(O)$.[76]

4. There are no generalizable stereochemical advantages of the W–E reaction over the Wittig reaction, since the tendency for both is to produce mainly *E*-alkenes when stabilized groups are attached to the carbanion. However, means have been discovered to increase the *Z*-alkene proportion in both reactions, but most effectively in the W–E reaction (see Section 10.2.3).

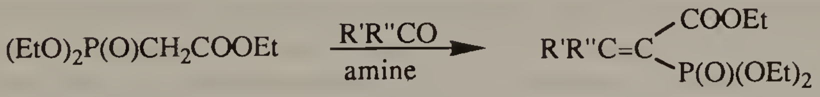
The W–E reaction also has several disadvantages with respect to the Wittig reaction (see also Section 10.2.4.4):

1. Stronger bases must be employed in the formation of the phosphonate carbanions than in the formation of ylides, leading to occasional carbonyl self-condensation or double-bond migration.

2. Phosphonate carbanions cannot be readily isolated and purified before use in alkene synthesis, whereas stabilized ylides usually are preformed and purified before reacting with a carbonyl compound.

3. The W–E reaction has been somewhat restricted to using phosphonate carbanions carrying stabilizing groups, usually keto, cyano, carbalkoxy, and phenyl, at least using mild conditions (however, see Section 10.2.1.2), whereas the Wittig reaction can be effected readily with nonstabilized, semistabilized, and some stabilized ylides.

4. Attempts to effect the W–E reaction in the presence of amines as bases often leads to a competing Knoevenagel reaction (Eq. 10.7),[70, 71, 77–79] although others recently have discovered means of preventing such reactions (see Section 10.2.1.1).



$$(EtO)_2P(O)CH_2COOEt \xrightarrow[\text{amine}]{R'R''CO} R'R''C{=}C\begin{matrix} \nearrow COOEt \\ \searrow P(O)(OEt)_2 \end{matrix} \qquad (10.7)$$

The Wittig and W–E reactions together have similar advantages over other methods for alkene synthesis:

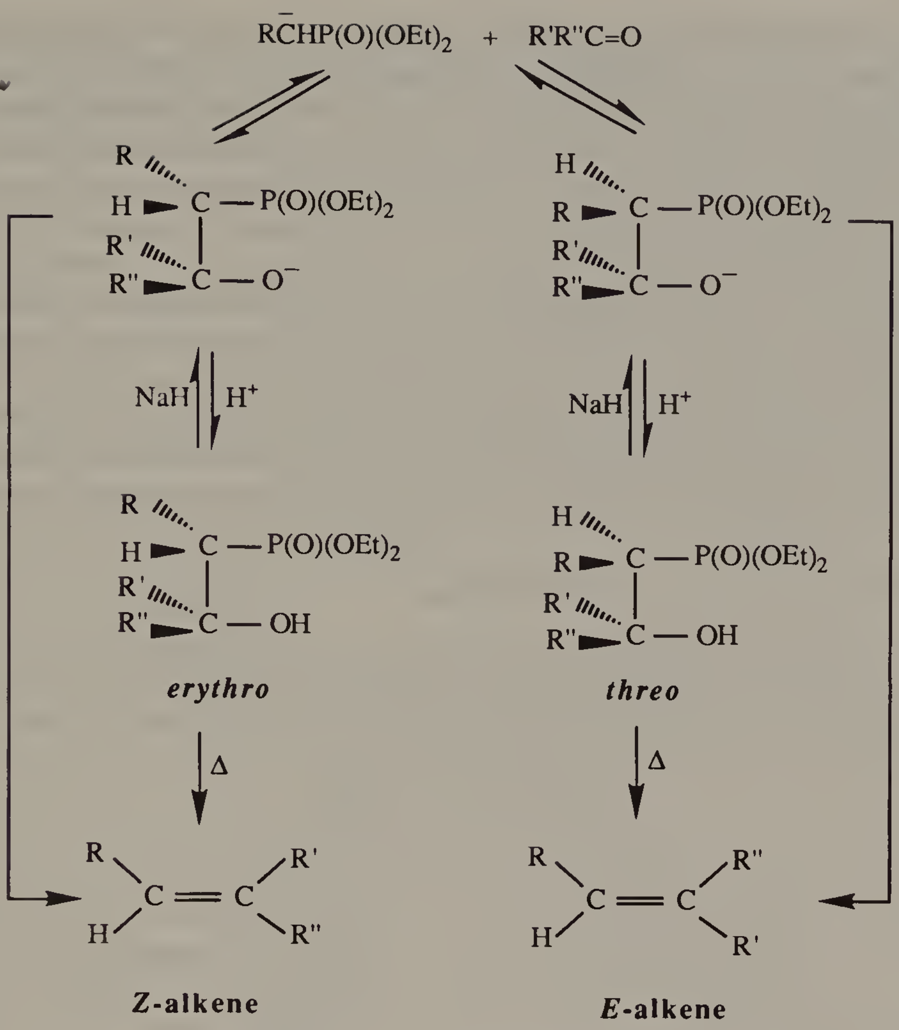
1. Side reactions are rare in both alkene-producing reactions.
2. The ability to substitute on the carbanions of both phosphonium ylides and phosphonate carbanions prior to carbonyl condensation, thereby providing access to more highly-substituted alkenes.
3. The regiospecificity of both reactions.

ment in yields. The addition of 15-crown-5 ether[111] or 18-crown-6 ether[112,113] led to significant improvement in yields of alkenes, and the latter also affected the stereochemistry of the reaction (see Section 10.2.3.4). A gas phase mixture of phosphonate and carbonyl compound, when passed over potassium carbonate in carbowax, produced modest yields of alkene, usually only the *E* isomer.[114] Electrolytic generation of the phosphonate carbanion also produced modest yields of alkene.[115]

The search for milder conditions for generating the phosphonate carbanion in the W–E reaction, in order to avoid complications such as aldol condensations and epimerization of the carbonyl compound, returned to amines, previously discarded because of Knoevenagel reaction competition.[70,71] Blanchette et al.[116] found that using DBU [1,8-diaza (5.4.0) bicycloundec-7-ene] or DEPA (diisopropylethylamine) with one equivalent of lithium chloride in dry acetonitrile afforded excellent yields of alkene with aldehydes, and demonstrated the existence of a phosphonate–DBU–LiCl complex in the reaction. Later, Rathke et al. showed that triethylamine could be employed in THF with the best yields resulting from LiBr or $MgBr_2$ complexes in reaction with aldehydes[117] and ketones.[118]

The W–E reaction also has been conducted in a polymer environment. Coupling of the phosphonate to a polystyrene chain through an alkoxy group, then reaction with a carbonyl compound in solution led to no advantage over the usual procedure.[119] Phosphonates also have been attached to the polymer chain through the carbanion.[120] Reaction of phosphonate with an anion exchange resin in the hydroxide form, followed by evaporation, produced a dry solid resin containing phosphonate carbanion which subsequently would react in a variety of solvents with aldehydes and ketones to afford mainly *E*-alkenes in excellent yield.[121]

***10.2.1.2 β-Hydroxyphosphonates.*** The earliest W–E reactions were conducted using phosphonates carrying electron-withdrawing groups attached to the α-carbon, most often carbethoxy, keto, cyano, and phenyl groups, from which alkenes were obtained directly. However, using diethyl methylphosphonate with benzophenone in the presence of butyllithium failed to produce the expected 1,1-diphenylethene, instead affording the β-hydroxyphosphonate (BHP) upon workup, presumed to result from phosphono carbanion addition across the carbonyl group (Eq. 10.9).[120] This led to the erroneous generalization that unless electron withdrawing groups were attached to the α-carbon of a phosphonate a W–E reaction could not take place. However, it was subsequently found that heating such BHPs in solution,[90,122–125] or treating them with a potassium,[90,126,127] sodium,[116,128] or cesium[129] base, would effect completion of the W–E reaction and produce alkenes. Such conversions were effected where the following groups were substituted on the methyl group (i.e., R in Eq. 10.9): hydrogen;[124,126,122] methyl;[126] alkoxy;[90,123] alkylthio;[122] and phenyl.[130] The BHPs also were obtained from cyclopropylphosphonates and they too could be converted to the expected alkenes.[127,128,131] Thus, it may be concluded that



(10.9)

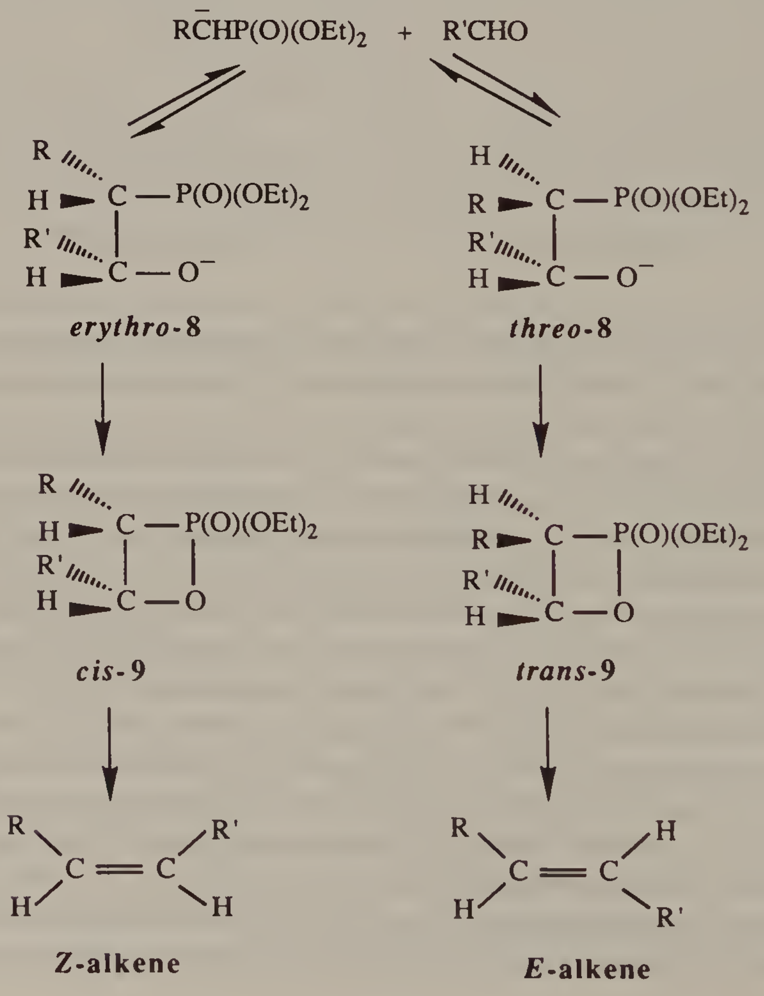
W–E reactions may be effected with both "stabilized" and "nonstabilized" phosphono carbanions, with the proviso that the latter require more strenuous conditions and the absence of lithium cations for the second alkene-forming step.

The Seyden–Penne group have been able to isolate BHPs from reaction of benzaldehyde with stabilized phosphono carbanions by using a lithium or magnesium base, both of which apparently complex with the intermediate betaine, permitting its stabilization and eventual isolation upon careful protonation (Eq. 10.9, $R = COOEt$ or CN or Ph; $R' = Ph$; $R'' = H$). By this means the carbethoxy-,[132] cyano-,[93,133] and phenyl-substituted[88,130] BHPs have been isolated in both their threo and erythro forms (the BHPs also have been prepared by independent routes[88]). In each instance they have been converted to alkene to complete the W–E reaction by thermal and/or base-catalyzed reaction. For the carbethoxy- and phenyl-substituted BHPs both the threo and erythro forms produced *only* the *E*-alkene, indicating that betaine formation was reversible. In the thermal decomposition of the cyano-substituted BHP the erythro form produced an 80:20 ratio of $Z:E$ alkenes, while the threo BHP produced a 10:90 ratio, indicating stereoselective decomposition with only little reversal of either betaine to starting materials. However, NaH-promoted decomposition of the two betaines produced 17:83 and 12:88 $Z:E$ ratios of cinnamonitriles, respectively, close to the ratio (15:85) produced in the direct and complete reaction of the cyano-substituted phosphono carbanion with benzaldehyde. The reversibility of betaine formation has been proven by trapping the reformed phosphono carbanions with the more electrophilic *p*-chlorobenzaldehyde.[93, 132, 133]

It may be concluded from the above that all W–E reactions *may* proceed via an intermediate betaine, which can be trapped in most instances, but which normally proceeds to alkene under mild or more severe reaction conditions, depending on the carbanion substituent. The stereochemical implications of this conclusion are discussed in Section 10.2.3. However, it should be cautioned that actual observation of a betaine in solution has not been reported to date.

### 10.2.2 Mechanism of the W–E Reaction

The W–E reaction of phosphonate carbanions with aldehydes, from its earliest days[74] and to the present, usually has been represented by a mechanism (Eq. 10.10) involving (i) initial nucleophilic attack of the carbanion on the electro-

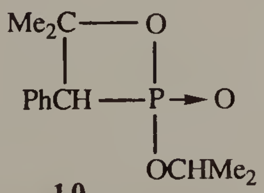


(10.10)

philic carbonyl carbon, perhaps to form betaines (**8**), (2) oxyanion attack at phosphorus possibly to form oxaphosphetanes (OPA) (**9**), and (3) ring opening to afford alkene and phosphate anion. Starting with triethyl phosphonoacetate (R = COOEt) and ethoxide as the base, the reaction has been shown to be third order, first order in each of ethoxide, phosphonate, and benzaldehyde (R′ = Ph).[41] The rate of alkene formation was approximately equal to the rate of carbonyl disappearance, and there was no other evidence for a build up of intermediate(s). Use of substituted benzaldehydes in the reaction provided a $\rho$ value of $+1.96$, lower than the 2.7–3.0 seen for the Wittig reaction but consistent with the higher nucleophilicity of the phosphonate carbanion. When the usual diethoxy phosphono group was replaced by the 2,3-butanedioxy phosphono group the reaction rate increased by a factor of 27, which has been explained by the release of strain when tetrahedral phosphorus in a five-membered ring was converted to trigonal bipyramidal phosphorus in the OPA intermediate (**9**), allowing the phospholane ring to assume apical–equatorial positions about phosphorus.[41,42]

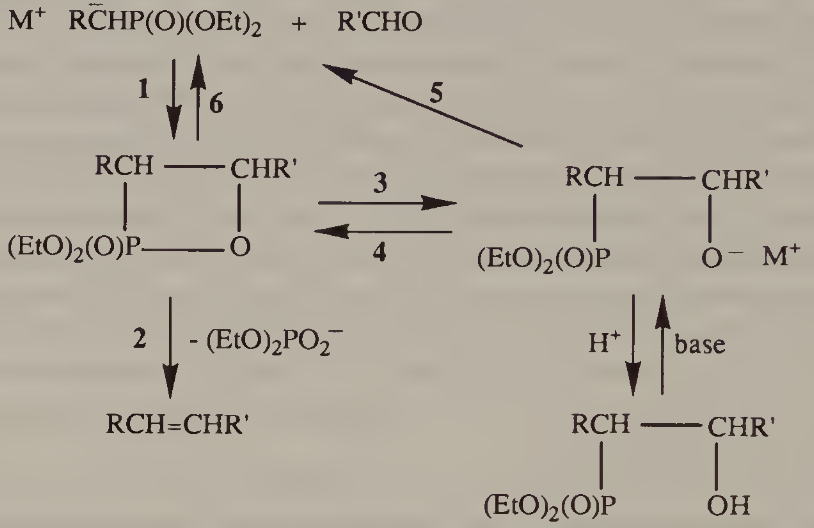
The issue of the precise nature of the intermediate in the W–E reaction still is very much open in that there have been no conclusive and repeatable observations of either a betaine (**8**) or an oxaphosphetane (**9**).[134] Most authors continue to represent the reaction as proceeding formally through a discrete betaine intermediate even though no NMR spectra have been reported for betaines during the course of W–E reactions, nor have any been isolated. $\beta$-hydroxyphosphonates (BHPs), the conjugate acids of betaines, have been isolated from numerous W–E reactions (see Section 10.2.1.2), leading to the assumption that they have been derived from betaines, but with no proof.[88] The fact that BHPs can be obtained from phosphonates carrying stabilizing groups only in the presence of effective complexing cations, such as lithium and magnesium, but not in the presence of sodium or potassium cations,[132] suggests that the free betaine may not exist in the latter instances.

The possible intermediacy of an OPA is consistent with Larsen's[41] relative rate observations for phospholane carbanions. There is only one brief report[135] noting $^{31}$P NMR absorption for a presumed oxaphosphetane intermediate, that being at $-34$ ppm at 0°C, but with no such observation at $-25$ or $-60$°C. It is strange that no follow-up on this 1979 experiment has been reported, either to confirm it or to demonstrate that the peak arose from a side product. Recently Tomioka et al.[136] have reported the isolation of a similar (but $\lambda^4$) species (**10**), but no characterizing data were provided, although it was thermally converted to an alkene and probably a metaphosphate.



**10**

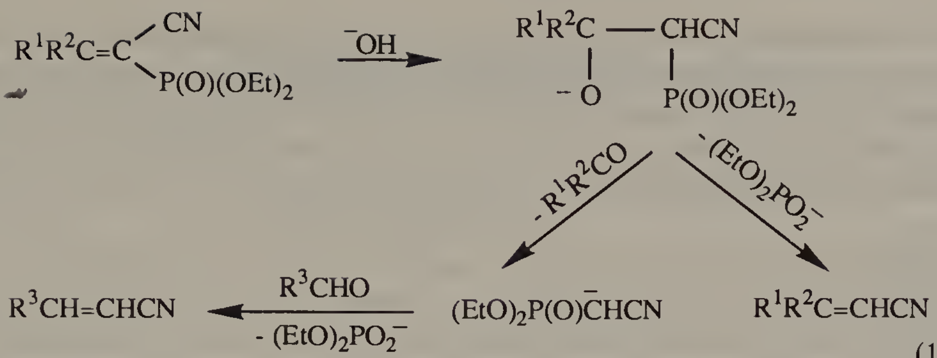
In view of this information, it may be more appropriate to represent the W–E reaction as proceeding via a mechanism similar to that now accepted for the Wittig reaction (see Chapter 9) and shown in Eq. 10.11, which proposes direct



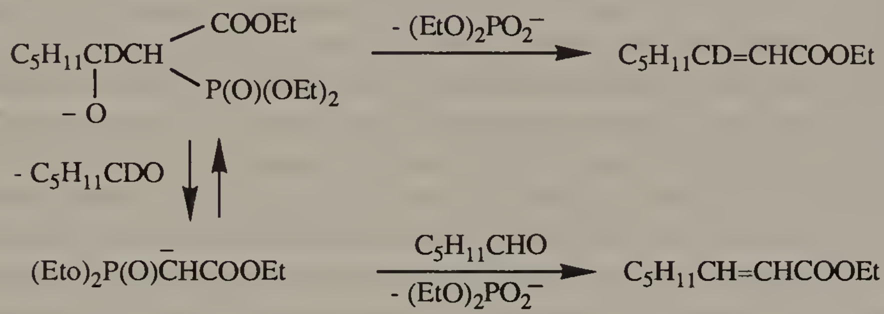
(10.11)

formation of the OPA[41] in step 1. The formation of betaines (step 3) could result from reaction of the OPA with complexing cations (e.g., lithium, magnesium[132]) or by protonation of those OPAs which are reluctant to proceed to alkene because of the absence of stabilization of the incipient double bond by a conjugating group. By this proposal betaines are not central to the process, but can be intercepted (step 3) and reintroduced (step 4 and/or step 5) to the reaction (see below). It is not clear whether OPA formation is reversible (step 6), but it is likely in order to explain the stereochemistry of the W–E reaction (see Section 10.2.3).

The condensation of phosphonate and carbanion in the W–E reaction has been claimed to be reversible because of copious evidence that formation of a betaine by proton removal from a BHP results in alkene and phosphate. The evidence that a betaine can *dissociate* to carbanion and carbonyl compound, and can *decompose* to alkene and phosphate, seems incontrovertible and multifaceted.[88,93,132,133] Danion and Carrie[137] found that hydroxide would add to α-cyanovinylphosphonates, presumably to form a betaine which produced a mixture of an acrylonitrile (decomposition) and a carbonyl compound (dissociation). Addition of a more reactive carbonyl would trap the phosphono carbanion formed by dissociation (Eq. 10.12). Durrant and Sutherland[125] found that a C-deutero β-hydroxyphosphonate, when converted to a betaine with sodium ethoxide in the presence of hexanal, afforded a 93% yield of trans ethyl 2-octenoate, of which 53% was monodeuterated, indicating that about half of the alkene had been formed by direct decomposition of the betaine and half was formed by dissociation to carbanion, which subsequently reacted with undeuterated hexanal (Eq. 10.13). Sturtz and Pondaven[138] reported inadvertent vinyl chloride formation from $(EtO)_2P(O)CHCl{-}CH_2OH$ upon treatment with base, and proposed a W–E decomposition of the intermediate.

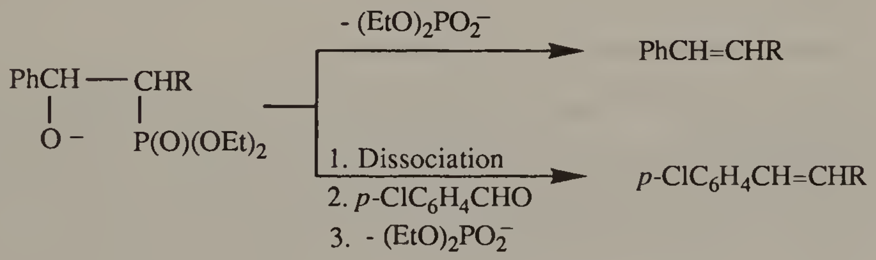


(10.12)



(10.13)

In an extensive series of papers the Seyden–Penne group reported obtaining the erythro and threo $\beta$-hydroxyphosphonates from cyano-,[133] carbethoxy-,[132] and phenyl-[88] substituted phosphonates and benzaldehyde. Treatment of both the threo and erythro BHPs from the latter two (R = Ph or COOEt) with base afforded *only* the *E*-alkenes, indicating that erythro BHPs had reverted to threo betaines (which produced *E*-alkene) either by direct interconversion or by reversal to carbanion and carbonyl compound (Eq. 10.14).[130] Repetition of the



(10.14)

reaction in the case of the carbethoxyphosphonate (R = COOEt), but in the presence of *p*-chlorobenzaldehyde, led to the formation of crossover alkenes, proving that the betaine reverted to carbanion, and that the erythro BHP did so to a larger extent than did the threo BHP.[132] Petrova et al.[130] recently have demonstrated that at low temperatures threo BHP could be converted to a mixture of threo and erythro BHPs. In the case of the cyano betaines (R = CN), reversal to carbanion also was indicated, with the same *Z*/*E* ratio of cinnamonitriles (15:85) being obtained from the threo and erythro betaines as was obtained from the original W–E reaction of benzaldehyde with the cyanomethylphosphonate.[93,133] However, the ratio of noncrossover to crossover cinnamonitrile was larger than that obtained for a W–E reaction with a 1:1 mixture of benzaldehyde and *p*-chlorobenzaldehyde, indicating that some direct interconversion of erythro to threo betaine may have occurred.[133] No further evidence on the nature of this process has been provided in the intervening 20 years!

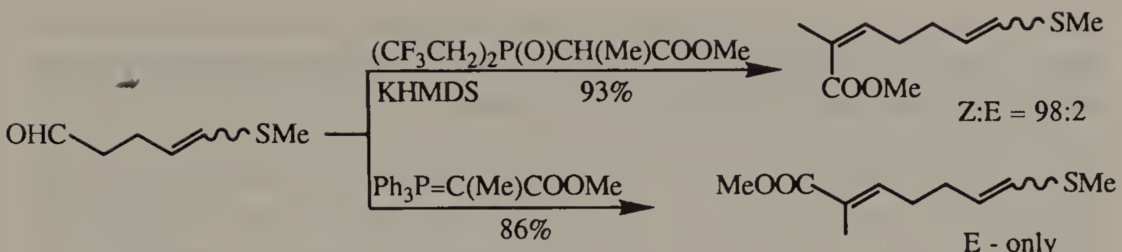
In studies of the effect of reaction conditions on the stereochemistry of the base-catalyzed conversion of BHPs to alkenes, it was shown that *Z*-alkene formation was enhanced by carrying out the reactions at low temperatures (e.g., −78°C) and by the use of noncomplexing cations such as potassium. The *E*-alkene formation was enhanced by higher reaction temperatures (e.g., 65°C) and the presence of complexing cations such as lithium. In other words, conditions that were likely to encourage dissociation of the betaine to carbanion, which could then recombine with carbonyl to form new betaine, facilitated formation of the thermodynamically more stable *E*-alkene.[95]

It is clear that *β*-hydroxyphosphonates can be converted to betaines which can both dissociate to phosphono carbanions or can proceed to alkenes by cycloelimination of phosphate. What has not been proven is whether these processes are tangential or central to the mechanism of the W–E reaction.

Finally, it is of interest to note that BHPs can be thermally stereoselectively, but not stereospecifically, converted to alkenes, with erythro BHPs affording mainly (e.g., 80:20) *Z*-alkenes and threo BHPs affording mainly (e.g., 90:10) *E*-alkenes.[133] The mechanism of this cycloelimination has not been determined, but it is apparent that intercepting a W–E reaction to isolate the stereoisomeric BHPs and their separate thermal cycloelimination provides access to both *E*- and *Z*-alkenes, albeit under strenuous conditions.

### 10.2.3 Stereochemistry of the W–E Reaction

In their original paper Wadsworth and Emmons[74] noted that benzaldehyde and $(EtO)_2P(O)CH_2CO_2Et$ reacted in the presence of sodium hydride to afford a 60% yield of stilbene, the trans isomer only being isolated. They surmised that "it is probable that the reaction is not stereospecific," and attributed their result to isomerization of the cis isomer, which they suggested undoubtedly also had been produced. Others[89,139] also concluded that the W–E reaction was not stereospecific, but the conventional wisdom soon changed to reflect the fact that in most cases studied, generally those with electron-withdrawing groups on the carbanion, the *E*-alkene was the dominant if not exclusive product,[140,2,85,141] similar to the results using the corresponding stabilized phosphonium ylides.[142] The W–E reaction now has developed to the point where it is an important complement to the Wittig reaction, with numerous examples known where a phosphonium ylide reacted with a carbonyl compound to afford the usual *E*-alkene, but the use of the corresponding phosphonate carbanion under specialized conditions provided dominant *Z*-alkene formation (Eq. 10.15).[143,144]



(10.15)

The W–E reaction with aldehydes and ketones most often produces a dominance of *E*-alkene, but many variables make the stereochemistry somewhat controllable. This section describes those variables and illustrate their outcomes. The *E*-alkene arises from a *trans*-OPA (**9**), perhaps involving a threo betaine (**8**) precursor, whereas the *Z*-alkene arises from the *cis*-OPA (**9**), perhaps involving an erythro betaine (**8**) (see Eqs. 10.10 and 10.11). It has been generally accepted, and the available evidence is consistent with the conclusion that the thermodynamically favored route is via *trans*-OPA to *E*-alkene. This has been the basis for explaining the observation that conditions which enhance reversibility of the W–E reaction increase the proportion of *E*-alkene, and vice versa.

***10.2.3.1 Effect of Phosphonyl Group.*** Most W–E reactions have been conducted with the diethoxy or dimethoxy phosphonyl group because of ease of access, and with most aryl or alkyl aldehydes the *E*-alkene is the exclusive or dominant product. It has been discovered that use of a 5-membered cyclic dialkoxy phosphonate, such as that derived from meso-2,3-butanediol, resulted in *Z*:*E* ratios as high as 2:1,[42,145,146] with similar six-membered ring-containing phosphonates having less of a *Z*-enhancing effect.[42,145–147] This pentacyclic ring effect has been attributed to the favorable energetics in formation of a pentavalent phosphorus intermediate (**9**) within a five-membered ring, thereby reducing its dissociation and the reversibility of the reaction.

Still and Gennari[148] discovered, and others[45,83,144,149] have used the fact that replacement of the two ethoxy groups in a phosphonoacetate with 2,2,2-trifluoroethoxy groups usually resulted in striking enhancement of the *Z*:*E* ratio of alkenes, for example, with benzaldehyde changing from 1:50 to a 50:1 ratio and octanal resulting in a 12:1 ratio of alkene.

Simple variation of the alkoxy groups attached to phosphorus has a modest effect on the stereoselectivity of the W–E reaction, with isopropoxy groups significantly enhancing the *E*:*Z* ratio.[45,150–154] This may be due to the increased bulkiness of the OPA and/or betaine intermediate, making the *trans*-OPA and threo betaine relatively more dominant in reversible reactions.

***10.2.3.2 Effect of Carbanion Substituents.*** Of the three most common substituents [R in $RCH_2P(O)(OEt)_2$], the phenyl[88] and carbethoxy[42,132] groups provided *E*:*Z* alkene ratios of near 100:1 under most conditions, whereas the cyano group[93] produced an 85:15 ratio. The increase in $Z$ proportion in the latter case has been attributed to the lesser steric requirement of the linear cyano group in the intermediate OPA and/or betaine.[132]

Several groups have found that replacing the common carbethoxy group with a larger group, such as the carboisopropoxy[152,155] or carbo-*t*-butoxy groups,[153,156] also resulted in increased proportions of the $E$-alkene. The amidophosphonate [$(EtO)_2P(O)CH_2CON(OMe)Me$] also has been employed to produce $\alpha,\beta$-unsaturated acid derivatives with high $E:Z$ ratios.[10,157]

The addition of a second substituent on the carbanion of the phosphonate results in formation of trisubstituted alkenes upon reaction with aldehydes. Whereas the Wittig reaction usually results in very high $E:Z$ ratios when using $\alpha,\alpha$-disubstituted ylides [e.g., $X = C(CH_3)COOEt$, with $X = Ph_3P$], the W–E synthesis [e.g., using $X = (EtO)_2(O)P$] of the same alkenes produced dominant proportions of $Z$-alkene.[143,158–160] When the phosphono carbanion in a W–E reaction carried two substituents, the proportion of $Z$-alkene usually increased significantly, and when the aldehyde reactant also was bulky, the $Z$-alkene usually dominated.[147,161–165] This increase in $Z$-alkene when both reactants have larger steric requirements at the reaction sites is somewhat surprising, in view of the increase in $E$-alkene formed when only one site has increased steric requirements or when the phosphono group has larger steric requirements. This unusual aspect is similar to that found in the Wittig reaction, and may portend unique geometry for a transition state leading to formation of an OPA intermediate.

***10.2.3.3 Effect of Carbonyl Reactant.*** In W–E reactions of ester phosphonate carbanions [$(EtO)_2(O)PCH{-}COOEt$] with aldehydes, the degree of branching of the aldehyde usually has very little effect on the stereoselectivity of the reaction, most resulting in $>95\%$ $E$-alkene.[145,161,165–167] Aliphatic and aromatic aldehydes produce almost identical $E:Z$ ratios of alkenes.[145] Ortho substitution in aromatic aldehydes produced a very modest increase in $Z$-alkene.[168]

When disubstituted phosphonate carbanions were used, the branched aliphatic aldehydes produced considerably larger $Z:E$ ratios, approaching 2:1, but the aromatic aldehydes remained dominant $E$-alkene producers.[95,161,163]

The W–E reaction of phosphonate carbanions with ketones affords tri- or tetrasubstituted alkenes. Two groups reported that increasing the steric requirements of one of the ketone substituents led to increasing proportions of $Z$-alkenes. Huff et al.[169] reported dominant $Z$-alkene formation using a disubstituted phosphonate carbanion and Jones and Maisey[170] found increasing, but not dominant, $Z$-alkene production using a monosubstituted phosphonate carbanion.

***10.2.3.4 Effect of Reaction Conditions.*** Early work indicated there was no significant solvent effect on the $Z:E$ alkene ratios from W–E reactions.[93,171]

However, some recent work indicates that nonpolar solvents increase the *Z*-component in certain W–E reactions.[172] For example, DME, and other less chelating solvents such as ether and benzene, produced larger *E*:*Z* ratios than did THF in the presence of lithium.[166] Hexamethylphosphoramide also has been shown to increase the *Z*-alkene proportion,[168] but not when used with bis-2,2,2-trifluoroethoxyphosphonates.[148]

The additions of crown ethers has been shown to affect the stereoselectivity of the W–E reaction. Two groups indicated the production of *E*-alkenes only,[111, 172] but two others indicated enhancement of the proportion of *Z*-alkene.[148, 160] The mechanism of these effects is unclear.

Lower reaction temperatures generally produce larger proportions of *Z*-alkenes,[81, 93, 172] in some instances making a striking difference.[45, 95, 162, 166] This effect is thought to result from decreased reversibility of the initial step of the reaction, leading to kinetic control of the stereochemistry, which produces more *Z*-alkene.

The nature of the cation present in the W–E reaction, dependent on the base chosen to generate the phosphonate carbanion, also influences the stereoselectivity of the reaction. Lithium cation generally produces the largest *E*:*Z* ratios while potassium cation generally produces the largest *Z*:*E* ratios.[95, 166] When a cyclic phosphonate was used, the effects of cation virtually disappeared.[42] The cation effect probably is associated with the degree of reversibility of the initial step of the reaction, and this influence can be seen in the crossover experiments as well, leading to more crossover (i.e., more reversal) with cations such as lithium which complex with the intermediate, slowing its cycloelimination to alkene.[93, 95] The effect of any single cation change may be modest [e.g., $(MeO)_2(O)PCH_2COOMe$ reacted with isobutyraldehyde to give *E*:*Z* alkene ratios of 1:3 with lithium cation and 1:1 with potassium cation[166]], but when employed in conjunction with solvent and temperature effects considerable stereoselectivity may be achieved, such as up to 12:1 in the previous example.[45, 166]

In summary, the use of the following reaction condition and reagent variables generally provides maximum stereoselectivity:

| | |
|---|---|
| *Maximize Z-alkene*: | low temperature, potassium base (KHDMS), less-polar solvent, crown ether addition, di(2,2,2-trifluoroethoxy)-phosphonate or five-membered cyclodialkoxy phosphonate. |
| *Maximize E-alkene*: | room temperature, lithium base, polar solvent (DME preferable), diisopropoxyphosphonate. |

The remaining variables are the structure of the carbonyl reactant and the nature of the carbanion substituents, both affecting the actual structure of the product. In general, increasing the bulk of one or the other produces more *E*-alkene, but if both reactants have large steric requirements, the *Z*-alkene usually will dominate.

### 10.2.4 Applications of the W–E Reaction

With its development in 1961, and especially with the appearance of two published reviews in 1974[140] and 1977,[2] the W–E reaction became a very important tool in organic synthesis. Its role mainly has been in alkene synthesis but in recent years the phosphonate carbanion has become a synthon for a number of functional entities. The W–E reaction has been utilized with a tremendous variety of phosphonates and carbonyl compounds. This section briefly describes the scope of the reaction in an exemplary, but not an encyclopedic, approach. Readers should refer to the reviews by Wadsworth[2] and Walker[85] for additional extensive tabulations through 1979.

***10.2.4.1 Phosphonate Reactants.*** A wide variety of phosphonates [$R^1R^2CHP(O)(OR)_2$], both monosubstituted ($R^1 = H$) and disubstituted have been employed in the W–E reaction to prepare alkenes. Table 10.1 contains a listing of many phosphonates which have been employed in the W–E reaction, together with mainly recent exemplary references to direct readers to their use.

Application of this variety of phosphonates in the W–E reaction makes available a wide variety of substituted alkenes. Monosubstituted phosphonates ($R^1 = H$; $R^2 \neq H$) with aldehydes produce 1,2-disubstituted alkenes and with ketones produce 1,1,2-trisubstituted alkenes. Disubstituted phosphonates ($R^1$ and $R^2 \neq H$) with aldehydes also produce 1,1,2-trisubstituted alkenes and with ketones produce 1,1,2,2,-tetrasubstituted alkenes. Most significantly, the latter seem readily available via the W–E reaction.[159,227,234,259]

**TABLE 10.1 Phosphonates [$R^1R^2CH–P(O)(OR)_2$] that have been Employed in the W–E Reaction with Aldehydes or Ketones**

| $R^1$ | $R^2$ | References |
|---|---|---|
| H | H | 20, 21, 22, 124 |
| Cyclopropyl | H | 131 |
| $CH_3$ | $CH_2Ar$ | 150 |
| $CH_2SiMe_3$ | H | 173 |
| $CF_3$ | $CF_3$ | 174 |
| $CH(OEt)_2$ | H | 175 |
| Ph | H | 88, 111, 176 |
| | $CH_3$ | 177 |
| $C_6H_4$–COOEt(*p*) | H | 178 |
| –$C_6H_4$–$C_6H_4$– | | 74 |
| 2–Pyridyl | H | 96 |
| Thienyl | H | 179 |
| Furyl | H | 179 |
| $CH{=}CH_2$ | H | 180 |
| $CH{=}CR{-}CH_3$ | H | 181 |
| CH=CH–Ph | H | 96 |
| CH=C(OEt)R | H | 182 |
| C(Me)=CHCOOR | H | 172 |
| $C(COOEt){=}CR^1R^2$ | H | 183 |

TABLE 10.1 Continued

| $R^1$ | $R^2$ | References |
|---|---|---|
| $CH{=}CH{-}CH_2{-}NR_2$ | H | 184 |
| $CH{=}CH{-}CH{=}NC_6H_{11}$ | H | 185, 186 |
| CH=CH–N–Phth | H | 187 |
| $CH{=}CH{-}C(Me){=}CH{-}CH_2{-}OBn$ | H | 188 |
| $CCSiMe_3$ | H | 13 |
| $CH{=}N{-}NMe_2$ | H | 189 |
| COOEt | H | 94, 145, 175 |
| $COOC_4H_9\text{-}t$ | H | 156 |
| $COO(CH_2)_8COOMe$ | H | 190 |
| COOEt | $CH_3$ | 163 |
| COOEt | $C_2H_5$ | 191 |
| | R | 160 |
| COSEt | H | 192 |
| $COO(CH_2)_2{-}$ | | 193 |
| $CONR_2$ | H | 109, 191, 194, 195 |
| CON(Me)OMe | H | 10, 157 |
| CONHCONR– | | 196 |
| COOH | H | 16, 197 |
| | F | 198 |
| | R | 199 |
| $COCH_3$ | H | 15, 58, 102, 200 |
| | $CH_3$ | 15, 200 |
| $COC_4H_9\text{-}t$ | H | 200 |
| $COC_5H_{11}\text{-}n$ | H | 201 |
| $COC_8H_{17}$ | H | 202 |
| $COCH_2COOEt$ | H | 203–205 |
| $COC(Me){=}C(Me)CH_2{-}$ | | 206 |
| $COCH_2NH_2$ | H | 207 |
| $COC_6H_5$ | H | 74 |
| CN | H | 133, 151, 162, 208 |
| | $CH_3$ | 162 |
| | $CH(Et)COOBu^t$ | 209 |
| F | H | 210 |
| | $CH_3$ | 210 |
| | CN | 211 |
| | COOMe | 212 |
| | $P(O)(OR)_2$ | 32 |
| | F | 49, 54, 213, 214 |
| Cl | Alkyl | 215 |
| | Aryl | 17, 216, 217 |
| | COOEt | 147, 165 |
| | COOH | 218 |
| | Cl | 219, 220 |
| Br | COOEt | 221 |
| | COR | 222 |
| | Br | 223 |
| OMe | H | 90, 224 |
| | Ph | 225 |

### 10.2.4 Applications of the W–E Reaction

With its development in 1961, and especially with the appearance of two published reviews in 1974[140] and 1977,[2] the W–E reaction became a very important tool in organic synthesis. Its role mainly has been in alkene synthesis but in recent years the phosphonate carbanion has become a synthon for a number of functional entities. The W–E reaction has been utilized with a tremendous variety of phosphonates and carbonyl compounds. This section briefly describes the scope of the reaction in an exemplary, but not an encyclopedic, approach. Readers should refer to the reviews by Wadsworth[2] and Walker[85] for additional extensive tabulations through 1979.

*10.2.4.1 **Phosphonate Reactants.*** A wide variety of phosphonates [$R^1R^2CHP(O)(OR)_2$], both monosubstituted ($R^1 = H$) and disubstituted have been employed in the W–E reaction to prepare alkenes. Table 10.1 contains a listing of many phosphonates which have been employed in the W–E reaction, together with mainly recent exemplary references to direct readers to their use.

Application of this variety of phosphonates in the W–E reaction makes available a wide variety of substituted alkenes. Monosubstituted phosphonates ($R^1 = H$; $R^2 \neq H$) with aldehydes produce 1,2-disubstituted alkenes and with ketones produce 1,1,2-trisubstituted alkenes. Disubstituted phosphonates ($R^1$ and $R^2 \neq H$) with aldehydes also produce 1,1,2-trisubstituted alkenes and with ketones produce 1,1,2,2,-tetrasubstituted alkenes. Most significantly, the latter seem readily available via the W–E reaction.[159, 227, 234, 259]

**TABLE 10.1 Phosphonates [$R^1R^2CH{-}P(O)(OR)_2$] that have been Employed in the W–E Reaction with Aldehydes or Ketones**

| $R^1$ | $R^2$ | References |
|---|---|---|
| H | H | 20, 21, 22, 124 |
| Cyclopropyl | H | 131 |
| $CH_3$ | $CH_2Ar$ | 150 |
| $CH_2SiMe_3$ | H | 173 |
| $CF_3$ | $CF_3$ | 174 |
| $CH(OEt)_2$ | H | 175 |
| Ph | H | 88, 111, 176 |
|  | $CH_3$ | 177 |
| $C_6H_4{-}COOEt(p)$ | H | 178 |
| $-C_6H_4{-}C_6H_4-$ |  | 74 |
| 2–Pyridyl | H | 96 |
| Thienyl | H | 179 |
| Furyl | H | 179 |
| $CH{=}CH_2$ | H | 180 |
| $CH{=}CR{-}CH_3$ | H | 181 |
| CH=CH–Ph | H | 96 |
| CH=C(OEt)R | H | 182 |
| C(Me)=CHCOOR | H | 172 |
| $C(COOEt){=}CR^1R^2$ | H | 183 |

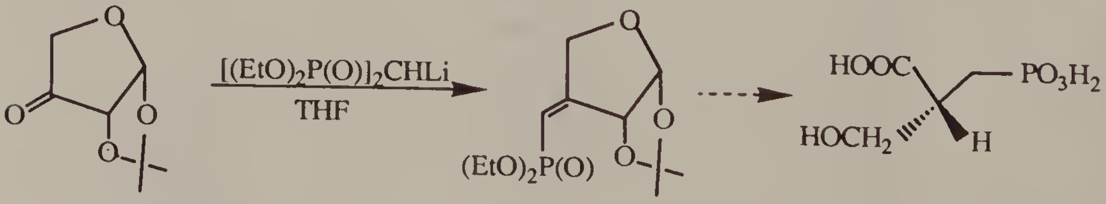
**TABLE 10.1** Continued

| $R^1$ | $R^2$ | References |
|---|---|---|
| $CH{=}CH{-}CH_2{-}NR_2$ | H | 184 |
| $CH{=}CH{-}CH{=}NC_6H_{11}$ | H | 185, 186 |
| CH=CH–N–Phth | H | 187 |
| $CH{=}CH{-}C(Me){=}CH{-}CH_2{-}OBn$ | H | 188 |
| $CCSiMe_3$ | H | 13 |
| $CH{=}N{-}NMe_2$ | H | 189 |
| COOEt | H | 94, 145, 175 |
| $COOC_4H_9$-*t* | H | 156 |
| $COO(CH_2)_8COOMe$ | H | 190 |
| COOEt | $CH_3$ | 163 |
| COOEt | $C_2H_5$ | 191 |
|  | R | 160 |
| COSEt | H | 192 |
| $COO(CH_2)_2{-}$ |  | 193 |
| $CONR_2$ | H | 109, 191, 194, 195 |
| CON(Me)OMe | H | 10, 157 |
| CONHCONR– |  | 196 |
| COOH | H | 16, 197 |
|  | F | 198 |
|  | R | 199 |
| $COCH_3$ | H | 15, 58, 102, 200 |
|  | $CH_3$ | 15, 200 |
| $COC_4H_9$-*t* | H | 200 |
| $COC_5H_{11}$-*n* | H | 201 |
| $COC_8H_{17}$ | H | 202 |
| $COCH_2COOEt$ | H | 203–205 |
| $COC(Me){=}C(Me)CH_2{-}$ |  | 206 |
| $COCH_2NH_2$ | H | 207 |
| $COC_6H_5$ | H | 74 |
| CN | H | 133, 151, 162, 208 |
|  | $CH_3$ | 162 |
|  | $CH(Et)COOBu^t$ | 209 |
| F | H | 210 |
|  | $CH_3$ | 210 |
|  | CN | 211 |
|  | COOMe | 212 |
|  | $P(O)(OR)_2$ | 32 |
|  | F | 49, 54, 213, 214 |
| Cl | Alkyl | 215 |
|  | Aryl | 17, 216, 217 |
|  | COOEt | 147, 165 |
|  | COOH | 218 |
|  | Cl | 219, 220 |
| Br | COOEt | 221 |
|  | COR | 222 |
|  | Br | 223 |
| OMe | H | 90, 224 |
|  | Ph | 225 |

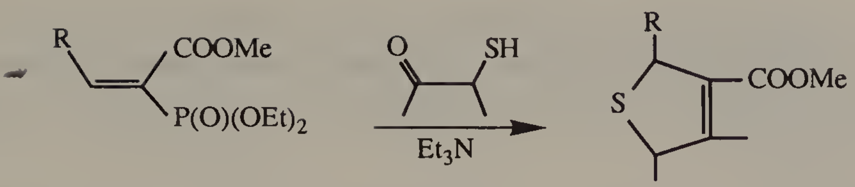
**TABLE 10.1** Continued

| $R^1$ | $R^2$ | References |
|---|---|---|
| OEt | H | 90 |
| $OCH_2CH_2OCH_3$ | H | 90, 123 |
| $OCH_2CH=CH_2$ | H | 226 |
| SMe | H | 122, 224, 227 |
| | Ph | 97, 224, 228 |
| | COOEt | 229 |
| | $CH_2CH_2COMe$ | 230 |
| SAr | H | 231, 232 |
| $S-CH_2-CH=CH_2$ | H | 226 |
| SR | OR | 228, 134 |
| | SR | 228, 233, 234 |
| SOMe | H | 235, 236 |
| SOAr | H | 97, 231, 237 |
| $SO_2Me$ | H | 109, 236, 238–240 |
| $SO_2Ph$ | H | 97, 109, 241, 242 |
| $SO_3R$ | H | 243 |
| S(O)(NTs)Ph | H | 244 |
| $^+S(Me)Ph$ | H | 245 |
| SeMe | R | 227, 246 |
| $N(CH_2)_4$ | H | 247 |
| NHR | COOMe | 248 |
| NHAr | Ar | 19 |
| N=CHR | R | 249 |
| NHCOR | COOR | 250 |
| NC | H | 251 |
| $^+N_2$ | H | 127, 252–255 |
| $^+PPh_3$ | H | 39, 256 |
| $P(O)(OR)_2$ | H | 32, 36, 91 |
| | $P(O)(OEt)CH_2P(O)(OEt)_2$ | 257 |
| $P(O)(OEt)_2$ | $P(NR_2)CH_2P(O)(OEt)_2$ | 258 |

Use of methylene bis-phosphonate [$R^1$ = H, $R^2$ = $P(O)(OEt)_2$] in the W–E reaction provides a high yield source of vinylphosphonates,[35, 36, 91] which themselves are useful intermediates. As examples, Blackburn and Rashid[37] produced an enantiomeric phosphonate by this means (Eq. 10.16), McIntosh and Siller[260] effected anion addition and eventual ring closure to 2,5-dihydrothiophenes using vinyl phosphonates (Eq. 10.17), Brooks and Palmer effected



(10.16)

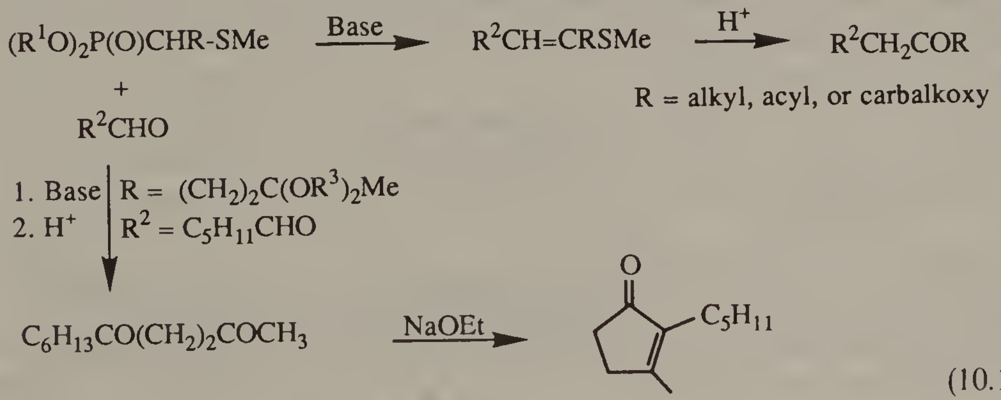


(10.17)

two consecutive W–E reactions,[261] and Mikolajczyk et al.[38] added acetone enolate to α-methylthiovinylphosphonate eventually to form 1,4-diketones which could be cyclized to cyclopentenones. Bis-phosphonates having their phosphono groups separated by at least two carbon atoms long have been known to undergo double W–E reactions[262] to form linear[263] and cyclic[264] dienes.

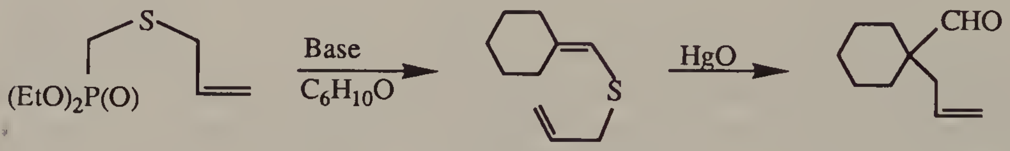
The presence of a vinyl group on the phosphonate carbanion usually has no deleterious effect on the W–E reaction. Carbanions prepared from allylic phosphonates are known to have some electron density at both their α- and γ-carbon atoms[180] (see Section 10.3), but the nucleophilic center in the W–E reaction usually remains the α-carbon,[172,182,187,188] producing dienes as expected. However, the geometry of the original allylic double bond usually is compromised in the basic medium to mainly *E*-alkene.[154,184] Gerber et al.[265] recently reported selected instances of γ-nucleophilicity under thermodynamic control conditions.

The carbanion group in a phosphonate has been shown to be the synthetic equivalent of several other groups useful in synthesis. For example, the $RCCl^-$ group[17,266] and $RCBr^-$ group[221] served as the equivalent of an alkyne group on phosphonate when involved in a W–E reaction with an aldehyde (R′CHO) to produce vinyl halides which then were dehydrohalogenated to alkynes. α-Thiomethylation of a phosphonate produced the equivalent of an acyl group [RCH(SMe) – ], since involvement in a W–E condensation and cleavage of the resulting α-methylthioalkene afforded ketones.[122] The same approach but changing the R group has afforded 1,2-diketones,[229] 1,4-diketones (cyclizable to cyclopentenones),[230] and α-ketoacids[267] (Eq. 10.18). Taylor and Davies[204] made the acetonylacetate group ($-CH_2COCH_2COOEt$) on phosphonate the equivalent of the propionate carbanion ($^-CH_2CH_2COOEt$) through the W–E reaction.

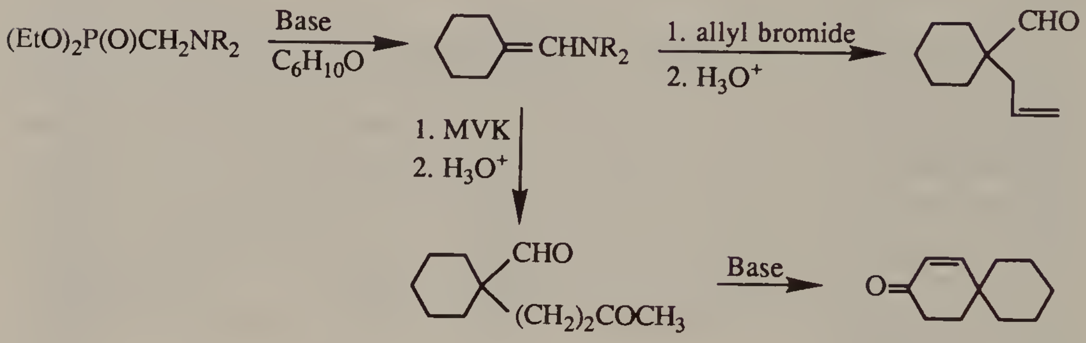


(10.18)

Corey and Shulman (Eq. 10.19),[226] and later Martin and Gompper (Eq. 10.20),[247, 268] used the W–E reaction as the initial step in converting a carbonyl group into a tetrasubstituted carbon which served as a starting point for spiro-annulation reactions.



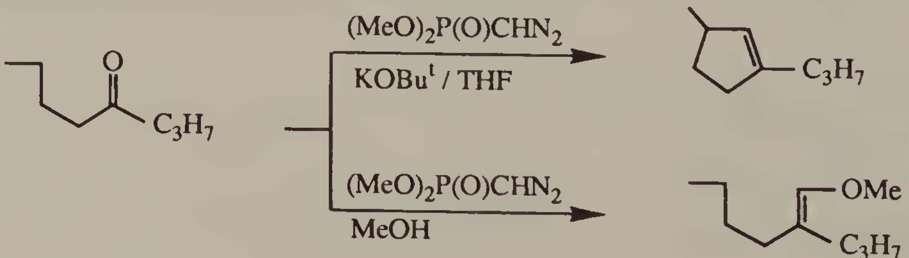
(10.19)



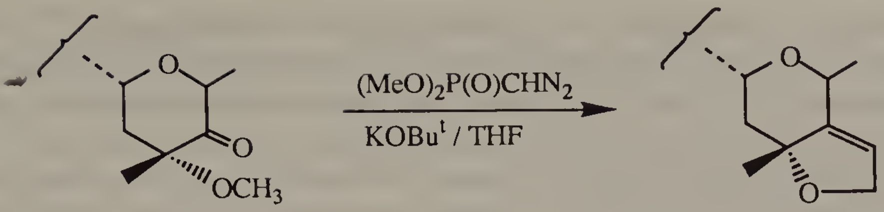
(10.20)

Dialkyl diazomethyl phosphonates [e.g., $(EtO)_2P(O)CHN_2$ = DAMP][269] have been used in three distinct reactions. With alkenes it underwent loss of nitrogen and afforded cyclopropylphosphonates which could be used in W–E reactions to produce alkylidenecyclopropanes.[127] With carbonyl compounds it effected an initial W–E reaction to produce an alkylidenediazo intermediate which, in the presence of an alcohol afforded an enol ether and in the presence of a secondary or primary amine afforded an enamine, both of which could be hydrolyzed to an aldehyde (Eq. 10.21).[270] The overall effect was the conversion of a carbonyl compound (C=O) to its one carbon homolog (CH–CHO). Four groups[252, 253, 271–273] have shown that in THF solvent DAMP will effect W–E reactions to produce alkylidenediazo intermediates which will lose nitrogen, form a carbene, and effect cyclization–insertion reactions (Eqs. 10.21 and 10.22).

Finally, two noncarbanion phosphonate anions have been used in W–E reactions. Phosphoramides, readily available from chlorophosphates and pri-



(10.21)



(10.22)

mary amines, lose a proton to sodium hydride to form phosphoramidate anions which react with carbonyl compounds (aldehydes, ketones, ketenes, isocyanates) to form good yields of the corresponding imines, ketenimines, and carbodiimides, respectively (Eq. 10.23).[274, 275] In these reactions they are similar to iminophosphoranes (see Section 13.5.5).

$$(EtO)_2P(O)NHR \xrightarrow{NaH} (EtO)_2P(O)\bar{N}R \xrightarrow[-\ (EtO)_2PO_2^-]{RR'C{=}O} RR'C{=}NR \quad (10.23)$$

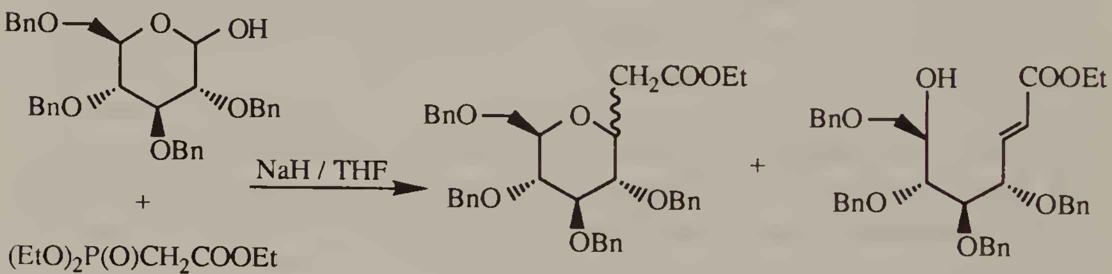
More recently an interesting group of phosphaphosphonates have been prepared and shown to undergo a W–E reaction with aldehydes and ketones to afford phosphaalkenes ($R_2C{=}P{-}R'$), all the while complexed to tungsten or molybdenum pentacarbonyl.[87, 276] The complexed phosphaalkenes were readily decomplexed, or the complexes could be trapped by addition of methanol across the C=P bond. Depending on the *P*-substituent, the phospha-anions reacted with both aldehydes and ketones, and with isobutyraldehyde the presence of the $W(CO)_5$ group did not affect the stereochemical outcome of the W–E reaction, the *P*-substituent and the isopropyl group being trans! The same phospha-anions could be converted to phosphadienes in W–E reaction with alkenals, but with alkenones a Michael addition occurred.[277]

***10.2.4.2 Carbonyl Reactants.*** Phosphonate carbanions (phosphono ylides) react with a nearly limitless variety of aldehydes and ketones to afford alkenes. From the simplest W–E reaction using formaldehyde to introduce a methylene group[272] to sterically hindered aldehydes[104, 161, 162, 166, 212, 219] it is rare to find an unreactive aldehyde. Similarly, most ketones react effectively with phosphonate carbanions,[111, 159, 185, 217, 239] even hindered ketones,[30, 170, 178, 184, 187, 197] but in a few instances ketones produced low yields.[118, 129, 137, 176, 199] Cycloalkanones normally are effective in the W–E reaction[220, 235, 278] and while diaryl ketones react, yields occasionally are low.[73, 134, 279] $\alpha,\beta$-Unsaturated aldehydes react in the normal manner,[78, 148, 187, 203] but $\alpha,\beta$-unsaturated ketones may undergo the W–E reaction at carbonyl or a conjugate addition (see Section 10.3.2.1). Reaction with *o*-quinones proceeds via a single W–E reaction, with the product undergoing subsequent transformations, often conjugate additions and cyclizations.[280]

Aldehydes clearly are more reactive than ketones[281, 282] and $\alpha$-ketoesters reacted with phosphonate carbanions at the ketonic carbonyl group.[167] There are conflicting reports on the reactivity of bicyclo[2.2.1]heptane ketones[220, 283] and also on steroidal ketones. The steroidal 3-ones clearly were reactive[284–287] but the 6 and 7 positions were reported to be less reactive.[284, 286] The 17-position[288] and the 20-position[289] both were quite reactive. A methyl bicyclooctyl ketone was reported not to react with triethyl phosphonoacetate, whereas it did react with the Reformatsky reagent.[290]

The phosphonate carbanion is more nucleophilic than the corresponding phosphonium ylide, and there have been numerous reports where specific ylides have been unreactive toward certain ketones while the corresponding phosphonate has effectively reacted to produce the desired alkene.[291] For example, Tadano et al.[292] found that a series of hexofuranoses would not react with triphenylphosphoniumcarbethoxymethylide, but would react in good yield with triethyl phosphonoacetate. Such distinctions usually are not found with aldehydes.

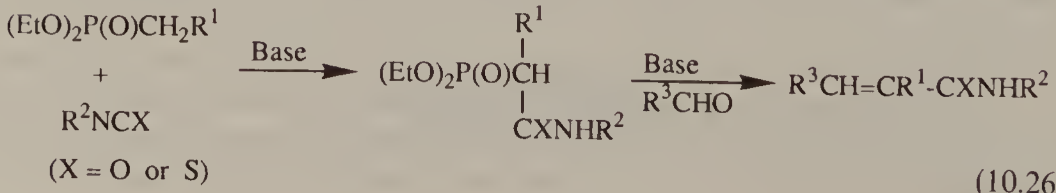
Phosphonate carbanions have been successfully reacted with numerous carbohydrates, both ketoses[292] and hemiacetals,[86] in circumstances where the Wittig reaction either failed or produced elimination byproducts. Thus, triethyl phosphonoacetate reacted with the masked aldehyde group to produce alkene and/or the recyclized derivatives (Eq. 10.24).[86, 293] The ratio of the two kinds of products was significantly controllable by solvent choice.



(10.24)

Ketenes have long been known to react with phosphonate carbanions to produce allenes,[74, 294] and recent techniques have improved the yields considerably (Eq. 10.25).[109, 240] However, isocyanates and isothiocyanates do not afford the analogous ketinimines, as did phosphonium ylides (Section 7.3.2), instead undergoing proton transfer to produce amidomethyl-phosphonates (Eq. 10.26).[33, 295–297] The latter have been employed in the W–E reaction to afford good yields of $E$-$\alpha,\beta$-unsaturated amides in high yields.[205]

$$(EtO)_2P(O)CH_2R^1 \quad + \quad R^2R^3C{=}C{=}O \xrightarrow[-\,(EtO)_2PO_2^-]{\text{Base}} R^2R^3C{=}C{=}CHR^1 \qquad (10.25)$$

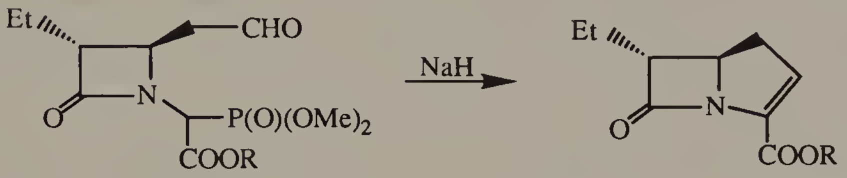


$$\begin{array}{c}(EtO)_2P(O)CH_2R^1\\ +\\ R^2NCX\\ (X = O \text{ or } S)\end{array} \xrightarrow{\text{Base}} \begin{array}{c}R^1\\ |\\ (EtO)_2P(O)CH\\ |\\ CXNHR^2\end{array} \xrightarrow[R^3CHO]{\text{Base}} R^3CH{=}CR^1\text{-}CXNHR^2$$

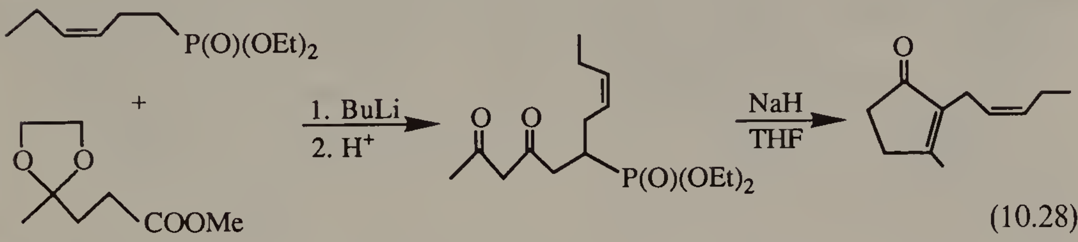
(10.26)

*10.2.4.3 Intramolecular W–E Reactions.* The intramolecular W–E reaction has become a mainstay for forming ring systems of from five to at least 38 members, and the subject has been reviewed by Wadsworth,[2] Walker,[85] Becker,[262] and most recently Maryanoff and Reitz.[298]

Five-membered rings have been formed by straightforward reaction of 5-carbonylalkylphosphonates, usually stabilized by an α-carboalkoxy or β-keto group, to produce compounds ranging from carbapenems (Eq. 10.27)[299] to variously substituted cyclopentenone derivatives[300–302] including *cis*-jasmone (Eq. 10.28)[303] and [3.3.0]bicyclic compounds.[304] Heteroatom-containing rings, such as butenolides[267, 305] and 2,5-dihydro-thiophenes[260] have been similarly prepared. Aristoff et al.[306] developed a general method for converting cyclic enol lactones, available from γ-ketoesters,[307] into same-sized cyclic enones by converting the ester into a ketophosphonate with dimethyl lithiomethylphosphonate and then effecting an intramolecular W–E reaction (see Section 10.3.1.2).

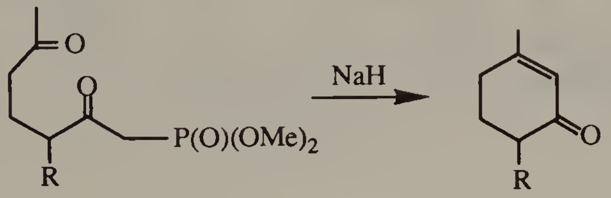


(10.27)

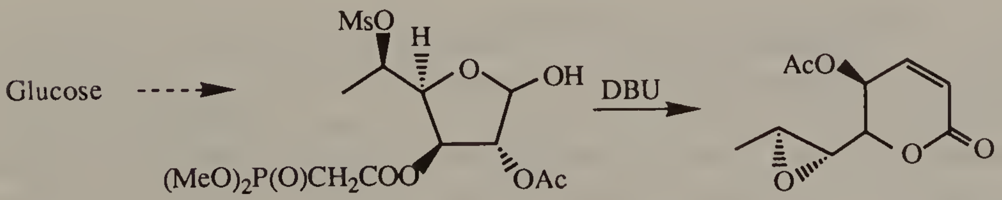


(10.28)

Six-membered rings have been formed from 6-aldehydo- or 6-ketoalkylphosphonates. Grieco et al.[308] converted open-chain 2,6-diketoheptylphosphonates to cyclohexenones (Eq. 10.29) and many others have applied this same principle to more complicated systems (Eq. 10.30).[31, 309–311]



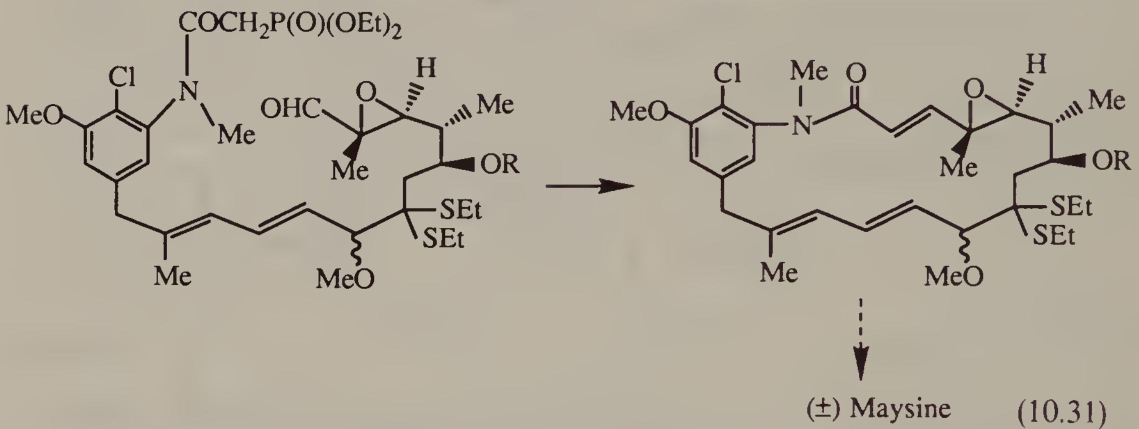
(10.29)



(10.30)

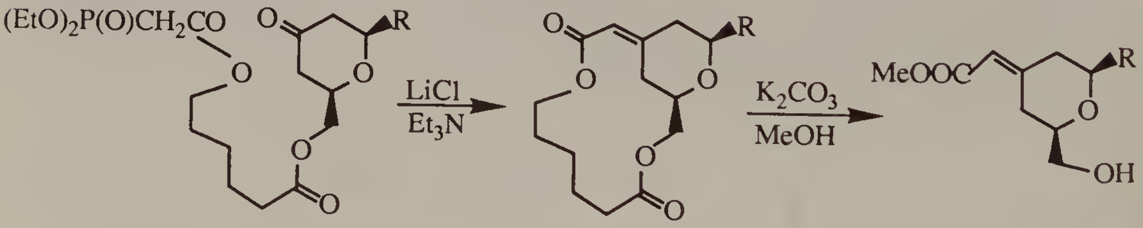
The reaction of diols with α-diazophosphonates served as a starting point for oxacycloalkene syntheses, the ring containing one more carbon than the diol.[312] Kolodiazhnyi[313] formed coumarins and quinolines by initial addition of *o*-hydroxy- and *o*-aminobenzaldehydes, respectively, to phosphonyl ketenes followed by intramolecular W–E reactions.

A wide variety of macrolide syntheses have relied on the W–E reaction for the ring closure step.[314] Most have used ordinary experimental procedures, such as potassium *t*-butoxide in THF and found it possible to minimize dimerization by using very dilute solutions[315] and to facilitate the reaction using crown ethers in toluene.[112, 113] As examples, Meyers et al.[316] completed a total synthesis of (±) maysine by obtaining only the *E*-alkene in the cyclization step (Eq. 10.31),



(10.31)

while recently Evans and Carreira[317] prepared a tethered model phosphonate, effected an intramolecular W–E reaction using lithium chloride and triethylamine, and then removed the tether, all to ensure the correct stereochemistry in the $C_{11}$–$C_{16}$ synthon to be incorporated into a total synthesis of bryostatin I (Eq. 10.32).



(10.32)

*10.2.4.4 Complications in the W–E Reaction.* There seem to be only three generic complications in the W–E reaction, one of which can be avoided. As mentioned in Section 10.2.1, attempted use of amines as a weaker than usual base often leads to a Knoevenagel dehydration instead,[77–79, 318] but conditions now have been described permitting use of amines and yet avoid this problem.[116–118, 317]

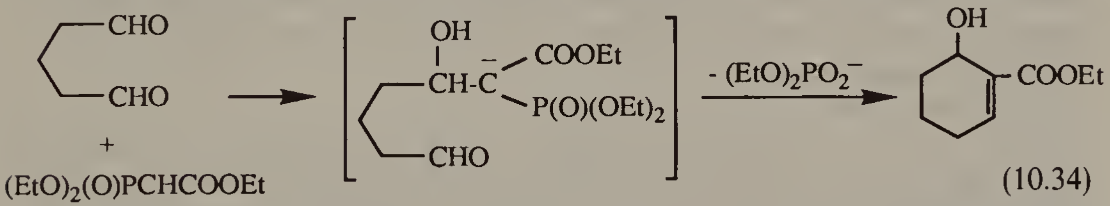
It has proven impossible to effect a W–E reaction with a phosphonate carrying a silyl group on the carbanion because of the competing Peterson elimination.[30, 319–321] For example, an α-trimethylsilyl phosphonate afforded, with a variety of aldehydes and ketones, good yields of vinyl phosphonates rather than vinyl silanes (Eq. 10.33).[322] However, normal W–E reactions

$$\mathrm{Me_3SiCH_2P(O)(OEt)_2} \xrightarrow[\mathrm{RR'C{=}O}]{\mathrm{BuLi}} \mathrm{RR'C{=}CHP(O)(OEt)_2} + \mathrm{Me_3SiOLi} \tag{10.33}$$

occurred when the trimethylsilyl group was one carbon removed from the carbanion.[173] Similarly, α-stannyl groups were eliminated in preference to the phosphonyl group in reaction with aldehydes.[323]

Some phosphonate carbanions react with α,β-unsaturated carbonyl compounds, most often ketones, at the β-position rather than at the carbonyl group, effecting conjugate addition and occasionally subsequent cyclization rather than a W–E reaction. This reaction is discussed in Section 10.3.2.1.

A number of miscellaneous examples of complications in W–E reactions are cited. α-Chloromethyl phosphonate carbanions, after initial addition to a carbonyl group, occasionally expelled chloride to produce an oxirane in a Darzen's-like condensation.[16, 219, 324–326] Reaction of phosphonate carbanions with cyclohexanones occasionally has resulted in migration of the initially formed exocyclic double bond to an endocyclic position.[101, 163, 192, 200, 237, 278] The interesting driving force for formation of six-membered rings was evident in the reaction of triethyl phosphonoacetate with glutaraldehyde, presumably proceeding via proton transfer in the first intermediate to form a new phosphonocarbanion which then cyclized (Eq. 10.34).[327] Ring opening of a cyclohexa-1,3-dione followed by reclosure has been reported recently,[328] and carbanion attack on the aromatic ring of p-nitrobenzophenone has been observed to compete with alkene formation.[232]



(10.34)

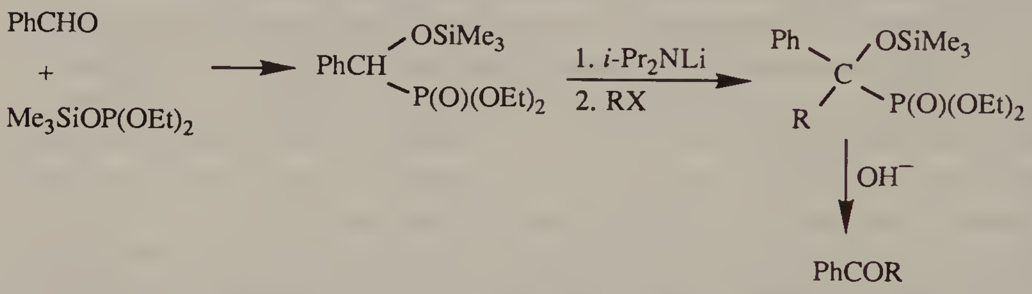
## 10.3 OTHER REACTIONS OF PHOSPHONATE CARBANIONS

### 10.3.1 Electrophiles

*10.3.1.1 Alkylation.* Alkylation of phosphonate anions with alkyl halides is a very old reaction, first having been reported by Arbusov et al.[1, 3] as the methylation, ethylation, and benzylation of triethyl phosphonoacetate, and nbutylation later was reported by Kosolapoff[329] and Wadsworth and Emmons.[74] Pudovik[330] reported carboethoxymethylation and Kosolapoff[331] reported stepwise dimethylation.

A wide variety of alkylating agents have been employed, usually without much complication from dialkylation, including trimethylsilyl chloride,[210, 219, 320] methyl sulfate,[210, 219] ethylsulfate,[219] *N*-(methylthiomethyl) piperidine hydrochloride,[332] allyl bromide,[210, 219, 333] and a variety of primary alkyl halides,[181, 334] although use of long-chain alkyl halides led to competing elimination reactions. Use of α,ω-dibromoalkanes led to formation of cycloalkylphosphonates in some cases,[335] but to normal monoalkylation in others.[336, 337] Difficulties have been reported by some in alkylating difluoromethylphosphonates.[214, 336, 337] Methylene bisphosphonate was readily converted to cyclopropane-1, 1-bisphosphonate by dialkylation.[338]

The alkylation of α-siloxyphosphonates, followed by hydrolysis, has provided an interesting means of homologating an aldehyde (Eq. 10.35).[339] Chlorine–lithium exchange of α,α-dichloromethylphosphonate with butyllithium, followed by the addition of catalytic quantities of cuprous bromide and an alkyl halide, resulted in replacement of chlorine with alkyl, and the process could be repeated to result in the substitution of two different alkyl groups on the α-carbon of phosphonate.[333]

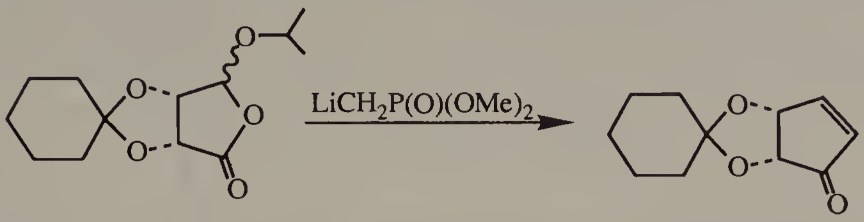


(10.35)

β-Ketophosphonates could be alkylated on the α-carbon[334] and/or on the γ-carbon, the latter possibly proceeding via an α,γ-dianion,[25,308] although recent reports claim the dianion is not necessarily formed.[205] Silylation of allylphosphonate was reported to occur first on the γ-carbon and then on the α-carbon,[180,340] and alkylation by a wide variety of alkyl groups produced the same results.[341] However, attachment of other substituents to the α-carbon resulted in either a mixture of α- and γ-alkylation or even complete α-alkylation.[340] Kondo et al.[181] reported only α-alkylation of γ,γ-disubstituted allyl phosphonates.

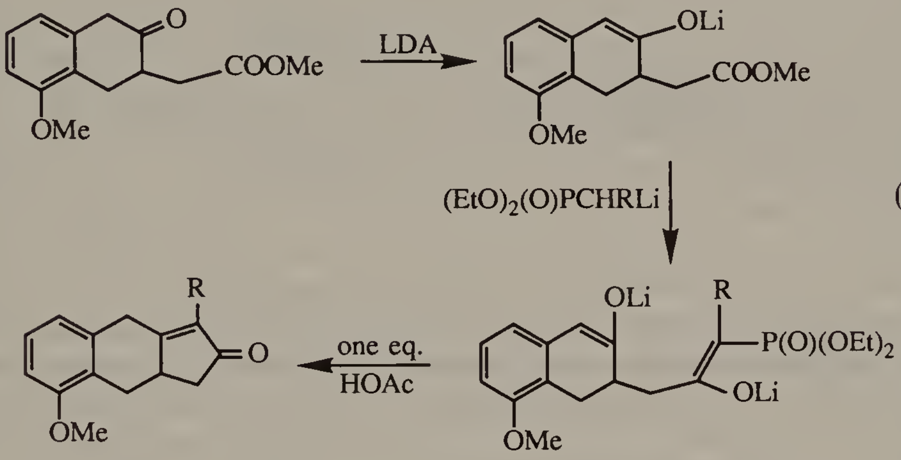
***10.3.1.2 Reaction with Lactones.*** Duggan et al.[342] found that diethyl cyanomethylphosphonate carbanion reacted with valerolactone and butyrolactone at the carbonyl group without ring opening to effect W–E reactions and produce enol ethers. More recently, a ketal lactone has been found to produce a cyclopentenone in high yield, presumably by nucleophilic ring opening to form a

$\beta$-ketophosphonate, deketalization, and an intramolecular W–E reaction of the $\beta$-ketophosphonate with the unmasked aldehyde group (Eq. 10.36).[343]



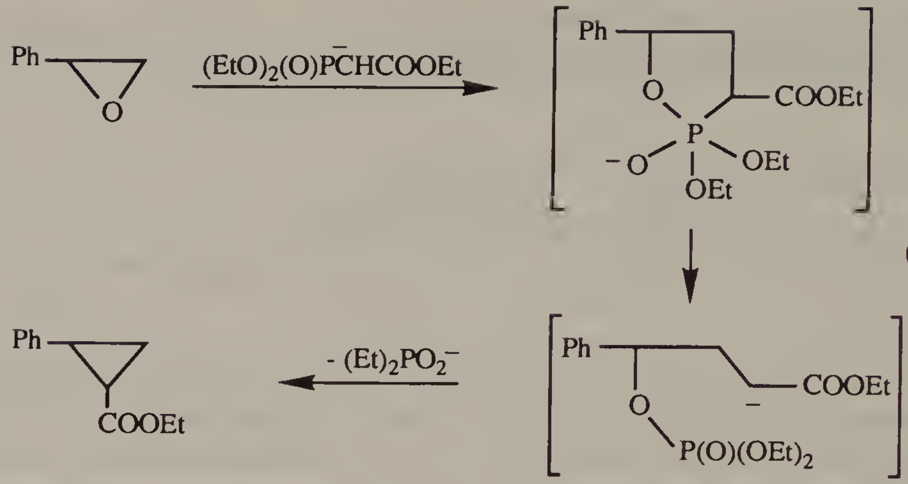
(10.36)

Reaction of phosphonate carbanions with enol lactones has become an effective means of preparing cyclopentenones, although it first was discovered by Henrick et al.[344] in the preparation of the A (six-membered) ring of testosterone acetate. More recently, Aristoff et al.[306] have improved the reaction yield to 85% and applied it to the synthesis of prostaglandin analogs. The process has been shortened to avoid separate preparation of the enol lactone, starting instead from the $\gamma$-ketoester (Eq. 10.37).[307]



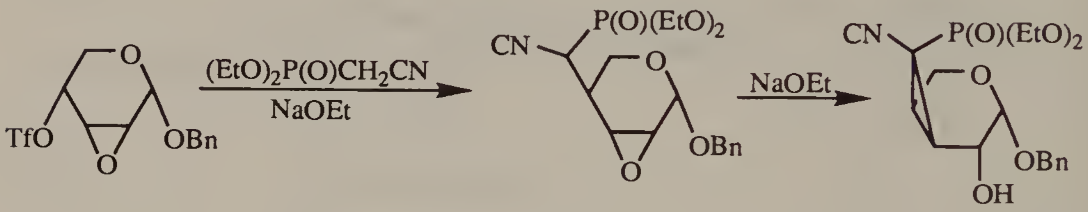
(10.37)

***10.3.1.3 Reaction with Oxiranes and Oxetanes.*** Substituted oxiranes react with phosphonate carbanions, under conditions milder than needed for phosphoranes, to produce substituted cyclopropanes in low to moderate yields. Triethyl phosphonoacetate afforded ethyl cyclopropane carboxylates,[72,345] while $\beta$-ketopropylphosphonates afforded methylcyclopropyl ketones.[200,207] Disubstituted phosphonates recently have afforded 1,1-disubstituted cyclopropanes upon reaction with oxirane.[346] Racemic styrene oxide with optically active carbomenthoxymethylphosphonate led to optically active 2-phenylcyclopropane carboxylic acid after hydrolysis.[345] Two groups demonstrated that the reaction mechanism involved inversion of configuration at *both* oxirane carbons, proceeding by ring opening to a pentacyclic intermediate which then dissociated in a stepwise manner involving nucleophilic displacement at the second carbon (Eq. 10.38).[345,347]



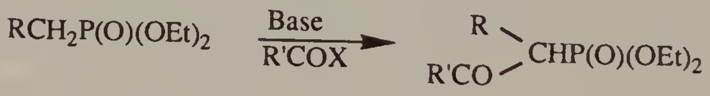
(10.38)

Fatima et al.[348] recently reported an interesting cyclopropane formation from an oxirane when a phosphonate carbanion was attached to the adjacent carbon (Eq. 10.39). The complexed phosphaphosphonates afforded numerous phosphirane complexes by analogous reaction with oxiranes.[349] Tanaka et al.[350] used a phosphonate carbanion to open an oxetane ring at the unsubstituted carbon, in the presence of a 2-deoxyfuranose ring, in the preparation of AZT analogs.



(10.39)

*10.3.1.4* ***Acylation.*** Acylation of phosphonate carbanions provides a route to $\beta$-carbonyl phosphonates (Eq. 10.40), a topic briefly addressed in Section 10.1.1.3. In contrast to the acylation of phosphonium ylides, in which there was occasionally competition from the olefination reaction, the W–E reaction with the carbonyl group of carboxylic acid derivatives normally does not compete with the acylation of phosphonates.



$$RCH_2P(O)(OEt)_2 \xrightarrow[R'COX]{Base} \begin{matrix} R \\ R'CO \end{matrix} \!\!> CHP(O)(OEt)_2$$

(X = Cl, NR$_2$, OR'', CN)
(R' = alkoxy, alkyl, aryl, alkenyl)

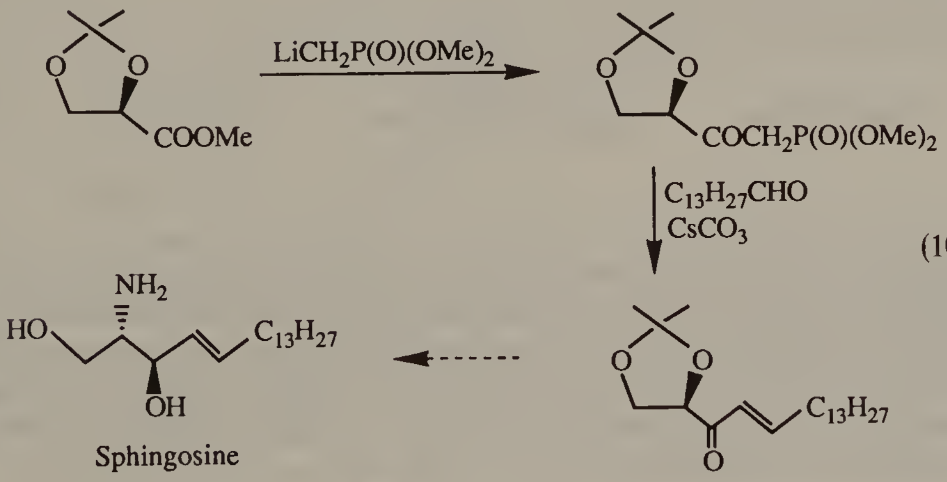
(10.40)

Acyl halides are effective acylating agents, with innumerable examples being known of the use of simple [23,125,210,351,352] or complex [202,353] acid chlorides, including ethyl chloroformate to produce the α-carbethoxyalkyl phosphonate.[147,354,355] The sodio- or lithio-phosphonocarbanion usually has been employed, but Savignac et al.[23,202] have found that conversion of the lithio salt to its cuprate salt before addition of the acid chloride resulted in better yields. Alkyl chlorothioformates[356] and methyl cyanoformate[310] have also been employed recently to introduce ester groups to the alkylphosphonate. Chlorophosphates and related compounds [$X_2P(O)Cl$] have also been employed.[42,242,357,358]

Amides have served as formylating agents. N-Formylmorpholine[359] and dimethylformamide[360] both are effective formylating agents for phosphono carbanions, providing the opportunity, through subsequent W–E reaction, to introduce a formylmethylene unit (=CH–CHO) in place of a carbonyl group.

Phosphono carbanions also react with carbon dioxide[229,325] to produce α-carboxyalkylphosphonates. Reaction also occurred with carbon disulfide[361,362] and subsequent methylation produced a ketene dithioacetal which, upon hydrolysis, afforded a methyl thioester.[356]

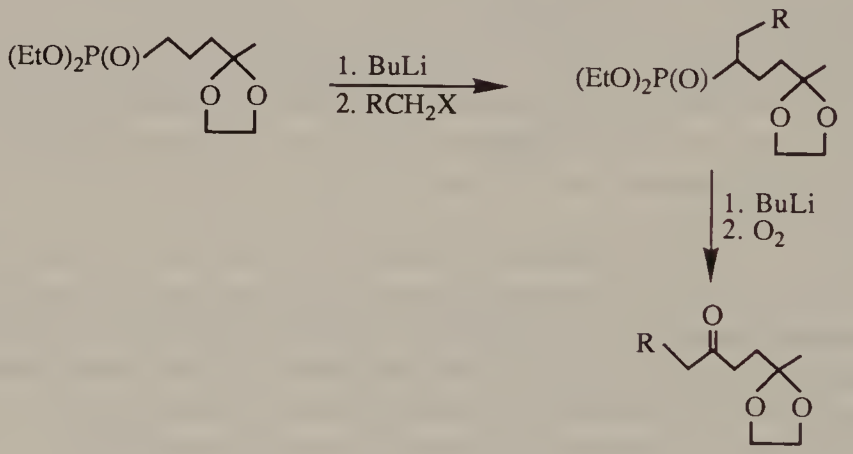
Esters are especially effective acylating agents, and there has been only one report of a competing olefination reaction (i.e., W–E reaction) at the carbonyl group, that being with diethyl oxalate and some phosphonates.[363] In contrast, many phosphonium ylides react with esters to produce enol ethers via a Wittig reaction (see Sections 6.5.3 and 8.2.2.7). Reported initially only in a footnote by Corey and Kwaitkowski,[20] the acylation of phosphono carbanions with a wide variety of esters has been significantly improved,[21] especially through use of lithium diisopropylamide as the base. The use of ethyl formate attached the formyl group[42] and the use of ethyl carbonate attached the carbethoxy group[165,332,364] to the phosphono carbanion. The reaction with esters has been widely employed in the synthesis of natural products in a chiral environment, such as syntheses leading to *cis*-jasmone,[303] prostaglandin analogs,[317] and sphingosine (Eq. 10.41).[365] Reaction of phosphono carbanions with diesters has produced bis-β-ketophosphonates which could be cyclized through intramolecular W–E reaction to afford functionalized cycloalkenones.[366]



(10.41)

***10.3.1.5 Miscellaneous Reactions.*** Halogenation of alkylphosphonates is facile, usually proceeding via the carbanion. Bromination occurred with bromine and sodium hydride[74] or with potassium hypobromite.[367] Fluorination occurred with perchloryl fluoride[283] and N-fluorobis(trifluoromethanesulfonyl)-imide[368] and iodination occurred with iodine and sodium hydride.[74] Diethyl trichloromethylphosphonate is best prepared from triethylphosphite and carbon tetrachloride in a Michaelis–Arbuzov reaction,[219,369] and it undergoes facile lithium–chlorine exchange[219,333,354] to afford dichloroalkylphosphono carbanions which can be alkylated or protonated. Sodium hypochlorite can lead to dichlorination of alkylphosphonates.[367] Benzenesulfonyl chloride recently has been used as a monochlorinating reagent for phosphonates.[215]

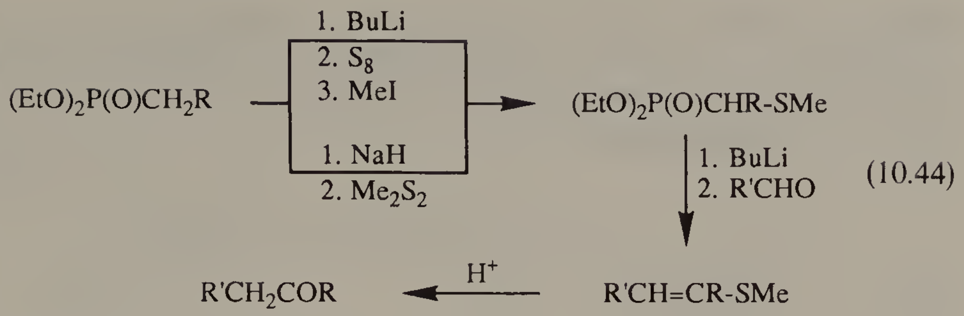
In a process similar to that undergone by phosphonium ylides, phosphono carbanions are subject to oxidation with molecular oxygen to produce carbonyl compounds. Although discovered over 30 years ago,[370] it still finds application (Eq. 10.42).[371,372] Its use permits the coupling of two alkyl groups to a phosphonate to eventually afford a ketone, the phosphonate carbanion becoming a carbonyl group (Eq. 10.43).



(10.42)

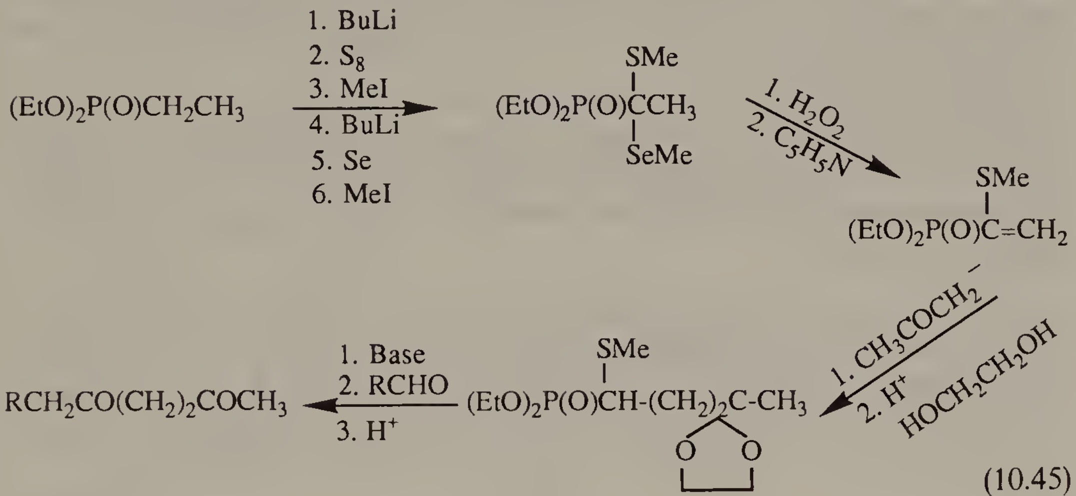
$$CH_3P(O)(OEt)_2 \xrightarrow[\text{3.Base, Oxidation}]{\substack{\text{1. Base, RCH}_2\text{X} \\ \text{2. Base, R'CH}_2\text{Y}}} RCH_2COCH_2R' \qquad (10.43)$$

Phosphono carbanions react with sulfur to afford α-thiols which are readily alkylated. A successive W–E reaction produced α-methylthioalkenes which could be hydrolyzed to ketones, permitting the phosphonate carbanion to serve as a masked carbonyl group (Eq. 10.44).[228,262] Alternatively, the phosphono carbanion could be reacted with dimethyl disulfide to directly obtain the methylthioalkylphosphonate.[229]



(10.44)

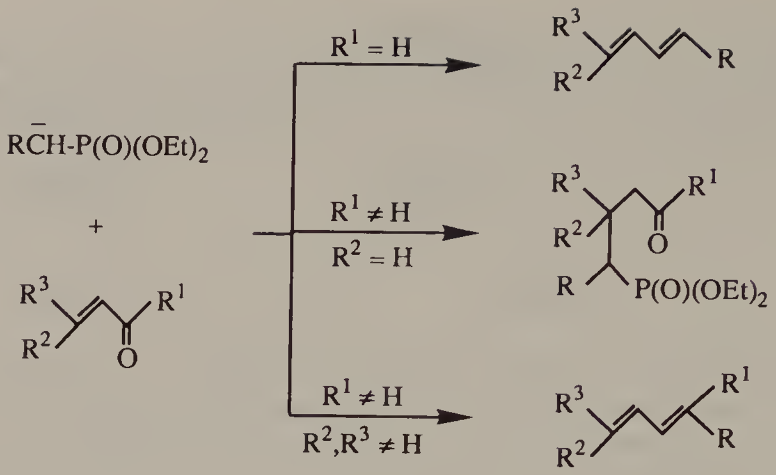
Selenium also reacts with phosphono carbanions to produce, from a subsequent reaction with methyl iodide, α-methylselenoalkylphosphonates.[38] Oxidation and elimination of selenic acid afforded vinylphosphonates. When selenation was preceded by sulfuration, the result of this process was α-methylthiovinylphosphonate, and addition of acetonide anion, protection of the ketone, and W–E reaction with aldehydes led to a new approach to 1,4-diketones (Eq. 10.45).[38] Thus, the $-CH_2-CH_3$ group of a reactant phosphonate became equivalent to the $-CO-CH_2-$ group of the final product. Selenation under stronger conditions led to carbanion–phosphorus cleavage, probably affording selenocarbonyl compounds which were trapped as selenoamides from reaction with secondary amines.[373]



(10.45)

### 10.3.2 Multiple-Bonded Compounds

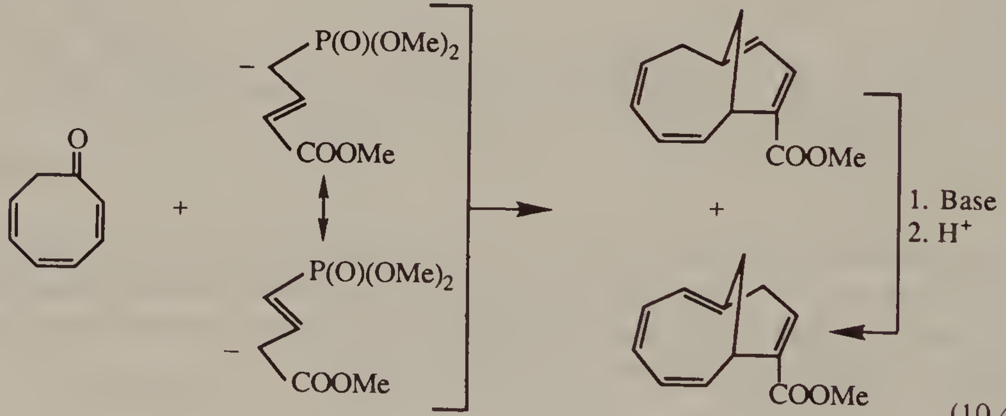
***10.3.2.1 Reaction with Conjugated Carbonyls.*** Reaction of phosphono carbanions with α,β-unsaturated *aldehydes* generally occurs at the carbonyl group in a normal W–E reaction to form a diene,[205,374] the alkene group having virtually no effect on the reaction. However, reaction with α,β-unsaturated *ketones* generally occurs as a conjugate addition.[375] If the β-carbon is disubstituted, addition generally reverts to the carbonyl group in a W–E reaction (Eq. 10.46).[208,375,376] It has been reported that the use of sodium ethoxide as the



(10.46)

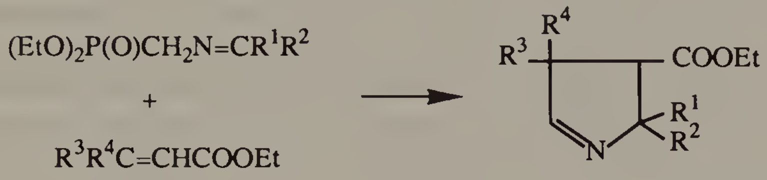
base in ethanol solution to generate the carbanion favored W–E reaction with α,β-unsaturated ketones, whereas use of aprotic conditions, such as sodium amide in ether, favored conjugate addition.[377] Further, cyanomethylphosphonate carbanions effected less conjugate addition than did carbethoxymethylphosphonate carbanions, presumably because of less delocalization in the cyano carbanion.[376]

When the phosphonate reactant was allylic, a 3+3-cyclization frequently occurred, presumably by conjugate addition of the γ-phosphono carbanion followed by subsequent intramolecular W–E reaction.[378,379] For example, cyclooctatrienone afforded the first example of a 1,5-methano-(10)-annulene system (Eq. 10.47).[380]

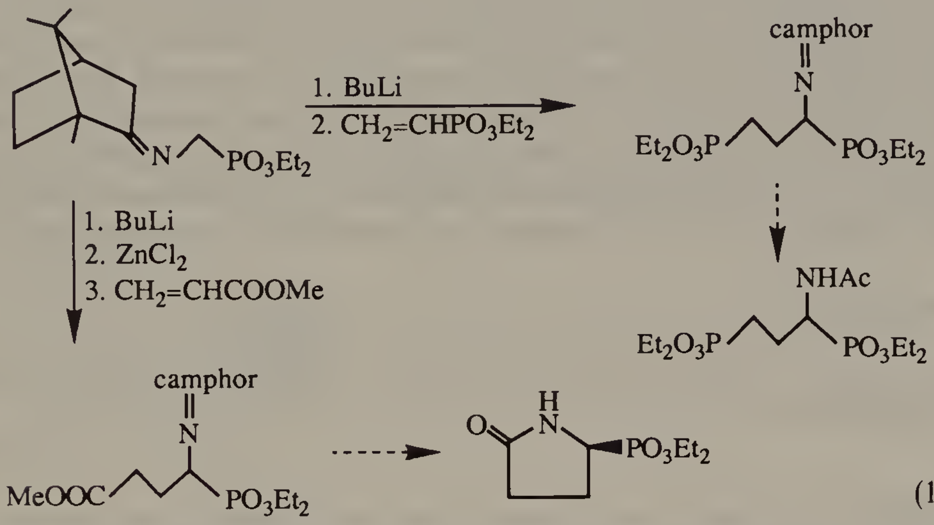


(10.47)

Phosphonate carbanion reaction with α,β-unsaturated esters has been known for a long time,[70] contrary to a recent claim,[381] with β-ketopropylphosphonate and α-carbethoxyphosphonate carbanions effecting conjugate addition to methyl acrylate. The *t*-butyl esters of substituted acrylates recently were found to undergo exclusive and stereoselective conjugate addition with the carbanions of alkylphosphonates, but the methyl, ethyl, and isopropyl acrylate esters afforded products both from conjugate addition and attack at the carbonyl group of the ester.[381] Conjugate addition, followed by cycloelimination of the phosphonate group, recently was employed as a means to prepare spin traps (Eq. 10.48).[382] The carbanion of an analogous Schiff base, obtained from (+)camphor and diethyl aminomethylphosphonate, effected conjugate addition to a vinyl phosphonate and ethyl acrylate with considerable stereoselectivity (Eq. 10.49).[383]

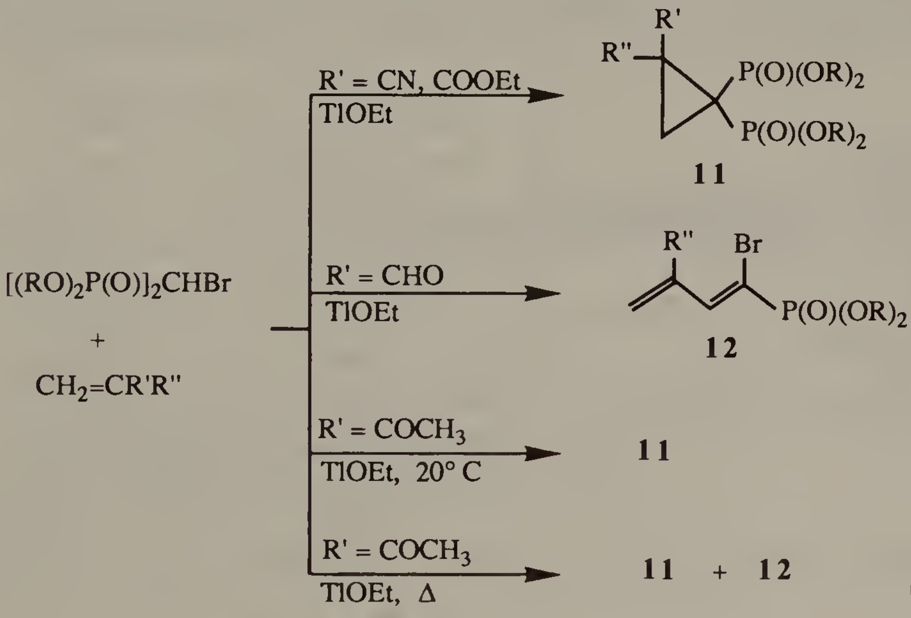


(10.48)



(10.49)

The recently reported reaction of bromomethylenebisphosphonate with conjugated aldehydes, ketones, and esters, all using thallium ethoxide as the base, presented the entire panoply of usually observed products, including W–E reaction and conjugate addition followed by cyclization (Eq. 10.50).[384] The



(10.50)

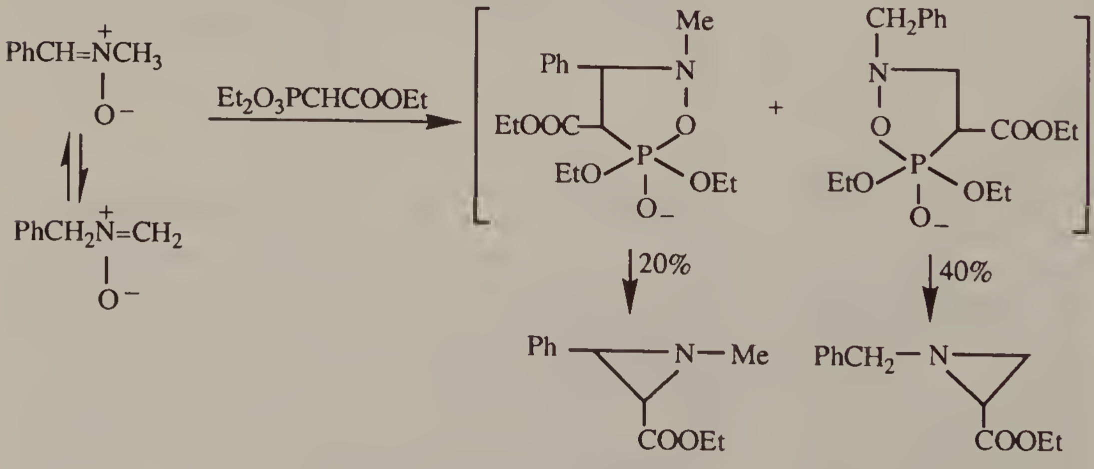
sequence of ester > ketone > aldehyde for preferred conjugate addition once more has held true.

*10.3.2.2* ***Reaction with Nitrogen-Containing Compounds.*** Phosphonate carbanions reacted with nitroso compounds in a manner analogous to the W–E reaction to produce imines and eliminate phosphate.[18,385] The carbanions also reacted with imines, normally to effect a simple addition, but in some cases the reaction continued to eject amidophosphate and produce alkenes. In those instances where the adduct was formed, it usually could be converted to the alkene with strong base.[386] This amounted to completion of a W–E type reaction. Reaction with ethoxymethylene aniline commenced in the same manner, but ethoxide was ejected to produce the phenylimine of an α-formylalkylphosphonate. This process was useful in that a subsequent W–E reaction with an aldehyde, followed by hydrolysis of the imine, accomplished transformation of the aldehyde to a homologated α,β-unsaturated aldehyde with the two substituents in a cis configuration (Eq. 10.51).[387] Phosphonate carbanions effected conjugate addition to conjugated imines such as $Ph_2C{=}NCOPh$.[388]

$$\begin{array}{c}(EtO)_2P(O)CH_2R\\ +\\ EtOCH{=}NPh\end{array} \longrightarrow Et_2O_3PCHRCH{=}NPh \xrightarrow[3.\ H_3O^+]{1.\ Base\quad 2.\ R'CHO} R'CH{=}CR\text{-}CHO$$

(10.51)

Nitrones also reacted with phosphonates and produced aziridines and/or enamines. N-Methyl-C-phenylnitrone reacted with sodio triethyl phosphonoacetate to produce two isomeric aziridines which presumably resulted from elimination of phosphate from two isomeric intermediate oxazaphospholidines (Eq. 10.52),[389] similar to the mechanism proposed for the reaction of oxiranes with phosphonate carbanions (Section 10.3.1.3). Only one aziridine resulted from a cyclic nitrone under the same conditions, but using a protic base instead



(10.52)

afforded only a small amount of the aziridine, the major product being an enamine.[390] The latter was the sole product when the more nucleophilic cyanophosphonate was employed under protic conditions.

## REVIEWS

**1966** Johnson, A. Wm. *Ylid Chemistry*, Academic: New York. A review of phosphonate carbanion chemistry.

**1974** Boutagy, J.; Thomas, R. *Chem. Revs. 74*, 87–99. A review of the W–E reaction.

**1977** Wadsworth, W. E. *Org. React. 25*, 73–253. A review of the W–E reaction.

**1979** Walker, B. J. In *Organophosphorus Reagents in Organic Synthesis*; Cadogan, J. I. G., Ed.; Academic: London; Chapter 3, pp. 155–205. A review of the W–E reaction.

**1981** Battacharya, A. K.; Thyagarajan, G. *Chem. Revs. 81*, 415–430. A review of the Michaelis–Arbuzov rearrangement to prepare phosphonates.

**1989** Maryanoff, B. E.; Reitz, A. B. *Chem. Revs. 89*, 863–927. A review of the W–E reaction.

**1992** Burton, D. J.; Yang, Z. Y. *Tetrahedron 48*, 189–275. A review of difluoromethylphosphonate carbanions.

**1992** Minami, T.; Motoyoshiya, J. *Synthesis* 333–349. A review of vinylphosphonates and their synthetic applications, especially nucleophile addition and subsequent W–E condensations.

## REFERENCES

1 Arbuzov, A. E.; Dunin, A. A. *Chem Ber.* **1927**, *60*, 291.

2 Wadsworth, W. E. *Org. React.* **1977**, *25*, 73.

3 Arbuzov, A. E.; Razumov, A. I. *J. Russ. Phys. Chem. Soc.* **1929**, *61*, 623; *Chem. Abstr.* **1929**, *23*, 4444.

4 Michaelis, A.; Kaehne, R. *Chem. Ber.* **1898**, *31*, 1048.

5 Crofts, P. C. *Quart. Rev.* **1958**, *12*, 341.

6 Arbuzov, B. A. *Pure Appl. Chem.* **1964**, *9*, 307.

7 Worms, K. A.; Schmidt-Dunker, M. In *Organic Phosphorus Compounds*; Kosolapoff, G. M. and Maier, L., Eds.; Wiley-Interscience: New York, 1976; Chapter 18, p. 22.

8 Battacharya, A. K.; Thyagarajan, G. *Chem. Revs.* **1981**, *81*, 415.

9 Lichtenthaler, F. W. *Chem. Revs.* **1961**, *61*, 607.

10 (a) Nuzillard, J. M.; Boumendjal, A.; Massiot, G. *Tetrahedron Lett.* **1989**, *30*, 3779; (b) Neetz, D.; Seidel J. L. *Tetrahedron Lett.* **1992**, *33*, 1957.

11 Michaelis, A.; Becker, T. *Chem. Ber.* **1892**, *30*, 1003.

12 Reference 7, p. 27.

13 Gibson, A. W.; Humphrey, G. R.; Kennedy, D. J.; Wright, S. H. R. *Synthesis* **1991**, 414.

[14] Sturtz, G.; *Bull. Soc. Chim. Fr.* **1964**, 2333.

[15] Normant, H.; Sturtz, G. *C. R. Seances Acad. Sci.* **1963**, *256*, 1800.

[16] Britelli, D. R. *J. Org. Chem.* **1981**, *46*, 2514.

[17] Zimmer, H.; Bercz, P. J.; Maltenieks, O. J.; Moore, M. W. *J. Am. Chem. Soc.* **1965**, *87*, 2777.

[18] Zimmer, H.; Bercz, P. J.; Hener, G. E. *Tetrahedron Lett.* **1968**, 171.

[19] Zimmer, H.; Servay, T. K., *Phosphorus Sulfur* **1991**, *61*, 201.

[20] Corey, E. J.; Kwaitkowski, G. T. *J. Am. Chem. Soc.* **1966**, *88*, 5654.

[21] Tang, K. C.; Coward, J. K. *J. Org. Chem.* **1983**, *48*, 5001.

[22] Aboujaoude, E. E.; Collignon, N.; Teulade, M. P.; Savignac, P. *Phosphorus Sulfur* **1985**, *25*, 57.

[23] Savignac, P.; Mathey, F., *Tetrahedron Lett.* **1976**, 2829.

[24] Chatta, M. S.; Aguiar, A. M. *J. Org. Chem.* **1973**, *38*, 2908.

[25] Grieco, P. A.; Pogonowski, C. S. *J. Am. Chem. Soc.* **1973**, *95*, 3071; Grieco, P. A.; Finkelhor, R. S. *J. Org. Chem.* **1973**, *38*, 2909.

[26] Calogeropoulou, T.; Hammond, G. B.; Wiemer, D. F. *J. Org. Chem.* **1987**, *52*, 4185.

[27] Lee, K.; Wiener, D. F. *Abstracts of Lectures*, 12th International Conference on Phosphorus Chemistry, Toulouse, France, 1992; p. 34.

[28] Schoen, W. R.; Parsons, W. H. *Tetrahedron Lett.* **1988**, *29*, 5201.

[29] Hong, S.; Chang, K.; Ku, B.; Oh, D. Y. *Tetrahedron Lett.* **1989**, *30*, 3307.

[30] Chang, K.; Ku, B.; Oh, D. Y. *Synth. Comm.* **1989**, *19*, 1891.

[31] Minami, T.; Kitajima, Y.; Chikugo, T. *Chem. Lett.* **1986**, 1229.

[32] Kleschik, W. A.; Heathcock, C. H. *J. Org. Chem.* **1978**, *43*, 1256.

[33] Bestmann, H. J.; Lehnen, H. *Tetrahedron Lett.* **1991**, *32*, 4279.

[34] Barbot, F.; Paraiso, E.; Miginiac, P. *Tetrahedron Lett.* **1984**, *25*, 4369.

[35] Minami, T.; Motoyoshiya, J. *Synthesis* **1992**, 333.

[36] Gupta, A.; Sacks, K.; Khan, S.; Tropp, B. E.; Engel, R. *Synth. Comm.* **1980**, *10*, 299.

[37] Blackburn, G. M.; Rashid, A. *J. Chem. Soc. Chem. Commun.* **1988**, 317.

[38] Mikolajczyk, M.; Grzejszczak, S.; Korbacz, K. *Tetrahedron Lett.* **1981**, *22*, 3097.

[39] Jones, G. H.; Hamamura, E. K.; Moffatt, J. G. *Tetrahedron Lett.* **1968**, 5731.

[40] Kandil, A. A.; Porter, T. M.; Slessor, K. N. *Synthesis* **1987**, 411.

[41] Larsen, R. O.; Aksnes, G. *Phosphorus Sulfur* **1983**, *15*, 219.

[42] Breuer, E.; Bannet, D. M. *Tetrahedron Lett.* **1978**, *34*, 997.

[43] Patois, C.; Ricard, L.; Savignac, P. *J. Chem. Soc. Perkin Trans. (1)* **1990**, 1577.

[44] Hatakeyama, S.; Satoh, K.; Sakavia, K.; Takano, S. *Tetrahedron Lett.* **1987**, *28*, 2713.

[45] Hensel, M. J.; Fuchs, P. L. *Synth. Comm.* **1986**, *16*, 1285.

[46] Polozov, A. M.; Polezhoeva, N. A.; Mustaphen, A. H.; Khotinen, A. V.; Arbuzov, B. A. *Synthesis* **1990**, 515.

[47] Hanaya, T.; Yamamoto, H.; Yamamoto, H. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 1154.

[48] Teulade, M. P.; Savignac, P. *Tetrahedron Lett.* **1987**, *28*, 405.

[49] Obayashi, M.; Kondo, K. *Tetrahedron Lett.* **1982**, *23*, 2327.

[50] Kawashima, T.; Ishii, T.; Inamoto, N. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 1831.

[51] Teulade, M. P.; Savignac, P.; Aboujaoude, E. E.; Collignon, N. *J. Organomet. Chem.* **1986**, *312*, 283.

[52] Teulade, M. P.; Savignac, P.; Jaudet, E. A.; Collignon, N. *Phosphorus Sulfur* **1988**, *40*, 105.

[53] Bordwell, F. G. *Acc. Chem. Res.* **1988**, *21*, 456.

[54] Burton, D. J.; Yang, Z. Y. *Tetrahedron* **1992**, *48*, 189.

[55] Corset, J. *Pure Appl. Chem.* **1986**, *58*, 1133.

[56] Seyden-Penne, J. *Bull. Soc. Chim. Fr.* **1988**, 238.

[57] Webb, G. A.; Simonnin, M. P.; Seyden-Penne, J.; Bottin-Strzalko, T. *Magn. Res. Chem.* **1985**, *23*, 48.

[58] Smith, S. J.; Zimmer, H.; Fluck, E.; Fischer, P. *Phosphorus Sulfur* **1988**, *35*, 105.

[59] Bottin-Strzalko, T.; Seyden-Penne, J.; Poutet, M. J.; Simonnin, M. P. *J. Org. Chem.* **1978**, *43*, 4346.

[60] Bottin-Strzalko, T.; Corset, J.; Froment, F.; Poutet, M. J.; Seyden-Penne, J.; Simonnin, M. P. *J. Org. Chem.* **1980**, *45*, 1270.

[61] Bottin-Strzalko, T.; Seyden-Penne, J.; Poutet, M. J.; Simonnin, M. P. *Org. Magn. Res.* **1982**, *19*, 69.

[62] Strzalko, T.; Seyden-Penne, J.; Froment, F.; Corset, J.; Simonnin, M. P. *J. Chem. Soc. Perkin Trans. (2)* **1987**, 783; *Can. J. Chem.* **1988**, *66*, 391.

[63] Zarges, W.; Marsch, M.; Harms, K.; Haller, F.; Frenking, G.; Boche, G. *Chem. Ber.* **1991**, *124*, 861.

[64] Macicek, J.; Angelova, O.; Petrov, G.; Kirilov, M. *Acta Cryst.* **1988**, *44C*, 626.

[65] Weiss, E.; Kopf, J.; Gardein, T.; Corbelin, S.; Schumann, U.; Kirilov, M.; Petrov, G. *Chem. Ber.* **1985**, *118*, 3529.

[66] Denmark, S. E.; Dorow, R. L. *J. Am. Chem. Soc.* **1990**, *112*, 864.

[67] Bottin-Strzalko, T.; Seyden-Penne, J.; Breuer, E.; Poutet, M. J.; Simonnin, M. P. *J. Chem. Soc. Perkin Trans. (2)* **1985**, 1801.

[68] Juaristi, E.; Cueves, G. *Tetrahedron* **1992**, *48*, 5019.

[69] Mikolajczyk, M. *Abstracts of Lectures*, 15th International Symposium on Organic Sulfur Chemistry, Caen, France; 1992, L19.

[70] Pudovik, A. N.; Lebedeva, N. M. *Dokl. Akad. Nauk SSSR* **1953**, *90*, 799; *Chem. Abstr.* **1956**, *50*, 2429.

[71] Patai, S.; Schwartz, A. *J. Org. Chem.* **1960**, *25*, 1232.

[72] Horner, L.; Hoffman, H.; Wippel, H. G. *Chem. Ber.* **1958**, *91*, 61.

[73] Horner, L.; Hoffmann, H.; Wippel, H. G.; Klahre, G. *Chem. Ber.* **1959**, *92*, 2499.

[74] Wadsworth, W. S.; Emmons, W. D. *J. Am. Chem. Soc.* **1961**, *83*, 1733.

[75] Pommer, H. *Angew. Chem.* **1960**, *72*, 811 and 911.

[76] Trippett, S.; Walker, D. M. *Chem. Ind.* **1961**, 990.

[77] Lehnert, W. *Tetrahedron* **1974**, *30*, 301.

[78] Minami, T.; Yamanouchi, T.; Tokumasu, S.; Hirao, I. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 2127.

[79] Reetz, M.; Peter, R.; von Itzstein, M. *Chem. Ber.* **1987**, *120*, 121.

[80] Tomoskozi, I.; Janzso, G. *Chem. Ind.* **1962**, 2085.

81 Gais, H. J.; Schmiedl, G.; Ball, W. A.; Bund, J.; Hellmann, G. H.; Erdelmeier, I. *Tetrahedron Lett.* **1988**, *29*, 1773.

82 Rehwinkel, H.; Kupsch, J. S.; Vorbruggen, H. *Tetrahedron Lett.* **1988**, *29*, 1775.

83 Lopez-Tudanca, P. L.; Jones, K.; Brownbridge, P. *J. Chem. Soc. Perkin Trans. (1)* **1992**, 533.

84 Shapiro, G.; Buechler, D.; Hennet, S. *Tetrahedron Lett.* **1990**, *31*, 5733.

85 Walker, B. J. In *Organophosphorus Reagents in Organic Synthesis*; Cadogan, J. I. G., Ed.; Academic; London, 1979, Chapter 3.

86 Allevi, P.; Ciuffreda, P.; Colombo, D.; Manti, D.; Speranza, G. *J. Chem. Soc. Perkin Trans. (1)* **1989**, 1281.

87 Marinetti, A.; Mathey, F. *Angew. Chem.* **1988**, *27*, 1382.

88 Bottin-Strzalko, T.; Seyden-Penne, J. *Bull. Soc. Chim. Fr.* **1984**, 161.

89 Wadsworth, D. H.; Schupp, O. E.; Seus, E. J.; Ford, J. A. *J. Org. Chem.* **1965**, *30*, 680.

90 Vo-Quang, Y.; Carniato, D.; Vo-Quang, L.; LeGoffic, F. *J. Chem. Soc. Chem. Commun.* **1983**, 1505.

91 Teulade, M. P.; Savignac, P.; Aboujaoude, E. E.; Lietge, S.; Collignon, N. *J. Organomet. Chem.* **1986**, *304*, 283.

92 Linke, S.; Kurz, J.; Lipinski, D.; Gau, W. *Liebigs Ann. Chem.* **1980**, 542.

93 Deschamps, B.; LeFebvre, B.; Redjal, A.; Seyden-Penne, J. *Tetrahedron* **1973**, *29*, 2437.

94 Wender, P.; Eissenstat, M.; Filosa, M. P. *J. Am. Chem. Soc.* **1979**, *101*, 2196.

95 Redjal, A.; Seyden-Penne, J. *Tetrahedron Lett*, **1974**, 1733.

96 Piechucki, C. *Synthesis* **1974**, 869; **1976**, 187.

97 Mikolajczyk, M.; Grzejszczak, S.; Midura, W.; Zatorski, A. *Synthesis* **1975**, 278.

98 Texier-Boullet, F.; Foucaud, A. *Synthesis* **1979**, 884.

99 Bouyssou, P.; Chenault, J. *Tetrahedron Lett.* **1991**, *32*, 5341.

100 Villieras, J.; Rambaud, M.; Kirschleger, B. *Phosphorus Sulfur* **1983**, *14*, 385.

101 Villieras, J.; Rambaud, M. *Synthesis* **1983**, 300.

102 Martinelli, M.; Peterson, B. C. *Tetrahedron Lett.* **1990**, *31*, 5401.

103 Mouloungui, Z.; Elmestour, R.; Delmas, M.; Gaset, A. *Tetrahedron* **1992**, *48*, 1219.

104 Mouloungui, Z.; Delmas, M.; Gaset, A. *Synth. Comm.* **1984**, *14*, 701.

105 Ibarra, C. A.; Arias, S.; Fernandez, M. J.; Sinisterra, J. V. *J. Chem. Soc. Perkin Trans. (2)* **1989**, 503.

106 Sinisterra, J. V.; Barrios, J.; Mouloungui, Z.; Delmas, M.; Gaset, A. *Bull. Soc. Chim. Belg.* **1991**, *100*, 267.

107 Texier-Boullet, F.; Foucaud, A. *Tetrahedron Lett.* **1980**, *21*, 2161.

108 Mouloungui, Z.; Delmas, M.; Gaset, A. *J. Org. Chem.* **1989**, *54*, 3936.

109 Fillion, H.; Refouvelet, B.; Pera, M. H.; Du Faud, V.; Luche, J. L. *Synth. Comm.* **1989**, *19*, 3343.

110 Sinisterra, J. V.; Fuentes, A.; Marinas, J. M. *J. Org. Chem.* **1987**, *52*, 3875.

111 Baker, R.; Sims, R. J. *Tetrahedron Lett.* **1981**, *22*, 161; *Synthesis* **1981**, 117; *J. Chem. Soc. Perkin Trans. (1)* **1981**, 3087.

112 Nicolaou, K. C.; Seitz, S. P.; Pavia, M. R. *J. Am. Chem. Soc.* **1982**, *104*, 2030.

[113] Still, W. C.; Gennari, C.; Noguez, J. A.; Reason, D. A. *J. Am. Chem. Soc.* **1984**, *106*, 260.

[114] Angeletti, E.; Tundo, P.; Venturello, P. *J. Chem. Soc. Perkin Trans. (1)* **1987**, 713.

[115] Niyazymbetov, M. E.; Petrosyan, V; Keitel, I.; Costisella, B.; Schwarz, K. H. *Tetrahedron Lett.* **1988**, *29*, 3007.

[116] Blanchette, M. A.; Choy, W.; Davis, J. T.; Essenfeld, A. P.; Masamune, S.; Roush, W. R.; Sakai, T. *Tetrahedron Lett.* **1984**, *25*, 2183.

[117] Rathke, M. W.; Nowak, M. *J. Org. Chem.* **1985**, *50*, 2624.

[118] Rathke, M. W.; Bouhel, E. *Synth. Comm.* **1990**, *20*, 869.

[119] Campa, C.; Font, J.; Roca, M. R.; Sanchez-Ferrando, F.; Virgili, A. *An. Quim. Ser. C.* **1986**, *82*, 51; *Chem. Abstr. 1987*, **107**, 39329.

[120] Sturtz, G.; Clement, J. C. *Polym. Bull.* **1983**, *9*, 125.

[121] Cainelli, G.; Contento, M.; Manescalchi, F.; Regnoli, R. *J. Chem. Soc. Perkin Trans. (1)* **1980**, 2516.

[122] Corey, E. J.; Shulman, J. I. *J. Org. Chem.* **1970**, *35*, 777.

[123] Kluge, A. F.; Cloudsdale, I. S. *J. Org. Chem.* **1979**, *44*, 4847.

[124] Fox, M. A.; Triebel, C. A.; Rogers, R. *Synth. Comm.* **1982**, *12*, 1055.

[125] Durrant, G.; Sutherland, J. K. *J. Chem. Soc. Perkin Trans. (1)* **1972**, 2582.

[126] Kawashima, T.; Ishii, T.; Inamoto, N. *Chem. Lett.* **1984**, 1097.

[127] Lewis, R. T.; Motherwell, W. B. *Tetrahedron Lett.* **1988**, *29*, 5033.

[128] Lewis, R. T.; Motherwell, W. B.; Shipman, M. *J. Chem. Soc. Chem. Commun.* **1988**, 948.

[129] Kawashima, T.; Ishii, T.; Inamoto, N. *Chem. Lett.* **1983**, 1375.

[130] Petrova, J.; Momchilova, S.; Vassilev, N. G. *Phosphorus Sulfur* **1992**, *68*, 45.

[131] Hirao, T.; Nakamura, T.; Hagihara, M.; Agawa, T. *J. Org. Chem.* **1985**, *50*, 5860.

[132] Bottin-Strzalko, T. *Tetrahedron* **1973**, *29*, 4199.

[133] Deschamps, B.; LeFebvre, G.; Seyden-Penne, J. *Tetrahedron* **1972**, *28*, 4209.

[134] Mikolajczyk, M.; Grzejszczak, S.; Zatorski, A.; Mlotkowska, B.; Gross, H.; Costisella, B. *Tetrahedron* **1978**, *34*, 3081.

[135] Breuer, E.; Zbaida, S.; Segall, E. *Tetrahedron Lett.* **1979**, 2203.

[136] Tomioka, H.; Watanabe, M.; Kobayashi, N.; Hirai, K. *Tetrahedron Lett.* **1990**, *31*, 5061.

[137] Danion, D.; Carrie, R., *C. R. Seances Acad. Sci.* **1968**, *267*, 735; *Tetrahedron* **1972**, *28*, 4223.

[138] Sturtz, G.; Pondaven-Raphalen, A. *Phosphorus Sulfur* **1984**, *20*, 35.

[139] Yanovskaya, L. A.; Kucherov, V. F. *Bull. Acad. Sci. USSR* **1965**, 1475.

[140] Boutagy, J.; Thomas, R. *Chem. Revs.* **1974**, *74*, 87.

[141] Gushurst, A. J.; Jorgensen W. L. *J. Org. Chem.* **1988**, *53*, 3397.

[142] Nesterov, N. I.; Belyaev, N. N.; Stadnichuk, M. D.; Mingaleva, K. S.; Sigolaev, Y. F. *J. Gen. Chem.* **1980**, *50*, 63.

[143] Oppolzer, W.; Grayson, J. I.; Wegmann, H.; Urrea, M. *Tetrahedron* **1983**, *39*, 3695.

[144] Denmark, S. E.; Sternberg, J. A. *J. Am. Chem. Soc.* **1986**, *108*, 8277.

[145] Larsen, R. O.; Aksnes, G. *Phosphorus Sulfur* **1983**, *16*, 339.

146 Kryshtal, G. V.; Serebryakov, E. P.; Suslova, L. M.; Yanovskaya, L. A. *Bull. Acad. Sci. USSR* **1990**, *39*, 1277.

147 Patois, C.; Savignac, P. *Synlett*. **1991**, 517.

148 Still, W. C.; Gennari, C. *Tetrahedron Lett*. **1983**, *24*, 4405.

149 Hammond, G. B.; Cox, M. B.; Wiemer, D. F. *J. Org. Chem*. **1990**, *55*, 128.

150 Meyers, A. I.; Tomioka, K.; Roland, D. M.; Comins, D. *Tetrahedron Lett*. **1978**, 1375.

151 Dugger, R. W.; Heathcock, C. H. *Synth. Comm*. **1980**, *10*, 509.

152 Nagaoka, H.; Kishi, Y. *Tetrahedron* **1981**, *37*, 3873.

153 Hutchinson, D. K.; Fuchs, P. L. *J. Am. Chem. Soc*. **1987**, *109*, 4755.

154 Kryshtal, G. V.; Serebryakov, E. P.; Suslova, L. M.; Yanovskaya, L. A. *Bull. Acad. Sci. USSR* **1988**, *37*, 2142.

155 Kryshtal, G. V.; Serebryakov, E. P.; Suslova, L. M.; Yanovskaya, L. A. *Bull. Acad. Sci. USSR* **1988**, *37*, 2146.

156 Fukuyama, Y.; Kirkemo, C. L.; White, J. D. *J. Am. Chem. Soc*. **1977**, *99*, 646.

157 Groesbeek, M.; Rood, G. A.; Lugtenburg, J. *Rec. Trav. Chim*. **1992**, *111*, 149.

158 Schmid, G.; Fukuyama, T.; Akasuka, K.; Kishi, Y. *J. Am. Chem. Soc*. **1979**, *101*, 259.

159 Bestmann, H. J.; Ermann, P.; Ruppel, H.; Sperling, W. *Liebigs Ann. Chem*. **1986**, 479.

160 Marshall, J. A.; DeHoff, B. S.; Cleary, D. G. *J. Org. Chem*. **1986**, *51*, 1986.

161 Kinstle, T. H.; Mandanas, B. Y. *J. Chem. Soc. Chem. Commun*. **1968**, 1699.

162 Deschamps, B.; Lampin, J. P.; Mathey, F.; Seyden-Penne, J. *Tetrahedron Lett*. **1977**, *22*, 1137.

163 Etemad-Moghadan, G.; Seyden-Penne, J. *Tetrahedron* **1984**, *40*, 5153.

164 Hoffmann, H. M.; Rabe, J. *J. Org. Chem*. **1985**, *50*, 3849.

165 Tay, M. K.; Jaudet, A. A.; Collignon, N.; Teulade, M. P.; Savignac, P. *Synth. Comm*. **1988**, *18*, 1349.

166 Thompson, S. K.; Heathcock, C. H. *J. Org. Chem*. **1990**, *55*, 3386.

167 Kryshtal, G. V.; Serebryakov, E. P.; Suslova, L. M.; Yanovskaya, L. A. *Bull. Acad. Sci. USSR* **1990**, *39*, 1280.

168 Seyden-Penne, J.; Lefebvre, G. *C. R. Seances Acad. Sci*. **1969**, *269*, 48.

169 Huff, R. K.; Moppett, C. E.; Sutherland, J. K. *J. Chem. Soc. (C)* **1968**, 2725.

170 Jones, G.; Maisey, R. F. *J. Chem. Soc. Chem. Commun*. **1968**, 543.

171 Bergelson, L. D.; Vaver, V. A.; Barsukov, L. I.; Shemyakin, M. M. *Bull. Acad. Sci. USSR* **1966**, 474.

172 Kryshtal, V. G.; Serebryakova, E. P.; Suslova, L. M.; Yanovskaya, L. A. *Bull. Acad. Sci. USSR* **1990**, *39*, 2301.

173 Gopalan, A.; Moerck, R.; Magnus, P. D. *J. Chem. Soc. Chem. Commun*. **1979**, 548.

174 Kadyrov, A. A.; Rokhlin, E. M. *Bull. Acad. Sci. USSR* **1983**, 1224.

175 Takahashi, H.; Fujiwara, K.; Ohta, M. *Bull. Chem. Soc. Jpn*. **1962**, *35*, 1498.

176 Petrova, J.; Vassilev, N. G.; Kirilov, M. *Phosphorus Sulfur* **1990**, *47*, 457.

177 Shahak, I.; Appelbaum, J. *Isr. J. Chem*. **1968**, *6*, 6.

178 Dawson, M. I.; Derdzinski, K.; Hobbs, P. D.; Rhee, S. W.; Yasuda, D. *J. Org. Chem*. **1984**, *49*, 5265.

[179] Kellogi, R. M.; Groen, M. B.; Wynberg, H. *J. Org. Chem.* **1967**, *32*, 3093.

[180] Kolodazhnyi, O. I.; Yastenko, S. N. *J. Gen. Chem.* **1990**, *60*, 610.

[181] Kondo, K.; Negishi, A.; Tunemoto, D. *Angew. Chem.* **1974**, *13*, 407.

[182] Sturtz, G.; Lavielle, G. *C. R. Seances Acad. Sci.* **1965**, *261*, 2697.

[183] Janecki, T.; Bodalski, R. *Synthesis* **1989**, 506.

[184] Nikaido, M.; Aslanian, R.; Scavo, P.; Helquist, P.; Akermark, B.; Backvall, J. *J. Org. Chem.* **1984**, *49*, 4738.

[185] Rein, T.; Akermark, B.; Helquist, P. *Acta Chem. Scand.* **1988**, *42B*, 569.

[186] Kann, N.; Rein, T.; Akermark, B.; Helquist, P. *J. Org. Chem.* **1990**, *55*, 5312.

[187] Connell, R. D.; Helquist, P.; Akermark, B. *J. Org. Chem.* **1989**, *54*, 3359.

[188] Takeda, K.; Kobayashi, T.; Saito, K.; Yoshii, E. *J. Org. Chem.* **1988**, *53*, 1092.

[189] Dolle, R. E.; Armstrong, W. P.; Shaw, A. N.; Novelli, R. *Tetrahedron Lett.* **1988**, *29*, 6349.

[190] Barrish, J. C.; Lee, H. L.; Baggiolini, E. G.; Uskokovic, M. R. *J. Org. Chem.* **1987**, *52*, 1372.

[191] Shahak, I.; Almog, J.; Bergmann, E. D. *Isr. J. Chem.* **1969**, *7*, 585.

[192] Liu, H. J.; Rose, P. A.; Sasaki, D. J. *Can. J. Chem.* **1991**, *69*, 934.

[193] Minami, T.; Niki, I.; Agawa, T. *J. Org. Chem.* **1974**, *39*, 3236.

[194] Landor, P. D.; Landor, S. R.; Odgek, O. *J. Chem. Soc. Perkin Trans. (1)* **1977**, 93.

[195] Tay, M. K.; Jaudet, E. A.; Collignon, N.; Savignac, P. *Tetrahedron* **1989**, *45*, 4415.

[196] Meanwell, N. A.; Roth, H. R.; Smith, E. C. R.; Wedding, D. L.; Wright, J. J. K. *J. Org. Chem.* **1991**, *56*, 6897.

[197] Coutrot, P.; Snoussi, M.; Savignac, P. *Synthesis* **1978**, 133.

[198] Coutrot, P.; Grison, C.; Sauvetre, R. *J. Organomet. Chem.* **1987**, *332*, 1.

[199] Coutrot, P.; Ghribi, A. *Synthesis* **1986**, 790.

[200] Sturtz, G. *Bull. Soc. Chim. Fr.* **1964**, 2349.

[201] Finch, N.; Fitt, J. J.; Hsu, I. H. S. *J. Org. Chem.* **1975**, *40*, 206.

[202] Durand, T.; Savignac, P.; Girard, J. P.; Escale, R.; Rossi, J. C. *Tetrahedron Lett.* **1990**, *31*, 4131.

[203] Bodalski, R.; Pietrusiewicz, K. M.; Monkiewicz, J.; Koszuk, J. *Tetrahedron Lett.* **1980**, *21*, 2287.

[204] Taylor, E. C.; Davies, H. M. L. *Tetrahedron Lett.* **1983**, *24*, 5453.

[205] Moorhoff, C. M.; Schneider, D. F. *Tetrahedron Lett.* **1987**, *28*, 559.

[206] Mikolajczyk, M.; Zatorski, A. *J. Org. Chem.* **1991**, *56*, 1217.

[207] Baboulene, M.; Sturtz, G. *Phosphorus* **1973**, *2*, 195.

[208] Geribaldi, S.; Rouillard, M. *Tetrahedron* **1991**, *47*, 993.

[209] Compagnone, R. S.; Rapoport, H. *J. Org. Chem.* **1986**, *51*, 1713.

[210] Blackburn, G. M.; Parratt, M. J. *J. Chem. Soc. Perkin Trans. (1)* **1986**, 1425.

[211] Baader, E.; Bartmann, W.; Beck, G.; Below, P.; Bergmann, A.; Jendralla, H. *Tetrahedron Lett.* **1989**, *30*, 5115.

[212] Etemad-Moghadam, G.; Seyden-Penne, J. *Bull. Soc. Chim. Fr.* **1985**, 448.

[213] Obayashi, M.; Ito, E.; Matsui, K.; Kondo, K. *Tetrahedron Lett.* **1982**, *23*, 2323.

[214] Martin, S. F.; Dean D. W.; Wagman, A. S. *Tetrahedron Lett.* **1992**, *33*, 1839.

[215] Lee, K.; Shin, W. S.; Oh, D. Y. *Synth. Comm.* **1992**, *22*, 649.

[216] Petrova, J.; Coutrot, P.; Dreux, M.; Savignac, P. *Synthesis* **1975**, 658.

[217] Crenshaw, M. D.; Zimmer, H. *J. Org. Chem.* **1983**, *48*, 2782.

[218] Savignac, P.; Snoussi, M.; Coutrot, P. *Synth. Comm.* **1978**, *8*, 19.

[219] Seyferth, D.; Marmor, R. S. *J. Organomet. Chem.* **1973**, *59*, 237.

[220] Savignac, P.; Petrova, J.; Dreux, M.; Coutrot, P. *Synthesis* **1975**, 535.

[221] Yamaguchi, A.; Okazaki, M. *Nippon Kagaku Kaishi* **1972**, 2103; *Chem. Abstr.* **1973**, *78*, 29372.

[222] Skuballa, W.; Schillinger, E.; Sturzebecher, C. S.; Vorbruggen, H. *J. Med. Chem.* **1986**, *29*, 313.

[223] Savignac, P.; Coutrot, P. *Synthesis* **1976**, 197.

[224] Green, M. *J. Chem. Soc.* **1963**, 1324.

[225] Schaumann, E.; Grabley, F. F. *Liebigs Ann. Chem.* **1977**, 88.

[226] Corey, E. J.; Shulman, J. I. *J. Am. Chem. Soc.* **1970**, *92*, 5522.

[227] Khan, N.; Morris, T. H.; Smith, E. H.; Walsh, R. *J. Chem. Soc. Perkin Trans. (1)* **1991**, 865.

[228] Mikolajczyk, M.; Grzejszczak, S.; Chefczynska, A.; Zatorski, A. *J. Org. Chem.* **1979**, *44*, 2967.

[229] Mikolajczyk, M. *Revs. Heteroatom Chem.* **1989**, *2*, 19.

[230] Mikolajczyk, M.; Grzejszczak, S.; Lyzwa, P. *Tetrahedron Lett.* **1982**, *23*, 2237.

[231] Hauske, J. R.; Rapoport H. *J. Org. Chem.* **1979**, *44*, 2472.

[232] Makosa, M.; Baran, J.; Dziewonska-Baran, D.; Golinski, J. *Liebigs Ann. Chem.* **1989**, 825.

[233] Kruse, C. G.; Brockhof, N. L. J. M.; Wijsman, A.; Van der Gen, A. *Tetrahedron Lett.* **1977**, 885.

[234] Yui, K.; Aso, Y.; Otsubo, T.; Ogura, F. *Chem. Lett.* **1986**, 551.

[235] Mikolajczyk, M.; Grzejszczak, S.; Zatorski, A. *J. Org. Chem.* **1975**, *40*, 1979.

[236] de Jong, B. E.; de Konig, H.; Huisman, H. O. *Rec. Trav. Chim.* **1981**, *100*, 410.

[237] Mikolajczyk, M.; Midura, W.; Grzejszczak, S.; Zatorski, A.; Chefczynska, A. *J. Org. Chem.* **1978**, *43*, 473.

[238] Posner, G. H.; Brunelle, D. J. *J. Org. Chem.* **1972**, *37*, 3547.

[239] Fillion, H.; Pera, M. H.; Rappa, J. L.; Luu-Doc, C. *J. Heterocycl. Chem.* **1978**, *15*, 753.

[240] Fillion, H.; Hseine, A.; Pera, M. H.; Dufaud, V.; Refouvelet, B. *Synthesis* **1987**, 708.

[241] Barnes, N. J.; Davidson, H.; Hughes, L. R.; Procter, G. *J. Chem. Soc. Chem. Commun.* **1985**, 1292.

[242] Lee, J. W.; Oh, D. Y. *Synth. Comm.* **1989**, *19*, 2209.

[243] Carretero, J. C.; Demillequand, M.; Ghosez, L. *Tetrahedron* **1987**, *43*, 5125.

[244] Craig, D.; Geach, N. J. *Synlett.* **1992**, 299.

[245] Kondo, K.; Kiu, Y.; Tunemoto, D. *J. Chem. Soc. Perkin Trans. (1)* **1974**, 1279.

[246] Mikolajczyk, M.; Grzejszczak, S.; Korbacz, K. *Tetrahedron Lett.* **1981**, *22*, 3097.

[247] Martin, S. F.; Gompper, R. *J. Org. Chem.* **1974**, *39*, 2814.

[248] Daumas, M.; Vo-Quang, L.; Vo-Quang, Y.; Le Goffic, F. *Tetrahedron Lett.* **1989**, *30*, 5121.

249 Dehnel, A.; Finet, J. P.; Lavielle, G. *Synthesis* **1977**, 474.

250 Schmidt, U.; Lieberknecht, A.; Wild, J. *Synthesis* **1984**, 53.

251 Schollkopf, U.; Schroder, R. *Tetrahedron Lett.* **1973**, 633.

252 Hauske, J. R.; Guadliana, M.; Desai, K. *J. Org. Chem.* **1982**, *47*, 5019.

253 Gilbert, J. C.; Blackburn, B. K. *J. Org. Chem.* **1986**, *51*, 3656.

254 Buxton, S. R.; Holm, K. H.; Skattebol, L. *Tetrahedron Lett.* **1987**, *28*, 2167.

255 Khare, A. B.; McKenna, C. E. *Synthesis* **1991**, 405.

256 McClard, R. W. *Tetrahedron Lett.* **1983**, *24*, 2631.

257 Gilmore, W. F.; Huber, J. W. *J. Org. Chem.* **1973**, *38*, 1423.

258 Gilmore, W. F.; Park, J. S. *Phosphorus Sulfur* **1987**, *29*, 287.

259 Erickson, T. J. *J. Org. Chem.* **1986**, *51*, 934.

260 McIntosh, J. M.; Siller, R. A. *Can. J. Chem.* **1978**, *56*, 226.

261 Brooks D. W.; Palmer, J. T. *Tetrahedron Lett.* **1983**, *24*, 3059.

262 Becker, K. B. *Tetrahedron* **1980**, *36*, 1717.

263 Horner, L.; Hoffmann, H.; Klink, W.; Ertel, H.; Toscano, V. G. *Chem. Ber.* **1962**, *95*, 581.

264 Whitlock, H. W. *J. Org. Chem.* **1964**, *29*, 3129.

265 Gerber, J. P.; Modro, T. A.; Muller, E. L.; Phillips, A. M. M. M. *Abstracts of Lectures*, 12th International Conference on Phosphorus Chemistry, Toulouse, France; 1992; p. 79.

266 Iseki, K.; Shinoda, M.; Ishiyama, C.; Hayasi, Y.; Yamada, S.; Shibasaki, M. *Chem. Lett.* **1986**, 559.

267 Mikolajczyk, M.; Midura, W. H. *Synlett.* **1991**, 245.

268 Martin, S. F. *J. Org. Chem.* **1976**, *41*, 3337.

269 Seyferth, D.; Marmor, R. S. *Tetrahedron Lett.* **1970**, 2493.

270 Gilbert, J. C.; Weerasooriya, U. *J. Org. Chem.* **1983**, *48*, 448.

271 Gilbert, J. C.; Giamalva, D. H.; Weerasooriya, U. *J. Org. Chem.* **1983**, *48*, 5251.

272 Mikolajczyk, M.; Zurawinski, R.; Kielbasinski, P. *Tetrahedron Lett.* **1989**, *30*, 1143.

273 Ohira, S.; Ishi, S.; Shinohara, K.; Nozaki, H. *Tetrahedron Lett.* **1990**, *31*, 1039.

274 Wadsworth, W. S.; Emmons, W. D. *J. Org. Chem.* **1964**, *29*, 2816.

275 Major, R. T.; Hedrick, R. J. *J. Org. Chem.* **1965**, *30*, 1268.

276 Marinetti, A.; Bauer, S.; Ricard, L.; Mathey, F. *Organometallics* **1990**, *9*, 793.

277 Marinetti, A.; Ricard, L.; Mathey, F. *Organometallics* **1990**, *9*, 788.

278 Wolinsky, J.; Erickson, K. L. *J. Org. Chem.* **1965**, *30*, 2208.

279 Bergmann, E. D.; Solomonovici, A. *Synthesis* **1970**, *2*, 183.

280 Boulos, L. S.; Abd. el-Rahman, N. M. *Phosphorus Sulfur* **1992**, *68*, 241.

281 Kovalev, B.; Altmark, E. M. *Zh. Org. Khim.* **1972**, *8*, 1582; *Chem. Abstr.* **1972**, *77*, 163967.

282 Lombardo, L.; Taylor, R. J. K. *Synth. Comm.* **1978**, *8*, 463.

283 Blackburn, G. M.; Parratt, M. J. *J. Chem. Soc. Perkin Trans. (1)* **1986**, 1417.

284 Drefahl, G.; Ponsold, K.; Schick, H. *Chem. Ber.* **1964**, *97*, 2011.

285 Kaneko, H.; Okazaki, M. *Tetrahedron Lett.* **1966**, 219.

286 Bose, A. K.; Dahill, R. T. *J. Org. Chem.* **1965**, *30*, 505.

287 Weiss, D.; Hobe, S.; Beckert, R.; Klemm, D.; Scheller, D.; Gruner, M. *J. Prakt. Chim.* **1990**, *332*, 367.

288 Wicha, J.; Bal, K.; Pickut, S. *Synth. Comm.* **1977**, *7*, 215.

289 Pettit, G. R.; Herald, C. L.; Yardley, J. P. *J. Org. Chem.* **1970**, *35*, 1389.

290 Mirrington, R. N.; Schmalzl, K. J. *J. Org. Chem.* **1972**, *37*, 2871.

291 Kovalev, B.; Yanovskaya, L. A.; Kucherov, V. F. *Bull. Acad. Sci. USSR* **1962**, 1788.

292 Tadano, K.; Idogaki, Y.; Yamada, H.; Suami, T. *J. Org. Chem.* **1987**, *52*, 1201.

293 Monti, D; Gramatica, P.; Speranza, G.; Mamitto, P. *Tetrahedron Lett.* **1987**, *28*, 5047.

294 Runge, W.; Kresze, G.; Ruch, E. *Liebigs Ann. Chem.* **1975**, 1361.

295 Hamlet, Z.; Mychajlowskij, W. *Chem. Ind.* **1974**, 829.

296 Barnikow, G.; Saeling, G. *J. Prakt. Chem.* **1974**, *316*, 534.

297 Schaumann, E.; Fittkau, S. *Synthesis* **1985**, 172.

298 Maryanoff, B. E.; Reitz, A. B. *Chem. Rev.* **1989**, *89*, 863.

299 Huang, N. Z.; Kalisch, V. J.; Miller, M. J. *Tetrahedron* **1990**, *46*, 8067.

300 Piers, E.; Abeysekera, B. *Can. J. Chem.* **1982**, *60*, 1114.

301 Poss, A. J.; Belter, R. K. *J. Org. Chem.* **1987**, *52*, 4810.

302 Altenbach, H. J.; Holzapfel, W. *Angew. Chem.* **1990**, *29*, 67.

303 Clark, R. D.; Kozar, L. G.; Heathcock, C. H. *Synth. Comm.* **1975**, *5*, 1.

304 Minami, T.; Nakayama, M.; Fujimoto, K.; Matsuo, S. *Abstracts of Lectures*, 12th International Conference on Phosphorus Chemistry, Toulouse, France; 1992, p. 83.

305 Katsumura, S.; Kimura, A.; Isoe, S. *Tetrahedron* **1989**, *45*, 1337.

306 Aristoff, P. A.; Johnson, P. D.; Harrison, A. W. *J. Am. Chem. Soc.* **1985**, *107*, 7967.

307 Lin, C. H.; Aristoff, P. A.; Johnson, P. D.; McGrath, J. P.; Timko, J. M.; Robert, A. *J. Org. Chem.* **1987**, *52*, 5594.

308 Grieco, P. A.; Pogonowski, C. S. *Synthesis* **1973**, 425.

309 Mikolajczyk, M.; Popielarczyk, M.; Grzejszczak, S. *Z. Chem.* **1984**, *24*, 377.

310 McClure, C. K.; Jung, K. Y. *J. Org. Chem.* **1991**, *56*, 2326.

311 Shing, T. K. M.; Aloui, M. *J. Chem. Soc. Chem. Commun.* **1988**, 1525.

312 Moody, C. J.; Sie, E. R. H. B.; Kulagowski, J. J. *Tetrahedron Lett.* **1991**, *32*, 6947; *Tetrahedron* **1992**, *48*, 3991.

313 Kolodiazhnyi, O. I. *J. Gen. Chem.* **1990**, *60*, 926.

314 Walker, B. J. In *Organophosphorus Chemistry*, A Specialist Periodical Report; Walker B. J.; Hobbs, J. B., Eds.; Royal Society of Chemistry, London, 1989; Vol. 20, Chapter 7, p. 294; also earlier volumes in the series.

315 Kodama, M.; Shiobara, Y.; Sumitomo, H.; Matsumura, K.; Tsukamoto, M.; Harada, C. *J. Org. Chem.* **1988**, *53*, 72.

316 Meyers, A. I.; Comins, D. L.; Roland, D. M.; Henning, R.; Shimizu, K. *J. Am. Chem. Soc.* **1979**, *101*, 7104.

317 Evans, D. A.; Carreira, E. M. *Tetrahedron Lett.* **1990**, *31*, 4703.

318 Singh, R. K.; Rogers, M. D. *J. Heterocycl. Chem.* **1985**, *22*, 1713.

319 Ager, D. J. *Org. React.* **1990**, *38*, 1–223.

320 Ahlbrecht, H.; Farnung, W.; Simon, H. *Chem. Ber.* **1984**, *117*, 2622.

321 Binder, J.; Zbiral, E. *Tetrahedron Lett.* **1986**, *27*, 5829.

322 Carey, F. S.; Court, A. S. *J. Org. Chem.* **1972**, *37*, 939.

323 Minouni, N.; About-Jaudet, E.; Collignon, N., *Abstracts of Lectures*, 12th International Conference on Phosphorus Chemistry, Toulouse, France; 1992; 37.

324 Martynov, V. F.; Timofeev, V. E. *J. Gen. Chem.* **1964**, *34*, 3950.

325 Perriot, P.; Villieras, J.; Normant, J. F. *Synthesis* **1978**, 33.

326 Coutrot, P.; Savignac, P. *Synthesis* **1978**, 34.

327 Kovalev, B. G.; Dormidontova, N. P. *J. Gen. Chem.* **1970**, *40*, 910.

328 Yamamoto, Y.; Furnta, T. *J. Org. Chem.* **1990**, *55*, 3971.

329 Kosolapoff, G. M.; Powell, J. S. *J. Am. Chem. Soc.* **1950**, *72*, 4198.

330 Pudovik, A. N.; Shchelkina, L. P.; Bashirova, L. A. *Z. Obshch. Khim.* **1957**, *27*, 2367; *Chem. Abstr.* **1958**, *52*, 7134.

331 Kosolapoff, G. M. *J. Am. Chem. Soc.* **1953**, *75*, 1500.

332 Mikolajczyk, M.; Balczewski, P. *Synthesis* **1984**, 691.

333 Villieras, J.; Reliquet, A.; Normant, J. F. *Synthesis* **1978**, 27.

334 Clark, R. D.; Kozar, L. G.; Heathcock, C. H. *Synthesis* **1975**, 635.

335 Nasser, J.; About-Jaudet, E.; Collignon, N. *Phosphorus Sulfur* **1990**, *54*, 171.

336 Bigge, C. F.; Drummond, J. T.; Johnson, G. *Tetrahedron Lett.* **1989**, *30*, 7013.

337 Halazy, S.; Ehrhard, A.; Danzin, C. *J. Am. Chem. Soc.* **1991**, *113*, 315.

338 Hutchinson, D. W.; Thornton, D. M. *Synthesis* **1990**, 135.

339 Hata, T.; Hashizume, A.; Nakajima, M.; Sekine, M. *Tetrahedron Lett.* **1978**, 363.

340 Ahlbrecht, H.; Farnung, W. *Chem. Ber.* **1984**, *117*, 1.

341 Hata, T.; Nakajima, M.; Sekine, M. *Tetrahedron Lett.* **1979**, *20*, 2047.

342 Duggan, A. J.; Adams, M. A.; Bryness, P. J.; Meinwald, J. *Tetrahedron Lett.* **1978**, 4323.

343 Borcherding, D. R.; Scholtz, S. A.; Borchardt, R. T. *J. Org. Chem.* **1987**, *52*, 5457.

344 Henrick, C. A.; Bohme, E.; Edwards, J. A.; Fried, J. H. *J. Am. Chem. Soc.* **1968**, *90*, 5926.

345 Tomoskozi, I, *Angew. Chem.* **1963**, *2*, 261; *Tetrahedron* **1963**, *19*, 1969.

346 Petter, R. C.; Banerjee, S.; Englard, S. *J. Org. Chem.* **1990**, *55*, 3088.

347 Izydore, R. A.; Ghirardelli, R. G. *J. Org. Chem.* **1973**, *38*, 1790.

348 Fatima, A.; Zaman, F.; Voelter, W. *Z. Naturforsch.* **1991**, *46B*, 1227.

349 Marinetti, A.; Ricard, L.; Mathey, F. *Synthesis* **1992**, 157.

350 Tanaka, H.; Fukui, M.; Haraguchi, K.; Masaki, M.; Miyasaka, T. *Tetrahedron Lett.* **1989**, *30*, 2567.

351 Villieras, J.; Perriot, P.; Normant, J. F. *Synthesis* **1978**, 29.

352 Thenappan, A.; Burton, D. J. *J. Org. Chem.* **1991**, *56*, 273.

353 Honda, M.; Katsuki, T.; Yamaguchi, M. *Tetrahedron Lett.* **1984**, *25*, 3857.

354 Villieras, J.; Perriot, P.; Normant, J. F. *Synthesis* **1978**, 31.

355 Kreutzkamp, N. *Chem. Ber.* **1955**, *88*, 195.

356 Schaumann, E.; Mergardt, B.; Fittkau, S. *Synthesis* **1990**, 47.

[357] Aboujaoude, E. E.; Lietje, S.; Collignon, N.; Teulade, M. P.; Savignac, P. *Tetrahedron Lett.* **1985**, *26*, 4435.

[358] Kolodiazhnyi, O. I.; Ustenko, S. N.; Grishkum, E. V. *J. Gen. Chem.* **1991**, *61*, 465.

[359] Olah, G.; Ohannesian, L.; Arvanaghi, M. *J. Org. Chem.* **1984**, *49*, 3856.

[360] Aboujaoude, E. E.; Collignon, N.; Savignac, P. *Synthesis* **1983**, 634.

[361] Schaumann, E.; Grabley, F. F. *Liebigs Ann. Chem.* **1979**, 1715.

[362] Neidlein, R.; Echinger, T. *Synthesis* **1991**, 1228.

[363] Grell, W.; Machleidt, H. *Liebigs Ann. Chem.* **1966**, *693*, 134.

[364] Aboujaoude, E. E.; Collignon, N.; Savignac, P. *J. Organomet. Chem.* **1984**, *264*, 9.

[365] Yamanai, T.; Akiyama, T.; Ishida, E.; Abe, H.; Amamiya, M.; Inazu, T. *Chem. Lett.* **1989**, 335.

[366] Mikina, M.; Mikolajczyk, M. *Abstracts of Lectures*, 12th International Conference on Phosphorus Chemistry, Toulouse, France; 1992, p. 160.

[367] Hutchinson, D. W.; Semple, G. *J. Organomet. Chem.* **1985**, *291*, 145.

[368] Xu, Z. Q.; DesMarteau, D. D., *J. Chem. Soc. Perkin Trans. (1)* **1992**, 313.

[369] Kosolapoff, G. M. *J. Am. Chem. Soc.* **1947**, *69*, 1002.

[370] Horner, L.; Hoffmann, H.; Klahre, G.; Toscano, V. G.; Ertel, H. *Chem. Ber.* **1961**, *94*, 1987.

[371] Zimmer, H.; Koenigkramer, R. E.; Cepulis, R. L.; Nene, D. M. *J. Org. Chem.* **1980**, *45*, 2018.

[372] Mikolaczyk, M.; Midura, W.; Grzejszczak, S. *Tetrahedron Lett.* **1984**, *25*, 2489.

[373] Okuma, K.; Ikari, K.; Ohta, H. *Chem. Lett.* **1992**, 131.

[374] Sundberg, R. J.; Bukowick, P. A.; Holcombe, F. O. *J. Org. Chem.* **1967**, *32*, 2938.

[375] Deschamps, B.; Seyden-Penne, J. *Tetrahedron* **1977**, *33*, 413.

[376] Cossentini, M.; Deschamps, B.; Anh, N. T.; Seyden-Penne, J. *Tetrahedron* **1977**, *33*, 409.

[377] Bergmann, E.; Solomonovici, A. *Tetrahedron* **1971**, *27*, 2675.

[378] Bohlmann, F.; Zdero, C. *Chem. Ber.* **1973**, *106*, 3779.

[379] Castello, J.; Font, J.; Ihara, T.; Llitjos, A.; Moreno-Manas, M. *An. Quim.* **1978**, *74*, 773.

[380] Masamune, S.; Brooks, D. W.; Mario, K.; Sobczak, R. L. *J. Am. Chem. Soc.* **1976**, *98*, 8277.

[381] Yamaguchi, M.; Tsukamoto, Y.; Hayashi, A.; Minami, T. *Tetrahedron Lett.* **1990**, *31*, 2423.

[382] Dehnel, A.; Griller, D.; Kanabus-Kaminska, J. M. *J. Org. Chem.* **1988**, *53*, 1566.

[383] Groth, U.; Richter, L.; Schollkopf, U. *Tetrahedron* **1992**, *48*, 117.

[384] Yuan, C.; Li, C.; Ding, Y. *Synthesis* **1991**, 854.

[385] Maasen, J. A.; Wajer, T. A. J. W.; de Boer, T. J. *Rec. Trav. Chim.* **1969**, *88*, 5.

[386] Kirilov, M.; Petrova, J. *Chem. Ber.* **1970**, *103*, 1047.

[387] Tay, M. K.; Aboujaoude, E. E.; Collignon, N.; Savignac, P. *Tetrahedron Lett.* **1987**, *28*, 1263.

[388] Kirilov, M.; van Huyen, L. *Tetrahedron Lett.* **1972**, 4487.

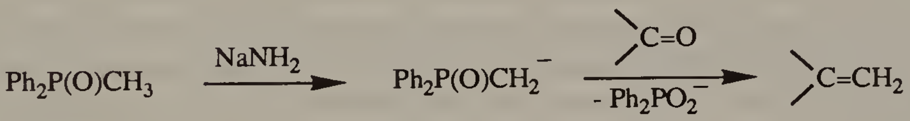
[389] Breuer, E.; Ronen-Braunstein, I. *J. Chem. Soc. Chem. Commun.* **1974**, 949.

[390] Breuer, E.; Zbaida, S.; Pesso, J.; Levi, S. *Tetrahedron Lett.* **1975**, 3103.

# 11

# PHOSPHINOXY CARBANIONS (PHOSPHINO YLIDES)

The chemistry of phosphinoxy (or phosphinoyl) carbanions began with the discovery by Horner et al.[1] of the acidity of alkyldiphenylphosphine oxides and reaction of the resulting carbanions with carbonyl compounds to form alkenes and diphenylphosphinate (Eq. 11.1). Development and refinement of this reaction has provided an alkene synthesis which complements the Wittig and Wadsworth–Emmons reactions. This chapter describes the preparation and properties of such carbanions, their use in the Horner reaction (alkene formation), and their use in other nucleophilic reactions.



$$Ph_2P(O)CH_3 \xrightarrow{NaNH_2} Ph_2P(O)CH_2^- \xrightarrow[-\ Ph_2PO_2^-]{>C=O} >C=CH_2 \qquad (11.1)$$

## 11.1 PREPARATION AND PROPERTIES

### 11.1.1 Preparation of Phosphine Oxides

Phosphinoxy carbanions for use in synthesis normally are prepared directly by proton removal from tertiary phosphine oxides (see Section 11.1.2), usually from alkyldiphenylphosphine oxides [$R'RCH–P(O)Ph_2$] which contain only one site adjacent to phosphorus for carbanion formation. However, carbanions have been prepared and used from other phosphine oxides ($R–CH_2–X$) containing X = phenylmethylphosphinoxy,[2] dimethylphosphinoxy,[3,4] diethylphosphinoxy,[3]

*Ylides and Imines of Phosphorus*, Edited by A. William Johnson.
ISBN 0-471-52217-1

di-*n*-butylphosphinoxy,[5] di-*n*-hexylphosphinoxy,[6] dibenzophosphole oxide,[7,8] and phospholene oxide[9] groups. The synthesis of alkydiphenylphosphine oxides is described briefly in the next section.

Complex phosphine oxides also have been elaborated by substitution reactions on simple phosphine oxides. For example, Maier and Rist[4] used chloromethyldimethylphosphine oxide as a substrate from which chloride could be displaced by alkali salts of numerous nitrogen heterocycles. Conversely, the readily accessible carbanion of methyldiphenylphosphine oxide has been used to effect displacement reactions on a wide variety of compounds, and these reactions, such as acylation and alkylation, are described in Section 11.3.

***11.1.1.1 Preparation of Alkyldiphenylphosphine Oxides.*** The standard means of preparing phosphine oxides have been described by Hays and Peterson,[10] and extensive tables of known compounds have been included. A few of these methods, which have been especially useful in the elaboration of unusual phosphinoxy carbanions, will be described.

Triphenylphosphine has been quaternized with alkyl halides and the resulting phosphonium salt hydrolyzed with sodium hydroxide, leading to displacement of a phenyl group and formation of the phosphine oxide (see also Section 5.1). This approach has been effective provided the alkyl group did not carry conjugating carbanion-stabilizing groups, in which case the alkyl group was displaced, and provided the system was otherwise stable to base.[11] Cyclopropylmethyldiphenylphosphine oxide was prepared in this manner,[12] as were phosphine oxides which served as precursors to $\beta,\gamma$- and $\gamma,\delta$-unsaturated ketones.[13,14]

The Michaelis–Arbuzov rearrangement of an alkyl halide with ethyl diphenylphosphinite has been an effective and mild synthesis. For example, it has been employed in the synthesis of oudemansins[15] and in the preparation of $\gamma,\delta$-unsaturated-$\beta$-ketoesters.[16]

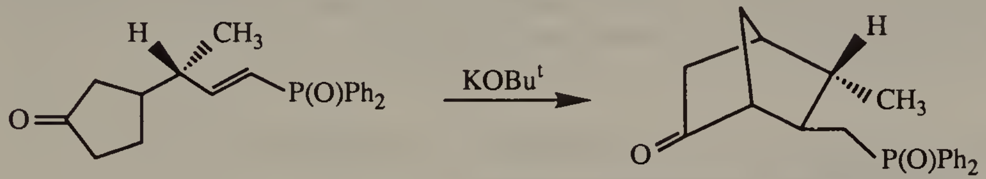
Allylic alcohols could be esterified with chlorodiphenylphosphine in the presence of pyridine to allyl phosphinites which were found to rearrange upon heating to allyldiphenylphosphine oxides with inverted allyl groups.[17] This technique has been applied to the preparation of numerous such phosphine oxides[18] and also with a propargylic alcohol for preparation of a ketenyldiphenylphosphine oxide.[19]

Secondary phosphine oxides have been metallated and then alkylated to tertiary phosphine oxides,[20] a method recently employed in the preparation of difluoromethyldiphenylphosphine oxide.[21] They also have been metallated and then added in a conjugate manner to $\alpha,\beta$-unsaturated ketones to afford $\beta$-diphenylphosphinoxy ketones.[13] In a novel reaction aldehydes (RCHO) and diphenylphosphine recently have been reported to produce phosphine oxides under $NbCl_5$ and $BF_3 \cdot Et_2O$ catalysis.[22]

Maleki et al.[23] discovered an effective and mild means of preparing $\alpha$-alkoxyalkyldiphenylphosphine oxides which avoided the use of $\alpha$-chloroethers. Reaction of chlorodiphenylphosphine with acetals proceeded simply as a

Michaelis–Arbuzov rearrangement,[24] and use of orthoformates produced α,α-dialkoxymethyldiphenylphosphine oxides which served as precursors to ketene acetals.[25]

*11.1.1.2 Addition to Unsaturated Tertiary Phosphine Oxides.* Nucleophiles add to the β-carbon of vinylphosphine oxide derivatives in a manner similar to that known for vinylphosphonium salts (see Section 4.2) and vinylphosphonates (see Section 10.1.1.4). Addition of secondary amines to vinyldiphenylphosphine oxide produced β-aminoalkyldiphenylphosphine oxides, which served as precursors to allylamines via a subsequent Horner reaction.[26] In a similar manner, organolithium reagents were added to the β-carbon of vinylphosphine oxides and the resulting carbanions were immediately reacted with carbonyl compounds to afford alkenes.[27] Bicyclic phosphine oxides were prepared by an intramolecular addition of enolate anion (Eq. 11.2).[28]



(11.2)

In an analogous manner alkynyldiphenylphosphine oxides added secondary amines to produce enamines which were hydrolyzed to β-ketophosphine oxides.[29] Addition of Grignard reagent to alkynylphosphine oxides followed by addition of the resulting carbanion to benzaldehyde afforded β-phosphinoxy-α-phenyl allyl alcohols, which would eliminate phosphinate to produce ketenes.[30]

### 11.1.2 Properties of Phosphinoxy Carbanions

Alkyldiphenylphosphine oxides are converted to their carbanions using strong bases such as sodamide,[1] sodium hydride,[31] lithium diisopropylamide,[32] sodium hexamethyldisilylamide,[33] *n*-butyllithium,[34,35] and potassium *t*-butoxide,[36] with the latter two being the most common. Tetrahydrofuran is the most common solvent. Most of the work with phosphinoxy carbanions has been with those that did not carry stabilizing groups on the carbanion other than the phosphinoxy group, but two groups have shown that carbethoxymethyldiphenylphosphine oxide has a p$K_a$ value in ethanol slightly lower than that for the corresponding phosphonate,[3,5] and in those instances sodium ethoxide was an effective base. The acidifying effect of the diphenylphosphinoxy group was comparable to that of the carbethoxy group,[37] but in aqueous media the inductive effect was less than that of the phosphonate or phosphonium groups. Horner showed that the phosphinoxy carbanion was less readily formed than the phosphonium carbanion (ylide), but that it was more nucleophilic.[38]

The stabilization of the phosphinoxy carbanion certainly is due significantly to the inductive effect of the phosphinoxy group ($\sigma^* = 1.68$),[37] but it has been suggested that delocalization of the $sp^2$-hybridized lone pair toward the phosphorus atom, utilizing vacant low-lying phosphorus $3d$-orbitals, also contributes.[10] Bottin–Strzalko et al.[39] have provided NMR evidence for the approximate planarity of the carbanion in two stabilized phosphinoxy carbanions, including increased $J_{PC}$ and $J_{CH}$ values and more positive $^{31}P$ values for the carbanions compared to the neutral species. Earlier Cram and Partos[40] had concluded, on the basis of deuterium exchange and racemization data, that chiral α-phosphinoxy carbanions had lost most of their asymmetry, perhaps owing to planarity and *d*-orbital overlap. Carbomethoxymethyldiphenylphosphine oxide carbanion was shown to exist in *Z*- and *E*- enolate forms in solution with the former dominating and a free energy of activation of 18.5 kcal/mole for interconversion. This carbanion also chelated well with lithium cation in THF or pyridine solutions, but less well in DMSO.[41] The *P*-phenyl groups seem not to interact conjugatively with the phosphorus atom, a behavior similar to that found in phosphonium ylides. Phosphinoxy carbanions have not been isolated and subjected to X-ray crystallographic analysis.

## 11.2 REACTION OF PHOSPHINOXY CARBANIONS WITH ALDEHYDES AND KETONES (THE HORNER REACTION)

Horner et al.[1] were the first to report the reaction of a phosphine oxide, in the form of its carbanion prepared with sodamide, with a carbonyl compound, obtaining from methyldiphenylphosphine oxide and benzophenone a 70% yield of 1,1-diphenylethene and a 96% recovery of diphenylphosphinic acid (Eq. 11.1). In view of the fact that Horner both discovered[1] and developed[42] the reaction of such carbanions with carbonyl compounds to form alkenes as a general olefination reaction, it deserves to be called only the **Horner reaction**, as proposed in Section 10.2. Most authors have used that terminology, but many still use Horner–Emmons, Wittig–Horner, and/or Horner–Wittig reaction, leading to confusion in the chemical literature.

Most examples of the Horner reaction have been conducted using "nonstabilized" phosphinoxy carbanions [$Ph_2(O)(P)–CH^-–R$], those without α-cyano, α-carbalkoxy, α-phenyl, or α-acyl groups (Note: such carbanions are known to react, contrary to popular notion, and are discussed later in this chapter). As a result, phosphinoxy carbanions have been viewed as olefinating reagents complementary to phosphonate carbanions in that the latter are more common with such stabilizing groups attached (see Section 10.2). As the Horner reaction and its two-step variant have evolved the following seem to be its advantages:

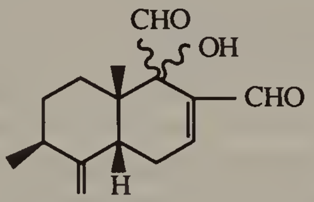
1. Facile formation and short-term storability of "nonstabilized" carbanions, in contrast to similar phosphonate carbanions which tend to dimerize on standing.

2. Ready elaboration of complex carbanions from simple carbanions through common processes such as alkylation and acylation.
3. Dominant formation of *E*-alkenes, in contrast to the Wittig reaction of alkylides which affords mainly *Z*-alkenes.
4. Ready separation of the phosphorus byproduct as a water-soluble phosphinate salt.
5. Sufficient reactivity for essentially all carbonyl compounds.

The major disadvantages of the phosphinoxy carbanion route to alkenes are the following:

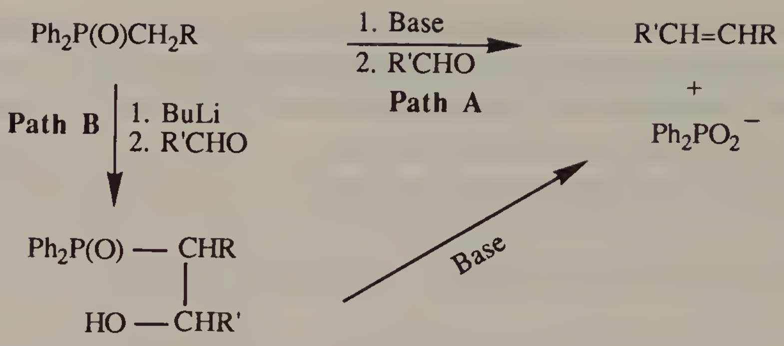
1. The necessity normally to employ very strong bases to generate the carbanion, potentially leading to side reactions among other reactants.
2. Conflicting reports of the lack of reactivity of β-keto carbanions $[Ph_2P(O)CH{-}COR^-M^+]$.[16,43,44]
3. Slightly better yields than the Wittig reaction in some cases[45] but poorer yields in others.[46]

Overall the Horner reaction is a useful complement to the Wadsworth–Emmons and Wittig olefination reactions. Each seems to have found its place in providing alternatives for difficult synthetic environments. For example, the Meinwald synthesis of the anti-feedant (±)-muzigadiol (**1**) relied on the Wittig reaction for incorporating the methylene group and its adjacent methyl group, but the Horner reaction for elaboration of the quaternary formyl group.[47]



**1**

The Horner reaction as originally discovered was a single-step conversion of a phosphine oxide and an aldehyde or ketone to an alkene, but as such depended on use of a base other than an organolithium. These authors fortuitously employed sodamide in their discovery work[1] and potassium *t*-butoxide subsequently.[42] It was soon noted, however, that in using organolithium bases alkenes were not obtained and instead, after protic workup, only β-hydroxyphosphine oxides (BHPOs) were obtained (Eq. 11.3).[6,42] These BHPOs could be converted into the same alkene(s) by treatment with a second base other than an organolithium base.[42,48] Accordingly the Horner reaction has a single step (path A) and a two-step (path B) variant, with the major difference being that any stereoisomers must be separated as alkenes when using path A, but could be



**BHPO**

(11.3)

separated either as alkenes or as BHPOs using path B. The latter separation has turned out to be much easier.[46]

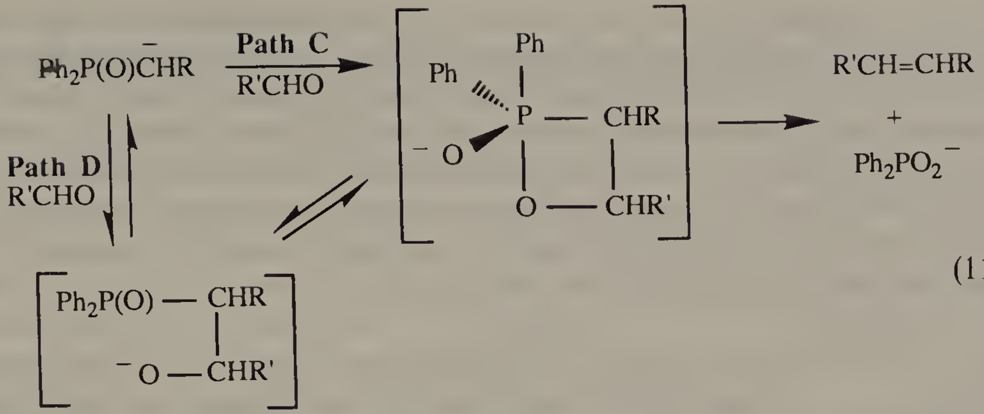
The use of organolithium bases at low temperatures (−78°C) invariably produces the BHPOs as products when conducted in the usual solvents, normally THF. However, use of butyllithium at room temperature[34] or lithium diisopropylamide at 0°C produced alkenes directly.[32] Also, addition of hexamethylphosphoric triamide (HMPA) after adduct formation using butyllithium resulted in alkene formation in moderate yield.[49] The standard reagent for conversion of BHPOs to alkenes in very high yields has become sodium hydride in DMF,[48] but others have used NaH in DMSO,[7] KH in THF/DMSO,[50] potassium hexamethyldisilylamide,[51] and DBU.[7]

The standard condition for single-step alkene formation (path A) has involved use of potassium *t*-butoxide[42,52] as the base, but others have used sodamide,[1] and both sodium and potassium hexamethyldisilylamide.[33]

## 11.2.1 Mechanism and Stereochemistry

***11.2.1.1 Mechanism of the Horner Reaction.*** The single-step Horner reaction has been shown to be a third-order reaction, first order in each of the base, the phosphine oxide, and the carbonyl compound.[5] The rate of aldehyde disappearance and alkene appearance were approximately the same, indicating no accumulation of intermediate. For reaction with substituted benzaldehydes, the $\rho$-value was $+2.33$, larger than that for comparable phosphinate ($+2.16$) and phosphonate ($+1.95$) carbanion reactions, but smaller than for comparable phosphonium ylide reaction ($+2.9$). This indicated that phosphinoxy carbanions were more nucleophilic than ylides, but less so than phosphinates or phosphonates; however, in all cases there was nucleophilic attack of the carbanion on the carbonyl carbon. Larsen and Aksnes[5] concluded that the reaction involved direct and rate-determining formation of a pentacoordinate oxaphosphetane intermediate which then dissociated to products, with the driving force being the formation of a new P–O bond (Eq. 11.4, path C). No other evidence for the existence of an oxaphosphetane has emerged.

Most authors have represented the Horner reaction as proceeding via an intermediate betaine (Eq. 11.4, path D), although no demanding evidence has



(11.4)

been provided. Schlosser et al[53] claimed that an NMR peak at 36 ppm indicated a lithium adduct of the betaine. There have been no authenticated reports of an uncomplexed betaine, but Edwards et al.[21] recently claimed that the betaine formed from difluoromethyldiphenylphosphine oxide and carbonyl compounds using lithium diisopropylamide at −50°C was stable to 27°C, and above that temperature decomposed to the expected alkenes.

Since β-hydroxyphosphine oxides are known to produce alkenes upon deprotonation,[42,48] it is obvious that betaines could be intermediates in the Horner reaction, but it is not clear whether they are the initial adducts which then decompose via oxaphosphetanes to alkenes (Eq. 11.4, path D) or whether they are derived from oxaphosphetanes upon complexation with lithium and subsequently isolated upon protonation (Eq. 11.4, path C). The BHPOs, and therefore betaines, are known to revert to reactants[54,55] since phosphinoxy carbanions formed in that manner have been trapped by more electrophilic carbonyl compounds,[55] and the carbonyl portion also has been trapped.[54]

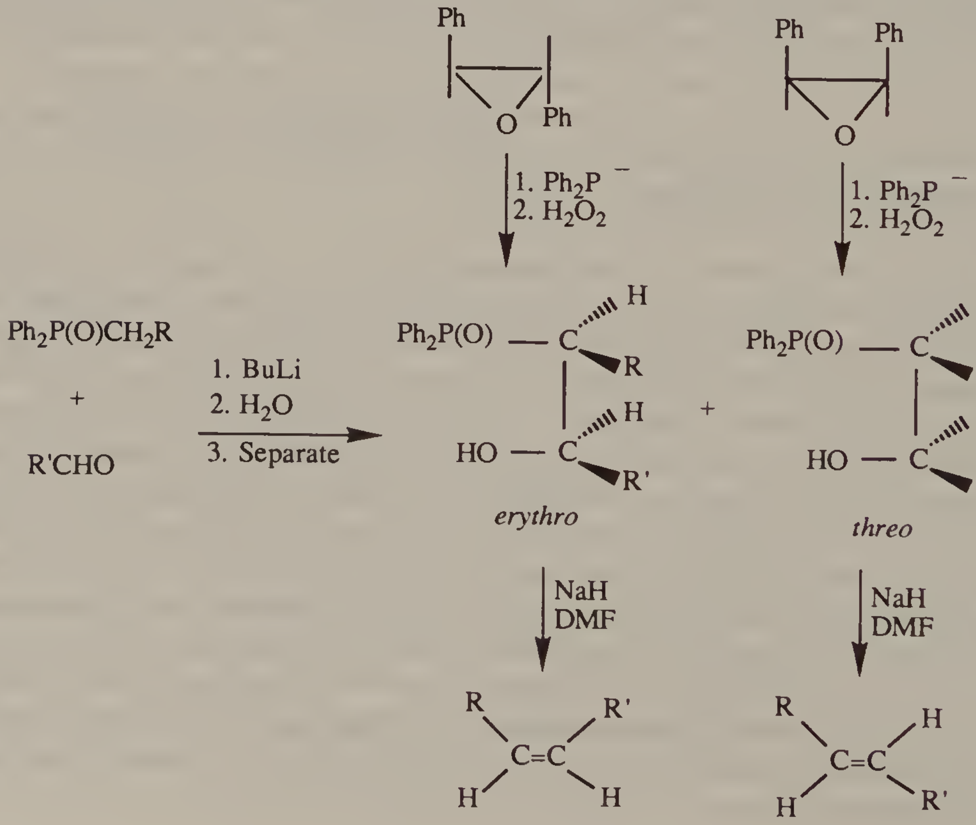
In summary, the detailed mechanism of the one-step Horner reaction remains unproven, especially regarding the possible relationship of a betaine and an oxaphosphetane intermediate.

***11.2.1.2 Stereochemistry of the One-step Horner Reaction.*** The one-step Horner reaction involves a syn elimination of the phosphorus group and the carbonyl oxygen atom, resulting in retention of configuration at phosphorus,[56] the same as for the Wittig reaction. Depending on the orientation of the two reactants, and whether envisaged as combining to form erythro and threo betaines or cis and trans oxaphosphetanes, the overall reaction could produce *Z*- or *E*-alkenes, respectively. When the phosphinoxy carbanion was "stabilized",[36,39,57] the dominant product was the *E*-alkene, the carbethoxy- and cyano-methyl carbanions affording 90–95% *E*-alkene. When the carbanion was disubstituted, as in $Ph_2P(O)C^-(F)COOMe$, the reaction was not stereoselective.[52] When the phosphinoxy carbanion was not "stabilized", the dominant product was also usually the *E*-alkene.[31,32,34,49] However, in spite of these stereoselectivities, the separation of the *Z*- and *E*-alkenes occasionally has been difficult.[49] No major solvent effect on the stereoselectivity of the reaction has been detected.[31]

The *E* stereoselectivity of the Horner reaction can be accounted for by the reversibility of the first step and the lower energy of the *trans*-oxaphosphetane and/or the threo betaine formed therein, both of which would afford the *E*-alkene. Conditions that diminish the reversibility of the carbanion attack on the carbonyl group would be expected to decrease the *E* stereoselectivity of the reaction.[7] It should be noted that *E* stereoselectivity occurred in spite of the dominance of erythro BHPO formation, eventually leading to *Z*-alkene, in the presence of lithium bases (see Section 11.2.1.3).

***11.2.1.3 Stereochemistry of the Two-Step Horner Reaction.*** Through the fortuitous use of organolithium bases to attempt Horner reactions, three groups[6,42,58] obtained *β*-hydroxyphosphine oxides (BHPOs) instead of alkenes, and two groups found that they could be converted to the expected alkenes using potassium *t*-butoxide (Eq. 11.3).[42,58] These observations led others, especially the Warren group, to investigate the stereochemistry of the two-step reaction through isolation and subsequent decomposition of the BHPOs, and thereby to develop even more stereoselective olefination processes.

Although Horner and Klink[54] were the first to investigate the stereochemistry of the two BHPOs produced from benzyldiphenylphosphine oxide and benzaldehyde, their assignment was incorrect and Buss et al.[55] showed that in this instance, and with most other phosphine oxides, the mixture of BHPOs was predominately (~ 85:15) the erythro BHPO, and the two isomers were readily separable (Eq. 11.5). The structures were confirmed by independent synthesis



(11.5)

from lithium diphenylphosphide and *trans*- and *cis*-stilbene oxides, which afforded the erythro and threo BHPOs, respectively, which could be identified by NMR.[55] Further confirmation was provided by X-ray analysis of an erythro isomer.[59] The mixture of BHPOs equilibrated in the presence of butyllithium to a 2:1 erythro:threo mixture.[55,59] Studying the effect of solvent and temperature indicated that the highest yields of the erythro isomer could be obtained at low temperatures (−78 to −100°C) in THF solvent,[35] conditions that should minimize reversal to reactants. The presence of $\alpha$-branched alkyl groups (e.g., isopropyl),[35] $\alpha$-alkoxy groups,[60] or $\beta$-amino groups[60] in the phosphine oxide reduced the dominance of erythro BHPO formation, but variation in the structure of the carbonyl reactant had little effect.[35]

The predominance of the erythro isomer was attributed to preferred antiorientation of the bulkiest groups in the betaine-forming transition state, those being the phosphinoxy and the complexed and solvated oxyanion group. Diminished solvation, such as in toluene solution, resulted in the absence of stereoselectivity in BHPO formation.[35]

Threo BHPOs, when treated with sodium hydride in DMF, afforded high yields of almost pure *E*-alkene,[35,48,55] demonstrating the syn elimination of the process as proposed earlier,[56] and the lack of reversal to carbanion and carbonyl. However, the low yields of threo BHPOs makes this an overall unattractive route to *E*-alkenes. Erythro BHPOs, under the same conditions, afforded mainly, but not exclusively, *Z*-alkenes with *Z*:*E* ratios of 75–90:1 being typical. The contaminant *E*-alkene was undoubtedly produced by dissociation of erythro betaine to reactants, as evidenced by trapping experiments with *m*-chlorobenzaldehyde.[56] Roberts and Whitham[7] later showed that an erythro BHPO prepared with a dibenzophosphole oxide group could be converted to a *Z*-alkene in high yield with a maximum 1% contamination by *E*-alkene. The absence of significant reversal to reactants presumably was due to the favourable geometry of the oxaphosphetane intermediate or transition state when spiro-connected to a five-membered ring at the phosphorus atom. The overall process, involving stereoselective formation of erythro BHPO, facile removal of threo betaine, then stereoselective decomposition of the erythro betaine to *Z*-alkene, provides results similar to the Wittig reaction for nonstabilized ylides, dominant formation of *Z*-alkenes. Thus, the impact of this process on synthetic chemistry has been minimal.

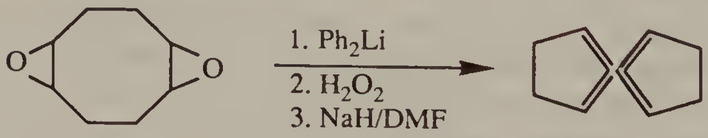
The Warren group[48,61] found that threo BHPOs, which serve as precursors with high stereoselectivity for *E*-alkenes, were best obtained by an alternate process which commenced with the same phosphine oxide, but involved initial acylation of the carbanion, usually with esters but occasionally with other reagents. Reduction of the resulting $\beta$-keto phosphine oxide with sodium borohydride afforded mixtures of BHPOs containing >90% threo isomer, with the erythro isomer being readily removable by chromatography. Sodium hydride converted the threo isomers to nearly pure *E*-alkenes in high yield (Eq. 11.6). It also was possible to perform the normal Horner reaction, isolate the mixture of erythro and threo BHPOs, oxidize both to the $\beta$-ketophosphine

$$\begin{tikzcd}
\text{Ph}_2\text{P(O)CH}_2\text{R} \arrow[r, "\text{BuLi/THF}", "\text{R'COOEt}"'] & \text{Ph}_2\text{P(O)-CHR-CO-R'} \arrow[d, "\text{NaBH}_4"] \arrow[ddr, "\text{NaBH}_4\ \text{CeCl}_3"] & \\
E\text{-alkene} & \textit{threo}\text{-BHPO} \arrow[l, "\text{NaH/DMF}"'] & \\
Z\text{-alkene} & & \textit{erythro}\text{-BHPO} \arrow[ll, "\text{NaH/DMF}"']
\end{tikzcd} \tag{11.6}$$

oxide, effect the $NaBH_4$ reduction to mainly threo BHPO, and then effect decomposition to alkene, thereby obtaining high yields and nearly exclusive formation of the *E*-alkene.[61] More recently the Warren group[62] found that while $NaBH_4$ produced the threo BHPO stereoselectively, the Luche modification thereof ($NaBH_4$, $CeCl_3$, MeOH, −78°C) afforded mainly the erythro BHPO. Therefore, using the alternate Warren route for the two-step Horner reaction from phosphine oxides and carbonyls to alkenes now provides the flexibility to obtain stereoselective production of the *Z*- or *E*-alkene (Eq. 11.6).

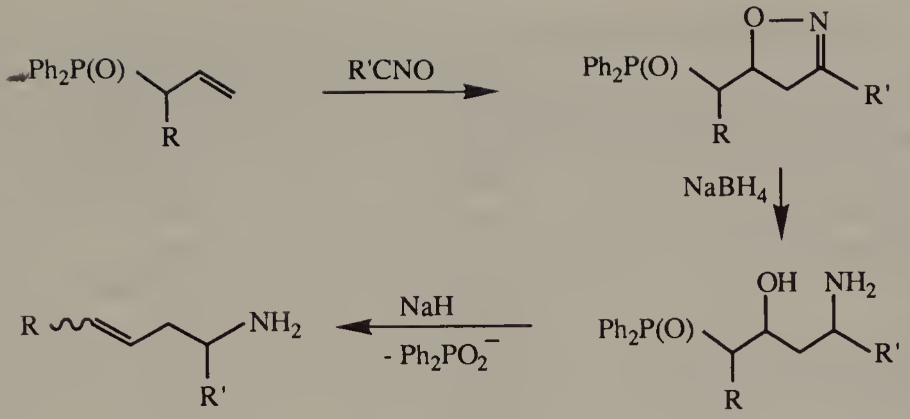
Understanding of the stereochemical processes described above has permitted many interesting syntheses. Bridges and Whitham[63] effected the conversion of *Z*-alkenes to *E*-alkenes and vice versa using the process shown in Eq. 11.7, for example converting *Z*,*Z*-cycloocta-1,5-diene to the *E*,*Z*-isomer. More recently, the diepoxide of 1,5-cyclooctadiene has been converted into *E*,*E*-cycloocta-1,5-diene (Eq. 11.8).[64] Addition of cyanates to allyldiphenylphosphine oxides and

$$\begin{tikzcd}
Z\text{-alkene} \arrow[r, "\text{(O)}"] & \textit{cis}\text{-oxirane} \arrow[d, "\text{1. Ph}_2\text{PLi}\ \ \text{2. (O)}"] \\
E\text{-alkene} & \textit{threo}\text{-BHPO} \arrow[l, "\text{NaH/DMF}"']
\end{tikzcd} \tag{11.7}$$



(11.8)

reduction of the resulting isoxazolines produced separable erythro and threo δ-amino-BHPOs which, when deprotonated with sodium hydride in DMF, afforded good yields of the separate *E*- and *Z*-homoallylic amines (Eq. 11.9).[65] Use of the two-step Horner reaction and the Warren modification has permitted efficient synthesis of many *Z*- and *E*-alkene-containing natural products.[66]



(11.9)

### 11.2.2 Applications of the Horner Reaction

The Horner reaction has been applied to alkene synthesis using a wide variety of phosphine oxides and carbonyl compounds. This section describes the scope of the reaction in an exemplary, but not encyclopedic, manner.

***11.2.2.1 Phosphine Oxide Reactants.*** Table 11.1 contains a listing of many of the phosphine oxides [$R^1R^2CH\text{-}P(O)Ph_2$], both monosubstituted ($R^1 \neq H$; $R^2 = H$) and disubstituted ($R^1, R^2 \neq H$), which have been employed in the Horner reaction, together with mainly recent exemplary references to direct

**TABLE 11.1 Phosphine Oxides [$R^1R^2CH–P(O)Ph_2$] Employed in the Horner Reaction with Aldehydes or Ketones**

| $R^1$ | $R^2$ | References |
|---|---|---|
| H | H | 6, 42, 58, 67, 68 |
| $CH_3$ | H | 34, 59, 69, 70 |
| $C_2H_5$ | H | 31, 35, 61 |
| $n\text{-}C_3H_7$ | H | 42, 61, 68 |
| $i\text{-}C_3H_7$ | H | 61 |
| $n\text{-}C_4H_9$ | H | 61 |
| $i\text{-}C_4H_9$ | H | 61 |
| $n\text{-}C_5H_{11}$ | H | 71 |
| $CH_3$ | $CH_3$ | 72 |
| $c\text{-}C_3H_5$ | H | 12 |
| $–CH_2–CH_2–$ | | 1, 50 |
| $–(CH_2)_5–$ | | 73 |
| $C_6H_5$ | H | 2, 34, 74–76 |
| | $C_6H_5$ | 77 |
| $CH_2=CH–$ | H | 27, 78 |
| $CH_3–CH=CH–$ | H | 18, 34, 79–81 |
| $c\text{-}C_6H_{10}=CH–$ | H | 81 |
| $C_6H_5–(CH=CH)_2–$ | H | 17 |

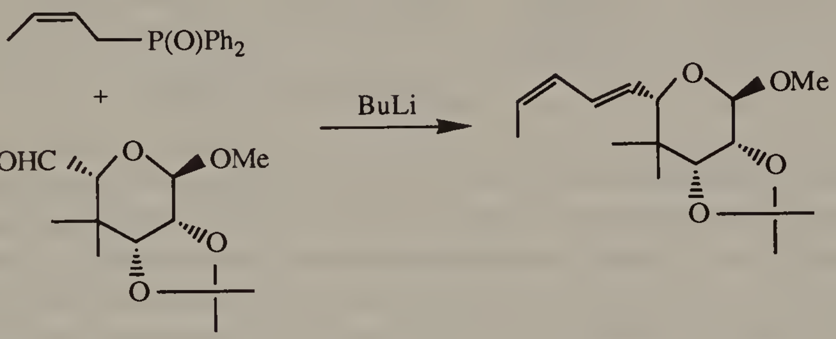
TABLE 11.1 Continued

| $R^1$ | $R^2$ | References |
|---|---|---|
| $CH_2{=}CH-$ | $CH_3$ | 17, 49, 82 |
| | $CH_3O$ | 24, 32, 83, 84 |
| $(CH_3)_2C{=}CH-CH_2-$ | H | 85 |
| $(C_6H_5)_2C{=}C{=}$ | | 19 |
| COOR | H | 5, 39, 86 |
| | $CH_3$ | 87 |
| | F | 52, 88 |
| $C(=O)CH_3$ | H | 43 |
| | $CH_3$ | 43 |
| C(=O)R | H | 29, 43 |
| $C(=O)-CH_2COOEt$ | H | 16 |
| 2-Cycloalkanone | H | 44 |
| 3-Cyclohexanone | H | 13 |
| $CH_3-CO-CH_2$ | H | 13, 89 |
| $CH_3CO-CH_2-CH_2$ | H | 14 |
| CN | H | 36, 39, 57 |
| Br | $C_6H_5$ | 90 |
| Cl | $C_6H_5$ | 90 |
| F | H | 21 |
| | F | 21 |
| $CH_3O$ | H | 23, 47, 60, 91, 92 |
| 2-Tetrahydropyranyl | H | 45 |
| 2-Tetrahydrofuranyl | H | 45 |
| $CH_3O$ | $CH_3O$ | 25 |
| $CH_3S$ | H | 11 |
| $C_6H_5S$ | $CH_3$ | 11, 93 |
| $-S-(CH_2)_3-S-$ | | 94 |
| $N(CH_3)C_6H_5$ | H | 95 |
| $N-(CH_2-CH_2)_2-O$ | H | 96 |
| $N-(CH_2)_5$ | H | 60 |
| $CH_2-N-(CH_2)_5$ | H | 26 |
| $CH_2-N-(CH_2)_4$ | H | 97 |
| $CH_2-NR-COC_6H_5$ | H | 97 |
| $N_2$ | H | 98 |
| | $C_6H_5$ | 90, 99, 100 |
| | $C_4H_9-C(=O)$ | 101 |
| N-Pyridinium | H | 102 |
| N-Imidazolium | H | 4 |
| $Ph_3P^+-$ | H | 103 |
| $Ph_2P(O)$ | H | 104 |
| $Ph_2P(O)-CH_2$ | H | 69, 105 |
| $Ph_2P(O)-CH_2-C_6H_4-$ | H | 69 |
| $Ph_2P(S)$ | H | 106 |
| $Ph_2P$ | H | 106 |
| Metals (Cr, Ti, Mn, Ce) | H | 68 |

readers to their use. Carbon substituents have been listed first followed by various heteroatom-containing substituents.

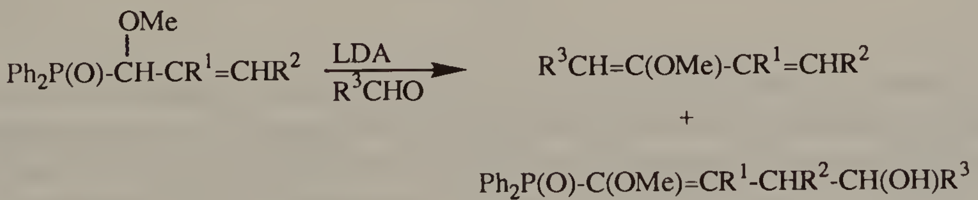
Application of this variety of monosubstituted phosphine oxides ($R^1 \neq H$, $R^2 = H$) in the Horner reaction with aldehydes produced 1,2-disubstituted alkenes[16,39,42,47,92,97] and with ketones produced 1,1,2-trisubstituted alkenes.[4,16,42,81,82,96] Use of disubstituted phosphine oxides ($R^1, R^2 \neq H$) with aldehydes produced 1,1,2-trisubstituted alkenes[11,25,26,32,45,52] and with ketones produced 1,1,2,2-tetrasubstituted alkenes.[21,25,50,89,94]

The presence of a vinyl group on the phosphinoxy carbanion, providing the opportunity for nucleophilic character at both the $\alpha$- and $\gamma$-carbons of the allylic system, normally provides no complications with nucleophilic attack occurring via the $\alpha$-carbon to afford dienes.[49,73,107] Thus, the phosphine oxides derived from geraniol and nerol both afforded conjugated dienes from $\alpha$-reaction.[46] In the total synthesis of milbemycin $B_3$ the coupling reaction between the northern and southern "hemispheres" occurred at the $\alpha$-carbon with retention of *E*-configuration of the preexisting double bond,[33] and in the total synthesis of vitamin $D_2$ the original position and stereochemistry of the vinylic double bond remained unchanged in the final triene.[108] Reaction of the carbanion from crotyldiphenylphosphine oxide also occurred at the $\alpha$-carbon and the original *Z*-configuration was retained (Eq. 11.10).[79,81]



(11.10)

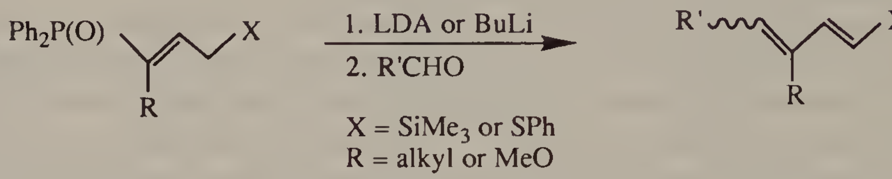
However, there are a few instances where the phosphinoxy carbanion reacted using its $\gamma$-carbanion site, thereby precluding alkene formation. In the $\alpha$-methoxycarbanion series addition to benzaldehyde and acetaldehyde normally occurred using the $\gamma$-carbon to produce $\alpha$-methoxy-$\delta$-hydroxy-$\alpha,\beta$-unsaturated phosphine oxides, unless the $\gamma$-carbon was substituted, in which case the expected diene resulted from $\alpha$ attack (Eq. 11.11).[83] Two other groups also



$$\mathrm{Ph_2P(O)\text{-}\overset{OMe}{\overset{|}{C}}H\text{-}CR^1{=}CHR^2} \xrightarrow[\mathrm{R^3CHO}]{\mathrm{LDA}} \mathrm{R^3CH{=}C(OMe)\text{-}CR^1{=}CHR^2} + \mathrm{Ph_2P(O)\text{-}C(OMe){=}CR^1\text{-}CHR^2\text{-}CH(OH)R^3}$$

(11.11)

reported isolated instances of $\gamma$ attack,[24,72] with the former group noting that initial complexation of the carbanion with titanium tetraisopropoxide returned the reaction to normal $\alpha$-attack, probably by initial complexation of titanium at the $\gamma$ site. The Warren group[82] and the Murray group[32] both noted instances where $\alpha$-diphenylphosphinoxyalkenes could be metallated at the $\gamma$ site with the resulting carbanion reacting with aldehydes only at the $\alpha$ site to produce dienes (Eq. 11.12).



(11.12)

The carbanion group in a phosphinoxy carbanion can serve as the synthetic equivalent of other groups useful in synthesis. Earnshaw et al.[91] reacted the $\alpha$-methoxy carbanion with aldehydes and ketones in a two-step Horner reaction to afford vinyl ethers which readily hydrolyzed to aldehydes, effecting a one-carbon homologation with the phosphinoxy carbanion being the equivalent of the formyl group (Eq. 11.13). In an analogous process Broekhof et al.[95,96] used

$$\mathrm{Ph_2P(O)\text{-}CH_2X} \xrightarrow[\substack{\text{2. RCHO}\\ \text{3. NaH}}]{\text{1. BuLi}} \underset{\mathrm{X = NR_2,\ OMe,\ or\ SPh}}{\mathrm{RCH{=}CHX}} \xrightarrow{\mathrm{H^+}} \mathrm{RCH_2CHO} \qquad (11.13)$$

$\alpha,\alpha$-disubstituted amino carbanions to obtain enamines which were hydrolyzed to aldehydes. Similarly, sulfenation of phosphinoxy carbanions followed by Horner reaction produced $\alpha$-phenylthioalkenes which were hydrolyzed to aldehydes. Use of $\alpha$-phenylthio-$\alpha$-alkylcarbanions $[\mathrm{R(C_6H_5S)C^-{-}P(O)Ph_2}]$ afforded ketones, the carbanion group being the synthetic equivalent of the acyl group (R–C=O).[11] Commencing with $\alpha$-phenylthiovinyldiphenylphosphine oxide and first adding an organolithium reagent, then effecting a Horner condensation, and finally hydrolyzing the thiovinyl ether afforded disubstituted acetones in which the phenylthiovinyl group was the synthetic equivalent of the $\mathrm{-CH_2{-}CO-}$ group (Eq. 11.14).[27]

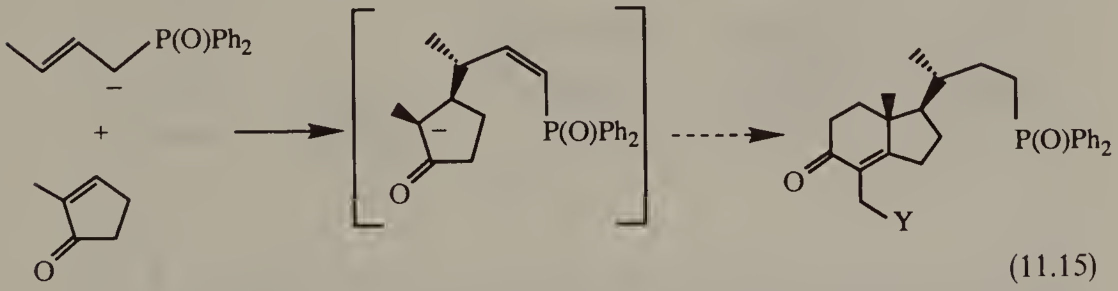
$$\mathrm{Ph_2P(O)\text{-}C(SPh){=}CH_2} \xrightarrow[\substack{\text{2. R'CHO}\\ \text{3. H}^+}]{\text{1. RLi}} \mathrm{R'CH_2CO\text{-}CH_2R} \qquad (11.14)$$

It should be noted that analogous phosphine sulfides reacted with aldehydes and ketones in the presence of strong base in a manner similar to the phosphine oxides. However, the carbanions were less nucleophilic, often not reacting with ketones,[94] and the $\mathrm{Ph_2P(S)}$ group was a poorer leaving group than the $\mathrm{Ph_2P(O)}$ group.[94,106]

*11.2.2.2* ***Carbonyl Reactants.*** Phosphinoxy carbanions reacted with most aldehydes and ketones (aryl, alkyl, and cycloalkyl) and regardless of the substitution pattern. Cycloalkanones also reacted readily. Aldehydes were more reactive than ketones in a competitive reaction,[68] as expected from the positive $\rho$ value for substituted benzaldehydes.[5] There is not as large a literature as with phosphonates of examples of the use of carbonyls which fully tests their reactivity with phosphinoxy carbanions, for example, the use of highly sterically hindered carbonyls. However, Saito et al.[19] did report high yields in the reaction of the carbanion of a cumulene phosphine oxide, $Ph_2P(O)–CH=C=CPh_2$, with pivaldehyde to form a butatriene. Phosphinoxy carbanions are not known to olefinate carboxylate derivatives, effecting only acylation instead (see Section 11.3.1.2).

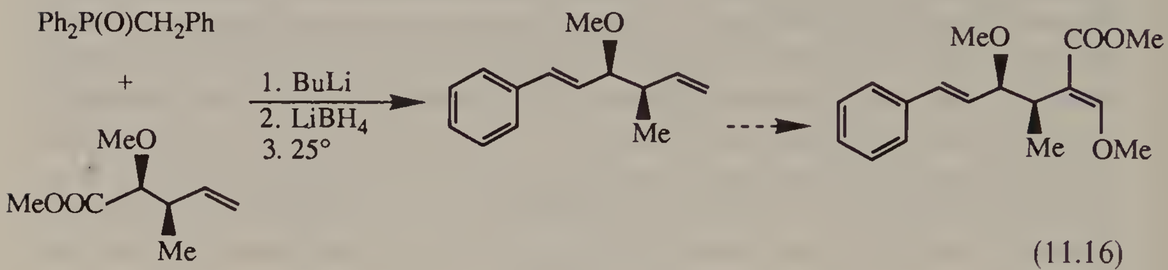
Reaction of phosphinoxy carbanions with $\alpha,\beta$-unsaturated aldehydes[82,109] and ketones[109,110] generally occurred at the carbonyl group to afford either BHPOs or dienes, depending on the conditions. However, there are a few exceptions, such as with $\alpha$-cyano[111] and $\alpha$-vinyl[80,18] phosphinoxy carbanions, which effected conjugate additions to $\alpha,\beta$-unsaturated ketones. The carbanion from acetonyldiphenylphosphine oxide effected a conjugate addition to methyl acrylate in modest yield.[43]

*11.2.2.3* ***Applications of the Horner Reaction.*** This section cites a few examples of the application of the Horner reaction, both the one- and two-step versions, as well as the Warren variant of the two-step version, to interesting synthetic problems. Lythgoe et al.[108] coupled the two major fragments using the Horner reaction in their total synthesis of vitamin $D_2$, and the process has been applied recently with excellent results in the synthesis of vitamin $D_3$ metabolites.[112] The C–D steroidal ring fragment with correct stereochemistry has been prepared using a phosphinoxy carbanion in a conjugate addition, with the phosphinoxy group being positioned to elaborate the side chain (Eq. 11.15).[18] The previously cited synthesis of *E,E*-cycloocta-1,5-diene (Eq. 11.8) is worthy of special mention, involving as it did a second-step Horner elimination from a BHPO.[64]

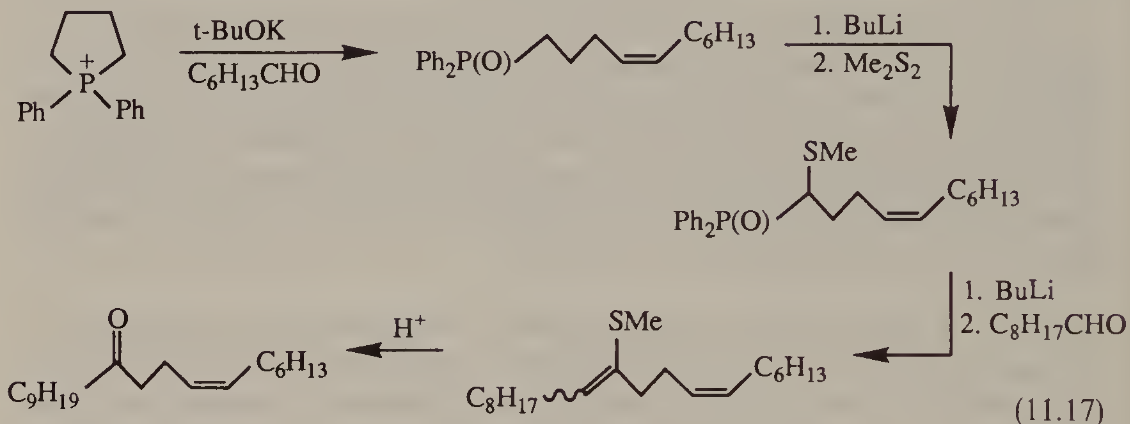


(11.15)

The introduction of the correct stereochemistry and the placement of several substituents in oudemansin A was made possible by the Warren variant of the two-step Horner reaction (Eq. 11.16).[75] A similar approach has been applied to the synthesis of dihydrocompactin precursors,[113] the synthesis of a number of pheromones,[66] and the *E* coupling of the $C_{10-18}$ and $C_{20-34}$ fragments of the immunosuppressant FK 506.[51] Using a Wittig reaction and a Horner reaction in tandem permitted the conversion of a cyclic phosphonium salt into the sex pheromone of the Japanese female peach moth (Eq. 11.17).[114]

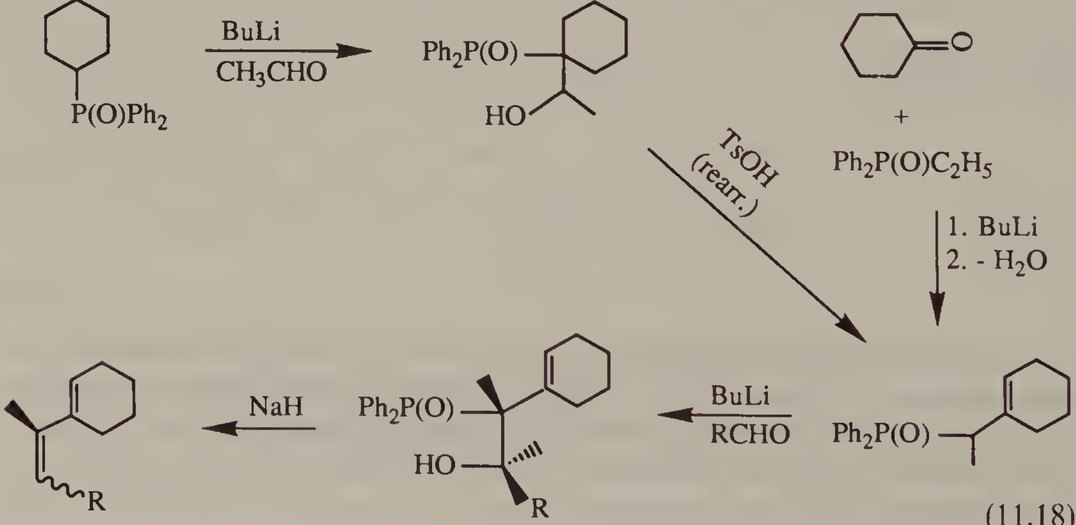


(11.16)



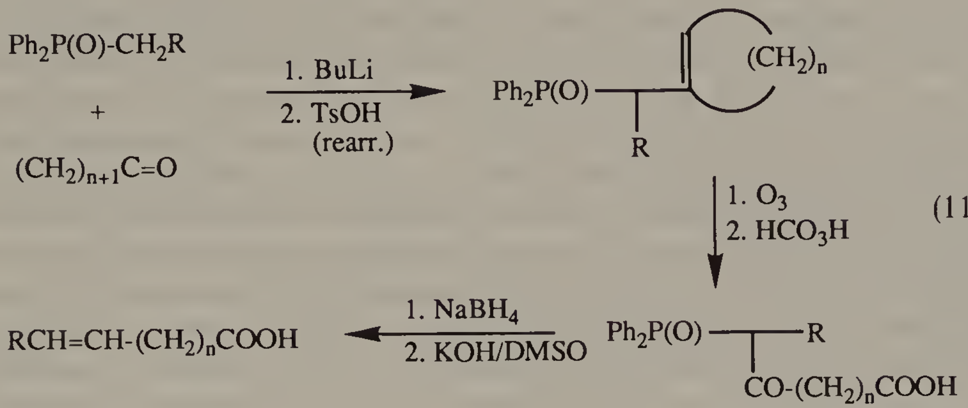
(11.17)

Warren and colleagues have developed a useful synthetic scheme based on Horner condensation, acid-catalyzed rearrangement of the isolated BHPO,[115] and a second Horner reaction to afford dienes. For example, both cyclohexyldiphenylphosphine oxide and acetaldehyde or ethyldiphenylphosphine oxide and cyclohexanone could be reacted and rearranged to afford separately the *E*- and *Z*-dienes (Eq. 11.18).[110] The rearrangement step even could be repeated before



(11.18)

the final Horner condensation. This process has been applied to the synthesis of unsaturated carboxylic acids, and separation of the BHPOs permitted obtaining the *E*- and *Z*-unsaturated acids stereoselectively (Eq. 11.19).[116]



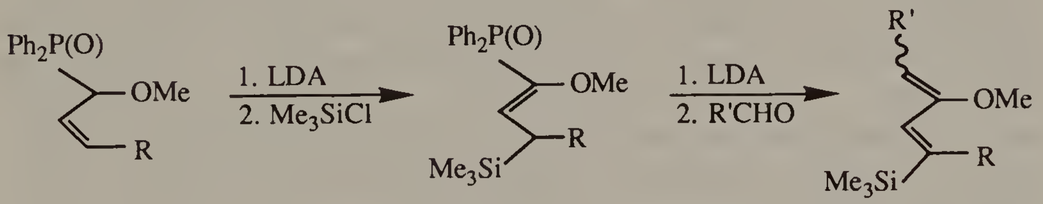
(11.19)

## 11.3 OTHER REACTIONS OF PHOSPHINOXY CARBANIONS

### 11.3.1 Electrophiles

***11.3.1.1 Alkylation and Related Reactions.*** The alkylation of alkyldiphenylphosphine oxides has been employed as a means of elaborating higher substitution on a phosphinoxy carbanion prior to its use in a Horner reaction. Such reactions proceeded readily using butyllithium as the base and methyl iodide,[85,93] higher alkyl iodides,[11] and benzyl bromide[117] as electrophiles. Allylic bromides, α-bromoketones, and α-bromoesters also have been effective.[43] The only complications seem to have been a risk of γ-alkylation of β-ketoalkylphosphine oxides[41] and γ-alkylation of allylic phosphine oxides.[83]

Reaction of trimethyl silyl chloride with the carbanion of allylic phosphine oxides afforded only the γ-silylated product which, in the presence of lithium diisopropylamide underwent a Horner reaction at the α-carbon (Eq. 11.20).[32,84]

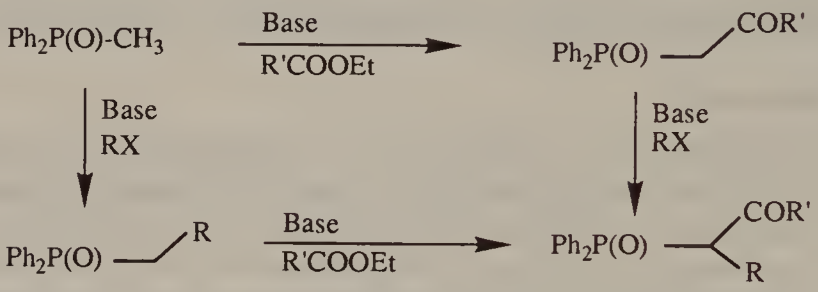


(11.20)

Sulfenation of phosphinoxy carbanions occurred readily with dimethyl disulfide or with diphenyl disulfide.[11] Reaction of the products with carbonyl compounds in a Horner reaction afforded α-methylthio- or α-phenylthioalkenes which were hydrolyzeable to carbonyl compounds, thus effecting a homologation reaction. However, with allylic phosphine oxides mixtures of α- and γ-sulfenated products usually resulted.[27,82,84]

Phosphinoxy carbanions have been metallated by reaction of their lithium salts with other metal halides, including chromium, titanium, manganese, and cerium, occasionally resulting in more than monosubstitution on the metal.[68]

*11.3.1.2 Acylation.* The attachment of the acyl group to the carbanion of a phosphine oxide has taken on added significance in the past decade owing to the Warren variant of the Horner reaction providing access in a stereoselective manner to threo BHPOs and *E*-alkenes (see Section 11.2.1.3). The historic means of effecting acylation has been to convert a phosphine oxide to its carbanion using potassium *t*-butoxide or butyllithium and acylating with ethyl carboxylates.[6,42] The reaction has been applied extensively to aromatic[61] and aliphatic[43,48] carboxylate esters, with no competition from olefination as with phosphonates and phosphonium ylides. Accordingly, a target-disubstituted phosphine oxide is available by two routes (Eq. 11.21).[43] Acylation was effected equally well using lactones, with carbonyl attack by the carbanion being the only observed course of reaction.[8,48,60]



(11.21)

Acylation was not effective with acid anhydrides in a single report[118] but has been very effective with acyl chlorides,[113,119] especially when the lithio carbanion was converted to its copper salt with CuI prior to addition of acyl chloride.[59,116,120] There is one report of acylation occurring on the γ-carbon of an allylic phosphine oxide, even when the carbanion initially was complexed with titanium, a technique which usually directed reactions to the α-carbon.[24]

Phosphinoxy carbanions were acylated with carbon dioxide to afford α-phosphinoxy acetic acids,[6,58] but here again with allylic phosphine oxides there was the complication of γ- as well as α-carboxylation.[72,107] Acylation with carbon disulfide, followed by deprotonation with LHMDS and methylation, afforded ketenedithioacetals, with allylic phosphone oxides attacking via the γ position.[121] Methylisothiocyanate acylated phosphinoxy carbanions to produce thioamides.[76]

β-Ketoalkylphosphine oxides also have been prepared by rearrangement of ω-carbalkoxyphosphine oxides, presumably via intramolecular acylation (Eq. 11.22).[60,120] Thus, reaction of ethylene oxide with phosphinoxy carbanions,

(11.22)

followed by acylation and rearrangement, provided a simple route to homoallylic alcohols.[60]

As is known both for phosphonium ylides and phosphonate carbanions, β-ketoalkylphosphine oxides, when heated with alkoxide bases, were converted to their carbanions, which underwent analogous intramolecular elimination of phosphinate to afford alkynes.[69,119]

***11.3.1.3 Miscellaneous Reactions.*** Phosphinoxy carbanions are oxidatively cleaved to carbonyl compounds by molecular oxygen as are phosphonium ylides and phosphonate carbanions. Use of a half equivalent of oxygen permitted the remaining carbanion to effect a Horner reaction to produce alkene,[75] but most often a full equivalent of oxygen was employed to obtain the carbonyl compound.[122,123] Oxidation of a macrocyclic α-thiophosphinoxy carbanion to a thiolactone was made very difficult by steric hindrance to carbanion formation.[124]

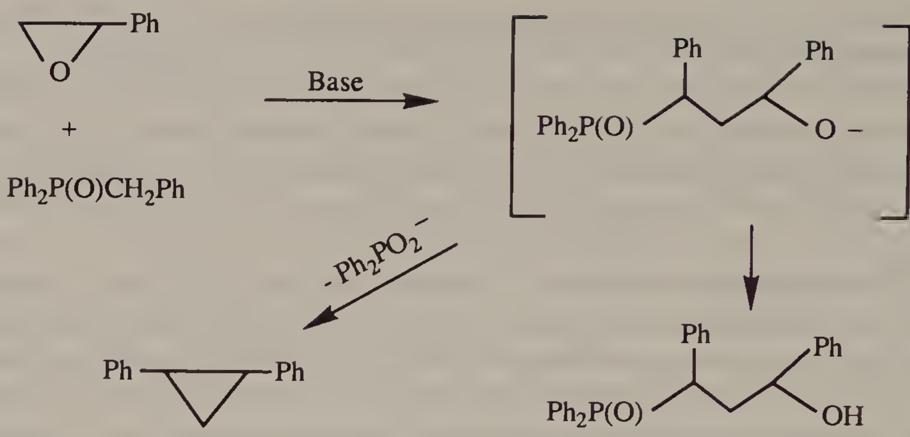
Horner et al.[89] brominated alkyldiphenylphosphine oxides on the α-carbon using N-bromosuccinimide and chlorinated them with *t*-butyl hypochlorite. Whereas phosphonium ylides displaced nitrogen from phenyl azide and formed iminophosphoranes, presumably by reacting with the internal nitrogen, the analogous phosphinoxy carbanion reacted with the terminal nitrogen in a direct coupling reaction without elimination of nitrogen.[125] Grim et al.[126] formed bidentate complexes of a phosphinoxy carbanion ($TrisO_2SLi$) with rhodium salts.

### 11.3.2 Multiple-Bonded Compounds and Oxiranes

Phosphinoxy carbanions reacted with nitrosobenzene in a manner exactly analogous to aldehydes in that they formed aldimines and phosphinate from attack at nitrogen, with the former being hydrolyzed to aldehydes during workup.[42] Similarly, phosphinoxy carbanions reacted with aldimines but via attack at carbon to afford alkenes and phosphinamide.[56]

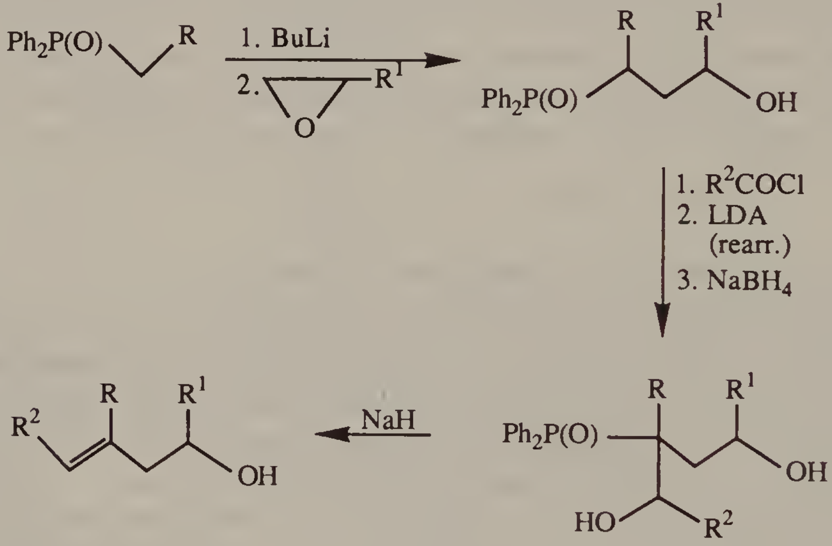
Phosphinoxy carbanions reacted with α,β-unsaturated carbonyl compounds generally at the carbonyl group to effect Horner reactions and alkene formation, but exceptions are known which produced δ-ketophosphine oxides by conjugate addition (see Section 11.2.2.2).

Horner et al.[74] found that phosphinoxy carbanions prepared using potassium *t*-butoxide reacted with oxiranes to afford cyclopropanes, but only in modest yields. Tomoskozi[2] showed that the reaction occurred with inversion of configuration when optically active styrene oxide was employed, indicating that the mechanism probably involved nucleophilic attack of the carbanion at the methylene group, contrary to Horner's supposition, and probably with subsequent attack of the oxyanion at phosphorus. However, when the reaction was conducted using butyllithium as the base, the intermediate γ-hydroxyphosphine oxide could be isolated,[74] presumably because of complexation with the lithium cation (Eq. 11.23) (note that the Horner structure probably is incorrect).

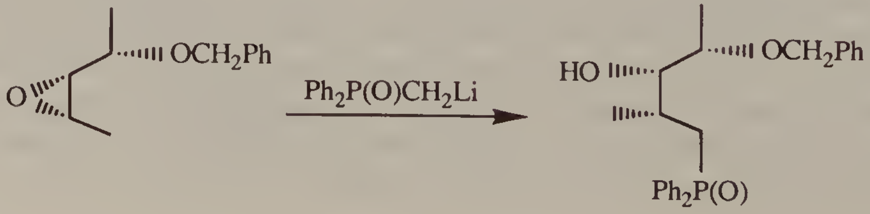


(11.23)

The major use of the reaction of phosphinoxy carbanions with oxiranes presently is for the formation of $\gamma$-hydroxyphosphine oxides and derived products.[13,60] *E*-Homoallylic alcohols (Eq. 11.24) were obtained from a multistep synthesis.[127] Others have applied the reaction with oxiranes to take advantage of the trans ring opening as a means of effecting stereochemical relationships,[70] for example synthesis of a fragment to be used for eventual Horner reaction coupling in the synthesis of avermectins (Eq. 11.25).[128]



(11.24)



(11.25)

## REVIEWS

**1966** Johnson, A. Wm. *Ylid Chemistry*, Academic: New York. A review of phosphinoxy carbanion chemistry.

**1972** Hays, H. R.; Peterson, D. J. In *Organic Phosphorus Compounds*; Kosolapoff, G. M.; Maier, L., Eds.; Wiley-Interscience: New York; Volume 3, Chapter 6, p. 341. A review of methods of synthesis of tertiary phosphine oxides.

**1977** Wadsworth, W. E. *Organic Reactions*, *25*, 73–255. A review of phosphoryl carbanions.

**1979** Walker, B. J. In *Organophosphorus Reagents in Organic Synthesis*; Cadogan, J. I. G., Ed.; Academic: London; Chapter 3, pp. 155–205. A review of phosphoryl reagents used in olefination reactions.

**1989** Maryanoff, B. E.; Reitz, A. B. *Chem. Revs.*, *89*, 863–927. A review of the Horner reaction.

## REFERENCES

[1] Horner, L.; Hoffmann, H.; Wippel, H. G. *Chem. Ber.* **1958**, *91*, 61.

[2] Tomoskozi, I. *Chem. Ind.* **1965**, 689.

[3] Petrov, E. S.; Tsvetkov, E. N.; Terekhova, M. I.; Malevannaya, R. A.; Shatenshtein, A. I.; Kabachnik, M. I. *Izv. Akad. Nauk SSSR* **1976**, 534.

[4] Maier, L.; Rist, G. *Phosphorus Sulfur* **1987**, *32*, 65.

[5] Larsen, R. O.; Aksnes, G. *Phosphorus Sulfur* **1983**, *15*, 229.

[6] Richard, J. J.; Banks, C. V. *J. Org. Chem.* **1963**, *28*, 123.

[7] Roberts, T. G.; Whitham, G. H. *J. Chem. Soc. Perkin Trans. (1)* **1985**, 1953.

[8] Elliott, J.; Warren, S. *Tetrahedron Lett.* **1986**, *27*, 645.

[9] Deschamps, B.; Lampen, J. P.; Mathey, F.; Seyden-Penne, J. *Tetrahedron Lett.* **1977**, 1137.

[10] Hays, H. R.; Peterson, D. J. In *Organic Phosphorus Compounds*; Kosolapoff, G. M.; Maier, L., Eds.; Wiley-Interscience: New York, 1972; Volume 3, Chapter 6, p. 341.

[11] Grayson, J. I.; Warren, S. *J. Chem. Soc. Perkin Trans. (1)* **1977**, 2263.

[12] Maercker, A. *Angew. Chem.* **1967**, *6*, 557.

[13] Bell, A.; Davidson, A. H.; Earnshaw, C.; Norrish, H. K.; Torr, R. S.; Trowbridge, D. B.; Warren, S. *J. Chem. Soc. Perkin Trans. (1)* **1983**, 2879.

[14] Cornish, C. A.; Warren, S. *J. Chem. Soc. Perkin Trans. (1)* **1985**, 2585.

[15] Kallmerten, J.; Wittman, M. D. *Tetrahedron Lett.* **1986**, *27*, 2443.

[16] van den Goorbergh, J. A. M.; van der Gen, A. *Tetrahedron Lett.* **1980**, *21*, 3621.

[17] Savage, M. P.; Trippett, S. *J. Chem. Soc. (C)* **1966**, 1842.

[18] Haynes, R. K.; Vonwiller, S. C. *J. Chem. Soc. Chem. Commun.*, **1987**, 92.

[19] Saito, I.; Yamaguchi, K.; Nagata, R.; Murahashi, E. *Tetrahedron Lett.* **1990**, *31*, 7469.

[20] Bodrin, G. V.; Mateeva, A. G.; Terekhova, M. I.; Matrosov, E. I.; Petrov, E. S.; Polikarpov, Y. M.; Kabachnik, M. I. *Bull. Acad. Sci. USSR* **1991**, *40*, 810.

[21] Edwards, M. L.; Stemerick, D. M.; Jarvi, E. T.; Matthews, D. P.; McCarthy, J. R. *Tetrahedron Lett.* **1990**, *31*, 5571.

[22] Hashimoto, T.; Maeta, H.; Matsumoto, T.; Morooka, M.; Ohba, S.; Suzuki, K. *Synlett.* **1992**, 340.

[23] Maleki, M.; Miller, A.; Lever, O. W. *Tetrahedron Lett.* **1981**, *22*, 365.

[24] Birse, E. F.; McKenzie, A.; Murray, A. W. *J. Chem. Soc. Perkin Trans. (1)* **1988**, 1039.

[25] van Schaik, T. A. M.; Henzen, A. V.; van der Gen, A. *Tetrahedron Lett.* **1983**, *24*, 1303.

[26] Cavalla, D.; Warren, S. *Tetrahedron Lett.* **1982**, *23*, 4505.

[27] Grayson, J. I.; Warren, S.; Zaslona, A. T. *J. Chem. Soc. Perkin Trans. (1)* **1987**, 967.

[28] Haynes, R. K.; Katsifis, A. G. *J. Chem. Soc. Chem. Commun.* **1987**, 340.

[29] Portnoy, N. A.; Morrow, C. J.; Chattha, M. S.; Williams, J. C.; Aguiar, A. M. *Tetrahedron Lett.* **1971**, 1397.

[30] Marszak, M. B.; Simalty, M.; Seuleiman, A. *Tetrahedron Lett.* **1974**, 1905.

[31] Bergelson, L. D.; Vaver, V. A.; Barsukov, L. I.; Shemyakin, M. M. *Bull. Acad. Sci. USSR* **1966**, 474.

[32] Ironside, M. D.; Murray, A. W. *Tetrahedron Lett.* **1989**, *30*, 1691.

[33] Schow, S. R.; Bloom, J. D.; Thompson, A. S.; Winzenburg, K. N.; Smith, A. B. *J. Am. Chem. Soc.* **1986**, *108*, 2662.

[34] Schlosser, M.; Tuong, H. B. *Chimia* **1976**, *30*, 197.

[35] Buss, A. D.; Warren, S. *Tetrahedron Lett.* **1983**, *24*, 3931.

[36] Etemad-Moghadan, G.; Seyden-Penne, J. *Synth. Comm.* **1984**, *14*, 565.

[37] Martin, D. J.; Griffin, C. E. *J. Org. Chem.* **1965**, *30*, 4034.

[38] Horner, L.; Klink, W.; Hoffmann, H. *Chem. Ber.* **1963**, 96, 3133.

[39] Bottin-Strzalko, T.; Etemad-Moghadan, G.; Seyden-Penne, J. *Nouv. J. Chem.* **1983**, *7*, 155.

[40] Cram, D. J.; Partos, R. D. *J. Am. Chem. Soc.* **1963**, *85*, 1093.

[41] Seyden-Penne, J. *Bull. Soc. Chim. Fr.* **1988**, 238.

[42] Horner, L.; Hoffmann, H.; Wippel, H. G.; Klahre, G. *Chem. Ber.* **1959**, *92*, 2499.

[43] Torr, R. S.; Warren, S. *J. Chem. Soc. Perkin Trans. (1)* **1983**, 1173.

[44] Mikolaczyk, M.; Kielbasinski, P.; Wieczorek, M. W.; Blaszczyk, J.; Kolbe, A. *J. Org. Chem.* **1990**, *55*, 1198.

[45] Ley, S. V.; Lygo, B.; Organ, H. M.; Wonnacott, A. *Tetrahedron* **1985**, *41*, 3825.

[46] Clough, J. M.; Pattenden, G. *Tetrahedron* **1981**, *37*, 3911.

[47] Bosch, M. P.; Camps, F.; Coll, J.; Guerrero, A.; Tatsuoka, T.; Meinwald, J. *J. Org. Chem.* **1986**, *51*, 773.

[48] Buss, A. D.; Warren, S. *J. Chem. Soc. Chem. Commun.* **1981**, 100; *J. Chem. Soc. Perkin Trans. (1)* **1985**, 2307.

[49] Caine, D.; Stanhope, B.; Fiddler, S. *J. Org. Chem.* **1988**, *53*, 4124.

[50] Meijs, G. F.; Eichinger, P. C. H. *Tetrahedron Lett.* **1987**, *28*, 5559.

[51] Jones, T. K.; Mills, S. G.; Redmer, R. A.; Askin, D.; Desmond, R.; Volante, R. P.; Shinkai, I. *J. Am. Chem. Soc.* **1989**, *111*, 1157.

52 Etemad-Moghadan, G.; Seyden-Penne, J. *Bull. Soc. Chim. Fr.* **1985** 448.

53 Schlosser, M.; Piskala, A.; Tarchini, C.; Tuong, H. B. *Chimia* **1975**, *29*, 341.

54 Horner, L.; Klink, W. *Tetrahedron Lett.* **1964**, 2467.

55 Buss, A. D.; Warren, S.; Leake, J. S.; Witham, G. H. *J. Chem. Soc. Perkin Trans. (1)* **1983**, 2215.

56 Horner, L.; Winkler, H. *Tetrahedron Lett.* **1964**, 3265.

57 Loupy, A.; Sugadji, K.; Seyden-Penne, J. *Synthesis* **1977**, 126.

58 Seyferth, D.; Welch, D. E.; Heeren, J. K. *J. Am. Chem. Soc.* **1964**, *86*, 1100.

59 Buss, A. D.; Cruse, W. B.; Kennard, O.; Warren, S. *J. Chem. Soc. Perkin Trans. (1)* **1984**, 243.

60 Buss, A. D.; Greeves, N.; Levin, D.; Wallace, P.; Warren, S. *Tetrahedron Lett.* **1984**, *25*, 357.

61 Buss, A. D.; Mason, R.; Warren, S. *Tetrahedron Lett.* **1983**, *24*, 5293.

62 Elliott, J.; Hall, D.; Warren, S. *Tetrahedron Lett.* **1989**, *30*, 601.

63 Bridges, A. J.; Whitham, G. H. *J. Chem. Soc. Chem. Commun.* **1974**, 142.

64 Boeckh, D.; Huisgen, R.; Noth, H. *J. Am. Chem. Soc.* **1987**, *109*, 1248.

65 Armstrong, S. K.; Warren, S.; Collington, E. W.; Naylor, A. *Tetrahedron Lett.* **1991**, *32*, 4171.

66 Buss, A. D.; Greeves, N.; Mason, R.; Warren, S. *J. Chem. Soc. Perkin Trans. (1)* **1987**, 2569.

67 Cavalla, D.; Warren, S. *Tetrahedron Lett.* **1983**, *24*, 295.

68 Kauffmann, T.; Schwartze, P. *Chem. Ber.* **1986**, *119*, 2150.

69 Horner, L.; Hoffmann, H.; Klink, W.; Ertel, H.; Toscano, V. G. *Chem. Ber.* **1962**, *95*, 581.

70 Levin, D.; Warren, S. *Tetrahedron Lett.* **1986**, *27*, 2265.

71 McElroy, A. B.; Warren, S. *Tetrahedron Lett.* **1985**, *26*, 1677.

72 Davidson, A. H.; Earnshaw, C.; Grayson, J. I.; Warren, S. *J. Chem. Soc. Perkin Trans. (1)* **1977**, 1452.

73 Davidson, A. H.; Warren, S. *J. Chem. Soc. Chem. Commun.* **1976**, 181.

74 Horner, L.; Hoffmann, H.; Toscano, V. G. *Chem. Ber.* **1962**, *95*, 536.

75 Wittmann, M. D.; Kallmerten, J. *J. Org. Chem.* **1987**, *52*, 4303.

76 Kunze, U.; Kruppa, V. *Phosphorus Sulfur* **1987**, *31*, 33.

77 Horner, L.; Hoffmann, H.; Klahre, G.; Toscano, V. G.; Ertel, H. *Chem. Ber.* **1961**, *94*, 1987.

78 Ikeda, Y.; Ukai, J.; Ikeda, N.; Yamamoto, H. *Tetrahedron* **1987**, *43*, 723.

79 Dolle, R. E.; Nicolaou, K. C. *J. Chem. Soc. Chem. Commun.* **1985**, 1016.

80 Binns, M. R.; Haynes, R. K.; Katsifis, A. A.; Schober, P. A.; Vonwiller, S. C. *Tetrahedron Lett.* **1985**, *26*, 1565.

81 Lythgoe, B.; Moran, T. A.; Nambudiry, M. E. N.; Ruston, S. *J. Chem. Soc. Perkin I* **1976**, 2386.

82 Blatcher, P.; Grayson, J. I.; Warren, S. *J. Chem. Soc. Chem. Commun.* **1978**, 657.

83 Maleki, M.; Miller, J. A.; Lever, O. W. *Tetrahedron Lett.* **1981**, *22*, 3789.

84 Devchand, D. K.; Murray, A. W.; Smeaton, E. *Tetrahedron Lett.* **1986**, *27*, 4635.

85 Buss, A. D.; Warren, S. *Tetrahedron Lett.* **1983**, *24*, 111.

[86] Bouyssou, P.; Chenault, J. *Tetrahedron Lett.* **1991**, *32*, 5341.

[87] Etemad-Moghadan, G.; Seyden-Penne, J. *Tetrahedron* **1984**, *40*, 5153.

[88] Baader, E.; Bartmann, W.; Beck, G.; Below, P.; Bergmann, A.; Jendralla, H. *Tetrahedron Lett.* **1989**, *30*, 5115.

[89] Earnshaw, C.; Torr, R. S.; Warren, S. *J. Chem. Soc. Perkin Trans. (1)* **1983**, 2893.

[90] Horner, L.; Hoffmann, H.; Ertel, H.; Klahre, G. *Tetrahedron Lett.* **1961**, 9.

[91] Earnshaw, C.; Wallis, C. J.; Warren, S. *J. Chem. Soc. Perkin Trans. (1)* **1979**, 3099.

[92] Campa, C.; Sanchez-Ferrando, F.; Tristan-Polo, M. *Nouv. J. Chem.* **1985**, *9*, 493.

[93] Warren, S.; Zaslona, A. T. *Tetrahedron Lett.* **1982**, *23*, 4167.

[94] Juaristi, E.; Gordillo, B.; Valle, L. *Tetrahedron* **1986**, *42*, 1963.

[95] Broekhof, N. L. J. M.; Jonkers, F. L.; van der Gen, A. *Tetrahedron Lett.* **1980**, *21*, 2671.

[96] Broekhof, N. L. J. M.; Jonkers, F. L.; van der Gen, A. *Tetrahedron Lett.* **1979**, 2433.

[97] Cavalla, D.; Cruse, W. B.; Warren, S. *J. Chem. Soc. Perkin Trans. (1)* **1987**, 1883.

[98] Kreutzkamp, N.; Schmidt-Samoa, E.; Herberg, K. *Angew. Chem.* **1965**, *4*, 1078.

[99] Regitz, M.; Anschutz, W.; Bartz, W.; Liedhegener, A. *Tetrahedron Lett.* **1968**, 3171.

[100] Eckes, H.; Regitz, M. *Tetrahedron Lett.* **1975**, 447.

[101] Corbel, B.; Hernot, D.; Haelters, J. P.; Sturtz, G. *Tetrahedron Lett.* **1987**, *28*, 6605.

[102] Wegener, W.; Schlippes, K. *Z. Chem.* **1972**, *12*, 334.

[103] Issleib, K.; Linder, R. *Liebigs Ann. Chem.* **1967**, *707*, 112.

[104] Kabachnik, M. I.; Medved, T. Y.; Matrosov, E. I. *Proc. Acad. Sci. USSR* **1965**, *162*, 460.

[105] Drehfal, G.; Hoerhold, H. H.; Wildner, H. *Chem. Abstr.* **1967**, *66*, 105346.

[106] Gloyna, D.; Henning, H. G. *Angew. Chem.* **1966**, *5*, 847.

[107] Davidson, A. H.; Warren, S. *J. Chem. Soc. Perkin Trans. (1)* **1976**, 639.

[108] Lythgoe, B.; Moran, T. A.; Nambudiry, M. E. N.; Tideswell, J.; Wright, P. W. *J. Chem. Soc. Perkin Trans. (1)* **1978**, 590.

[109] McElroy, A. B.; Warren, S. *Tetrahedron Lett.* **1985**, *26*, 1677.

[110] Brown, P. S.; McElroy, A. B.; Warren, S. *Tetrahedron Lett.* **1985**, *26*, 249.

[111] Cossentini, M.; Deschamps, B.; Anh, N. T.; Seyden-Penne, J. *Tetrahedron* **1977**, *33*, 409.

[112] Mascarenas, J. L.; Mourino, A.; Castedo, L. *J. Org. Chem.* **1986**, *51*, 1269.

[113] Burke, S. D.; Saunders, J. O.; Oplinger, J. A.; Murtiashaw, C. W. *Tetrahedron Lett.* **1985**, *26*, 1131.

[114] Yamamoto, I.; Tanaka, S.; Fujimoto, T.; Ohta, K. *J. Org. Chem.* **1989**, *54*, 747.

[115] Warren, S. *Acc. Chem. Res.* **1978**, *11*, 401.

[116] Levin, D.; Warren, S. *J. Chem. Soc. Perkin Trans. (1)* **1988**, 1799.

[117] Pietrusiewicz, K. M.; Zablocka, M. *Tetrahedron Lett.* **1989**, *30*, 477.

[118] Levin, D.; Warren, S. *Tetrahedron Lett.* **1985**, *26*, 505.

[119] Gough, S. T. D.; Trippett, S. *J. Chem. Soc.* **1962**, 2333.

[120] Greeves, N.; Warren, S. *Tetrahedron Lett.* **1986**, *27*, 259.

[121] Schaumann, E.; Fittkau, S. *Bull. Soc. Chim. Belg.* **1985**, *94*, 463.

[122] Davidson, A. H.; Warren, S. *J. Chem. Soc. Chem. Commun.* **1975**, 148.
[123] Vedejs, E.; Mastalerz, H.; Meier, G. P.; Powell, D. W. *J. Org. Chem.* **1981**, *46*, 5253.
[124] Vedejs, E.; Buchanan, R. A.; Watanabe, Y. *J. Am. Chem. Soc.* **1989**, *111*, 8430.
[125] Hoffmann, H. *Chem. Ber.* **1962**, *95*, 2563.
[126] Grim, S. O.; Ketter, P. B.; Thoden, J. B. *Organometallics*, **1991**, *10*, 2399.
[127] Wallace, P.; Warren, S. *J. Chem. Soc. Perkin Trans. (1)* **1988**, 2971.
[128] Barrett, A. G. M.; Miller, T. A. *Tetrahedron Lett.* **1988**, *29*, 1873.

# 12

# OTHER PHOSPHORUS YLIDES/CARBANIONS

As follows from the definition elaborated in the opening chapter of this book, the term "*phosphorus ylides*" broadly encompasses all those compounds where a carbanion is attached to any phosphorus atom which carries a substantial degree of positive charge and on which the positive charge is created by sigma bonding of the substituents to the phosphorus. Accordingly, there are three common groups of organophosphorus derivatives, those with O-, N-, or C-based substituents, whose members might be expected readily to form carbanions and which may provide interesting ylide-type chemistry. These groups are as follows:

A. *Phosphonium-Based Ylides* ($R^1R^2R^3P{=}CR^4_2$): There are a total of 10 possible combinations of alkyl/aryl, alkoxy, and disubstituted-amino groups which could produce phosphonium or "quasi-phosphonium" ylides of this type.

B. *Phosphoryl-Based Ylides* ($R^1R^2P(O){=}CR^4_2$): There are a total of six possible combinations of alkyl/aryl, alkoxy, and disubstituted-amino groups which could produce phosphoryl ylides (carbanions) of this type.

C. *Thiophosphoryl-Based Ylides* ($R^1R^2P(S){=}CR^4_2$): There are a total of six possible combinations of alkyl/aryl, alkoxy, and disubstituted-amino groups which could produce thiophosphoryl ylides (carbanions) of this type.

## 12.1 PHOSPHONIUM-BASED YLIDES

Of the 10 possible combinations of carbon, nitrogen, and oxygen-based substituents which are possible for phosphonium ylides ($R^1R^2R^3P{=}CR^4_2$), nine are

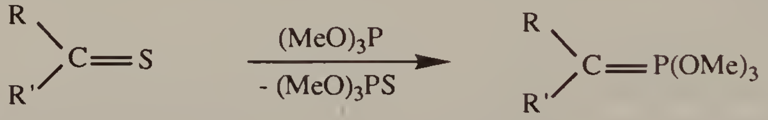
*Ylides and Imines of Phosphorus*, Edited by A. William Johnson.
ISBN 0-471-52217-1

known; these are listed below and their chemistry is described in this section. The first three are of important synthetic use, but the others are chemical curiosities.

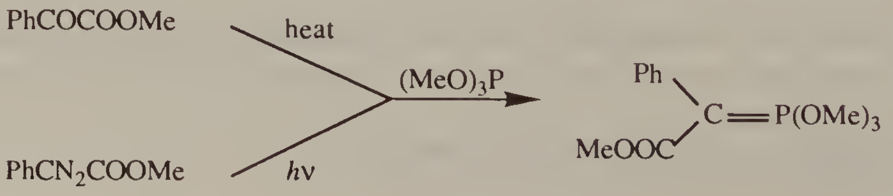
| $R^1$ | $R^2$ | $R^3$ | Reference |
|---|---|---|---|
| Alkl/aryl | Alkyl/aryl | Alkyl/aryl | Chapter 3 |
| Alkoxy | Alkoxy | Alkoxy | Section 12.1.1 |
| Amino | Amino | Amino | Section 12.1.2 |
| Alkyl/aryl | Alkyl/aryl | Alkoxy | Section 12.1.3 |
| Alkyl/aryl | Alkyl/aryl | Amino | Section 12.1.4 |
| Alkyl/aryl | Alkoxy | Alkoxy | Section 12.1.5 |
| Alkyl/aryl | Amino | Amino | Section 12.1.6 |
| Alkoxy | Amino | Amino | Section 12.1.7 |
| Alkoxy | Alkoxy | Amino | Section 12.1.8 |

### 12.1.1 Tris-alkoxyphosphonium Ylides

There are three distinct approaches to the preparation of these ylides, also called phosphitemethylenes or phosphite ylides. The first is the desulfurization of thiones and related compounds first disclosed in two patents issued two months apart.[1,2] Reaction of hexafluorothioacetone,[2,3] thiofluorenone,[3] and numerous cyclic trithiocarbonates[4,5] with trimethylphosphite afforded the ylides, which usually were not isolated, along with trimethyl thiophosphate (Eq. 12.1). The same process has been used to desulfurize phosphonodithioformates[6] and thiophosgene[1,7] to produce stabilized phosphite ylides. Griffiths et al.[8] obtained phosphite ylides in a deoxygenation process applied to aroylphosphonates, and proved that the process involved carbonyl deoxygenation to form a carbene which then was trapped by the phosphite. Recently Tomioka et al.[9] reported that α-keto esters (thermally) and α-diazo esters (photochemically) reacted with trimethylphosphite to afford identical phosphite ylides (Eq. 12.2). Seebach found that tris(phenylmercapto)methyl lithium apparently dissociated to a carbenoid species which also could be trapped by trimethylphosphite to form bis(phenylmercapto)methylenetrimethoxyphosphorane.[10]

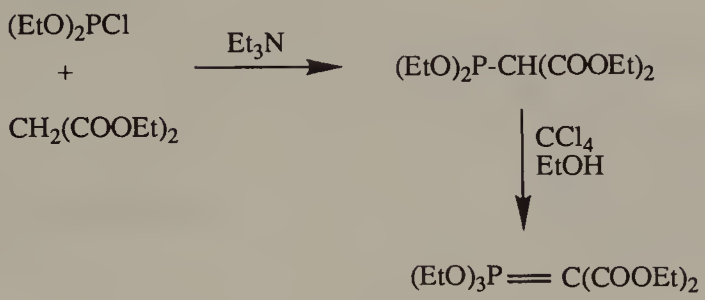


(12.1)



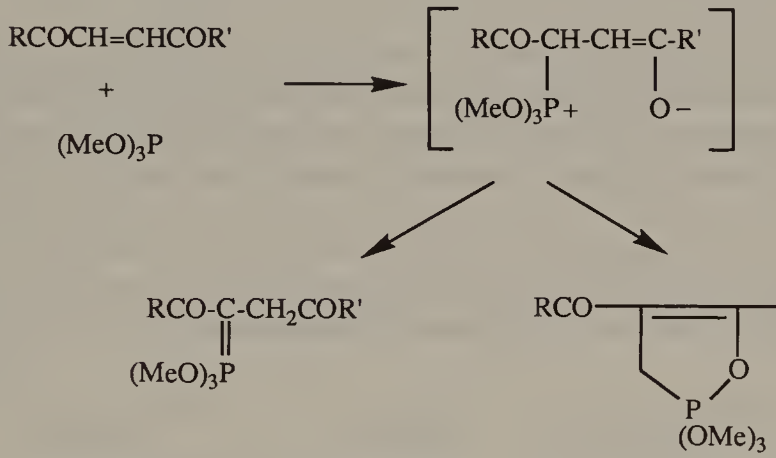
(12.2)

The second method involves the oxidation of readily available phosphonites using the Atherton–Openshaw–Todd[11] process ($CCl_4 + EtOH$) by which a stabilized P-chloroylide first was formed which then underwent nucleophilic displacement by ethanol (Eq. 12.3).[12,13]



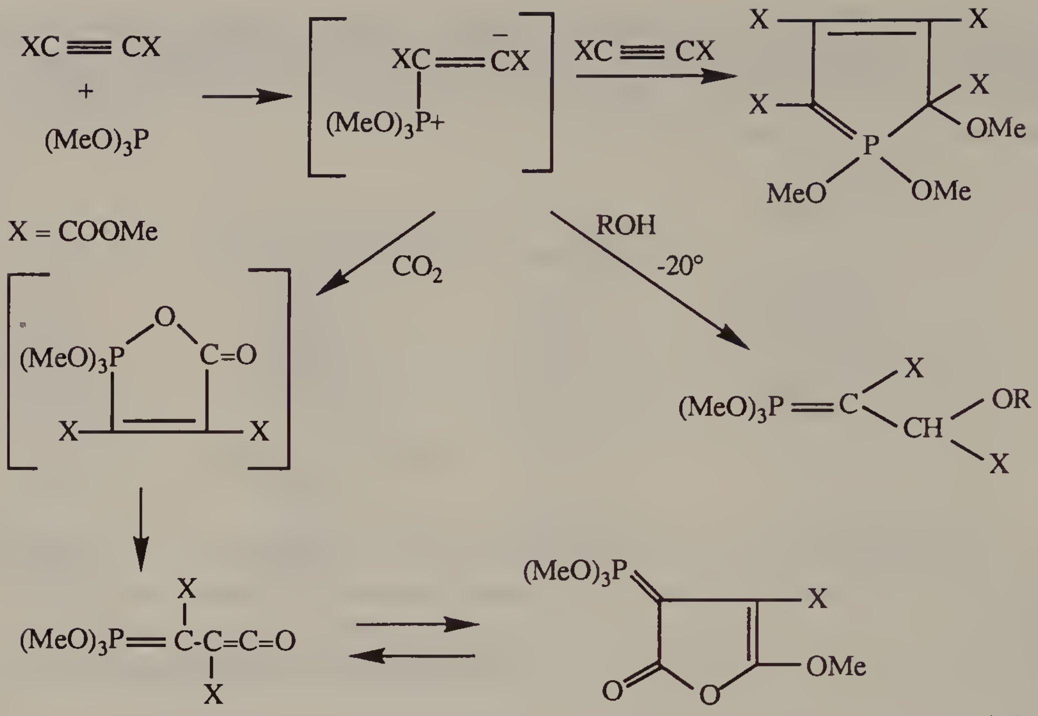
(12.3)

The third general route involves the addition of phosphites to conjugated alkenes or alkynes. Ramirez et al.[14] added trimethylphosphite to dibenzoylethylene and isolated the ylide resulting from proton transfer, but in some related instances a phosphorane was obtained instead (Eq. 12.4).[15] More recently, trimethylphosphite has been added to dimethyl acetylenedicarboxylate under three sets of conditions with two of them[16,17] leading to phosphite ylides, the third forming a cyclic ylide (Eq. 12.5).[18] Cyclic phosphites also have been added in the presence of various proton sources (YH), with the same initial zwitterionic adduct first undergoing protonation followed by nucleophilic addition of $Y^-$ either at phosphorus, to form vinylphosphoranes, or at vinylic carbon to produce ylides.[19]



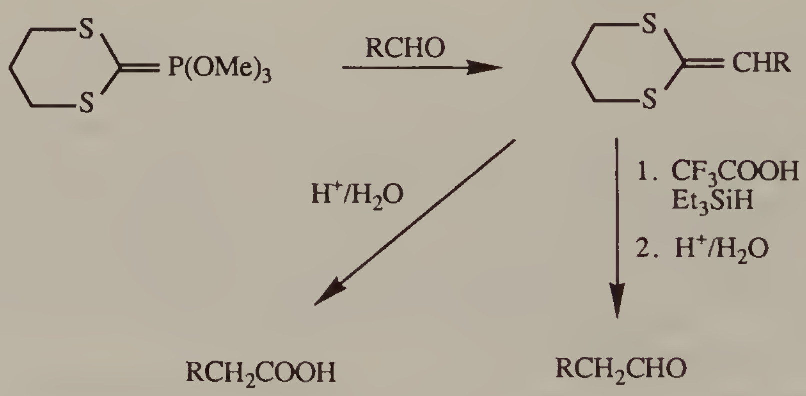
(12.4)

The phosphite ylides have been characterized by $^{31}$P NMR spectroscopy, typically showing a peak near 50 ppm.[6,8,14] Warming trimethoxy ylides generally leads to methyl migration to the ylide carbanion in a Steven's-type rearrangement to form $\alpha$-methylalkyl phosphonates,[3,4,8,14] and treatment with acid or water leads to protonation and demethylation to a phosphonate.[3,7,8] $\beta$-Carbonyl trimethoxyphosphonium ylides were O-alkylated, but in the process



(12.5)

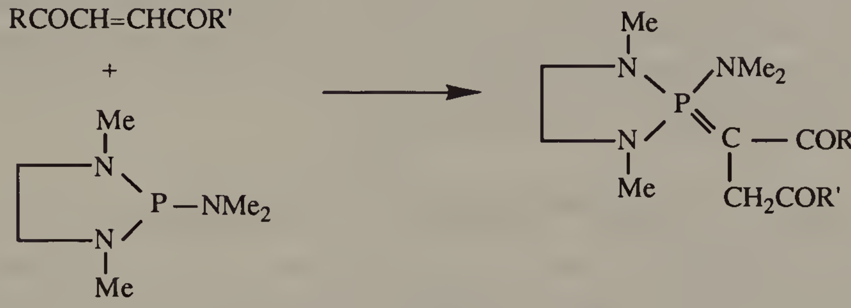
also were demethylated,[6,14] as they were upon C-halogenation.[3] The α,α-dithioylides would undergo a Wittig-type reaction, but only with aldehydes, to produce alkenes which could be cleaved to carboxylic acids or aldehydes, thereby effecting overall homologation reactions (Eq. 12.6).[4,5,10] Tomioka's ylides (see Eq. 12.2) did not react with aldehydes or ketones under normal conditions, but did react with both under photochemical conditions to afford good yields of alkenes.[9] More complex phosphite ylides would not react with carbonyls, probably because of "excess" delocalization of the carbanion.[6,17]



(12.6)

### 12.1.2 Tris-(dialkylamino)phosphonium Ylides

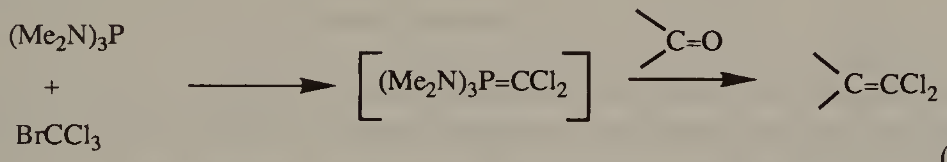
Alkylation of tris-(dialkylamino)phosphines with alkyl halides is the standard route to the phosphonium salts which then can be deprotonated to distillable ylides using a variety of strong bases.[20-24] More recently Leroux et al.[25,26] have added cyclic and acyclic tris-(dialkylamino)phosphines to symmetrical $\alpha,\beta$-unsaturated ketones and esters, and to some alkynyl ketones,[27] and obtained the corresponding ylides, similar to the Ramirez process with phosphites. (Eq. 12.7).[14]



(12.7)

These ylides would effect normal Wittig-type reactions with aldehydes and ketones.[20, 23] They also have been silylated in the normal manner and deprotonation then afforded silylated tris-amino ylides.[22]

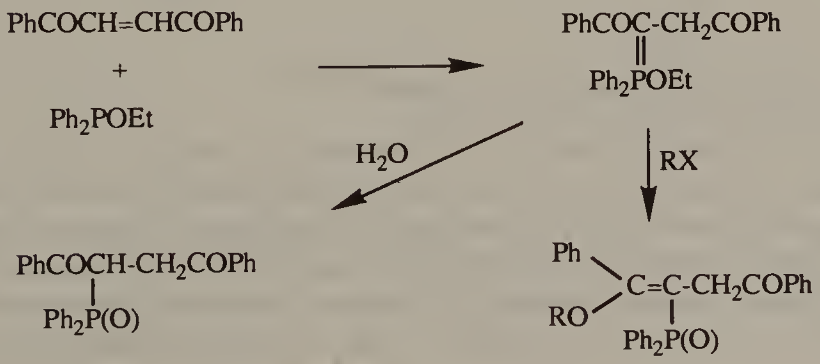
The use of tris(dialkylamino) substituents on phosphorus in place of the usual triphenyl substituents increased ylide reactivity in the Wittig reaction of dichloro- and difluoroylides. Naae and Burton[28] produced a stable olefinating solution of $(Me_2N)_3P{=}CF_2$ from dibromodifluoromethane and hexamethyl triphosphorous amide which reacted with aldehydes and ketones in excellent yield to afford *gem*-difluoroethenes. Similarly, Salmond[29] used bromotrichloromethane and the amide to produce the analogous dichloro ylide which reacted with aldehydes, but poorly with ketones, to afford *gem*-dichloroethenes (Eq. 12.8).



(12.8)

### 12.1.3 Alkoxydiphenylphosphonium Ylides

Ramirez et al.[30] added ethyl diphenylphosphinite to dibenzoylethylene and obtained a modest yield of the corresponding ylide (Eq. 12.9). The ylide was



(12.9)

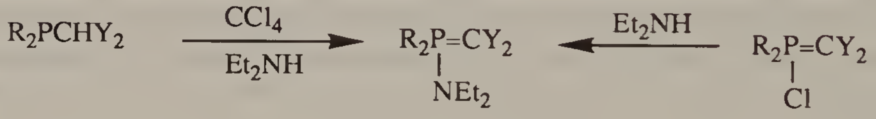
sensitive to water, hydrolyzing to the phosphine oxide and undergoing deethylation during O-alkylation. No Wittig-type reaction has been reported for such ylides.

Whereas ethyl di-*t*-butylphosphinite effected a normal Arbuzov rearrangement with α-chloroketones annd α-chloroesters, through attack of phosphorus on carbon, with α-chloroacetonitrile phosphorus attacked chlorine instead, the carbanion then displacing chloride eventually to form a low yield of the phosphinite ylide which was stable to moisture.[31]

### 12.1.4 Dialkyl- or Diaryl(dialkylamino)phosphonium Ylides

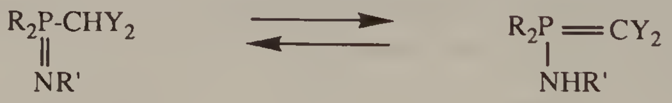
Methylation of dimethyldimethylaminophosphine to the phosphonium salt with methyl iodide was facile, as was subsequent deprotonation with sodium amide to afford the corresponding ylide [$(CH_3)_2N(CH_3)_2P{=}CH_2$)]. The latter was not isolated but would serve as a nucleophile, for example reacting with chlorophosphines.[32]

Kolodiazhnyi and co-workers prepared several highly stabilized phosphonium ylides with two alkyl or two aryl groups on phosphorus together with a single dialkylamino group. Many were prepared from precursor phosphines by amination procedures (Eq. 12.10).[33] Some were prepared with an alkylamino group, and ylide formation relied on the tendency for a tautomeric shift from carbon to nitrogen when the resulting carbanion (ylide) could be highly stabilized.[34] Depending on the nature of the carbon and nitrogen substituents, the tautomeric equilibrium which existed could be forced in either direction (Eq. 12.11).



$$R_2PCHY_2 \xrightarrow[Et_2NH]{CCl_4} \underset{\substack{|\\ NEt_2}}{R_2P{=}CY_2} \xleftarrow{Et_2NH} \underset{\substack{|\\ Cl}}{R_2P{=}CY_2}$$

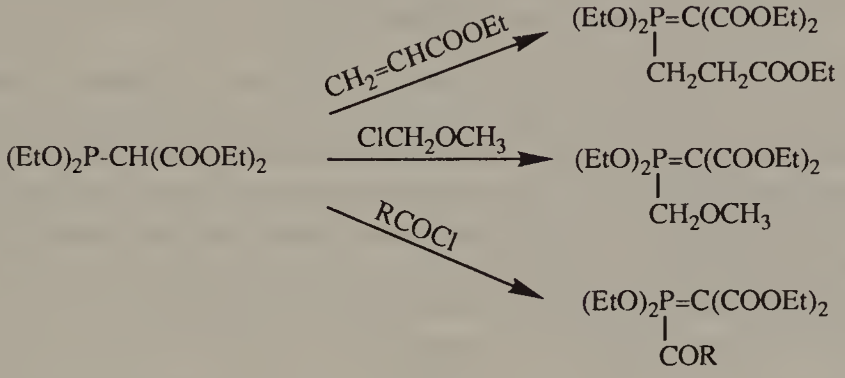
Y = COOEt, $SO_2Ph$, etc. (12.10)



$$\underset{\substack{\|\\ NR'}}{R_2P\text{-}CHY_2} \rightleftarrows \underset{\substack{|\\ NHR'}}{R_2P{=}CY_2} \qquad (12.11)$$

### 12.1.5 Alkyldialkoxyphosphonium Ylides

Although no significant chemistry has resulted, for the sake of completeness it should be noted that a phosphonite [$(EtO)_2PCH(COOEt)_2$] has been converted into ylides by two methods. The phosphonite effected a conjugate addition to ethyl acrylate, with the intermediate carbanion abstracting a proton from the malonate group to afford an ylide.[35] The same phosphonite was alkylated with chloromethyl ether and the expected Arbuzov rearrangement did not occur because of the same type of proton transfer.[36] Finally, acylation of the same phosphonite produced a *P*-acyl ylide, but this required proton removal by an added amine.[37] All of these ylide formations depended on the large stabilization provided by the dicarbethoxymethyl group, and failed in less stabilizing environments (Eq. 12.12).

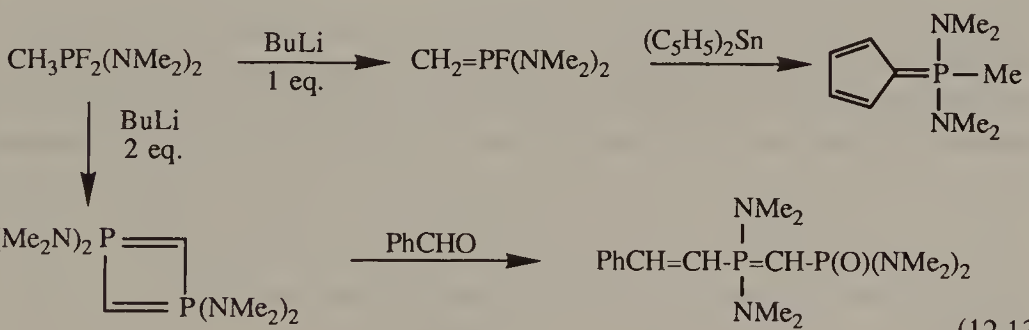


(12.12)

### 12.1.6 Bis-(dialkylamino)alkylphosphonium Ylides

Alkylbis-(dialkylamino)phosphines were readily converted into phosphonium methylides by methylation and proton removal.[21,22,32] Bis-dimethylaminophenylphosphine was converted into benzyl and carbethoxymethyl salts by alkylation, both of which could be deprotonated to the corresponding ylides which effected Wittig reactions with aldehydes and ketones.[38]

In an interesting reaction Plass et al.[39] obtained methylbis(dimethylamino) phosphoniumcyclopentadienylide from dicyclopentadienyl stannane and fluorobis(dimethylamino)phosphoniummethylide. The latter compound was obtained from a phosphorane [$CH_3PF_2(NMe_2)_2$] with one equivalent of butyllithium,[40] but with two equivalents it afforded a cyclic bis-dimethylamino-bis-ylide which underwent a Wittig-type reaction with benzaldehyde (Eq. 12.13).[41] In a somewhat related reaction, Kolodiazhnyi and Golokov[42] found



(12.13)

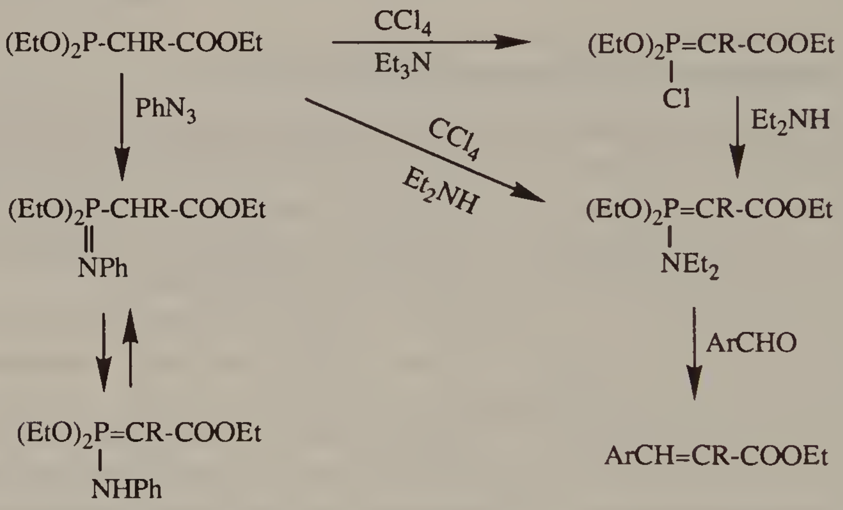
that bisdiethylaminofluorophosphonium ylides also reacted with carbonyl compounds to afford isolable oxaphosphetane adducts ($^{31}$P, −42 to −56 ppm) but which decomposed by HF elimination to allylphosphonamides rather than by Wittig-type elimination.

### 12.1.7 Bis-(dialkylamino) alkoxyphosphonium Ylides

Alkylation of bis-(dialkylamino) alkoxyphosphines with ethyl bromoacetate followed by proton removal with sodium hydride afforded the expected ester ylides. These ylides underwent a Wittig reaction with *m*-nitrobenzaldehyde.[43]

### 12.1.8 Dialkylaminodialkoxyphosphonium Ylides

Amination of dialkylphosphonites using $CCl_4$ and primary or secondary amines[12,13,44] or using azides[45] and relying on imine–ylide tautomerism afforded numerous such ylides, but only in cases where the resulting ylide was highly stabilized (Eq. 12.14). The position of the tautomeric equilibria between such iminophosphoranes and phosphonium ylides was a function of the delocalizing ability of substituents attached to nitrogen and carbon.[46] Such ylides would effect a Wittig reaction with aldehydes.[44]



(12.14)

## 12.2 PHOSPHORYL-BASED YLIDES

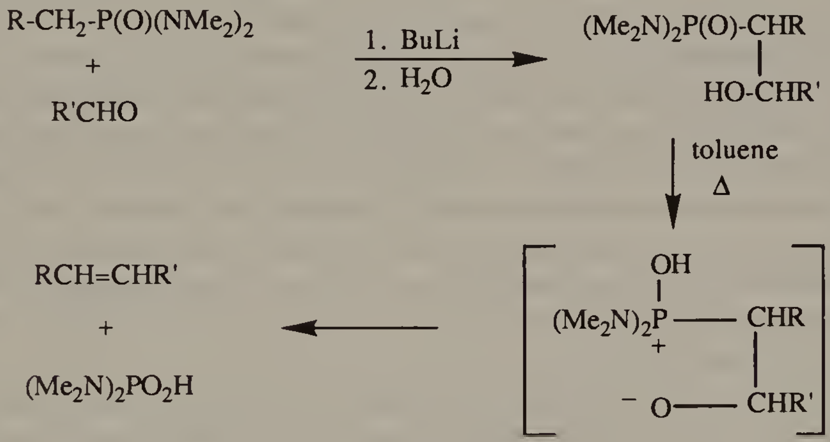
Phosphoryl-based ylides $[R^1R^2P(O){=}CR^4_2]$ are known containing all of the six possible combinations of alkyl, alkoxy, and amino P-substituents; these are listed below, and their chemistry is described in this section. The latter three have been curiosities only, but the first three have been of significant synthetic value.

| $R^1$ | $R^2$ | Reference |
|---|---|---|
| Alkyl/aryl | Alkyl/aryl | Chapter 11 |
| Alkoxy | Alkoxy | Chapter 10 |
| Amino | Amino | Section 12.2.1 |
| Alkyl/aryl | Alkoxy | Section 12.2.2 |
| Alkyl/aryl | Amino | Section 12.2.3 |
| Alkoxy | Amino | Section 12.2.4 |

### 12.2.1 Phosphonamide Carbanions

Phosphonamides [$RP(O)(NR'_2)_2$] are readily accessible from the reaction of secondary amines with phosphonic acid dihalides[47] and are readily converted to their carbanions using butyllithium[48] or potassium diisopropylamide.[49] Alkyl phosphonamides are commonly used but are readily converted into more complex phosphonamides by acylating the carbanions with esters[50, 51] or by alkylation.[48]

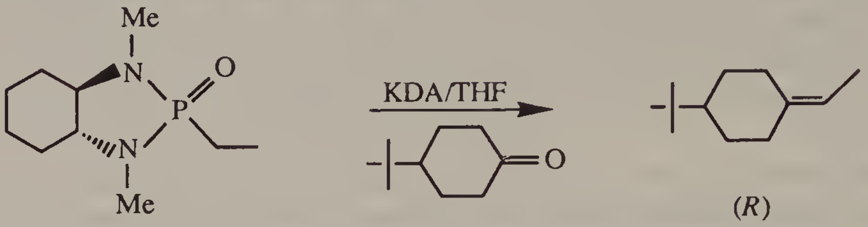
Alkyl phosphonamide carbanions reacted with aldehydes and ketones in THF to afford excellent yields of adducts which, upon protonation, were isolated as the $\beta$-hydroxyphosphonamides (BHPAs). The reaction was nonstereoselective, the erythro and threo isomers usually being separable, and with the erythro isomer normally predominating. Heating the separated BHPAs in toluene solution afforded excellent yields of alkenes, the erythro producing *Z*- and the threo producing *E*-alkene, thus indicating a cis elimination of diamidophosphate (Eq. 12.15).[48, 52] The anions of the BHPAs did not undergo elimination, in contrast to the phosphonium and phosphonyl analogs, leading to speculation that intramolecular proton transfer to produce more positive charge on phosphorus occurred before elimination as shown in Eq. 12.15.[53]



(12.15)

A variety of alkyl phosphonamides have been employed in reactions with carbonyls, including alkoxy-substituted derivatives,[54] but always afforded modest stereoselectivities. The best route to *E*-alkenes employing phosphonamide carbanions was to acylate with the ester (R′COOEt) corresponding to the intended aldehyde (R′CHO) of a carbonyl reaction, to reduce the resulting ketone to the BHPA with sodium borohydride which afforded high stereoselectivity for the threo BHPA, and then effect thermal elimination. High *E*-isomeric purities ($>90\%$) have been achieved,[48,51] similar to that from the Warren variant of the Horner reaction (see Section 11.2.1.3), providing a complement to the Wittig reaction which provides *Z*-stereoselectivity.

Recently, Hanessian et al.[49] have prepared enantiomeric phosphonamides and demonstrated that the resulting carbanions have a high stereofacial bias in that reaction of the *R*,*R*-form with *t*-butylcyclohexanone afforded a 95:5 ratio of the *R*- and *S*-alkene and the *S,S*-form afforded a 5:95 ratio (Eq. 12.16). Other examples were reported, as well as stereoselectivity in α-alkylation of the same carbanion.

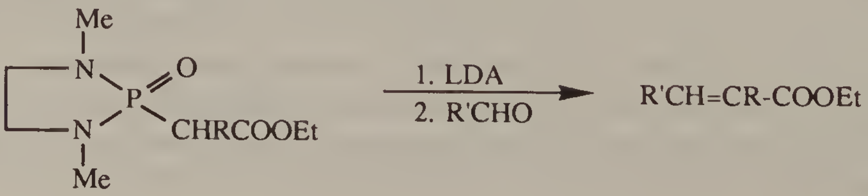


(*R,R*) (*R*) (12.16)

Use of allylphosphonamide carbanions, with their inherent possibility of α and γ nucleophilicity, resulted in exclusive γ addition to ketones under normal conditions,[52] but use of a cyclic diamine in the phosphonamide resulted in predominate α addition.[52] The substitution pattern of the electrophile and the reaction conditions both affect the α:γ ratio.[55]

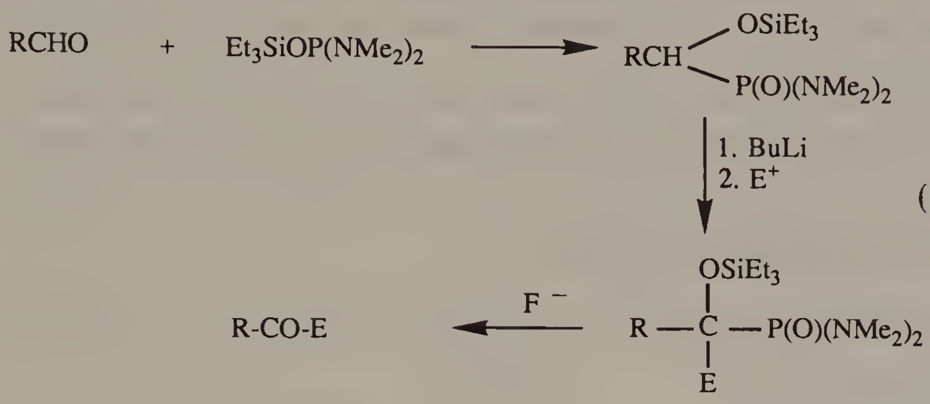
Benzylphosphonamide carbanions reacted with aldehydes to produce mixtures of erythro and threo BHPAs under the normal reaction conditions of −70°C, but if the reaction was allowed to warm to 20°C for one-half hour before workup, the erythro isomer was stereoselectively formed. Thermal elimination then produced excellent yields of nearly pure *Z*-alkenes.[53, 56] The erythro BHPA was shown to be the thermodynamically controlled product, possibly owing to the geometry of that lithio salt being most favorable for a tetracoordinate chain polymer excluding solvent. Such stereochemical control was not possible with ketone reactants.[57] Recently, such erythro BHPAs have been shown to stereoselectively afford *Z*-stilbenes by warming in ethanolic hydrogen chloride, but to produce a mixture of *E*- and *Z*-stilbenes in aqueous hydrogen chloride. The mechanism for conversion of the erythro BHPA to *E*-alkene is unknown.[58]

The reactions of stabilized phosphonamide carbanions with carbonyl compounds also have been studied, but in these instances BHPAs were not isolated, the alkenes being formed directly. Dauben et al.[50] found that the 2-ketobutyl phosphonamide carbanion was very unreactive. α-Cyanoethyl phosphonamide was reactive, affording mainly *E*-alkene with benzaldehyde and mainly *Z*-alkene with isobutyraldehyde.[59] Carbethoxymethyl phosphonamide carbanions, prepared from 2-alkyl-2-oxo-1,3-dimethyl-1,3,2-diazaphospholidine, also afforded excellent yields of *Z*-alkenes from aldehydes, with stereoselectivities usually > 90% (Eq. 12.17).[60, 61] The *Z*-isomer proportion was increased further by lower reaction temperatures and higher dilution.



(12.17)

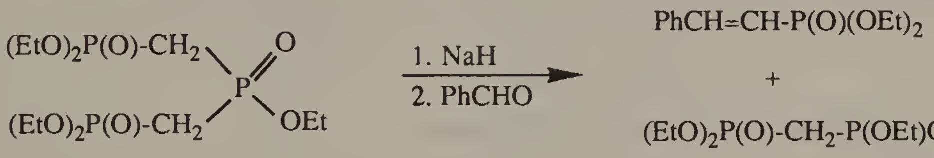
The acidifying effect of the phosphonamide group has been employed by Evans et al.[62] to create an acyl anionic synthon (Eq. 12.18). Addition of a silyl phosphoramidite across a carbonyl group, followed by removal of the α-proton and reaction of the resulting carbanion with an electrophile, and finally desilylation with fluoride, produced homologated carbonyls.



(12.18)

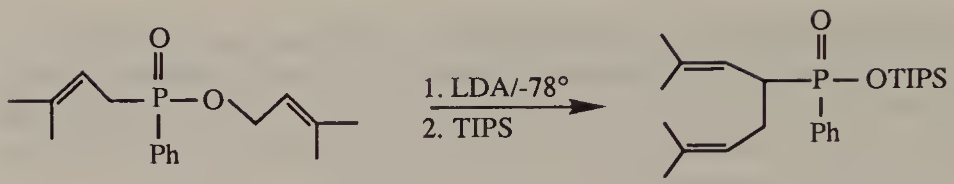
## 12.2.2 Phosphinate Carbanions

Since Horner's initial report in 1962[63] of the reaction of ethyl benzylphenylphosphinate carbanion with benzaldehydes to produce stilbenes in modest yield, there have been sporadic reports of the application of phosphinate carbanions to olefination reactions. The phosphorus has been attached to a polymer backbone[64] for reaction with aldehydes and ketones, and an optically active carbanion, based on phosphorus chirality, has been shown to induce chirality in the alkene product from reaction with unsymmetrically substituted cyclic ketones.[65] The rate of the reaction of phosphinate carbanions with aldehydes has been shown to be third order, with the reaction faster than that using phosphine oxides but slower than that using phosphonates, and a $\rho$ value for the aldehydes between those of the other two carbanions.[66] In a competitive reaction, Gilmore and Huber found the phosphinate group to be eliminated in preference to the phosphonate group in a Wittig-type reaction (Eq. 12.19).[67]



(12.19)

Allylic phosphinate carbanions have been found to undergo intermolecular alkylation and allylation (without transposition of the migrating allyl group) (Eq. 12.20), and this unique C–C bond-forming process recently has been applied to the conversion of farnesyl farnesylphenylphosphinate to squalene.[68] Cyclic phosphinates, such as phospholanate esters, also afforded carbanions

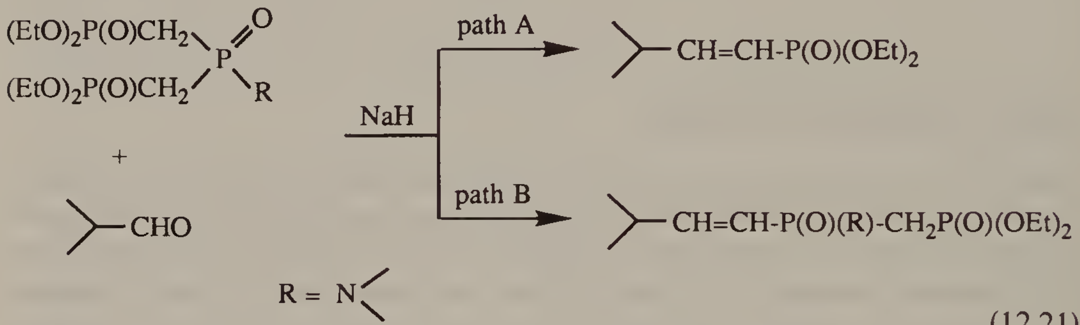


(12.20)

which were monoalkylated to form mixtures of *syn*- and *trans*- (to the phosphoryl oxygen) 2-monoalkyl-phospholanates, and these in turn were alkylated for a second time to mixtures of *cis*- and *trans*-2,5-dialkyl products.[69] The diameric phosphinates could be converted to diameric phosphine oxides which have the potential to be chiral olefinating reagents in the Horner reaction.

### 12.2.3 Phosphinamide Carbanions

Gilmore and Park[70] found that in a competitive reaction (Eq. 12.21) either the

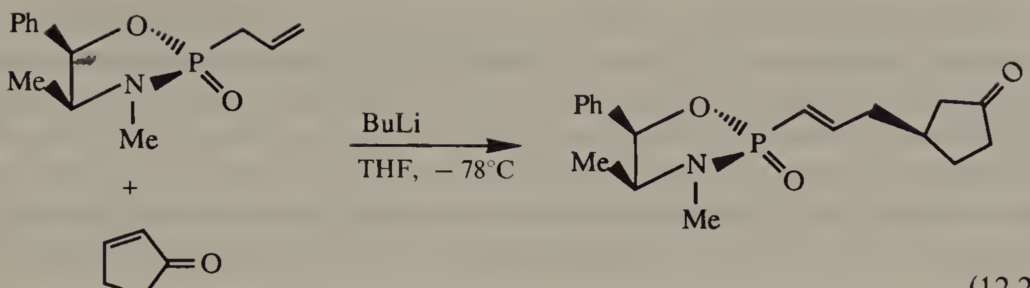


(12.21)

phosphinamide group (path A) or the phosphonate group (path B) could be eliminated preferentially in an olefination reaction of the carbanion with isobutyraldehyde depending on the steric bulk of the amino group R, with increasing bulk of the amino group (R) leading to more phosphonate elimination. When R = NHPh the product was 93% from path A, but when R = $NPr_2$ it was 88% from path B. Interestingly, no hydroxyphosphinamide adducts were reported, in contrast to the phosphonamide system. Apparently, the oxyanion was able to attack phosphorus directly, and did so at the aminophosphorus group (path A) until the steric requirements of R became too large.

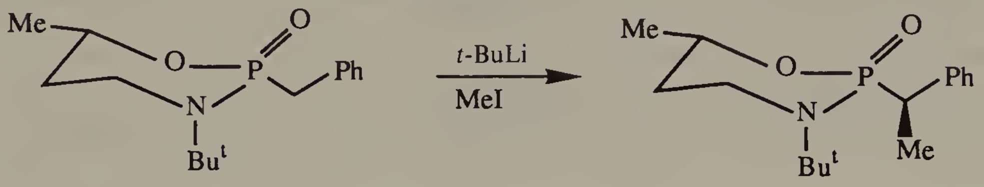
### 12.2.4 Phosphonate Monoamide Carbanions

Two groups recently have prepared such carbanions from enantiomeric hydroxyamines and detected significant stereoselective reactions thereof. Hua et al.[71] obtained both isomers of a monoamide from reaction of ( − ) ephedrine and dichloroallylphosphonate. Reaction of the carbanion from the 2*S*,4*S*,5*R*-diamer with cyclopentenone led to conjugate addition by the γ-carbon of the allyl group to produce an 80% yield of cycloalkanone with about 70% optical yield (Eq. 12.22). Bulkier substituents on nitrogen led to a substantial increase in



(12.22)

the optical yield. Denmark and Dorow[72] found that a 2*S*,6*S*-diamer carbanion was methylated in 85% yield to a 95:5 ratio of diamers, and the 2*R*,6*S*-diamer was methylated to an 83:17 ratio (Eq. 12.23). Therefore, the local chirality of the phosphorus atom was inducing stereoselectivity in the alkylation process and probably will in other processes, such as alkene formation. Further, hydrolysis and esterification afforded enantiomeric alkylated phosphonates potentially of use in Wadsworth–Emmons reactions.



(12.23)

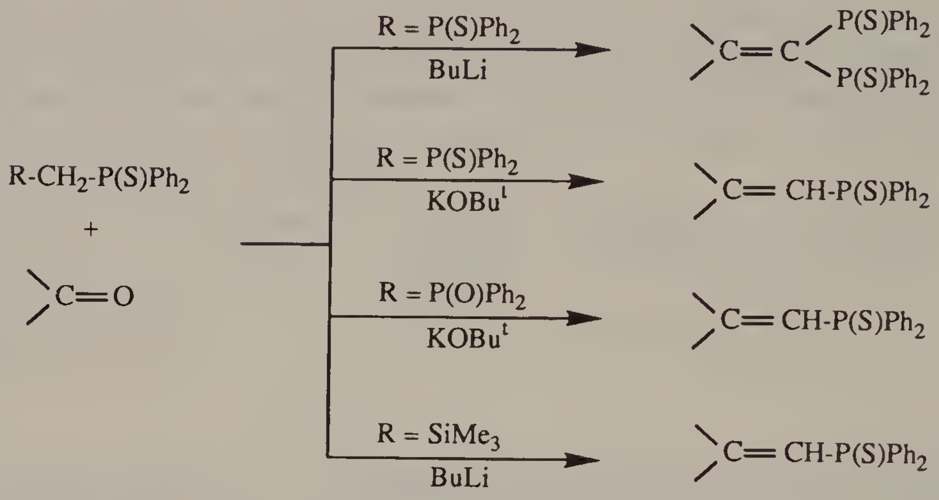
## 12.3 THIOPHOSPHORYL-BASED YLIDES

Of the six possible combinations of alkyl, alkoxy, and amino groups as P-substituents in thiophosphoryl carbanions [$R^1R^2P(S){=}CR^4_2$], three are known; they are listed below and their chemistry is described in this section.

| $R^1$ | $R^2$ | Reference |
|---|---|---|
| Alkyl/aryl | Alkyl/aryl | Section 12.3.1 |
| Alkoxy | Alkoxy | Section 12.3.2 |
| Alkyl/aryl | Amino | Section 12.3.3 |

**12.3.1 Phosphinethioxy Carbanions.** Alkyldiphenylphosphine sulfides are readily deprotonated to the carbanion with strong bases such as butyllithium and potassium *t*-butoxide. However, Seyferth and Welch[73] also found that methyllithium would cleave triphenylphosphine sulfide, as it had triphenylphosphine oxide, to afford the methylcarbanion [$Ph_2(S)CH_2Li$] which could be trapped with carbon dioxide, hydrogen bromide, and alkylating agents.

Diphenylphosphinethioxy carbanions reacted with carbonyl compounds to produce alkenes directly, without the isolation of $\beta$-hydroxyphosphine sulfides. Yields were modest and these carbanions were less reactive than the analogous phosphinoxy carbanions, occasionally failing to react with ketones.[74] When the carbanion also carried a diphenylphosphinoxy group, reaction with carbonyls led to elimination of the phosphinoxy group rather than the phosphinethioxy group (Eq. 12.24).[75,76] When the diphenylphosphinoxy group was replaced by a second diphenylphosphinethioxy group, elimination of one of those two groups did occur when potassium-*t*-butoxide was the base, but was reported not to occur when butyllithium was the base. Instead, the initial adduct was reported to lose lithium hydroxide to form 1,1-bis-(diphenylphosphinethioxy)ethene![76] When the carbanion carried a trimethylsilyl group the usual Peterson elimination occurred to afford diphenylphosphinethioxy alkene.[77] Thus, the phosphinethioxy carbanion seems to be less nucleophilic than the oxygen counterpart, but at the same time the phosphorus atom is less susceptible to oxyanion attack in a Wittig-type reaction.

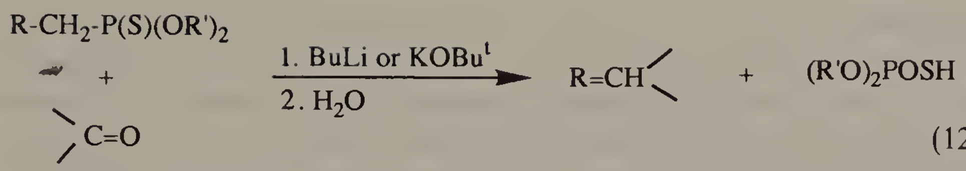


(12.24)

### 12.3.2 Phosphonothioate Carbanions

These carbanions are readily formed from dimethyl- or diethyl alkylphosphonothioates [$RCH_2P(S)(OR')_2$] using butyllithium or potassium *t*-butoxide as bases. They underwent normal alkylation reactions,[78,79] thereby providing a means for elaborating more complex carbanions.

Both stabilized ($R = H$, $R' = COOEt$)[78] and nonstabilized ($R,R' = H$ or alkyl)[79] carbanions reacted readily with carbonyl compounds to afford alkenes in good yield (Eq. 12.25). The carbanions were claimed to form slower than the corresponding phosphonate carbanions, but modest warming of the reaction was necessary to effect monothiophosphate elimination and alkene formation.[79]

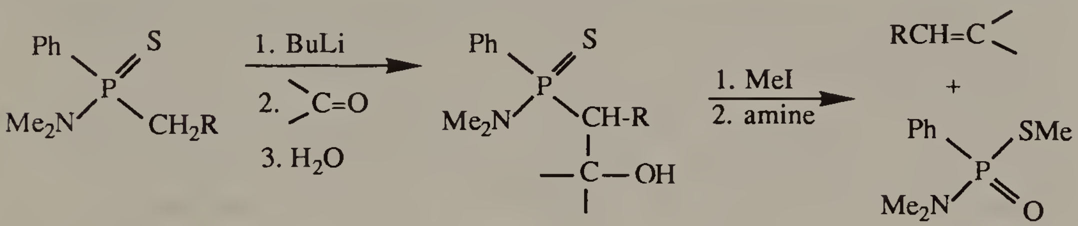


(12.25)

However, such elimination clearly was easier than with the corresponding phosphonate, especially with alkyl (nonstabilized) carbanions.

### 12.3.3 Phosphinothioylamide Carbanions

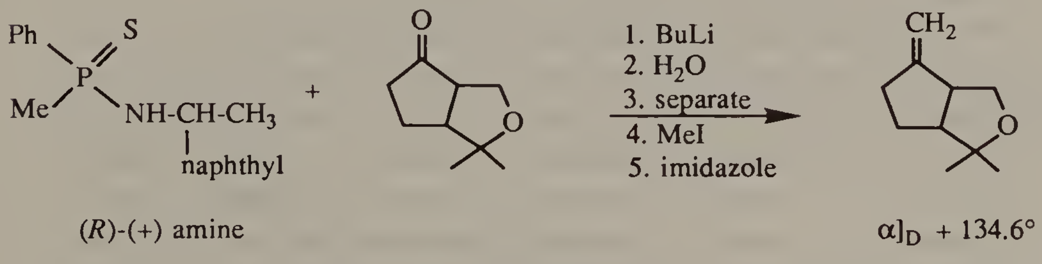
Johnson and Elliott[80] prepared a series of these carbanions from phenylalkylphosphinethioate N,N-dimethylamide using butyllithium. The carbanions could be alkylated in good yield to more complex amides. Mono- and di-substituted carbanions reacted readily with aldehydes and ketones to afford adducts which did not eliminate the phosphorus-containing group. However, methylation and treatment of the $\beta$-hydroxy-quasi-phosphonium salts with an amine base at room temperature resulted in methylthiophosphonate amide elimination and alkene formation (Eq. 12.26). Yields were poor with simple



(12.26)

aldehydes but good with ketones, and good with both mono- and di-substituted carbanions. The erythro and threo protonated adducts from benzaldehyde and the ethylide ($R = CH_3$) could be separated and converted stereospecifically to the respective *Z*- and *E*-alkenes.

Replacement of the dimethylamino group in the starting amide with an optically active primary amine [*R*( + )-1-naphthylethylamine], and reaction with the appropriate ketone afforded a 3:2 ratio of adducts which could be separated. Separate decomposition with methyl iodide and imidazole afforded the two enantiomers of Japanese hop ether (Eq. 12.27).[81]



(12.27)

## REVIEWS

**1966** Johnson, A. Wm. *Ylid Chemistry*; Academic: New York; pp. 212–215. A review of the chemistry of miscellaneous phosphorus ylides.

**1983** Kolodiazhnyi, O. I.; Kukhar, V. P. *Russian Chem. Revs. 52*, 1096–1112. A review of P-heterosubstituted phosphorus ylides.

## REFERENCES

[1] Birum, G. H. *Chem. Abstr.* **1963**, *58*, 7975.

[2] Middleton, W. J. *Chem. Abstr.* **1963**, *58*, 11402.

[3] Middleton, W. J.; Sharkey, W. H. *J. Org. Chem.* **1965**, *30*, 1384.

[4] Corey, E. J.; Markl, G. *Tetrahedron Lett.* **1967**, 3201.

[5] Carey, F. A.; Neergaard, J. R. *J. Org. Chem.* **1971**, *36*, 2731.

[6] Bulpin, A.; Masson, A.; Sene, A. *Tetrahedron Lett.* **1990**, *31*, 1151.

[7] Masson, A.; Sene, A.; Hutchinson, D. W.; Thornton, D. M. *Phosphorus Sulfur* **1988**, *40*, 1.

[8] (a) Griffiths, D. V.; Tebby, J. C. *J. Chem. Soc. Chem. Commun.* **1986**, 871. (b) Griffiths, D. V.; Griffiths, P. A.; Whitehead, P. S.; Tebby, J. C. *J. Chem. Soc. Perkin Trans. (1)* **1992**, 479.

[9] Tomioka, H.; Ichikawa, N.; Murata, H. *J. Chem. Soc. Chem. Commun.* **1992**, 193.

[10] Seebach, D. *Chem. Ber.* **1982**, *105*, 487.

[11] Atherton, F. R.; Openshaw, H. P.; Todd, A. R. *J. Chem. Soc.* **1945**, 660.

[12] Kolodiazhnyi, O. I.; Repina, L. A.; Gololobov, Y. G. *J. Gen. Chem.* **1975**, *45*, 535.

[13] Kolodiazhnyi, O. I. *J. Gen. Chem.* **1979**, *49*, 88.

[14] Ramirez, F.; Madan, O. P.; Smith, C. P. *J. Org. Chem.* **1965**, *30*, 2284.

[15] Ramirez, F.; Madan, O. P.; Heller, S. R. *J. Am. Chem. Soc.* **1965**, *87*, 731.

[16] Burgada, R.; Khoshnieh, Y. O. E.; Leroux, Y. *Tetrahedron* **1985**, *41*, 1207.

[17] Caesar, J. C.; Griffiths, D. V.; Griffiths, P. A.; Tebby, J. C. *J. Chem. Soc. Perkin Trans. (1)* **1990**, 2329.

[18] Caesar, J. C.; Griffiths, D. V.; Tebby, J. C. *J. Chem. Soc. Perkin Trans. (1)* **1988**, 175.

[19] Ben Jaafar, B.; El Manouni, D.; Burgada, R.; Leroux, Y. *Phosphorus Sulfur* **1990**, *47*, 67.

[20] Oediger, H.; Eiter, K. *Liebigs Ann. Chem.* **1965**, *682*, 58.

[21] Schmidbaur, H.; Pichl, R. *Z. Naturforsch.* **1985**, *40b*, 352.

[22] Schmidbaur, H.; Pichl, R.; Muller, G. *Chem. Ber.* **1987**, *120*, 789.

[23] Wittig, G.; Weigmann, H. D.; Schlosser, M. *Chem. Ber.* **1961**, *94*, 676.

[24] Mizrakh, L. I.; Polonskaya, L. Y.; Ivanova, T. M. *J. Gen. Chem.* **1978**, *48*, 1733.

[25] Leroux, Y.; El Manouni, D.; Burgada, R. *Tetrahedron Lett.* **1981**, *22*, 3393.

[26] El Manouni, D.; Leroux, Y.; Burgada, R. *Phosphorus Sulfur* **1985**, *25*, 319.

[27] El Manouni. D.; Leroux, Y.; Burgada, R. *Tetrahedron* **1986**, *42*, 2435.

[28] Naae, D. G.; Burton, D. G. *Synth. Comm.* **1973**, *3*, 197.

29 Salmond, W. G. *Tetrahedron Lett.* **1977**, 1239.

30 Ramirez, F.; Madan, O. P.; Smith, C. P. *J. Am. Chem. Soc.* **1964**, *86*, 5339.

31 Dahl, O. *J. Chem. Soc. Perkin Trans. (1)* **1978**, 947.

32 Issleib, K.; Lischewski, M. *J. Prakt. Chem.* **1970**, *312*, 135.

33 Kolodiazhnyi, O. I.; Kukhar, V. P. *J. Gen. Chem.* **1975**, *45*, 2509; *J. Org. Chem. USSR* **1977**, *13*, 248.

34 Kolodiazhnyi, O. I.; Kukhar, V. P. *J Gen. Chem.* **1979**, *49*, 1752.

35 Malenko, D. M.; Gololobov, Y. G. *J. Gen. Chem.* **1978**, *48*, 2533.

36 Malenko, D. M.; Kasukhin, L. F.; Ponomarchuk, M. P.; Gololobov, Y. G. *J. Gen. Chem.* **1980**, *50*, 1569.

37 Malenko, D. M.; Gololobov, Y. G. *J. Gen. Chem.* **1979**, *49*, 267.

38 Hudson, R. F.; Chopard, P. A.; Salvadori, G. *Helv. Chim. Acta* **1964**, *47*, 632.

39 Plass, W.; Heckmann, G.; Fluck, E. *Phosphorus Sulfur* **1990**, *54*, 181.

40 Svara, J.; Fluck, E. *Phosphorus Sulfur* **1985**, *25*, 129.

41 Plass, W.; Heckmann, G.; Fluck, E. *Phosphorus Sulfur* **1991**, *55*, 19.

42 Kolodiazhnyi, O. I.; Golokov, D. B. *J. Gen. Chem.* **1989**, *59*, 252.

43 Kim, T. V.; Kiseleva, I. E.; Loktionova, R. A.; Gololobov, Y. G. *Zh. Obshch. Khim.* **1980**, *50*, 1889; *Chem. Abstr.* **1980**, *93*, 220864.

44 Kolodiazhnyi, O. I.; Yakovlev, V. N.; Kukhar, V. P. *J. Gen. Chem.* **1979**, *49*, 2170.

45 Kolodiazhnyi, O. I.; Repina, L. A.; Gololobov, Y. G. *J. Gen. Chem.* **1974**, *44*, 1253.

46 Kolodiazhnyi, O. I. *J. Gen. Chem.* **1975**, *45*, 539.

47 Worms, K. H.; Schmidt-Dunker, M. In *Organic Phosphorus Compounds*; Kosolapoff, G. M.; Maier, L., Eds.; Wiley–Interscience: New York, 1972; Vol. 7, Chapter 18, p. 60.

48 Corey, E. J.; Kwaitkowski, G. T. *J. Am. Chem. Soc.* **1968**, *90*, 6816.

49 Hanessian, S.; DeLorme, D.; Beaudoin, S.; Le Blanc, Y. *J. Am. Chem. Soc.* **1984**, *106*, 5754.

50 Dauben, W. G.; Beasley, G. H.; Broadhurst, M. D.; Muller, B.; Peppard, D. J.; Pesnelle, P.; Suter, C. *J. Am. Chem. Soc.* **1975**, *97*, 4973.

51 Hill, R. A.; Macaulay, G. S.; MacLachlan, W. S. *J. Chem. Soc. Perkin Trans. (1)* **1987**, 2209.

52 Corey, E. J.; Cane, D. E. *J. Org. Chem.* **1969**, *34*, 3053.

53 Petrova, J.; Momchilova, S.; Kirilov, M. *Phosphorus Sulfur* **1985**, *24*, 243.

54 Levielle, G.; Reisdorf, D. *C. R. Seances Acad. Sci.* **1971**, *272*, 100.

55 Kirilov, M.; Petrova, J.; Zdravkova, Z. *Phosphorus Sulfur* **1985**, *21*, 301.

56 Petrova, J.; Kirilov, M.; Momchilova, S. *Phosphorus Sulfur* **1983**, *17*, 29.

57 Momchilova, S.; Petrova, J.; Kirilov, M. *Phosphorus Sulfur* **1988**, *35*, 319.

58 Petrova, J.; Kirilov, M.; Momchilova, S.; Kasser, K. *Phosphorus Sulfur* **1988**, *40*, 69.

59 Deschamps, B.; Lampin, J.; Mathey, F.; Seyden-Penne, J. *Tetrahedron Lett.* **1977**, *22*, 1137.

60 Patois, C.; Savignac, P. *Tetrahedron Lett.* **1991**, *32*, 1317.

61 Patois, C.; Savignac, P. *Synlett.* **1991**, 517.

62 Evans, D. A.; Takacs, J. M.; Hurst, K. M. *J. Am. Chem. Soc.* **1979**, *101*, 371.

[63] Horner, L.; Hoffmann, H.; Klink, W.; Ertel, H.; Toscano, V. G. *Chem. Ber* **1962**, *95*, 581.

[64] Qureshi, A. E.; Ford, W. T. *Br. Polym. J.*, **1984**, *16*, 231; *Chem. Abstr.* **1985**, *102*, 220504.

[65] Musierowicz, S.; Wroblewski, A.; Krawczyk, H. *Tetrahedron Lett.* **1975**, 437.

[66] Larsen, R. O.; Aksnes, G. *Phosphorus Sulfur* **1983**, *15*, 229.

[67] Gilmore, W. F.; Huber, J. W. *J. Org. Chem.* **1973**, *38*, 1423.

[68] De, B.; Corey, E. J. *Tetrahedron Lett.* **1990**, *31*, 4831.

[69] Polniaszek, R. P.; Foster, A. L. *J. Org. Chem.* **1991**, *56*, 3137.

[70] Gilmore, W. F.; Park, J. S. *Phosphorus Sulfur* **1987**, *29*, 287.

[71] Hua, D. M.; Chen-Yu-King, R.; McKie, J. A.; Meyer, L. *J. Am. Chem. Soc.* **1987**, *109*, 5026.

[72] Denmark, S. S.; Dorow, R. L. *J. Org. Chem.* **1990**, *55*, 5926.

[73] Seyferth, D.; Welch, D. E. *J. Organomet. Chem.* **1964**, *2*, 1.

[74] Juaristi, E.; Gordillo, B.; Valle, L. *Tetrahedron* **1986**, *42*, 1963.

[75] Gloyna, D.; Henning, H. G. *Angew. Chem.* **1966**, *5*, 847.

[76] Goli, M. B.; Grim, S. O. *Tetrahedron Lett.* **1991**, *32*, 3631.

[77] Peterson, D. J. *J. Organomet. Chem.* **1967**, *9*, 373.

[78] Michalski, J.; Musierowicz, S. *Tetrahedron Lett.* **1964**, 1187.

[79] Corey, E. J.; Kwiatkowski, G. T. *J. Am. Chem. Soc.* **1966**, *88*, 5654.

[80] Johnson, C. R.; Elliott, R. C. *J. Am. Chem. Soc.* **1982**, *104*, 7041.

[81] Johnson, C. R.; Elliott, R. C.; Meanwell, N. E. *Tetrahedron Lett.* **1982**, *23*, 5005.

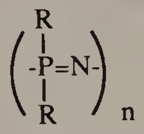
# 13

# IMINOPHOSPHORANES AND RELATED COMPOUNDS

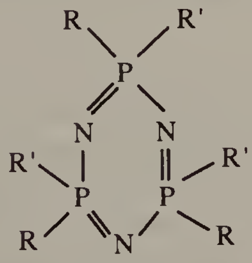
The chemistry of iminophosphoranes (**1**), compounds of general structure $R_3P{=}NR'$ with four-coordinate phosphorus and incorporating a formal phosphorus–nitrogen double bond, is so analogous to that of phosphorus ylides as to warrant treatment in the same book. Such compounds have been variously described as phosphinimines, iminophosphines, phosphinimides, phosphazo compounds, $\lambda^5$-phosphazenes, and (mono-) phosphazenes. Iminophosphoranes are closely related to several other types of compounds which will not be discussed herein, but to which leading references are cited, including linear polyphosphazenes (**2**),[1] cyclic polyphosphazenes (phosphonitriles) (**3**),[2] two-coordinate phosphimines (**4**),[3,4] and three-coordinate phosphimines (**5**).[3,5] The

$$R_3P{=}NR' \longleftrightarrow R_3\overset{+}{P}\text{—}\overset{-}{N}R'$$

**1**



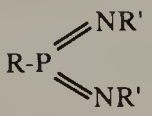
**2**



**3**

R-P=N-R'

**4**



**5**

*Ylides and Imines of Phosphorus*, Edited by A. William Johnson.
ISBN 0-471-52217-1

first two listed groups have become important materials of commerce, with much of their chemistry deriving from that discovered through iminophosphoranes.[2,6] The iminophosphoranes (**1**) to be described herein are those that are structurally and chemically most analogous to phosphorus ylides.

Iminophosphoranes first were reported by Staudinger and Meyer in 1919[7] but virtually no additional chemistry was reported until the late 1950s. Much chemistry has been discovered in the intervening 35 years with numerous applications to organic synthesis and increasing application in complex ion chemistry. This chapter reports the current state of iminophosphorane chemistry, including their preparation, molecular structure, reactions, and involvement in metal complexes. In addition, the closely related phosphazines ($R_3P{=}N{-}N{=}CR'_2$), phosphiteimines [$(RO)_3P{=}NR'$], P-haloiminophosphoranes ($X_3P{=}NR$), and phosphoramidate anions [$(RO)_2P(O)N^-R$] are described in Section 13.5.

## 13.1 PREPARATION OF IMINOPHOSPHORANES

Iminophosphoranes have been prepared by two different approaches, the direct union of nitrogen and phosphorus fragments or the indirect approach of substituting on a previously prepared simple iminophosphorane. N-Substituted iminophosphoranes are best directly prepared through two major routes, the Staudinger reaction of azides with tertiary phosphines (Section 13.1.1) and the Kirsanov reaction of tertiary phosphine dibromides with amines (Section 13.1.2). Some other direct methods, described in Sections 13.1.3 and 13.1.4, are also available, but are less generally applicable.

The indirect approach to iminophosphoranes involves preparation of the parent imine ($Ph_3P{=}NH$) and later substitution on nitrogen using electrophilic reagents. Processes such as halogenation, alkylation, and acylation are well known and are described in Section 13.4.2. Iminotriphenylphosphorane itself is readily available through the Staudinger reaction (Section 13.1.1), the Kirsanov reaction (Section 13.1.2), from chloroamine (Section 13.1.3), and from hydrolysis of N-silyliminotriphenylphosphorane (Section 13.4.1).

### 13.1.1 The Staudinger Reaction

First reported by Staudinger and Meyer in 1919 in the reaction of phenyl azide with triphenylphosphine, which eliminated molecular nitrogen and afforded N-phenyliminotriphenylphosphorane,[7] the reaction of azides with tertiary phosphines has been widely employed for the high-yield synthesis of an immense variety of imines (Eq. 13.1). The reaction has been thoroughly reviewed by Gololobov et al.[8] in 1981 and again in 1992, and briefly reviewed by Scriven and Turnbull[9] in 1988.

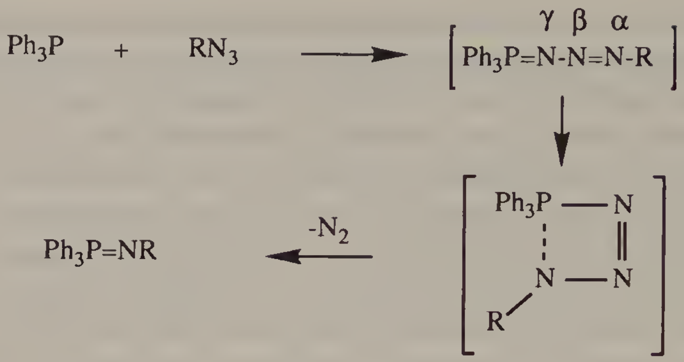
$$R_3P \quad + \quad R'N_3 \longrightarrow \left[ R_3PN_3NR' \right] \xrightarrow{-N_2} R_3P{=}NR' \qquad (13.1)$$

When the purpose of preparing the iminophosphorane was subsequently to employ it in synthesis, triphenylphosphine usually has been used because of the stability of the resulting imine. However, the reaction also occurred with a wide variety of tertiary phosphines, including trialkylphosphines,[10,11] mixed alkylaryl phosphines,[12] unsaturated phosphines,[13] aminophosphines,[14,15] cyclic phosphines,[16] bicyclic phosphines,[17] and polymeric phosphines.[18] Table 13.1 (Section 13.1.5) lists with references many known iminophosphoranes carrying different phosphorus substituents, many of which were prepared using the Staudinger reaction. The reaction also occurred with other trivalent derivatives of phosphorus, especially oxygen- and halogen-carrying derivatives, as will be described later in this chapter (Section 13.5).

An immense variety of azides have been employed in the Staudinger reaction, with the only limits apparently being the availability of the requisite azide (usually obtained by displacement of a halide using sodium azide) but also the thermal and shock stability of azides. Aromatic,[7,19] aliphatic,[20–22] heterocyclic,[23] olefinic,[24,25] carbonyl,[7,26] carbalkoxy,[27] carbamido,[28] tosyl,[29] hydrogen[30] and bis[18,31] azides have been employed. In addition, silyl,[10,15,32] germanyl,[32] stannyl[33] and many other metallic azides have been used. Table 13.2 (Section 13.1.5) lists imines carrying a wide variety of N-substituents, many of which have been prepared using the Staudinger reaction.

*13.1.1.1* ***Mechanism of the Staudinger Reaction.*** In most instances reaction of an organic azide with triphenylphosphine in ether or methylene chloride at 0°C results in the visible elimination of nitrogen and direct formation of the iminophosphorane in nearly quantitative yield. In the earliest reported such reaction,[7] that between triphenylphosphine and phenyl azide, the presence of a labile intermediate was reported when the reaction was conducted at $-80$°C. Later,[32,34,35] triphenylmethyl azide was reported to afford an isolable phosphazide, and since then numerous examples have been isolated.[8,36–40] In most instances such isolable phosphazides have been formed from sterically hindered components or the electronic effects of substituents have been such as to increase the electron density on phosphorus or decrease it on the alpha nitrogen of the azide, thereby inhibiting ring closure of the phosphazide to the necessary four-centered transition state.

The Staudinger reaction proceeds by nucleophilic attack by the phosphine on the terminal ($\gamma$) nitrogen of the azide to afford a linear phosphazide, usually not detectable, which then dissociates to products, probably via a four-centered transition state (Eq. 13.2). In those instances where the phosphazide was not especially stable, the reaction was second order[41–44] with electron-withdrawing groups on the azide and electron-donating groups on the phosphine facilitating the reaction. Rho values for phosphorus substituents ranged from $-0.73$ to $-1.19$[42,43] and values for aryl azides ranged from $+0.78$ to 1.36.[42–45] Substituent effects were reversed in those instances where the phosphazide was stable and the slow step involved attack of the $\alpha$-nitrogen on the phosphorus via a four-membered transition state.[43] Steric effects from phosphine or azide

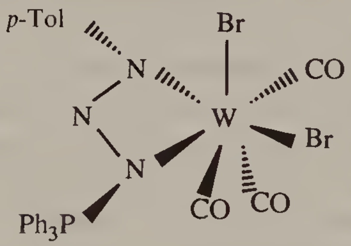


(13.2)

substituents seemed nonexistent on the first step of the reaction, but increasing bulk hindered the second step,[46,47] as would be expected.

Bock and Schnoller[48] demonstrated, using $^{15}$N labelled azide, that the α-nitrogen of the original azide is that which appears in the imine product, the β- and γ-nitrogens being evolved as molecular nitrogen. It has been demonstrated that the phosphorus atom retained its configuration through imine formation,[12,16,29] supporting the four-centered transition state proposal, but that reaction of a chiral phosphine with a racemic azide led to only slight asymmetric induction.[12]

The structure of the intermediate phosphazides had been a matter of some controversy [linear structure (P–N–N–N–C) vs. branched ($P–N(N_2)–C$) structure[3,32,35]], but it has been resolved unequivocally by X-ray crystallographic analysis in favor of the linear proposal, first of a tungsten complex (**6**)[49] and more recently of three isolated phosphazides (**7**–**9**).[50–52] Prior to these



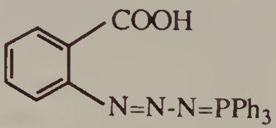
**6**

$(O_2N)_3C_6H_2\text{-N=N-N=}P(N(CH_2CH_2)_2O)_3$

**7**

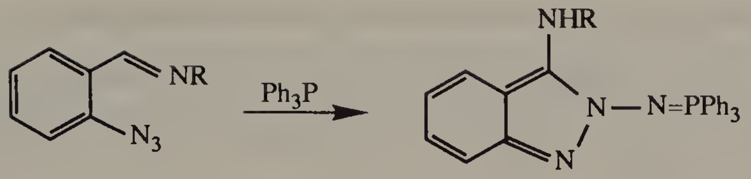
$HO(CH_2)_3N\text{=N-N=}P(NMe_2)_3$

**8**



**9**

determinations it had been concluded that the phosphazide was linear, based partially on the similarity of the imine and phosphazide $^{31}$P NMR peaks, with the imine peaks at higher field by about 10–20 ppm.[39,40,53,54] Much earlier,[55] and again recently,[56] a phosphazide was trapped in an intramolecular reaction to produce an indazole which could only result from a linear phosphazide (Eq. 13.3). In the phosphazides the P=Nγ bonds were longer than in the corresponding iminophosphoranes (1.61–1.65 Å vs 1.54–1.62 Å), the $C–N_\alpha$ bonds were of normal length for amines, the $N_\beta–N_\gamma$ bonds were shorter than

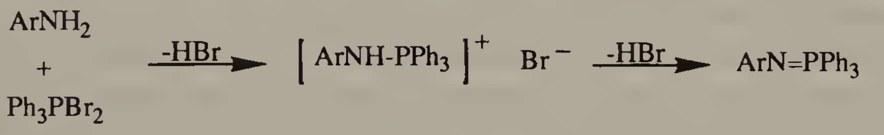


(13.3)

expected, the $N_\alpha$–$N_\beta$ bonds were about normal length, the P atoms were approximately tetrahedral, the P–N–N–N–C framework was approximately planar, and the orientation of substituents about the $N_\alpha$–$N_\beta$ and $N_\beta$–$N_\gamma$ bonds was *E*. The *E* geometry in these isolable phosphazides probably accounts for their stability by making more difficult ring closure to the four-membered transition state necessary for nitrogen elimination and imine formation.

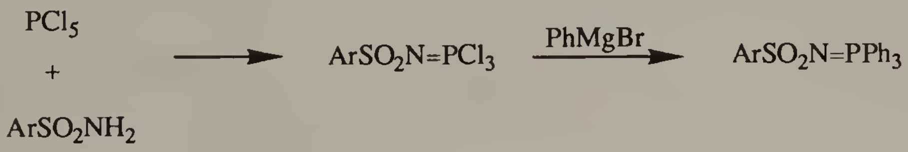
### 13.1.2 The Kirsanov Reaction

Horner and Oediger[57] found that conversion of triphenylphosphine to its dibromide in solution, followed by reaction with a wide variety of aromatic amines in the presence of two equivalents of triethylamine, afforded good yields of N-aryliminophosphoranes. The reaction appeared to proceed by nucleophilic displacement of bromine from phosphorus by nitrogen, followed by deprotonation (Eq. 13.4). Later, Zimmer and Singh[58] applied the same process to alkylamines, but found that the reaction stopped at the aminophosphonium salt stage. However, separate deprotonation with sodamide produced the N-alkyliminophosphoranes. Use of ammonia,[59] hydrazines,[60,61] hydrazides,[62] hydrazones,[63] and sulfonamides[64] also afforded the corresponding imines.



$$\begin{matrix}\mathrm{ArNH_2}\\+\\\mathrm{Ph_3PBr_2}\end{matrix}\xrightarrow{-\mathrm{HBr}}\left[\mathrm{ArNH\text{-}PPh_3}\right]^+\ \mathrm{Br}^-\xrightarrow{-\mathrm{HBr}}\mathrm{ArN{=}PPh_3}\qquad(13.4)$$

In the USSR literature this reaction is referred to as the Kirsanov reaction, because its principle was discovered by Kirsanov[65] in 1950 in the reaction of phosphorus pentachloride with benzenesulfonamide to produce N-benzenesulfonylimino-P,P,P-trichlorophosphorane. The latter was later converted to N-benzenesulfonyliminotriphenylphosphorane using phenylmagnesium bromide (Eq. 13.5).[66] The full range of reactions of mono- and diorgano-substituted derivatives of $PCl_5$ with amines is discussed in Section 13.5.3.



$$\begin{matrix}\mathrm{PCl_5}\\+\\\mathrm{ArSO_2NH_2}\end{matrix}\longrightarrow\mathrm{ArSO_2N{=}PCl_3}\xrightarrow{\mathrm{PhMgBr}}\mathrm{ArSO_2N{=}PPh_3}\qquad(13.5)$$

The reaction with triphenylphosphine dibromide continues to be effective for conversion of amines directly to iminophosphoranes, for example, with aminocephalosporin,[67] chiral amines,[68] heterocyclic amines,[69] and diamines.[57,70]

### 13.1.3 The Reaction of Haloamines with Tertiary Phosphines

The second oldest method for the preparation of iminophosphoranes was reported in 1937 and involved the reaction of tertiary phosphines with anhydrous chloramine-T (Eq. 13.6).[71] It has been applied only occasionally

$$Ph_3P \quad + \quad TsNClNa \quad \longrightarrow \quad TsN{=}PPh_3 \qquad (13.6)$$

since then,[72–74] but led to the development of a more useful variant by Appel. Reaction of triaryl- or trialkylphosphines with either hydroxylamine-O-sulfonic acid[75] or, more commonly, chloroamine[76–78] produced the aminophosphonium salt which then afforded iminotriphenylphosphorane upon treatment with sodamide (Eq. 13.7). N-Chlorourea[79] and tris-N-chloromelamine[80] reacted

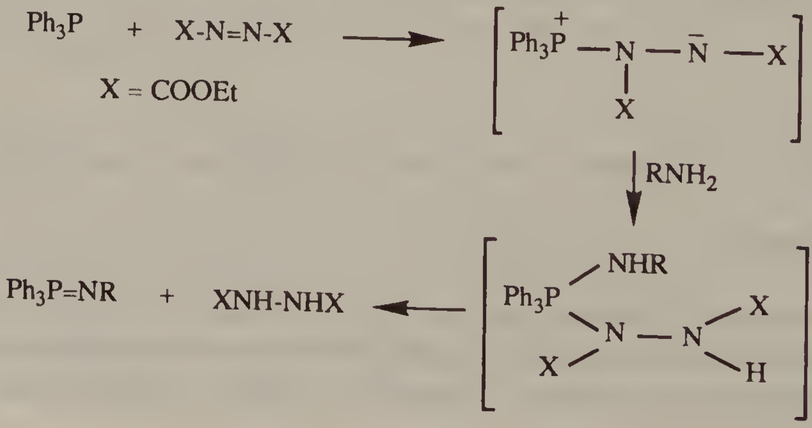
$$Ph_3P \quad + \quad NH_2Cl \longrightarrow Ph_3\overset{+}{P}\text{-}NH_2 \quad Cl^- \xrightarrow{NaNH_2} Ph_3P{=}NH \qquad (13.7)$$

analogously. In a slight variant N,N-dichloroamines have been reacted with tertiary phosphines also to afford imines.[73,81,82]

Heesing and Steinkamp[29] have clarified the different stereochemistries at phosphorus of many of these reactions, finding that with a chiral phosphine the following resulted: (1) with hydroxylamine-O-sulfonic acid retention occurred, presumably via phosphorus attack on nitrogen; (2) with chloroamine there was racemization, presumably by pseudorotation in a pentavalent P-amino-P-chloro intermediate; (3) with chloramine-T there was inversion, indicating initial phosphorus attack on chlorine rather than on nitrogen, followed by displacement of chlorine by nitrogen.

### 13.1.4 Other Syntheses

A relatively recent adaptation of the Mitsunobi condensation to involve reaction of a tertiary phosphine, diethyl azodicarboxylate, and an amine derivative under mild conditions afforded excellent yields of iminophosphoranes (Eq. 13.8).[83] The reaction so far seems generally limited to aroyl amides, sulfonyl

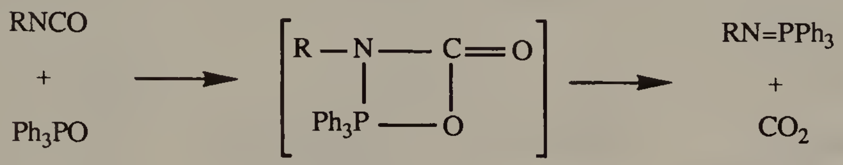


(13.8)

amides, and aromatic amines with electron-withdrawing groups on the ring,[84] but it also was successful with urea and related compounds, other diamides, and even cyanamide.[85] Using a chiral phosphine resulted in a racemic imine, verifying the probable intermediacy of a pentavalent structure.[29]

The Atherton method[86] for making phosphorus nitrogen bonds has been adapted by Appel et al.[87] for the preparation of iminophosphoranes. A tertiary phosphine, carbon tetrachloride, and an amine afforded an aminophosphonium salt which was deprotonated with potassium amide to the imine. Later Weinberger and Fehlhammer[88] were able to use triethyl amine as the base.

Iminophosphines (RN=PR′) are known to oxidatively add halogens, alcohols, and even $CCl_4$ to result in iminophosphoranes.[89,90] Phosphonium ylides reacted with azides[91] and with carbonyl imines[92] to afford iminophosphoranes. The reaction of a carbamido phosphonium ylide ($Ph_3P{=}CHCONH_2$) with methyl acrylate in an aprotic solvent recently has produced an iminophosphorane ($Ph_3P{=}NCOCH_2CH_2COOMe$) in an interchange-type reaction.[93] Phosphine oxides catalyzed the conversion of isocyanates to carbodiimides (Eq. 13.9),[94] and the mechanism has been shown to involve intermediate



(13.9)

formation of an iminophosphorane.[95,96] Hall and Smith[97] isolated the imine and showed that it formed from the phosphine oxide with retention of configuration. In a similar reaction N-sulfinyl-amides and phosphine oxides were found to produce iminophosphoranes and sulfur dioxide.[98]

### 13.1.5 Exemplary Iminophosphoranes

A wide variety of iminophosphoranes have been prepared with a great many being isolated and characterized. The listing in Table 13.1 is exemplary only and is designed to indicate the variety of P substituents which have been incorporated into imines, even though the majority of those prepared for use in synthesis used the triphenylphosphonium group. Table 13.2 also is exemplary but illustrates the wide variety of N substituents that are known, all with the triphenylphosphonium group. In both tables references are included to lead readers to one or more exemplary preparations, but the list of references is not claimed to be exhaustive. In 1972 Bestmann and Zimmerman[405] published an extensive list of iminophosphoranes to which readers are referred.

*13.1.5.1 Conjugated Iminophosphoranes.* Iminophosphoranes carrying conjugating groups such as N-vinyl and N-imino (i.e., phosphazines, see Section 13.5.2) are known, and their chemistry has been examined especially for evidence

**TABLE 13.1 Phosphorus Substituents in Iminophosphoranes ($R^1R^2R^3P{=}N{-}R^4$)[a]**

| $R^1$ | $R^2$ | $R^3$ | References |
|---|---|---|---|
| Me | Me | Me | 173 |
| Et | Et | Et | 10, 11 |
| *n*-Pr | *n*-Pr | *n*-Pr | 10 |
| *n*-Bu | *n*-Bu | *n*-Bu | 10, 212 |
| *t*-Bu | *t*-Bu | *t*-Bu | 271 |
| Me | Alkyl | Ph | 585 |
| Me | Cycloalkyl | Ph | 585 |
| Me | Me | $CH_2Ph$ | 141 |
| Me | Me | Ph | 72 |
| Et | Et | Ph | 31 |
| Et | Ph | Ph | 213 |
| Neomenthyl | Ph | Ph | 12 |
| Allyl | Ph | Ph | 13 |
| Ferrocenyl | Ph | Ph | 372 |
| Ph | Ph | Ph | Table 13. 2 |
| $Me_2N$ | $Me_2N$ | $Me_2N$ | 39, 53, 59, 60, 139, 323, 535 |
| $CH_3C(CH_2NH)_3$ | | | 39 |
| $P(CH_2NH)_3$ | | | 39 |
| PhNH | PhNH | PhNH | 586 |
| $O(CH_2CH_2)_2N$ | $O(CH_2CH_2)_2N$ | $(CH_2CH_2)_2N$ | 126 |
| $N(Ph)CH_2CH_2N(Ph)$ | | $NMe_2$ | 130 |
| *t*-Bu | *t*-Bu | $NH_2$ | 319 |
| Ph | Ph | $NH_2$ | 373 |

[a] Excluding P-alkoxy and P-halo Imines; see Section 13. 5

**TABLE 13.2 Exemplary Nitrogen Substituents in Iminotriphenylphosphoranes ($Ph_3P{=}N{-}R$)**

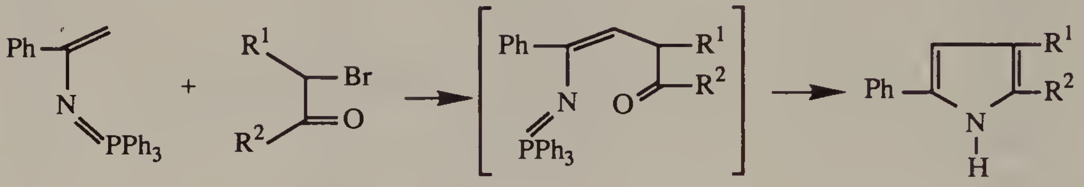
| R | References |
|---|---|
| H | 30, 76–78, 587 |
| Me | 58, 180, 348, 354 |
| *n*-Pr | 58, 354 |
| *t*-Bu | 58, 68, 346, 353, 354 |
| $CH_2Ph$ | 183, 186, 254, 354 |
| $CPh_3$ | 34, 291, 306 |
| $CH_2COOEt$ | 186, 254 |
| 2-Adamantyl | 212 |
| Carbohydrate | 195, 214, 596, 598 |
| $CH_2{=}CH{-}$ | 24, 106, 345 |
| $CH_2{=}CH{-}CH_2{-}$ | 251 |
| Cycloheptatrienyl | 108 |
| Ferrocenyl-$CH_2$– | 185 |

TABLE 13.2 Continued

| R | References |
|---|---|
| $C_6H_5$ | 7, 57 |
| $C_6H_4X$ | 16, 45, 52, 57, 60, 133, 143–145 |
| Naphthyl | 57, 189, 251 |
| Pyridyl | 583, 597 |
| Heteroaryl | 244, 583 |
| PhCO | 41, 84, 125, 147, 247, 248, 250, 352 |
| RCS | 588 |
| COOMe | 80, 137, 354, 589 |
| CONHR | 28, 137, 232 |
| CN | 85, 120, 249, 331, 590, 591 |
| NC | 88, 592 |
| $F((Me_2N)_3P{=}NF)$ | 305 |
| Cl | 301, 321 |
| Br | 301 |
| I | 301, 321 |
| $NH_2$ | 60, 194, 234, 452 |
| $NR_2$ | 61 |
| NHCOR | 62, 225 |
| $N{=}CR_2$ (phosphazines) | Section 13.5.2 |
| $N{=}PPh_3$ | 192 |
| $Ph_2P(O)$ | 397, 595 |
| $Ph_3P^+$ | Section 13.5.1.1 |
| $PCl_2$ | 320 |
| $^+PCl_3$ | 321 |
| $P(O)Cl_2$ | 321 |
| $P(CF_3)_2$ | 401 |
| ArS | 328, 576 |
| ArSO | 328, 593 |
| $ArSO_2$ | 64, 66, 73, 74, 84, 98, 148, 327, 328 |
| $RSO_2$ | 84 |
| $ClSO_2$ | 327, 530, 594 |
| $Me_3Si$ | 10, 172, 262, 324, 371, 386, 535, 585 |
| $Me_2XSi$ | 318 |
| $Me_3SiCH_2$ | 21 |
| $Ph_3Si$ | 32, 418 |
| Group IIB metalloalkyls | 30 |
| Group IIIA metalloalkyls | 30, 383 |
| Group IVA metalloalkyls | 32, 33, 316, 351 |

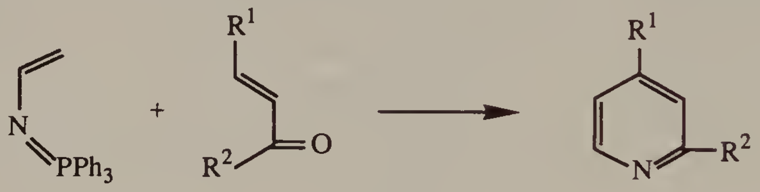
of nucleophilicity at both the atoms $\alpha$ and $\gamma$ to the phosphorus. Such evidence was obtained for similar phosphonium ylides (Section 3.4.1).

Although N-vinyliminotriphenylphosphoranes, both unsubstituted[99] and with various substituents on the vinyl carbons,[100] reacted normally with phenylisocyanate and aldehydes in Aza–Wittig reactions, two other reactions have demonstrated reactivity at the $\gamma$ position of the imine. N(1-Phenylvinyl)-iminotriphenylphosphorane reacted with $\alpha$-bromoketones in the presence of triethylamine to afford 2-phenylpyrroles, with the reaction probably proceeding through alkylation by the $\gamma$-carbon, imine reformation, and an Aza–Wittig cyclization (Eq. 13.10).[101] Another example of such an alkylation recently has been reported.[102]

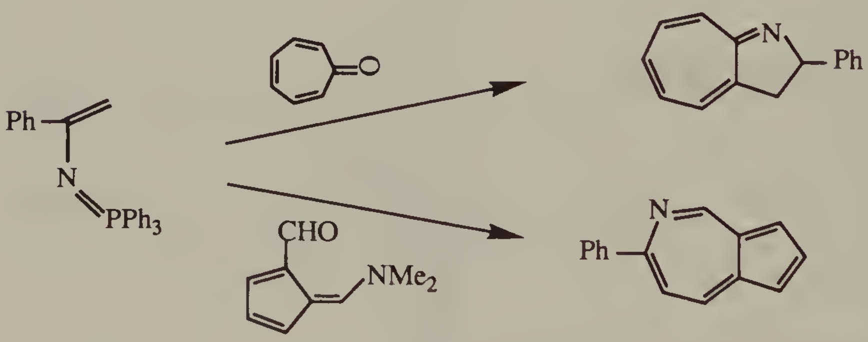


(13.10)

Several examples of N-vinylimine reactions with $\alpha,\beta$-unsaturated aldehydes or ketones have been reported which involve nucleophilic attack by the $\gamma$-carbon of the imine, all involving eventual cyclization via an Aza–Wittig reaction of the reformed imine. The N-vinylimine afforded pyridines in modest yield using linear enones (Eq. 13.11),[24,103] and use of cycloalkenones afforded 2,4-pyridinophanes.[104] Use of tropone afforded 1-azaazulenes,[105] and use of a fulvene derivative afforded 5-azaazulenes (Eq. 13.12).[106] N-Cycloheptatrienyliminotriphenylphosphorane reacted with enones[107] or $\alpha$-bromoketones[108] in a similar manner to produce fused six- or five-membered rings, respectively.

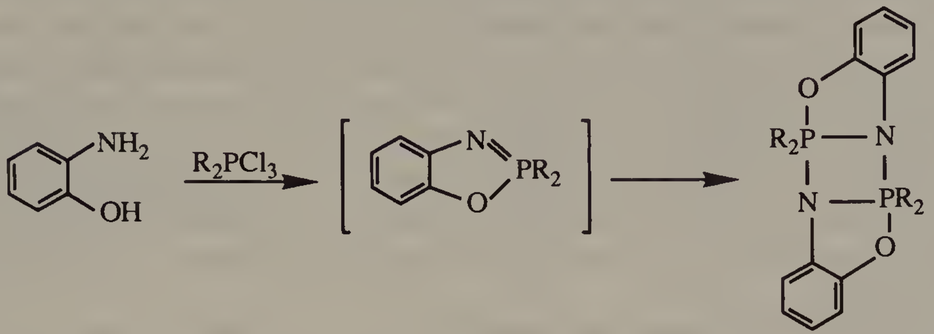


(13.11)



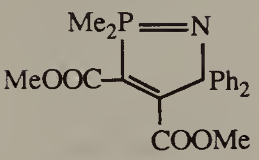
(13.12)

*13.1.5.2 Cyclic Iminophosphoranes.* Relatively few cyclic iminophosphoranes are known in which a *single* P=N group is endocyclic (a general exception, of course, are the di-, tri-, and tetracyclophosphazene compounds which are cyclic polyimines, but which are not discussed in this book, see ref. 2). No four-membered cyclomonoimines have been reported, but several five-membered cycloimines are known. Two groups prepared 2,2-dialkylbenzo-1,3,2-oxazaphosphole but found that it existed as a dimer (Eq. 13.13),[109,110] although

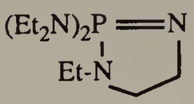


(13.13)

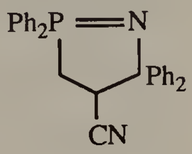
the dimer was cleaved to the monomeric hydrochloride with HCl. Several other phosphole derivatives, such as triaza,[111] diazaoxa,[112] and diazathia[113] derivatives, also dimerized across the P=N bond. However, a few other five-membered cycloimines (**10**,[114] **11**,[115] and **12**[116]) have been obtained in their monomeric form.



**10**

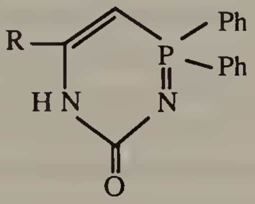


**11**

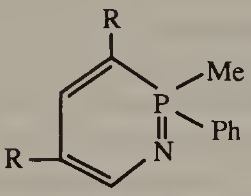


**12**

Two examples of six-membered cycloiminophosphoranes have been reported recently, but little is known of their properties. In one instance a linear imine was cyclized to the first 1,3,4-diazaphosphinine (**13**)[117] and in the other a 1,2-$\lambda^3$-azaphosphinine was converted to a 1,2-$\lambda^5$-azaphosphinine (**14**).[118] The latter was very susceptible to hydrolysis.



**13**



**14**

## 13.2 PHYSICAL PROPERTIES OF IMINOPHOSPHORANES

In comparison to phosphonium ylides ($Ph_3P{=}CHR$), the analogous and isoelectronic iminophosphoranes ($Ph_3P{=}NR$) are considerably more stable. Iminophosphoranes have been isolable since their first discovery in 1919 when

Staudinger and Meyer[7] prepared and purified crystalline N-phenyliminotriphenylphosphorane. Therefore, physical studies of such imines are not unique.

An intriguing feature of iminophosphoranes has been the nature of the phosphorus–nitrogen bond, the ease with which it is formed and its chemical stability, but most chemists seem to have had no qualms about representing this bond in the literature as a formal double bond. By contrast there has been considerable debate about the corresponding phosphorus–carbon double bond! In addition to the stable N-phenyl compound a wide spectrum of imines carrying other N-substituents, from the simplest when R = H[10,76] to the very complex (see Table 13.2), have been isolated and subjected to physical and chemical study.

The stability of iminophosphoranes ($RR'N^-$, $R = {}^+PPh_3$) to protic solvents (Section 13.4.1) certainly indicates that the nitrogen atom in the phosphonio amide carries far less negative charge than an ordinary amide anion ($RR'N^-$, $R,R' \neq {}^+PPh_3$). The unusual stabilization of such imines has been attributed to the nature of the phosphorus–nitrogen bond, and in particular to delocalization of electron density from nitrogen to phosphorus. Evidence regarding the nature of the phosphorus–nitrogen bond is discussed in this section, including structural measurements, basicity, spectra, dipole moments, and calculations.

### 13.2.1 Molecular Structure

Interest in the molecular structure of iminophosphoranes has focused on the phosphorus–nitrogen bond and the geometry about the nitrogen atom. Although other options have been debated, it appears that the nitrogen atom is approximately trigonally hybridized, with one lone pair of electrons in an $sp^2$ hybrid orbital and the other pair in a $2p$ orbital, and with a predicted bond angle at nitrogen of 120°. The phosphorus atom appears to be approximately tetrahedrally hybridized, with predicted bond angles of 109.5° between phosphorus substituents. The nitrogen–phosphorus bond is thought to be approximately double, with overlap of the filled nitrogen $2p$-orbital with the vacant $3d_{xy}$ or $3d_{xz}$ orbitals of phosphorus, providing a bond order greater than 1.0 and approaching 2.0. The sums of the phosphorus–nitrogen covalent radii are 1.84 Å for a P–N single bond and 1.62 Å for a P=N double bond.[119] Table 13.3 lists the P–N bond distances and the P–N–R bond angles for most of the iminotriphenylphosphoranes which have been studied using X-ray crystallography or electron diffraction to date.

In iminophosphoranes containing the triphenylphosphonium group the data reveals that the bond angles about phosphorus are usually $109 \pm 6°$ and the P-phenyl distances usually are $1.80 \pm 0.03$ Å, consistent with the proposed tetrahedral hybridization for tetravalent phosphorus. The P-phenyl groups often are oriented in a propeller manner about phosphorus.[120] The P–N bond lengths reported in Table 13.3 range from 1.54 to 1.64 Å, with the majority being under 1.60 Å, clearly in the range predicted by the sum of the Pauling double-bond radii.

**TABLE 13.3 Structural Data for N-Substituted Iminotriphenylphosphoranes ($Ph_3P{=}N{-}R$)**

| R | P=N (Å) | P–N–R (deg) | Reference |
|---|---|---|---|
| $C_6H_5$ | 1.602 | 130.4 | 391 |
| $C_6H_4Br(p)$ | 1.567 | 124.2 | 573 |
| 1-(8-Aminonaphthyl) | 1.575 | 128.5 | 574 |
| 1-(8-Triphenylphosphonio-aminonaphthyl) | 1.598 | 126.4 | 123 |
| COPh | 1.626 | 117.8 | 125 |
| CN | 1.595 | 123.0 | 120 |
| 1-(2,3,3,4,4,5,5-Heptacyanocyclopentenyl) | 1.615–1.618 | 130.0–130.2 | 575, 599 |
| SPh | 1.566 | 123.1 | 576 |
| $SO_2C_6H_4Me(p)$ | 1.579 | 126.4 | 577 |
| $^+S(C_6H_5)_2$ | 1.60 | 123.6 | 578 |
| $S_3N_3$ | 1.645 | 121.0 | 579 |
| $S_3N_3 \cdot C_7H_8$ | 1.583 | 123.5 | 580 |
| $N_3P_3Cl_5$ | 1.597 | 134.8 | 581 |
| $^+P(C_6H_5)_3$ | 1.539–1.59 | 137–180 | Section 13.5.1 |
| $(CF_3)_2P$ | 1.576 | 131 | 401 |
| 2-(4-Chloro-6-dimethylamino-1,3,5-triazenyl) | 1.622 | 121 | 307 |
| 2,4,6-trinitro-3,5-di-(triphenylphosphoranylimino)phenyl | 1.54–1.57 | 137 (av.) | 582 |

It must be noted that the phosphorus–nitrogen bond lengths for three aminophosphonium cations, $(C_6H_5)_2(C_6H_5CH_2)P^+N(C_2H_5)_2$, $(C_6H_5)_3P^+(NH_2)$, and $(C_6H_5)_3P^+(NHC_{10}H_7{-}1)$, are 1.63,[121] 1.615,[122] and 1.63 Å,[123] respectively. Thus, the major shortening ( ~ 0.2 Å) of the P–N bond in the hypothetical conversion of $R_2P{-}NHR'$ to $R_3P{=}NR'$ appears to occur upon quaternization of the phosphorus atom (i.e., conversion to $R_3P^+NHR'$), with only slight additional shortening ( ~ 0.05 Å) occurring upon conversion of the nitrogen to an anion as in an imine (i.e., to $R_3P^+N^-R'$). Thus, there already may be considerable overlap from the lone pair electrons of trivalent nitrogen to the 3*d* orbitals of tetravalent positively charged phosphorus, leading to this major bond shortening. In the conversion of an aminophosphonium salt to an iminophosphorane the overlap may simply be improved by using either the 2*p* electrons of divalent nitrogen or there may even be some measure of triple bonding using both lone pair electrons of nitrogen. In any event it seems clear that the P–N bond in iminophosphoranes has a significant multiple bond character which may account for their stability and surprisingly low basicity, especially when compared to phosphonium ylides.

The effect of variations in N substituents on P–N bond length is not clear from the limited data available since most of the substituents were aromatic. The shortest P–N bond lengths were observed in the PNP cation, $[(C_6H_5)_3P]_2N^+$, especially in those few instances where the P–N–P bonds were linear[124] (these cations are discussed in detail in Section 13.5.1). The attachment of a benzoyl group to the imine nitrogen ($R_3P{=}N{-}COC_6H_5$)[125,126] resulted in a planar P–N–C–O group with the C=O bond 0.04 Å longer than usual, presumably owing to delocalization through the carbonyl group, and, in one instance,[125] a longer than normal P=N bond. N-Metal substituted iminophosphoranes, which are discussed separately in Section 13.4.4, generally showed P–N bond lengths slightly under 1.60 Å, similar to those listed in Table 13.3.

Replacement of the triphenylphosphonio group with other phosphonio groups lead to some shortening in the P–N bond lengths, but some of these effects may be due to the effect of the different N substituents. Other imines studied and their reported P–N bond lengths include $[O(CH_2CH_2)_2N]_3P{=}NCOC_6H_5$ (1.591 Å),[126] $Me_3P{=}NSiMe_3$ (1.542 Å),[127] and $Ph_2PCH_2(Ph)_2P{=}NSiMe_3$ (1.529 Å).[128] The three reports of incorporation of the phosphorus atom in five- (1.543[129] and 1.539 Å[130]) or six-membered (1.523 Å[131]) rings and with an exocyclic P=NPh group produced shorter than average P–N bond lengths.

The P–N–R bond angles in iminophosphoranes ranged from 117 to 137°, with the majority being 124 ± 4°, consistent with the proposed $sp^2$ hybridization of nitrogen. The exceptions are three reports of linear PNP cations, in particular metal complexes, which are discussed in Section 13.5.1.

It may be concluded that the P=N bond length and the bond angles about P and N are consistent with iminophosphorane formulation as a tetrahedral phosphorus multiply bonded to a trigonal nitrogen.

### 13.2.2 Basicity

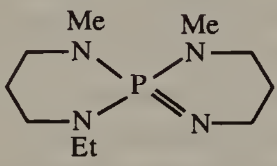
Iminophosphoranes are basic, with the nitrogen atom serving as the site of proton attack.[123,132] They are considerably more basic than anilines,[8] N-phenyliminotriphenylphosphorane showing a $pK_a$ of 7.6 in 95% ethanol. At the same time, the acidifying effect of an N-triphenylphosphonio group on aniline is impressive.

A determination of the $pK_a$ of imines has been used to determine the effect of both P and N substituents on the basicity of imines and to shed light on the electronic effects of imine substituents. Using N-(substitutedphenyl)iminotriphenyl phosphoranes, Johnson and Wong[133] found that their $pK_a$'s correlated with $\sigma^\circ$ constants to give a $\rho$ value of $+3.5$, indicating modest resonance and inductive interactions between the nitrogen anion and N-phenyl substituents. Kukhar et al.[134] reached similar conclusions. Edelman and Stepanov[135] found that analogous imines, but with a diethylphenylphosphonium group, correlated best with $\sigma^-$ constants, indicating a higher degree of resonance interaction from nitrogen to N-phenyl substituents when ethyl groups replaced two phenyl groups on phosphorus. This is the direction of change to be expected, since the alkyl groups should decrease the net charge on phosphorus, leading to poorer $\pi$

overlap with nitrogen, providing more opportunity for the substituted N-phenyl ring to delocalize the negative charge from nitrogen. The Kukhar group[134] also demonstrated that the triphenylphosphoranylimino group served as an electron donating substituent on a phenyl ring, in the meta position being a better donor ($\sigma^\circ = -0.33$) than the dimethylamino group ($\sigma^\circ = -0.15$), but in the para position being a slightly poorer donor ($\sigma^\circ = -0.40$ vs. 0.44). Ivanova et al.[136] also determined that N-phenyl substituents affected the basicity of the imine nitrogen by measuring complex formation of imines with iodine.

The nature of the interaction between the nitrogen anionic center and P-phenyl substituents also has been revealed by p$K_a$ studies. From studies of N-phenylimino(substituted-phenyl)phosphoranes it has been concluded that there is not a direct resonance interaction between the phosphonium atom and a P-phenyl substituent. The $\rho$ values have been determined to be $+3.1$[133] and $+1.79$[137] using $\sigma$ constants to correlate the p$K_a$ values. Thus, the tetravalent phosphonium atom served as somewhat of a resonance insulator between nitrogen and a P-phenyl substituent.

Schwesinger has used the basicity of iminophosphoranes in creating a series of neutral very strong bases, one of which (**15**)[138] is nearly $10^4$ stronger than DBU, and another of which (**16**)[139] is the strongest neutral base known, comparable in strength to KHDMS. The latter has been designated **reagent of the year** for 1992 and Schwesinger has received the Fluka Prize for its discovery and application. The special advantages of these imine bases are that they are crystalline solids, stable in both water and in organic solvents, and are very poor nucleophiles. Accordingly, they are especially useful for deprotonation reactions, such as dehydrohalogenations and aldol condensations, where alkylations often compete. For example, with isopropyl bromide, the alkylation–elimination ratios were 27 for DBU but only 0.96 for **15**[138].



**15**

$$[(Me_2N)_3P{=}N]_3P{=}NBu^t$$

**16**

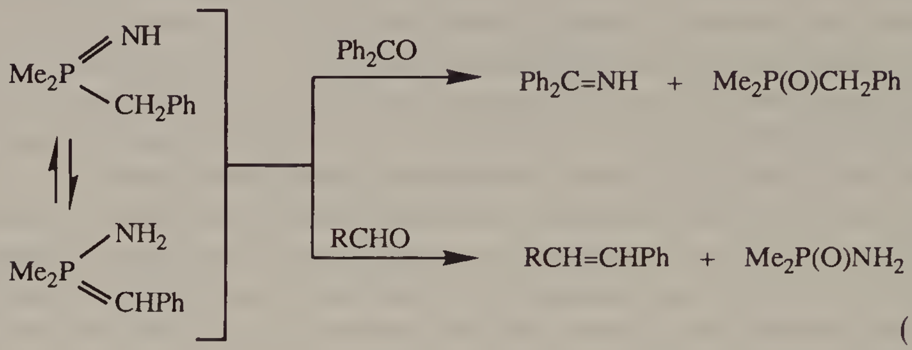
In certain structural environments tautomerism of iminophosphoranes has been observed when a phosphorus substituent carried a somewhat labile proton. Kolodiazhnyi[140] was able to detect both ylide and imine forms of **17**, with the

$$R\text{-}NH\text{-}P(OR')_2{=}C(COOMe)_2 \rightleftharpoons R\text{-}N{=}P(OR')_2\text{-}CH(COOMe)_2$$

**17**

imine predominating only when R was electron withdrawing, such as tosyl or *p*-nitrophenyl. More recently Wannagat and Munstedt[141] reported that a

P-benzylimine reacted with aldehydes as an ylide but with ketones as an imine (Eq. 13.14).



(13.14)

### 13.2.3 Other Physical Properties

*13.2.3.1* ***NMR Spectra.*** Considerable information now is available regarding NMR spectra of iminophosphoranes, especially $^{31}P$ spectra, but also some $^{13}C$ and $^{15}N$ spectra.

The $^{31}P$ absorption for aminophosphonium salts generally is about + 30–45 ppm, whereas that for the corresponding iminophosphoranes generally is shifted upfield and in the + 10–0 range, all with respect to 85% $H_3PO_4$. Thus, the salt-to-imine $^{31}P$ shift invariably is negative, usually 10–30 ppm,[122, 142, 143] with the phosphorus being more shielded in the imine than in the salt.

The nature of both the nitrogen and phosphorus substituents on imines affects the $^{31}P$ chemical shift. Unfortunately, spectra have not been reported for most N-alkyl substituted imines. Table 13.4 presents representative data on the effect of nitrogen substituents on the $^{31}P$ chemical shift of iminophosphoranes. It can be seen that electron-withdrawing substituents generally decreased the shielding of phosphorus, presumably by withdrawing electron density from nitrogen. Several groups have demonstrated Hammett correlations of these $^{31}P$ chemical shifts in N(substituted-phenyl)iminotriphenylphosphoranes, with two correlations being claimed using $\sigma$ constants[143, 144] and the most recent with $\sigma^-$ constants.[145] The $^{31}P$–$^{15}N$ coupling constants have been determined for the same arylimines, but they did not correlate with $\sigma^-$; instead they correlated with $\sigma_R$ constants. It was concluded that the chemical shift values did not directly reflect $p\pi$–$d\pi$ bonding, but that the P–N coupling constants probably did.[146] When the aryl ring was insulated from the nitrogen atom by a carbonyl group ($Ph_3P{=}NCOC_6H_4R$)[147] or by a sulfonyl group ($Ph_3P{=}NSO_2C_6H_4R$),[148] the $^{31}P$ chemical shifts did not correlate with $\sigma^-$, but did correlate with $\sigma_m$ and $\sigma_p$, indicating no direct conjugation of N with R.

The question of the ease of rotation about the phosphorus–nitrogen (double) bond has been addressed using $^{31}P$ NMR spectra. Albright et al.[141] could find only one set of resonances in $Ph_3P{=}NPh$ and concluded there was rapid rotation about the P–N bond. Calculations for $Ph_3P{=}N{-}CH{=}CH_2$ indicated

**TABLE 13.4** $^{31}P$ **NMR Chemical Shifts of N-Substituted Iminotriphenylphosphoranes (R–N=PPh$_3$)**

| R | $\delta^{31}P$ | References |
|---|---|---|
| H | 25.2 | 122 |
| $CH_2C_6H_5$ | 12.6 | 288 |
| $CH_2CH_2CH(CH_3)_2$ | 19.0 | 288 |
| $CPh_3$ | $-10.3$ to $-12.3$ | 142, 156 |
| $SiMe_3$ | $-1.8$ to $-1.5$ | 142, 172 |
| $SiPh_3$ | 2.99 | 156 |
| $COC_6H_5$ | 20.6 | 142 |
| CN | 25.1 | 85 |
| $C_6H_5$ | 3.0–3.29 | 142–144 |
| $C_6H_4OCH_3$ (p) | 2.06–2.65 | 143, 144 |
| $C_6H_4CH_3$ (p) | 2.60–2.93 | 143, 144 |
| $C_6H_4Cl$ (p) | 4.00–4.25 | 143, 144 |
| $C_6H_4CN$ (p) | 7.20 | 143 |
| $C_6H_4NO_2$ (p) | 7.45–7.73 | 143, 144 |
| $SO_2C_6H_4CH_3$ (p) | 14.6–15.29 | 142, 148 |
| 4-Pyridyl | 7.30 | 583 |
| 2-Pyridyl | 13.60 | 583 |

rotational barriers of about 2 kcal/mol.[142,149] Katti and Cavell[150] reported that $Ph_2P{-}CH_2(Ph)_2P{=}NSiMe_3$ ($\delta^{31}P = -1.38$) could be reversibly thermally converted to two other isomeric forms proposed to be rotational isomers about the P=N axis.

In 1972 Tarasevich and Egerov[151] calculated substituent electronegativities and bond orders based on $^{31}P$ spectra of imines and concluded that the P–N bond order increased as the electronegativity of P substituents increased and the electronegativity of N substituents decreased. Power et al.[152] used solid-state $^{31}P$ NMR of aryliminotriphenylphosphoranes to determine dipolar coupling constants and chemical shift tensors, and then to calculate bond lengths. The calculated P–N length for the N-phenyl imine was 1.60 Å, almost identical to the sum of the covalent double-bond radii and consistent with many measured bond lengths (see Section 13.2.1.).

Changing the substituents on phosphorus also affected the $^{31}P$ chemical shift of iminophosphoranes. Table 13.5 lists examples of various P-substituted imines and their $^{31}P$ NMR peaks. Few conclusions can be drawn because of the paucity of comparable series, most known imines carrying P-phenyl groups. It does appear that replacement of P-phenyl with increasingly branched alkyls deshielded the phosphorus, as was the case with phosphonium ylides (Section 3.2.1.2). Similarly, when the P-phenyl groups carried increasingly electron-donating substituents, the phosphorus was increasingly deshielded. It would appear that the major shielding arises from the nitrogen atom of the imine sharing electron density with phosphorus, the P substituents simply determining

**TABLE 13.5** $^{31}$P **Chemical Shifts of P-Substituted Iminophosphoranes (R–N=PX$_3$)**

| X | R | $\delta^{31}$P | References |
|---|---|---|---|
| $C_6H_5$ | H | 25.2 | 122 |
| $C_4H_9$-*t* | H | 55.0 | 586 |
| $Et_2N$ | H | 21.8 | 60 |
| $C_6H_4OCH_3$ (p) | $C_6H_5$ | 3.93 | 153 |
| $C_6H_4CH_3$ (p) | $C_6H_5$ | 4.23 | 153 |
| $C_6H_5$ | $C_6H_5$ | 3.0–3.73 | 142–144, 153 |
| $C_6H_4Cl$ (p) | $C_6H_5$ | – 0.28 | 153 |
| $C_6H_4CN$ (p) | $C_6H_5$ | – 4.16 | 153 |
| $Me_2N$ | $C_6H_5$ | 16.6 | 154 |
| $Me_2N$ | $CH_3$ | 32.6 | 53 |
| $Me_2N$ | $C_2H_5$ | 21.5 | 154 |
| $Me_2N$ | $NH_2$ | 37.7 | 60 |
| $C_6H_5$ | $SiMe_3$ | – 1.5 | 172 |
| Me | $SiMe_3$ | – 3.5 | 172 |
| Et | $SiMe_3$ | 14.1 | 172 |
| *n*-Pr | $SiMe_3$ | 8.3 | 172 |
| *i*-Pr | $SiMe_3$ | 23.7 | 172 |
| *t*-Bu | $SiMe_3$ | 31.9 | 172 |

to what extent there is $p\pi$–$d\pi$ overlap. Thus, the nature of the dipole of the P substituent seems to be the major factor in the $^{31}$P chemical shift.[153]

The $^{15}$N NMR spectra have been reported for a few iminophosphoranes. For N-(substituted-phenyl)iminotriphenylphosphoranes the chemical shifts correlated with $\sigma^-$, reflecting the direct effect of substituents on nitrogen electron density,[143] and varied in a manner similar to anilines. Similarly, replacing an N-phenyl group with an N-ethyl group led to an expected increase in nitrogen shielding.[154]

Several groups have reported $^{13}$C NMR spectra of N-aryl and P-aryl groups. The ipso carbon of an N-phenylimine was more shielded when electron withdrawing groups were on the ring, and less shielded when electron donating groups were attached. The $^{13}$C chemical shifts correlated well with $\sigma^-$.[145] The value of $J_{P-C}$ipso increased on converting the imine to its hydrobromide, reflecting phosphorus rehybridization from $sp^3d$ to $sp^3$, thereby increasing the *s* character of the P–C$_{ipso}$ bond.[155] The P–C coupling constants also decreased slightly and steadily as an N-phenyl group became more electron withdrawing due to substitution, such changes correlating with $\sigma^-$.[145] It appears that both $J_{P-N}$ and $J_{P-C}$ reflected the extent of $p\pi$–$d\pi$ overlap in iminophosphoranes.

Finally, $^{19}$F NMR spectra of iminophosphoranes have been employed to detect the nature of interactions between the P–N group and phenyl rings. The $Ar_3P$=N– group has been shown to be an effective electron donor, approximately as effective as the $NH_2$ group, with some disagreement as to whether slightly better[156,157] or slightly poorer.[145] It also could be concluded that there was little conjugative interaction between a P-aryl ring and the phosphorus atom in an imine,[156,157] consistent with conclusions reached in the phosphonium ylide series.

*13.2.3.2 Miscellaneous Properties of Iminophosphoranes.* Iminophosphoranes have sizeable dipole moments, comparable to those of phosphonium ylides. Iminotriphenylphosphorane has a dipole moment of 4.21 D,[158] N-phenyliminotriphenylphosphorane has a moment of 4.40–4.85 D,[136,158,159] and substituted N-phenyl derivatives have the following values: *p*-methyl = 4.54; *p*-chloro = 5.99; *p*-nitro = 9.14–9.58. Thus, electron-withdrawing groups on the nitrogen raised the dipole moment by increasing the charge separation between nitrogen and phosphorus. Lutskii et al.[158] and Goetz and Probst[160] also showed that increasing the electronegativity of phosphorus substituents *decreased* the dipole moment, presumably by increasing the P–N $p\pi$–$d\pi$ overlap. The P–N bond moments were calculated[161] to be 3.8 for $Ph_3P{=}NH$, 3.1 for $Ph_3P{=}NPh$, and 2.6 for $Cl_3P{=}NCCl_3$.

There remain some inconsistencies in the reported infrared absorptions for the P=N bond in imines. Horner and Oediger[57] assigned the P–N stretch for the $Ph_3P{=}NPh$ series at 1160–1180 $cm^{-1}$ but Zhmurova et al.[162] assigned the 1325–1385 $cm^{-1}$ region. Later[163,164] the P–N stretch in $Ph_3P{=}NH$ was assigned 1193 $cm^{-1}$ and that in $Ph_3P{=}NPh$ was assigned 1344 $cm^{-1}$. More recently[149] the P–N stretch in $Me_3P{=}NMe$ was assigned the 1239 $cm^{-1}$ peak. The P=N absorption range therefore seems to be from 1140 to 1370 $cm^{-1}$.

The ultraviolet spectra of N-phenyliminophosphoranes are very similar to those of the analogous anilines, again indicating similar electronic effects for the $NH_2$– group and the $Ph_3P{=}N$– group.[59,165–167] The spectra have little character to them, with maxima ranging from 260 to about 360 nm, and reflect conjugation between the electron-rich nitrogen and the attached phenyl ring. The maxima for a series of N-(*p*-nitrophenyl)iminophosphoranes were near 385 nm, the $P{=}NC_6H_4NO_2$ chromophore being similar to *p*-nitroaniline.[160]

The ESCA studies of iminophosphoranes showed binding energies for nitrogen ($N_{1s}$) of ~397 ev, indicating very high electron densities on nitrogen, higher than azide and close to that in cyanide ion.[156,168] The phosphorus binding energies of ~137 ev indicated considerable positive charge, more so for imines than for ylides.[169] Recent repetition of these measurements led to the conclusion that charges were + 0.9 on phosphorus and – 0.5 on nitrogen.[170] The photoelectron spectra of imines usually showed two ionizations (e.g., 8.29 and 9.25 ev for $Me_3P{=}NH$), from the $N\pi$ and $N\sigma$ orbitals, respectively.[171] N-Alkyl and N-phenyl imines had lower N ionization potentials. P-Phenyl imine ionization potentials were still lower. The $P_{3s}$ ionizations were at 17.7 ev, also indicating more positive charge on phosphorus than for the analogous ylides. Mossbauer spectra also have been reported for a few imines.[172] Dissociation energies of the P=N bond have been calculated for $Me_3P{=}NEt$ (97 kcal/mol) and $Ph_3P{=}NEt$ (126 kcal/mol), leading to a difference of 28 ± 8 kcal/mol, such a difference being in the opposite direction of that for comparable phosphine oxides.[173]

### 13.2.4 Calculations

There have been four[174–176a,b] recent theoretical studies of the iminophosphorane system, all using $H_3P$–NH as the model system (the four sets of data that follow are from these references, respectively, which used 4-31G, 6-31G*, 6-31G*, and 6-31G* as basis sets in ab initio calculations). The calculated bond lengths were very similar (1.532, 1.525, 1.545, and 1.571 Å) and the P–N–H bond angles were calculated to be 119.16, 130.2, 121.6, and 116.4°. The N–P–H angles were found to vary between 108 and 126°, the H–P–H angles were calculated to be 100°,[174] and the dihedral angle H–N–P–H was reported to be from 116 to 180°. The nitrogen was found to be trigonally hybridized and the three phosphorus–hydrogen bonds were oriented pyramidally about phosphorus. The P–N stretching frequency was calculated to be 1294 $\mathrm{cm}^{-1}$,[175] within the experimental range of 1140–1370 $\mathrm{cm}^{-1}$ (see Section 13.2.3.2). The dipole moment was calculated to be 3.2, 2.9, or 3.4 D, close to the empirically determined P=N bond moment of 3.1[161] (see Section 13.2.3.2). The overlap populations for the P=N bond were calculated to be 0.51, 1.24, or 0.59. The net charge on phosphorus was calculated to be + 0.73 or + 0.91, and the net charge on nitrogen was calculated to be − 1.02 and − 0.86. The barrier to rotation about the P–N bond was calculated to be small, 8 kJ/mol, comparing well with the experimental data (see Section 13.2.3.1). Three groups attributed the multiple bond character of the P–N bond to *p–d* orbital interactions, the overlap populations being almost constant among conformations with varying dihedral angles, as expected from *d*-orbital orientations.[142,174,176a] The most recent study indicated that net atomic charges were very large, the molecule was very polar,[176b] and two groups argued that there was partial P–N *triple* bonding,[174,176b] one claiming little or no involvement of *d*-orbitals.[176b]

Two groups[174,175] were concerned with the energetics of the tautomeric conversion of the iminophosphorane ($H_3P{=}NH$) into the aminophosphane ($H_2P{-}NH_2$). The energy difference between the two was calculated to be 71 kJ/mol[174] and 31.8 kcal/mol,[175] with the aminophosphane being the more stable. The free entropy of activation was negligible and the free energy of activation was 51.7 kcal/mol.[175]

Other calculations on iminophosphoranes have been performed in conjunction with experimental work. In an ab initio approximation the P–N overlap populations were calculated to be about 1.15 using *d*-orbitals for the series of imines, $Ph_3P{=}NC_6H_4R$, with a linear correlation found between $J_{PN^{15}}$ values and the populations as a function of substituent R.[145] Thus, $J_{PN^{15}}$ values may reflect the extent of $p\pi$–$d\pi$ overlap, although there are other possibilities. The $^{31}P$ NMR spectra of the unsubstituted imine (R = H) in the solid state has yielded information on the $^{31}P$ chemical shielding tensors and dipolar coupling constants from which a P–N bond length of 1.60 Å was calculated.[152] Two groups[177, 178] earlier had performed Huckel MO calculations on the same series of imines to effect correlations with ultraviolet spectra. Assuming the P–N bond length was 1.57 Å net charges of about $-0.55$ for nitrogen and $+0.71$ for phosphorus, and a $\pi$-electron density of $+0.61$ for the P–N bond, were calculated.[177] The CNDO calculations giving a P–N bond length of 1.66 Å and a trigonally hybridized nitrogen were used to provide a fit with photoelectron spectral data.[171] Trinquier[179] calculated the P=N bond lengths to be 1.61 Å in a cyclodiphosphazene ring $(H_2P{=}N)_2$ and 1.65 Å in a cyclotriphosphazene ring $(H_2P{=}N)_3$, both considerably longer than lengths calculated by others (see above) for acyclic phosphazenes (iminophosphoranes).

## 13.3 REACTION OF IMINOPHOSPHORANES WITH CARBONYL-CONTAINING COMPOUNDS

The reaction of carbonyl-containing compounds with iminophosphoranes was discovered by Staudinger over 70 years ago. First reported in the reaction of N-phenyliminotriphenylphosphorane with diphenylketene and carbon dioxide,[7] and later expanded to reaction with aldehydes, ketones, carbon disulfide, and isocyanates,[180] the reaction has become widely used to create the C=N functional group and additional uses have been discovered. This section describes the various classes of such reactions.

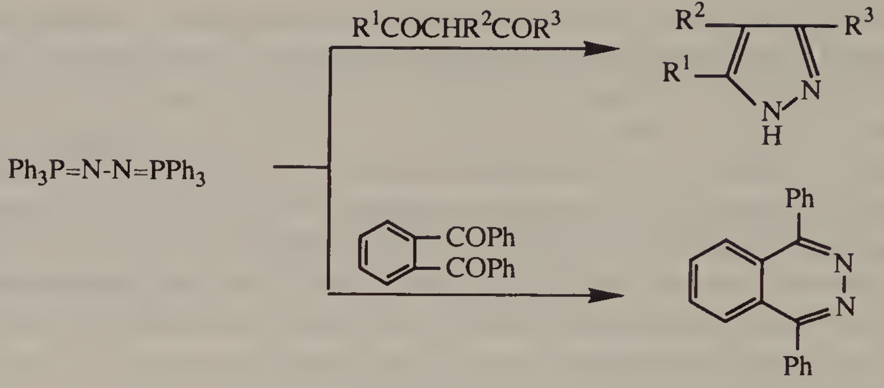
### 13.3.1 Aldehydes and Ketones (The Aza–Wittig Reaction)

Staudinger and his students used the reaction between N-phenyliminotriphenylphosphorane and benzaldehyde and benzophenone to produce carbonyl imines (Schiff bases) (Eq. 13.15). Probably since Staudinger's name became associated

$$Ph_3PN{=}R^1 \quad + \quad R^2R^3C{=}O \xrightarrow{-Ph_3PO} R^2R^3C{=}NR^1 \qquad (13.15)$$

with the formation of iminophosphoranes from azides and phosphines, an alternate name was needed for the reaction with aldehydes and ketones, and recently it has come to be called the Aza–Wittig reaction. The analogy with the reaction of phosphonium ylides with carbonyl compounds (Chapter 8) is obvious. The Aza–Wittig reaction usually is conducted in neutral solvents in the absence of catalysts, generally at mild reflux temperatures, and usually proceeds in high yield.

The Aza–Wittig reaction has been conducted with a wide variety of aldehydes and ketones, including benzaldehydes,[21, 59, 62, 133, 180–183] aliphatic aldehydes,[21, 100, 184–186] heterocyclic aldehydes,[187] dialiphatic ketones,[21, 188, 189] aromatic–aliphatic ketones,[190] and diaromatic ketones.[57] Monoimines have reacted with bis-aldehydes,[183] bis-imines have reacted with mono-aldehydes,[191] and bis-imines have reacted with bis-ketones, the latter reaction producing heterocycles[192] (Eq. 13.16). Iminophosphoranes attached to a polystryene chain

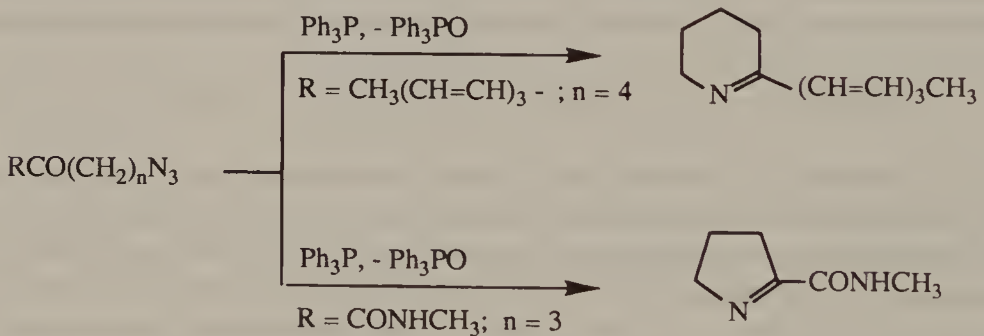


(13.16)

also have been reacted with benzaldehydes to produce polymeric Schiff bases.[193]

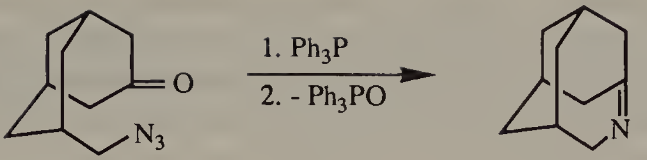
A wide variety of iminophosphoranes (i.e., with different N substituents) have been employed in reactions with carbonyl compounds. Exemplary N substituents have included aryl groups,[57,133,180,181,189] ferrocenylmethyl,[185] benzyl,[183] trimethylsilyl,[188] trimethylsilylmethyl,[21] amino,[194] benzamido,[62] and glucosyl.[195] The unsubstituted iminophosphorane, $Ph_3P{=}NH$, also reacted with aldehydes and ketones to produce the corresponding N-unsubstituted carbonyl imines.[59,76,196]

***13.3.1.1 The Intramolecular Aza–Wittig Reaction.*** The first application of the Aza–Wittig reaction in an intramolecular environment was the synthesis of nigrifactine, a tetrahydropyridine-based streptomyces alkaloid, in only 11% yield from a $\delta$-azidoketone (Eq. 13.17).[197] Similar cyclization to form a pyrroline later was applied to a $\gamma$-azidoketone (Eq. 13.17).[198] More recently other



(13.17)

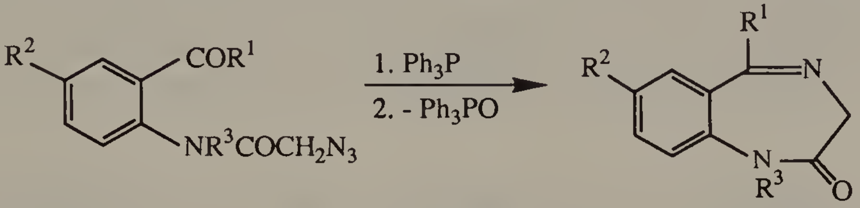
tetrahydropyridines have been prepared in high yields using this reaction.[199] The cyclization has been successful with $\gamma$, $\delta$ and $\varepsilon$-azido ketones and aldehydes to form many five- to seven-membered imine-containing heterocycles,[200–203] but has failed to form eight-membered rings.[200,201] The cephalosporin ring system also has been formed by closing the six-membered ring with the Aza–Wittig reaction.[204] The cyclization even has provided fleeting access to unstable bridgehead tricyclic imines, whose existence was proven by trapping (Eq. 13.18).[205] In most of these reactions the iminophosphorane was formed



(13.18)

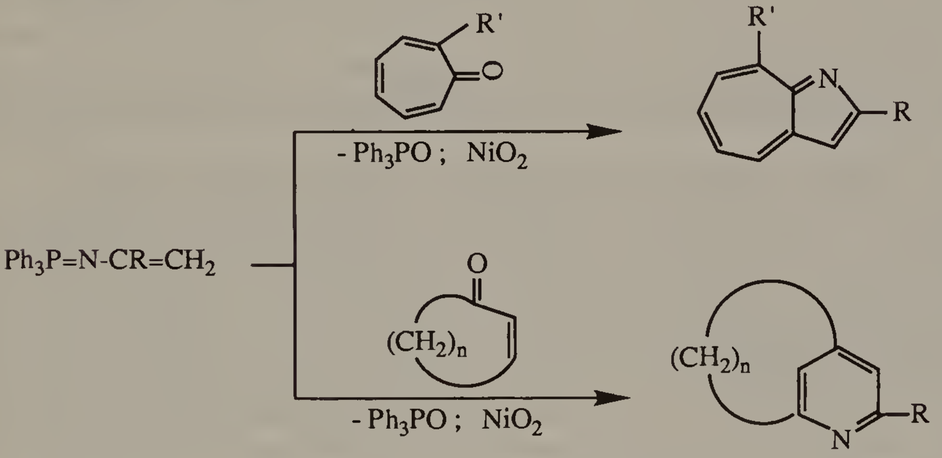
in situ from the azide and triphenylphosphine, was not isolated, and was reacted immediately with the carbonyl group.

Intramolecular Aza–Wittig reactions using ortho-substituted phenylketones afforded seven-membered heterocycles (Eq. 13.19).[202] Vinylic imines effected



(13.19)

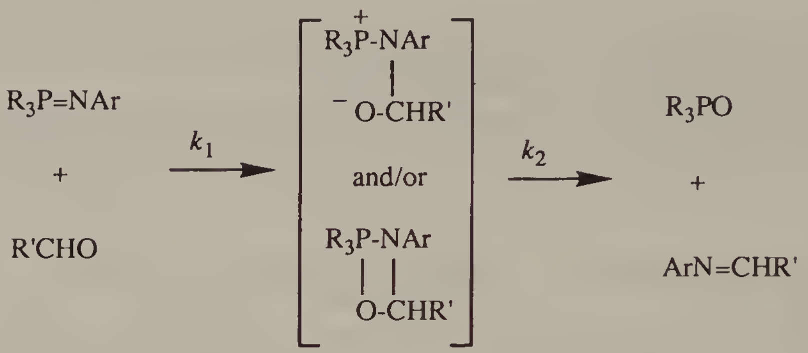
conjugate addition to enones, followed by cyclizations of the resultant ε-keto iminophosphoranes eventually to form aza-azulenes[105] and pyridinophanes[104] (Eq. 13.20).



(13.20)

Dimerization is an alternative to intramolecular cyclization for N-(carbonyl-substituted)iminophosphoranes. β-Carbonyl-substituted iminophosphoranes underwent intermolecular reaction, appearing to dimerize to form hexacyclic heterocycles.[62, 206, 207] N-(*o*-Formyl-phenyl)iminotriphenylphosphorane, a γ-carbonyl derivative, neither dimerized to an eight-membered ring nor cyclized to an azacyclobutadiene.[38, 181] The structurally analogous N(2-formylcyclohexenyl)iminotriphenylphosphorane, another γ-carbonyl imine, was reported to dimerize under severe conditions to a known bis-annelated pyridine, but involving the unexplained loss of one nitrogen.[208]

***13.3.1.2 Mechanism of the Aza–Wittig Reaction.*** The broad outlines of the mechanism of the Aza–Wittig reaction are known, but essential information regarding intermediates and/or transition states remains unavailable. There is considerable similarity with the mechanism of the Wittig reaction, with the reaction proceeding via nucleophilic attack of the imine nitrogen on carbonyl carbon followed by transfer of oxygen to phosphorus (Eq. 13.21).



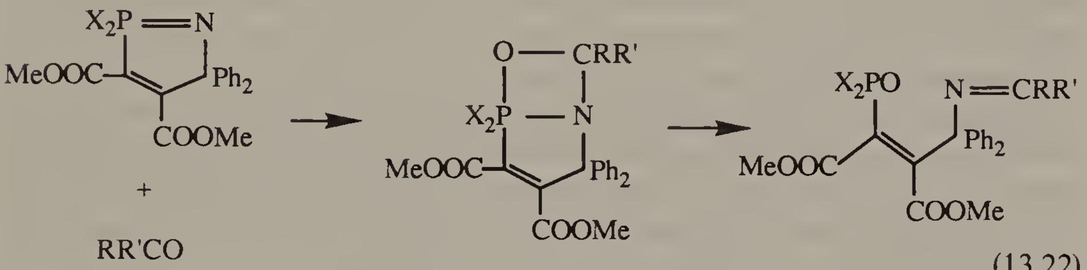
(13.21)

Johnson and Wong[133] demonstrated that the reaction rates increased with increasing electrophilicity of benzaldehyde carbonyl groups, a Hammett correlation with $\sigma$ leading to a $\rho$ value of $+2.1$, similar to those found for the Wittig reaction. The reactions were second order, first order in each reactant, with low energies of activation ($\sim 8$ kcal/mol) and large negative entropies of activation ($-35$ to $-45$ eu).[133,209] The reaction has not been demonstrated to be reversible, in spite of assumptions to the contrary.[209] There was not a major solvent effect,[209] contrary to an earlier conclusion,[133] although hydrogen-bonding solvents and added carboxylic acids did increase the rates up to a factor of 10.

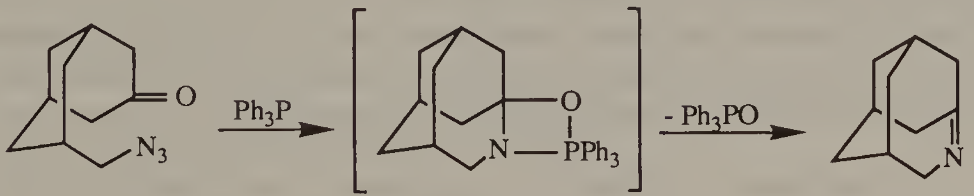
Imine substituents also affected the rates of the reaction. Increased nucleophilicity of the imine should increase the rate of the first step ($k_1$), whereas the rate of the second step ($k_2$) should be increased by substituents that facilitated oxygen transfer to phosphorus. For a series of N-phenyliminotri-(substituted-phenyl)phosphoranes, the $\rho$ value was $-0.70$.[133] This value was consistent with the relative rates being $k_2 > k_1$, electron-withdrawing substituents on nitrogen decreasing the nucleophilicity of the imine nitrogen. The small effect per substituent suggests there was only a small difference in the rates of the two steps of the reaction. Similarly, in reaction of N-phenyliminotriphenylphosphorane, stepwise replacement of the P-phenyl groups with P-ethyl groups led to increases in the rates of the reaction by a factor of about 10 for each replacement.[209] The P-ethyl groups would be expected to increase $k_1$ but decrease $k_2$, again indicating that $k_1$ was the slow step.

For reaction of a series of N-(substituted-phenyl)iminotriphenylphosphoranes with several benzaldehydes variation in the nature of the N-phenyl substituent led to "concave down" Hammett correlations with $\sigma$. The fastest rates were with the unsubstituted imine—with electron donating substituents the $\rho$ value was $+0.95$, and with electron withdrawing substituents the $\rho$ value was $-2.4$.[133,210] This behavior was indicative of a change in the rate-determining step, indicating that for this Aza–Wittig reaction the rates of the two steps were similar. The change of substituent on either nitrogen or phosphorus affected the reaction rate, and each change had the opposite effect on the two steps of the reaction.

The nature of the intermediate in the Aza–Wittig reaction has not been proven, neither a betaine nor an oxazaphosphetane having been observed in ordinary reactions. While earlier rationalized in terms of a betaine, the kinetic data and substituent effects can equally well be rationalized in terms of an oxazaphosphetane formed approximately synchronously from the two reactants.[205] The large negative values for the entropy of activation and the absence of significant solvent effects are consistent with this proposal. Two reports of oxazaphosphetanes have appeared since that proposal. Schmidpeter and Criegern[211] were able to isolate adducts formed from a cyclic iminophosphorane and ketones carrying trifluoromethyl groups (Eq. 13.22). Aldehydes proceeded directly to Aza–Wittig products, no intermediates being observed. The key characteristics of the intermediate were the $^{31}P$ NMR peaks at − 35 to − 55 ppm, consistent with an oxazaphosphetane but not a betaine structure, and the observation that their formation was reversible. Further, heating the intermediates produced imine product accompanied by some starting materials. The structure of the intermediate has been determined by X-ray crystallography.[114] More recently, observation of the formation and disappearance of an oxazaphosphetane intermediate by $^1H$ and $^{13}C$ NMR spectroscopy was reported during the formation of a highly strained imine using the Aza–Wittig reaction (Eq. 13.23).[205]



(13.22)



(13.23)

Based on the information now available, it seems appropriate to portray the Aza–Wittig reaction as a two-step reaction, with the rates of the two steps being similar, and involving the intermediacy of an oxazaphosphetane formed approximately synchronously from the two reactants.

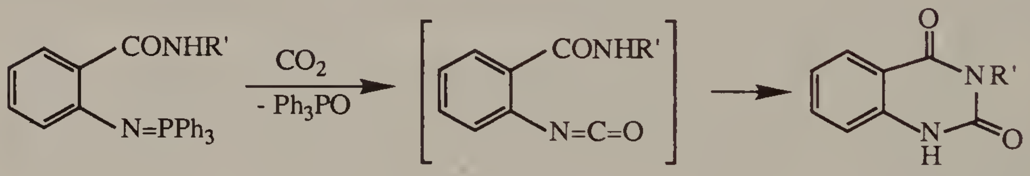
### 13.3.2 Other Carbonyl Compounds

*13.3.2.1* ***Reaction with Carbon Dioxide.*** One of the oldest reactions of iminophosphoranes is that with carbon dioxide, which usually resulted in the formation of isocyanates (Eq. 13.24). Staudinger et al.[7,180] produced phenylisocyanate by this route and many others have employed this reaction,[45,57,59,76]

$$\mathrm{Ph_3P{=}NR} + \mathrm{CO_2} \xrightarrow{\mathrm{-Ph_3PO}} \mathrm{RNCO} \xrightarrow[\mathrm{-Ph_3PO}]{\text{imine}} \mathrm{R{-}N{=}C{=}N{-}R} \qquad (13.24)$$

including Eguchi et al.,[212] who prepared adamantyl-1-isocyanate and Tsuge et al.,[21] who prepared trimethylsilylmethyl isocyanate. The carbon dioxide reaction also has been employed as a nonhydrolytic means of converting an iminophosphorane to a phosphine oxide.[213] In a few instances[18,214] using only one-half equivalent of carbon dioxide resulted in further reaction of the isocyanate product with unchanged imine to form carbodimides, a well-known reaction (see Section 13.3.2.3).

Molina et al. have employed the reaction of iminophosphoranes with carbon dioxide to form isocyanates, which then underwent various ring closure reactions to form a wide variety of heterocycles. In all instances a substituent located at the ortho position to the newly formed isocyanate added across the latter group to form the new ring, such substituents including amido (Eq. 13.25),[19,215] imino,[23,216] amino,[217] and ω-nitrovinyl[218,219] groups.

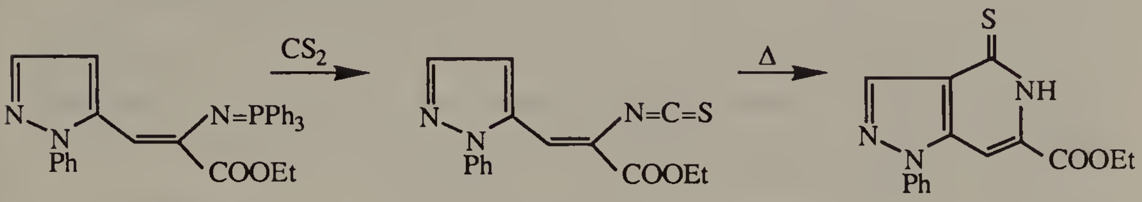


(13.25)

In somewhat related reactions iminophosphoranes have been found to react with carbon monoxide. N-Phenyliminotriphenylphosphorane reacted with CO in the presence of $PdCl_2$, probably via attack of nitrogen at carbon with subsequent elimination of triphenylphosphine oxide and resulting in a nitrile complex.[220] Iron pentacarbonyl reacted similarly (Eq. 13.26).[221] Imine formation also appears to have been involved in the reaction of iminophosphoranes with $Fe_2(\mu\text{-}CH_2)(CO)_8$ eventually to form pyridones.[222,223].

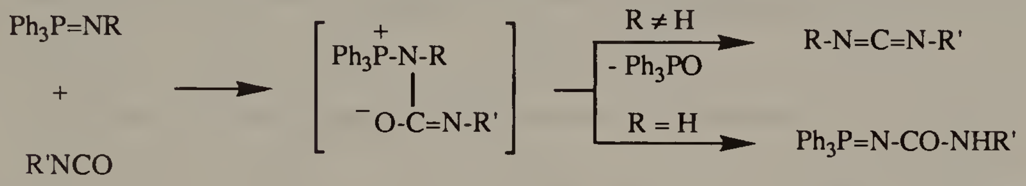
$$\mathrm{Ph_3P{=}NAr} + \mathrm{Fe(CO)_5} \xrightarrow[\mathrm{-\ Ph_3PO}]{} \mathrm{Fe(CO)_4(ArCN)} \qquad (13.26)$$

*13.3.2.2* ***Reaction with Carbon Disulfide.*** Staudinger and Hauser[180] found that carbon disulfide reacted with iminophosphoranes in an identical manner to afford isothiocyanates. Many additional examples of this reaction are known, for example, producing aryl,[45] 1-adamantyl,[212] trimethylsilylmethyl,[222] and trimethylsilyl isothiocyanates,[224] with no reports of carbodiimides being formed for subsequent reaction of product with imine. This method of isothiocyanate formation has been followed by various cyclization strategies in producing heterocyclic thiones, with cyclization involving nearby amide,[19,225] imine,[216] amine,[217] and even aromatic ring groups (Eq. 13.27).[226,227] Cyclization could not be effected in one structurally analogous case where the ring juncture needed to be made at a nonaromatic carbon.[218]



(13.27)

***13.3.2.3 Reaction with Isocyanates and Isothiocyanates.*** Iminophosphoranes normally react with isocyanates in an Aza–Wittig reaction to produce carbodiimides and phosphine oxides (Eq. 13.28). Staudinger and Hauser[180] dis-

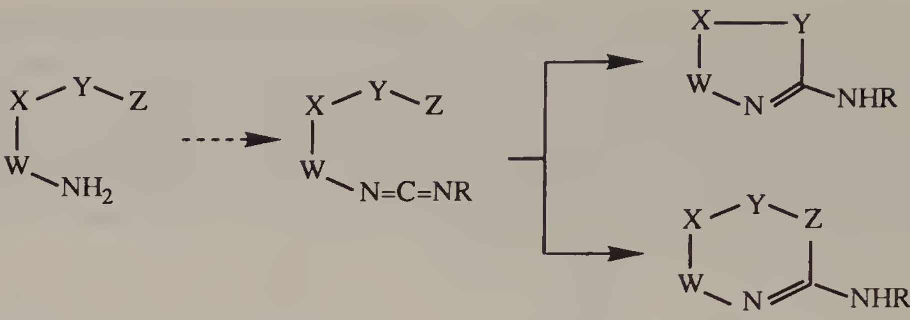


(13.28)

covered this reaction using phenyl isocyanate and the N-phenylimine, and it has been used frequently since with imines carrying a wide variety of N substituents, including: aryl,[45,228] vinylic,[229] amido,[225] alkyl,[21,212,230] β-ketoalkyl,[231] and polystyrylmethyl.[193] The reaction probably occurred by attack of the nucleophilic nitrogen on the isocyanate carbonyl group. When the iminophosphorane substituent was hydrogen, phosphine oxide elimination did not occur, proton transfer occurring instead to produce an N-carbamidoiminophosphorane (phosphoranyl urea).[232–234] When the N substituent was trimethylsilyl, mixtures of products occurred, including the expected carbodiimide, but also products from silyl group migration and from imine interchange.[224]

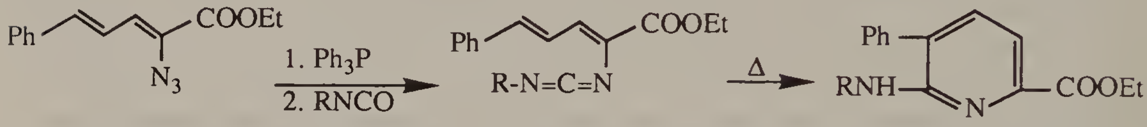
Isothiocyanates reacted identically with iminophosphoranes, although they occasionally appeared less reactive.[21,212,225,228]

The conversion of aromatic amines into azides and then to iminophosphoranes, followed by reaction with isocyanates or isothiocyanates to form carbodiimides which cyclized to form heterocycles has been exploited by Molina and others,[235] and recently has been summarized.[8,236] By this means a wide variety of five- and six-membered heterocycles have been made available through the general approach shown in Eq. 13.29, with Y or Z being a source of electrons, including from a multiple bond. For example, an α-azidodienyl ester



(13.29)

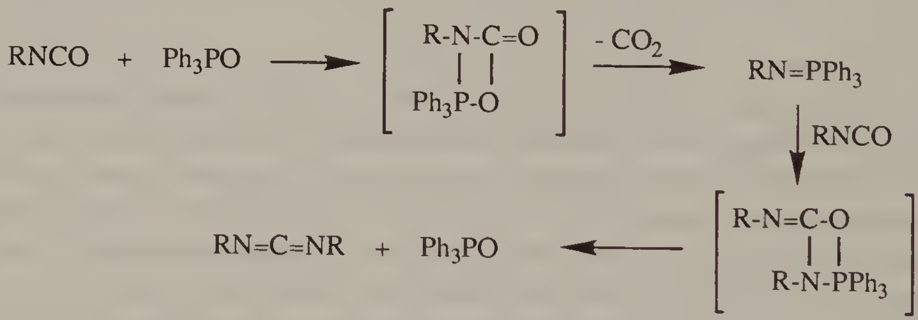
reacted with triphenylphosphine and isocyanates to form the carbodiimides which cyclized to α-aminopyridines simply on refluxing in toluene (Eq. 13.30).[218,237] Ring closures have involved attack on the central carbon of



(13.30)

carbodiimides by C-3 of indole,[226] C-4 of pyrazole,[227] C-5 of carbazole,[238] N-1 and C-2,3 or 4 of pyridine,[239] nitrovinyl carbon,[219,240] meta-aryl carbon,[241] amine nitrogen,[23,56,217] imine nitrogen,[216,242] amide nitrogen,[19,215] and hydroxyl.[243] In a few instances the intermediate heterocyclic carbodiimides have not cyclized, but instead have dimerized[244] or reacted further with the iminophosphorane.[176]

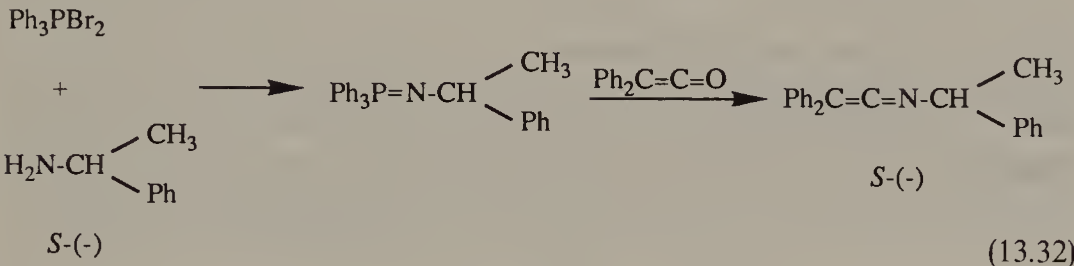
As mentioned earlier (Section 13.1.4), tertiary phosphine oxides have been shown to catalyze the dimerization reaction of isocyanates to afford carbodiimides and carbon dioxide (Eq. 13.31). The reaction has been shown,



(13.31)

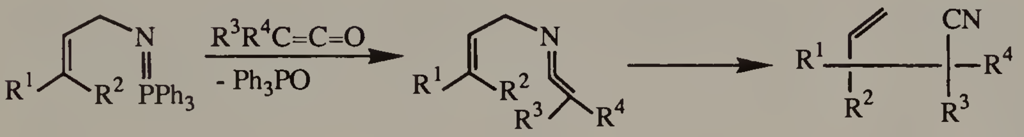
through kinetic studies[96,245] and $^{18}O$ transfer studies,[95] to involve slow formation of an iminophosphorane, followed by a rapid Aza–Wittig reaction with additional isocyanate to produce carbodiimide and regenerate phosphine oxide. In a reaction similar to the first step of the example given above, N-sulfinylmethanesulfonamide ($MeSO_2NSO$) and N-sulfinyl-*p*-toluenesulfonamide (TsNSO) reacted with triphenylphosphine oxide or sulfide to afford, respectively, N-(methanesulfonyl)- or N-(*p*-toluenesulfonyl)iminotriphenylphosphorane.[98]

*13.3.2.4* ***Reaction with Ketenes.*** One of the first reactions reported for iminophosphoranes by Staudinger and Meyer[7] was that with diphenylketene to produce triphenylketenimine and triphenylphosphine oxide, a typical Aza–Wittig reaction. Horner and Gross[45] reported additional examples of the reaction and more recent examples have been reported for N-substituted imines such as the trimethylsilylmethyl,[21] ω-bromostyryl,[246] β-ketoalkyl,[207] amido,[207] amidomethyl,[207] and a cephalosporin imine.[67] Use of an enantiomeric amine for preparation of the iminophosphorane led to the availability of the corresponding ketenimine with complete retention of configuration (Eq. 13.32).[68]



(13.32)

Ketenimines prepared from ketenes also have been used for in situ cyclization reactions,[227] and in one instance the ketenimine rearranged before isolation (Eq. 13.33).[25]

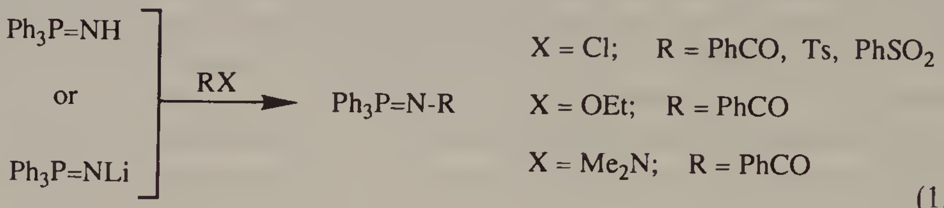


(13.33)

### 13.3.3 Carboxylic Acid Derivatives

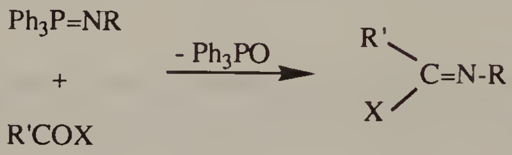
The reaction of iminophosphorances with derivatives of carboxylic acids could, in principle, proceed to two kinds of products. Reaction could lead to acylation of the imine to form an acylaminophosphonium salt, which might be stable or might decompose by cleavage of the phosphorus–nitrogen bond. Alternatively, reaction could lead to olefination of the carbonyl group, in effect an Aza–Wittig reaction. Phosphonium ylides underwent both types of reactions with acid derivatives (Section 6.5), whereas phosphonate (Section 10.3.1.4) and phosphinoxy (Section 11.3.1.2) carbanions underwent acylation almost exclusively. The following sections report the reactions of N-substituted iminophosphoranes with various derivatives of carboxylic acids. Gusar recently, but briefly, reviewed the reactions with esters and amides.[236]

In contrast to phosphorus carbanions, many of which carried a proton on the α-carbon and therefore underwent substitution by an acyl group with reformation of a new stabilized carbanion, all but one iminophosphorane do not have a proton on the nitrogen available for substitution. The only one which does, iminotriphenylphosphorane, and its anion,[247] reacted with acylating agents, including acid chlorides,[76, 248–250] esters,[247] and amides,[247] to afford only the acylated imines, there being no evidence for Aza–Wittig reactions (Eq. 13.34).



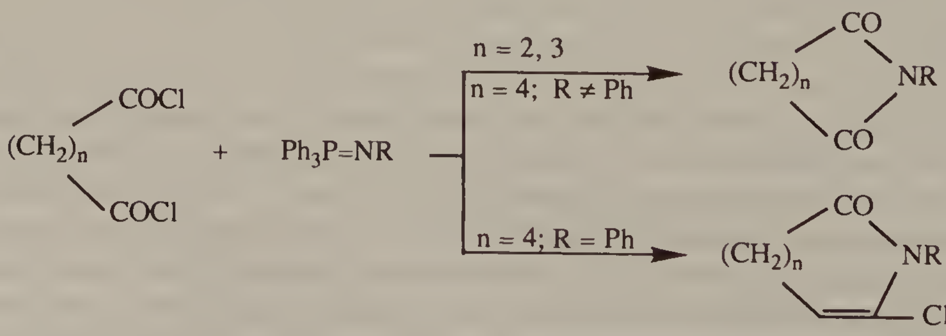
(13.34)

***13.3.3.1 Reaction with Acid Chlorides.*** Acid chlorides generally have undergone Aza–Wittig reactions with N-substituted iminophosphoranes. Zbiral and Bauer[251] found that several iminotriphenylphosphoranes reacted at room temperature with acid chlorides, bromides, and iodides to form imidoyl halides in moderate yields, the result of Aza–Wittig reactions (Eq. 13.35). Upon acylation of an imine carrying a $\beta$-lactam group on nitrogen, the corresponding acylated amine was obtained (i.e., loss of phosphorus), but the product probably resulted from an Aza–Wittig reaction followed by partial hydrolysis of the imidoyl halide.[182] When the N substituent was the trimethylsilyl group, acylation occurred with subsequent displacement of the trimethylsilyl group to afford the N-acyliminotriphenylphosphorane.[27] Zbiral et al.[189, 252] found that initial N-acylation usually occurred with imines, but anions such as azide would then add to the acylated imine, the resulting oxyanions eliminating triphenylphosphine oxide and forming heterocycles, a reaction that has been reviewed.[253]



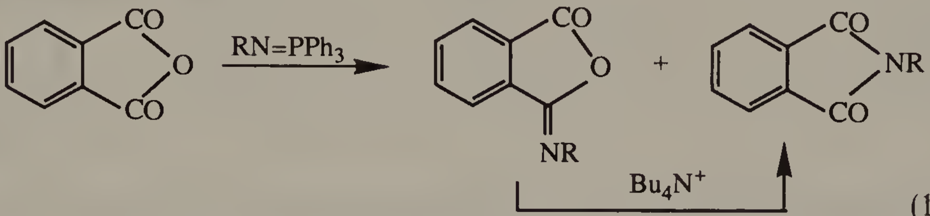
(13.35)

More recently, Aubert et al.[254] have reported reaction of iminophosphoranes with acid chlorides of dicarboxylic acids. With succinoyl and glutaroyl dichlorides bis-acylation resulted to afford the corresponding N-substituted imide. However, with adipoyl and similar chlorides an initial Aza–Wittig reaction was followed by an acylation in some instances (Eq. 13.36).



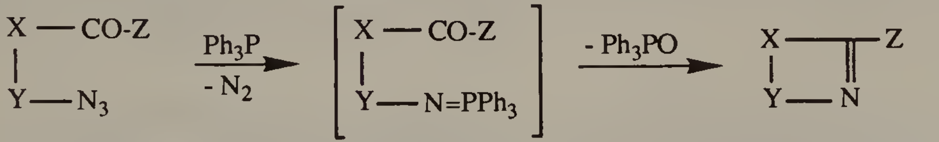
(13.36)

*13.3.3.2 Reaction with Acid Anhydrides.* N-Trimethylsilyliminotriphenylphosphoranes reacted with linear[27, 224] or cyclic[224] anhydrides with displacement of the trimethylsilyl group to produce N-acyliminophosphoranes. However, other imines probably effected Aza–Wittig reactions with cyclic anhydrides initially to form isoimides,[255, 256] which then rearranged to imides in some instances (Eq. 13.37).[256] This latter reaction has been employed to convert carbohydrate alkyl halides to protected primary amines via azides, iminophosphoranes, and phthalimides.[11, 255] The course of the reaction of N-substituted imines with linear anhydrides is unreported.



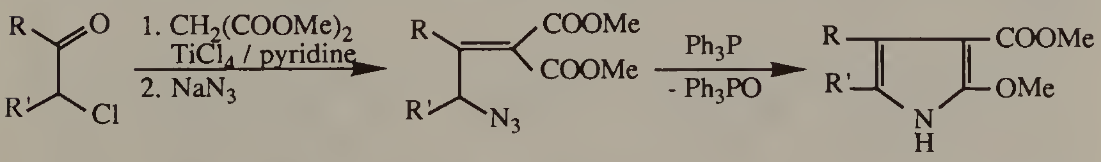
(13.37)

*13.3.3.3 Reaction with Esters.* The reaction of esters with N-substituted iminotriphenylphosphoranes, first reported only in recent years, invariably resulted in Aza–Wittig reactions with the products being enol ethers or derivatives thereof. This reaction seems to have been applied only in an intramolecular environment, usually in a "one-pot" reaction with the azide and triphenylphosphine, and has been used for the synthesis of a wide variety of heterocycles containing at least one nitrogen atom (Eq. 13.38). The synthesis of five-membered heterocycles has been accomplished, including pyrroles[257] (Eq. 13.39), oxazoles,[258] oxazolines,[22] and oxadiazoles.[259] Six-membered heterocycles synthesized include benzoxazinones[260–262] (Eq. 13.40) and pyridines.[263] Seven-membered heterocycles have been synthesized similarly (13.41).[264, 265]

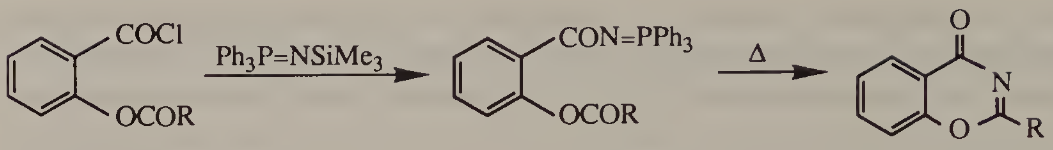


X = O or Z = OR
Y = 2 to 4 atoms

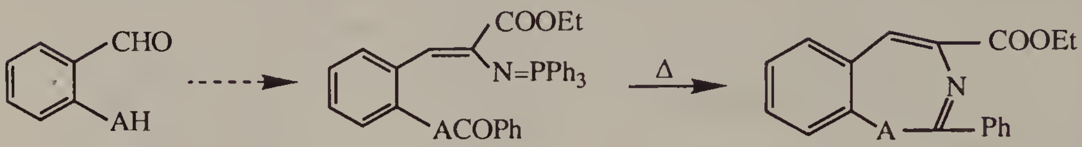
(13.38)



(13.39)



(13.40)

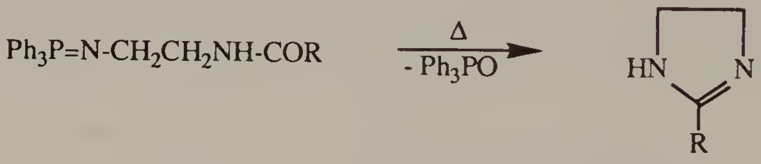


(A = O or NH)

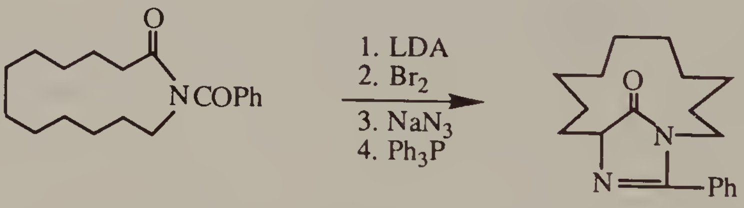
(13.41)

As discussed in Section 13.5.4, triethylphosphite frequently and earlier had been used in such Aza–Wittig cyclizations.

***13.3.3.4 Reaction with Amides and Imides.*** Muchowski[266] found that N-substituted iminophosphoranes effected an Aza–Wittig reaction with dimethyl formamide to afford formamidines. Gololobov et al.[22] reported that N-(β-amidoethyl)iminotriphenylphosphoranes produced imidazolines upon heating via an intramolecular Aza–Wittig reaction (Eq. 13.42). Flitsch and Mukidjam[203] fused a six-membered ring to an azaazulenone and Takeuchi et al.[267] converted a 13-membered cyclic amide into a fused imidazolinone using this cyclization reaction (Eq. 13.43).

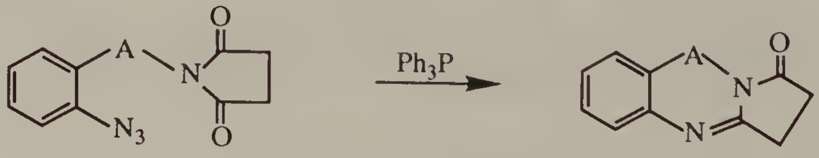


(13.42)



(13.43)

Cyclization reactions involving imides and iminophosphoranes also have been reported by four groups within the space of two years. Three reported using succinimide derivatives to form fused heterocyclic systems[268–270] (Eq. 13.44). The use of phthalimide also has been reported.[268, 270] Formation of heterocycles such as imidazolinones[267] from linear imides also has been reported.



(13.44)

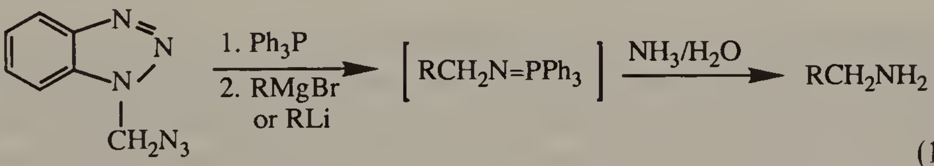
A = CH$_2$, CO, or no group

## 13.4 OTHER REACTIONS OF IMINOPHOSPHORANES

### 13.4.1 Cleavages and Decompositions

*13.4.1.1* ***Hydrolysis.*** Iminophosphoranes ($RN{=}PPh_3$) are cleaved to amines and phosphine oxides under acidic or basic hydrolysis conditions, with the ease of the reaction depending on the N-substituent. The parent imines (N = H), other than that derived from tris-*t*-butylphosphine,[271] hydrolyze rapidly in moist air,[76, 78, 272]; alkylimines (R = alkyl) also often hydrolyze in air,[58] but arylimines (R = aryl) generally are stable in air and often in water, but hydrolyze in dilute acid or base.[7, 57] Acid-catalyzed hydrolysis occurred by protonation of the imine followed by attack of water on phosphorus, whereas base-catalyzed hydrolysis occurred by attack of hydroxide on phosphorus, both processes leading to expulsion of the amino group and inversion of configuration at phosphorus.[273]

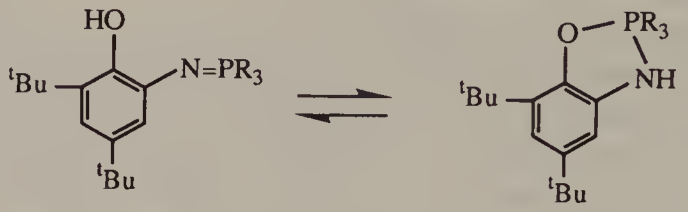
The imine hydrolysis process has been applied to the synthesis of primary amines, first by Horner and Gross[45] who converted α-bromocarboxylic acids to α-amino acids by displacement with azide, formation of imine with triphenylphosphine, and hydrolysis. This approach has been reviewed as a means to convert azides to amines other than by reduction[8, 9] and has been applied to the synthesis of oligonucleotide amines.[274] 3-Aminooxetane was prepared from its tosylate in excellent yield in this manner,[20] polyvinylbenzylamine was obtained from its imine,[193] and Vaultier et al.[275] devised a "one-pot" high-yield procedure from azide to amine. Using the same concept, but triethylphosphite in place of triphenylphosphine, Koziara et al. [276] converted alkyl halides to alkylamines using acid-catalyzed hydrolysis as the final step. In their preparation of homologous amines, Katritzky et al.[277] employed iminophosphorane intermediates which were hydrolyzed in situ (Eq. 13.45).



(13.45)

*13.4.1.2* ***Alcoholysis.*** Most iminophosphoranes do not react with alcohols, as evidenced by the formation of unsubstituted imines in methanolic solution. The exception is N-trimethylsilyliminophosphoranes, carrying either the triphenyl or trialkylphosphorus group, which reacted with methanol and sulfuric acid at low temperatures to afford the unsubstituted imines ($R_3P{=}NH$).[10, 271, 272, 278] The reaction presumably occurred by protonation of the imine, followed by attack of methanol on silicon, rather than on phosphorus as in hydrolysis.

Stegmann et al.[279] demonstrated that phenolic groups would add across an adjacent iminophosphorane P=N bond to afford oxazaphosphoranes. The imine and the oxazaphospholines were shown to be in equilibrium in solution, with the concentration of the latter being higher at lower temperatures (Eq. 13.46).[280] Later Cadogan et al.[281] isolated the benzoxazaphospholine from

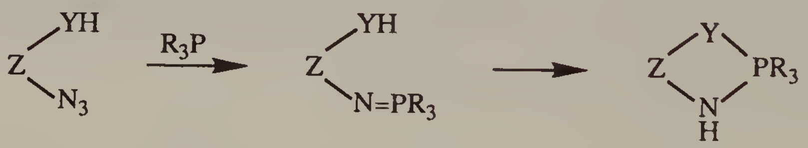


(13.46)

*o*-azidophenol and methyl diphenylphosphinite which showed the expected high field $^{31}$P NMR absorption at − 36 ppm. At about the same time, Sanchez et al.[282] found that secondary amines appropriately distanced from an N-phenylimino group would effect similar addition to produce a phosphorane (Eq. 13.47). Cadogan et al.[283] subsequently provided numerous examples of the

(13.47)

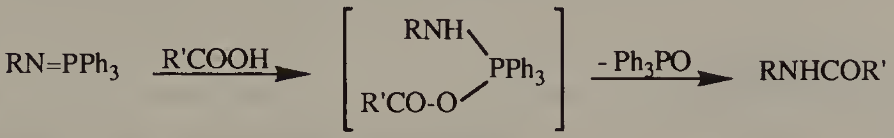
addition of alcoholic, phenolic, and amino groups across the P=N group to afford pentavalent phosphorus derivatives, all fitting a general pattern shown in Eq. 13.48, with the phosphorane ring being five or six-membered, Y being



(13.48)

oxygen or nitrogen, and Z being *o*-diphenyl or various two-carbon groups. They also effected reaction between diols and N-phenylimines which involved addition of the OH group across the P=N bond.[284] An improved preparation of azetidine was effected by forming the imine from 3-azidopropanol and triphenyl- or tributylphosphine and then heating, a reaction whose mechansim is unknown but which might have involved OH addition across the P=N bond, followed by $Ph_3PO$ elimination.[285] Alternatively, imine displacement of hydroxyl might have been involved, as had been proposed for the conversion of 2-azido-2-phenylethanol to 2-phenylaziridine.[286]

*13.4.1.3 Acidolysis.* As shown in Section 13.2.2 iminophosphoranes are basic, and they produced amino-phosphonium salts when treated with hydrogen halides.[57, 180] Reaction with carboxylic acids proceeded further, however, with cleavage of the P–N bond and formation of an amide of the carboxylic acid,[11, 57, 287] probably by formation of a phosphorane intermediate which eliminated phosphine oxide (Eq. 13.49).[288] Recently this reaction has been applied to the synthesis of peptides, for example, azido acetic ester and a dipeptide affording a 70% yield of the tripeptide (Eq. 13.50).[289]



(13.49)

$$\underset{\displaystyle R}{H_2NCH}CONH\underset{\displaystyle R'}{CH}COOH \xrightarrow[N_3CH_2COOEt]{Ph_3P} \underset{\displaystyle R}{H_2NCH}CONH\underset{\displaystyle R'}{CH}CONHCH_2COOEt$$

(13.50)

*13.4.1.4* ***Photolysis.*** There are only two reports on the photochemistry of iminophosphoranes. N-Arylimines were cleaved to triphenylphosphine and azobenzene derivatives, but it was not possible to trap nitrenes inter- or intramolecularly.[290] Highly stabilized imines (N substituents = sulfonyl, carbonyl, etc.) could not be cleaved. N-Alkyliminophosphoranes underwent P–N and N–C cleavage, with the former normally dominating, and in the case of the *t*-butyl substituent there was evidence of free radical formation.[291]

*13.4.1.5* ***Thermolysis.*** Most iminophosphoranes are thermally stable. The bisimine ($Ph_3P{=}N{-}N{=}PPh_3$) dissociated to triphenylphosphine and nitrogen upon heating.[194] First Staudinger and Hauser,[180] then others,[45, 292–294] reported that N-benzoyliminotriphenylphosphorane thermally decomposed to benzonitrile and triphenylphosphine oxide, presumably via the enolate, a reaction well known in the phosphonium ylide series (Section 5.4).

*13.4.1.6* ***Oxidation.*** Corey et al.[295] discovered that N-alkyliminophosphoranes could be oxidized with three equivalents of ozone to produce good yields of alkyl nitro compounds, providing a useful means for converting azides to nitro groups. Aldehydes occasionally were significant byproducts. The P=N bond was subject to cleavage by $ReOCl_3(PPh_3)_2$, resulting in phosphine oxide and iminorhenium compounds.[296] Electrochemical oxidation of N-arylimines involved one-electron transfer from nitrogen and tail-to-tail para-aryl coupling products, with the CV peak potentials correlating well with $\sigma^+$ values of the ring substituents.[145, 297] Imines with more electron-withdrawing substituents, such as carbonyl or sulfonyl groups, were more difficult to oxidize.

*13.4.1.7* ***Reduction.*** Lithium aluminum hydride reduced N-phenyliminophosphoranes to aniline and the tertiary phosphine.[117] This reduction complements the hydrolysis reaction which produced phosphine oxide and amine. Earlier, Hassner and Galle[298] had effected reduction of an aminotriphenylphosphonium salt under the same conditions and in high yield.

Electrochemical reduction of N-arylimines first was studied in the early 1970s and revealed considerable resistance to reduction.[299, 300] Two one-electron reductions were proposed with cleavage of the P–N bond producing amine.[145]

### 13.4.2 Electrophiles

*13.4.2.1 Halogenation.* Iminotriphenylphosphorane was halogenated by chlorine, bromine, and iodine to afford one-half equivalent of the N-haloiminotriphenylphosphorane and one-half equivalent of aminotriphenylphosphonium halide.[196, 301] That N-(iodoimino)triphenylphosphorane was obtained from iodine monochloride indicates the reaction proceeded by attack of nucleophilic nitrogen on iodine, followed by "transylidation."

Iodination of the N-phenylimine afforded N-(*p*-iodophenyl)iminophosphorane, proposed to result from initial formation of the N-iodo-N-phenylimine, which served as an iodinating agent on another molecule of imine, the imino group serving as an activator and para-directing group.[302] Zbiral had reported that the hydrogen iodide salt of the N-phenylimine afforded the same product upon oxidation with lead tetraacetate, presumably by formation of molecular iodine.[303] Gutsch earlier had reported a similar bromination.[304] Ivanova et al.[136] studied the charge-transfer complex formation between N-arylimines and iodine, with the extent of complex formation being a function of the electron density on nitrogen, as influenced by the aryl substituent.

An N-fluoroimine was prepared from the N-trimethylsilylimine using xenon difluoride.[305]

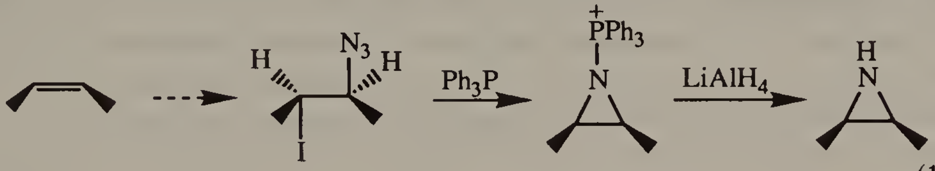
*13.4.2.2 Alkylation.* Reaction of the N-unsubstituted imine, $Ph_3P{=}NH$, with ethyl[196] or methyl[247] iodide resulted in formation of one-half equivalent of N,N-dialkylaminophosphonium salt and one-half equivalent of aminophosphonium salt, the result of alkylation followed by transylidation to form an N-alkylimine, then a second alkylation. If the original imine first was converted to its anion with butyllithium, and then alkylated, a full equivalent of N,N-dialkylaminophosphonium salt resulted.[247] When a bulky alkylating agent such as trityl chloride was used, monoalkylation followed by transylidation occurred to afford the N-tritylimine.[306] In a similar reaction Cameron et al.[307] arylated the unsubstituted imine with a chlorotriazine derivative. Koidan et al.[59] effected dialkylations with α,ω-dibromides to afford piperidino- and pyrrolidinophosphonium salts.

N-Aryliminotriphenylphosphorane[45, 57, 308, 309] underwent simple monoalkylation with alkyl halides to afford N-alkyl-N-aryl aminophosphonium salts. Such salts formed paramagnetic complexes with TCNQ, with the methyl and ethyl derivatives showing conducting behavior, but the N-propyl and N-butyl salts being insulators.[310]

The nitrogen atom of N-(*p*-hydroxyphenyl)imines, rather than the phenolic group, was methylated by methyl sulfate.[311] Similarly, the imine nitrogens and not the amino nitrogens of N-amino imines were alkylated.[60, 61] The bis-imine, $Ph_3P{=}N{-}N{=}PPh_3$, underwent monomethylation.[194]

N-Alkylimines also underwent simple alkylation with alkyl halides, but when the alkylating agent was larger than ethyl, the imine was a sufficiently strong base to effect dehydrohalogenation.[58, 312] However, the conversion of alkyl halides into secondary amines was made possible by the alkylation route when followed by the ready hydrolysis of the N,N-dialkylaminophosphonium salt (Eq. 13.51).[312] Katritzky et al.[313] intercepted the imines prepared in his benzotriazole method (see Eq. 13.45) and effected alkylations, thereby providing another synthesis route to secondary amines. Hassner and Galle[298] employed a stereospecific intramolecular alkylation of an imine in converting *cis*- and *trans*-2-butene to *cis*- and *trans*-aziridines, respectively, in high yield (Eq. 13.52).

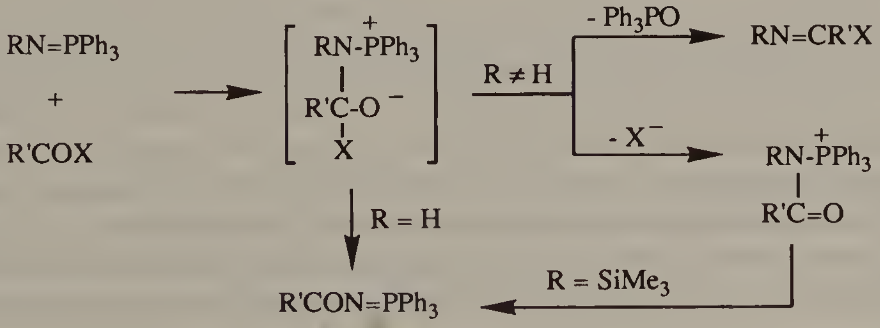
$$RX \xrightarrow[2.\ Ph_3P]{1.\ NaN_3} RN{=}PPh_3 \xrightarrow{R'X} RR'N\text{-}\overset{+}{P}Ph_3 \xrightarrow[-\ Ph_3PO]{^{-}OH} RR'NH \tag{13.51}$$



(13.52)

The only major complication in imine alkylations, other than dehydrohalogenation of the alkylating reagent, has been a few instances where conjugated imines, such as N-vinylic[101, 314] and N-cyano[315] imines, have undergone alkylation at the $\beta$-carbon rather than at the imine nitrogen.

*13.4.2.3* ***Acylation.*** Reaction of iminophosphoranes with acylating agents was discussed in Section 13.3.3. N-Substituted imines with acid halides, anhydrides, esters, amides, and imides invariably effected an Aza–Wittig reaction at the carbonyl group, through expulsion of triphenylphosphine oxide from the intermediate, rather than through anion explusion to form an amidophosphonium salt or subsequent product (Eq. 13.53, $R \neq H$). The only exception has been when the N substituent was trimethylsilyl, in which case the anion ($X^-$) attacked silicon leaving an N-acylated imine.[27, 224, 262]

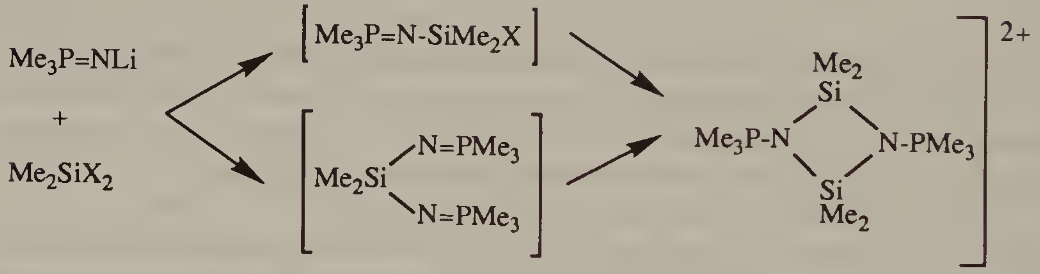


(13.53)

Normal acylation occurred with N-unsubstituted imines (Eq. 13.53, R = H) in their reaction with acid halides, anhydrides, and sulfonyl halides[76, 196, 234, 249, 250] to produce N-acylated or N-sulfonated imines. Cristau et al.[247] effected acylation of the anion of iminotriphenylphosphorane with esters, amides, and acid chlorides to produce the same compounds in good yield.

**13.4.2.4 *Reaction with Silicon Halides.*** Using their nucleophilic nitrogen, iminophosphoranes have reacted with a wide variety of compounds containing halide as a potential leaving group. Such reactions have been of use with the unsubstituted imine ($Ph_3P{=}NH$) as a means of attaching different substituents to nitrogen, and the same result has been accomplished using N-trimethylsilyl-iminophosphoranes in reactions in which the trimethylsilyl group was replaced. The imine anion produced with butyllithium ($Ph_3P{=}N^-Li^+$) also effected such substitutions. This section and the next three sections review such reactions; those with metallic halides are discussed in Section 13.4.4.

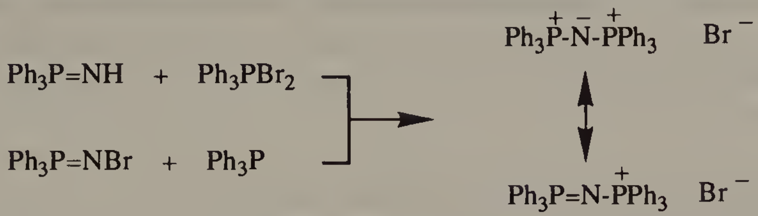
Imine anions, both with trialkylphosphonium[271, 316] and triphenylphosphonium[316] groups, reacted with trimethylsilyl halides to produce N-trimethylsilyliminophosphoranes. Use of dimethylsilyl dihalides afforded bis-imines[317] or halosilylimines,[318] which reacted further to form what appeared to be cyclic dimers, but instead were the result of intramolecular silylations (Eq. 13.54). Similar reactions occurred with germanyl and stannyl chlorides.[316, 319]



(13.54)

The N-trimethylsilyl group is important in that it has been found to be readily replaceable by other substituents, the trimethylsilyl group leaving under attack by various nucleophiles, including halide. It has been replaced by carbonyl,[27, 224] phosphorus (see below), sulfur (see below), hydrogen,[10, 271, 272, 317] and many metallic groups (see Section 13.4.4).

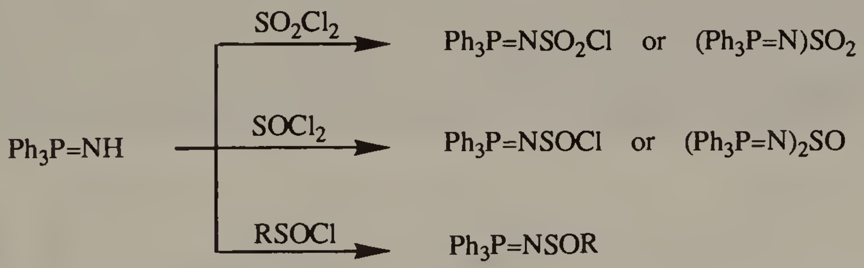
**13.4.2.5 *Reaction with Phosphorus Halides.*** The parent imine ($Ph_3P{=}NH$) reacted with chlorodiphenylphosphine to displace chlorine and produce N-(diphenylphosphino) iminotriphenylphosphorane.[250] Similarly, reaction with phosphorus trichloride[320] and phosphorus oxychloride[321] resulted in replacement of only a single chlorine and formation of a new phosphorus-containing imine. Reaction with triphenylphosphine dibromide afforded the important cation known as PNP (see Section 13.5.1.1) by essentially a simple substitution reaction, the same cation having been produced by quaternizing triphenylphosphine with N-bromoiminotriphenylphosphorane (Eq. 13.55).[196]



(13.55)

Reaction of N-trimethylsilylimine with $PCl_3$, $MePCl_2$, or $Me_2PCl$ resulted in replacement of all chlorines by imine groups to produce a series of tri-, di-, and monoiminophosphines.[322, 323] On the other hand, Noth et al.,[324] in an oral report, indicated that two equivalents of chlorodiphenylphosphine reacted with an N-trimethylsilylimine to afford the N,N-bis(diphenylphosphino)aminophosphonium salt. Bartsch et al.[325] found that two of three chlorines of $PCl_3$ were replaced by imines and that two of three fluorines of $Ph_2PF_3$, but two of four in $PhPF_4$, were replaced. Thus, the trimethylsilyl group of imines is readily replaced by phosphorus-containing groups, but it is difficult to predict how many new nitrogen–phosphorus bonds will be formed.

*13.4.2.6* ***Reaction with Sulfur Halides.*** Iminotriphenylphosphorane reacted with sulfuryl chloride with replacement of either one or both halides to produce N-sulfonated imines[326, 327] (Eq. 13.56). Use of thionyl chloride[327] also gave



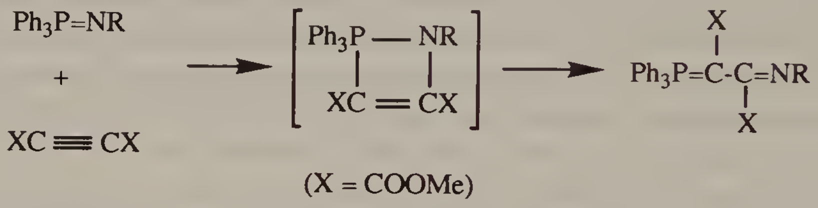
(13.56)

mono- or disubstituted imines, in both cases depending on the ratio of reactants, excess imine affording the disubstituted imines. Sulfinyl chlorides also were substituted, and the product could be oxidized to sulfonyl imines.[328, 329] The unsubstituted imine even reacted with sulfur dioxide, but in an Aza–Wittig reaction to produce N-sulfinylaniline.[180] Reaction of an N-trimethylsilylimine with sulfur trioxide initially afforded the trimethylsilyl sulfonate of the imine, but addition of unsubstituted imine displaced the siloxy group to afford a sulfonyl bis-imine.[330]

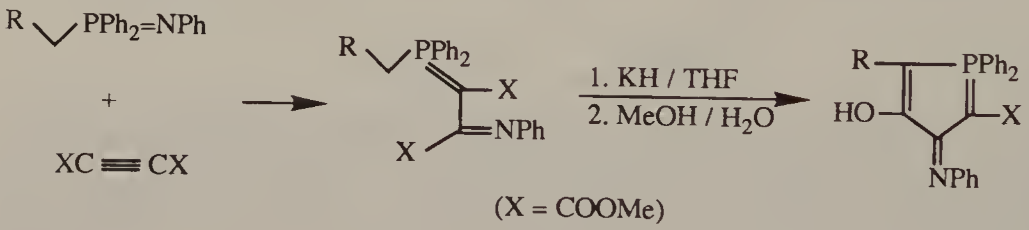
*13.4.2.7* ***Reaction with Miscellaneous Halides.*** N-Cyanoiminotriphenylphosphorane has been prepared by reaction of the unsubstituted imine with cyanogen bromide[249, 250] or phenyl cyanate.[249] Reaction of the N-trimethylsilyl imine with cyanogen chloride afforded the same product.[331] Reaction of N-substituted imines with nitrosyl chloride afforded diazonium salts and triphenylphosphine oxide.[273, 332] Benzene diazonium chloride phenylated the N-phenylimine on nitrogen.[333] Imines with or without N substituents formed complexes with boron compounds, including boranes,[334] boron trifluoride,[306, 335] and triphenylboron.[306]

### 13.4.3 Multiple-Bonded Compounds and Oxiranes

***13.4.3.1 Reaction with Alkynes.*** Brown et al.[30, 336, 337] found that iminophosphoranes reacted with dimethylacetylene dicarboxylate (DMAD) in a manner identical to that of phosphonium ylides (Section 7.1.2), inserting DMAD between the phosphorus and nitrogen to form a homologated imine that was a phosphonium ylide[338] (Eq. 13.57). The reaction was effective with the unsubstituted imine and with N-substituted imines provided the substituent was not too electron withdrawing, such as –COOEt. Replacement of the triphenylphosphonio group with the tris(dimethylamino) phosphonio group led to the same reaction, but again the N substituent could not be too electron withdrawing.[54] Barluenga et al. applied the addition reaction to the eventual synthesis of a 4-aza-1,1-diphenylphosphabenzene[339] and a $3H$-$\lambda^5$-phosphole[340] (Eq. 13.58). Similar addition of N-phenyliminotriphenylphosphorane to a propargyltriphenylphosphonium salt afforded a phosphonium ylide which, through two Wittig reactions, afforded a novel route to divinyl ketones, the original adduct being a synthon for the =CH–CO–CH= group.[341]



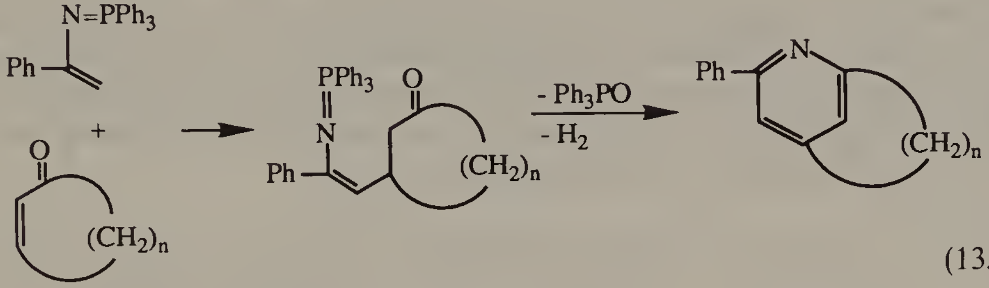
(13.57)



(13.58)

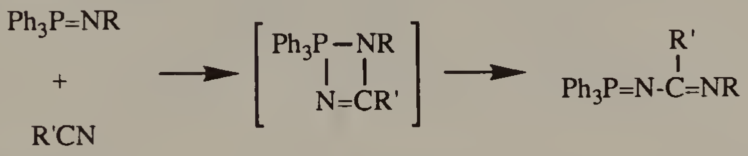
Two groups[314, 342] claimed that addition of N-vinylic imines with DMAD did not result in normal addition by the imine group. Instead a 1,2-addition was proposed between the vinylic group and DMAD, followed by ring opening to a diene. However, the latter group[342] did not publish any proof of structure, thereby not foreclosing an alternate structure resulting from "normal" imine addition.

*13.4.3.2* ***Reaction with Alkenes.*** Iminophosphoranes normally do not react with isolated alkenes and there has been only one reported reaction of an ordinary N-substituted imine with conjugated carbonyl compound.[343] It has been reported that N-vinylic imines effected conjugate addition to α,β-unsaturated ketones, with the nucleophilic attack originating with the β-carbon of the imine at the β-carbon of the conjugated ketone. In all cases the reaction was completed via a subsequent Aza–Wittig reaction and dehydrogenation to form a nitrogen-containing heterocycle. Thus N-vinyliminotriphenylphosphorane with vinylketones afforded pyridines[24] (Eq. 13.11). Nitta et al.[102,107,344–346] recently reported several examples of such additions, including formation of 1- and 5-azaazulene derivatives[105,107] (Eq. 13.12). Reaction of N-(1-phenylvinyl)-imine with cycloalkenones in the presence of a dehydrogenation agent afforded pyridinophanes[104] (Eq. 13.59).



(13.59)

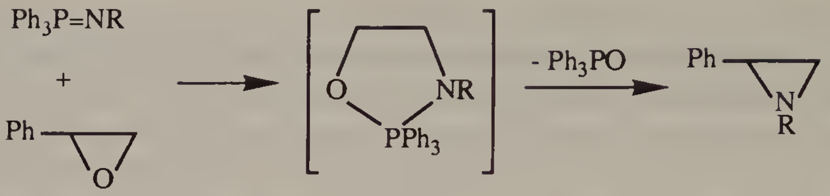
*13.4.3.3* ***Reaction with Nitriles.*** Iminophosphoranes, both with[347] and without[249,272] N substituents, reacted with nitriles carrying strong electron withdrawing groups (CN, $CF_3$, $CCl_3$) by adding across the triple bond and forming new imines (Eq. 13.60). A four-membered intermediate may have been



$$Ph_3P{=}NR + R'CN \longrightarrow \left[\begin{array}{c} Ph_3P-NR \\ |\quad\;\; | \\ N{=}CR' \end{array}\right] \longrightarrow Ph_3P{=}N{-}\overset{R'}{\overset{|}{C}}{=}NR \qquad (13.60)$$

involved as the nitrile inserted itself between the N and P atoms just as did the alkyne group of DMAD (see Section 13.4.3.1). Zbiral[303] probably was the first to observe this addition in the course of a very different reaction involving a thiocyanate group.

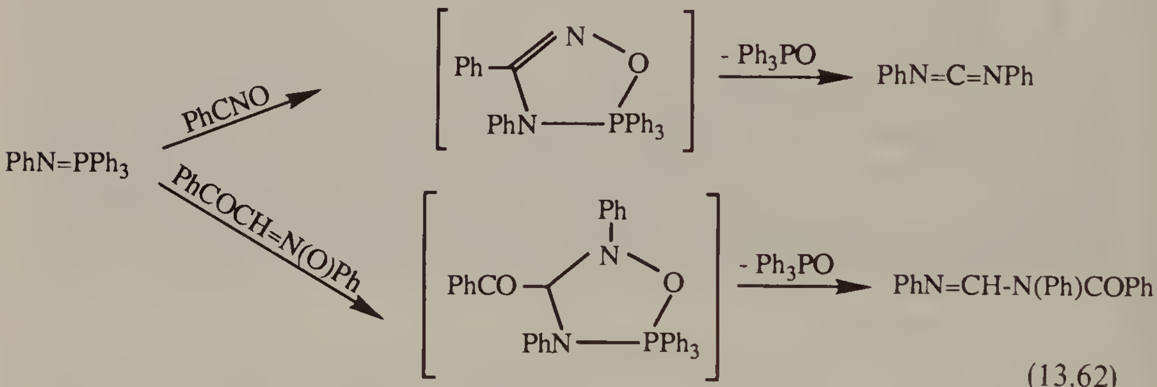
*13.4.3.4* ***Reaction with Oxiranes.*** Appel and Halstenberg[348] converted styrene oxide into 1-substituted-2-phenylaziridines by reaction with N-substituted iminotriphenylphosphoranes. The reaction probably involved nucleophilic ring opening at the terminal carbon of the oxirane ring by the imine, followed by formation of a phosphorane intermediate which ejected triphenylphosphine oxide (Eq. 13.61). The intermediate was isolated when using phenoxymethyloxirane.[348] Shortly thereafter Ittah et al.[286] effected a similar conversion of styrene



(13.61)

oxide to 2-phenylaziridine using sodium azide and triphenylphosphine, probably forming the imine in situ. Earlier they had found that the phosphoramidate analog of the imine reacted with styrene oxide also to form aziridines.[349] Katritzky et al.[313] recently prepared substituted aziridines using the reaction of oxiranes with imines.

*13.4.3.5* ***Reaction with 1,3-Dipoles.*** Huisgen and Wulff[350] reported the reaction of iminophosphoranes with nitrile oxides, nitrones, and nitrilimines. All three reactions appeared to proceed identically for the first step at least, with nucleophilic nitrogen adding to the positive end of the 1,3-dipolar compound, and a phosphorane intermediate probably being involved in the first two cases (Eq. 13.62). In the first two cases triphenylphosphine oxide was ejected and in the latter a betaine was isolated.



(13.62)

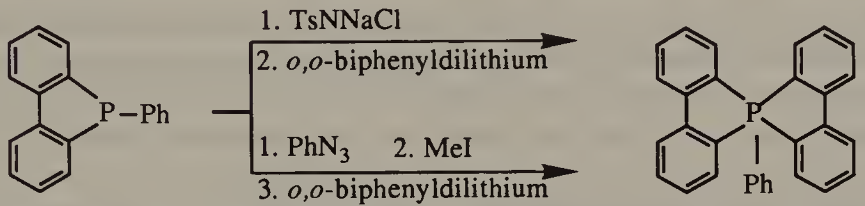
## 13.4.4 Metallic Compounds

*13.4.4.1* ***Reaction with Organolithiums.*** Iminotriphenyl- or trialkylphosphoranes, $R_3P{=}NH$, are deprotonated by organolithium reagents to form imine anions ($R_3P{=}N^-$),[316] strong nucleophiles which have been employed extensively to prepare various N-substituted imines. The lithium salt of the anion appeared to exist as a cyclic trimer.[247] Reaction with trimethylsilyl chloride, trimethylgermanyl chloride, and trimethylstannyl chloride[271,316,351] afforded the organometallic substituted imines (Eq. 13.63), some of which were not accessible by the Staudinger method. More recently, Cristau et al. have subjected the imine anion to acylation[247,352] and alkylation,[247,353,354] and subsequent hydrolysis of the alkylated imines afforded primary or secondary amines.

$$Ph_3P{=}NH \xrightarrow{BuLi} Ph_3P{=}NLi \xrightarrow{Me_3YCl} Ph_3P{=}N\text{-}YMe_3 \qquad (13.63)$$

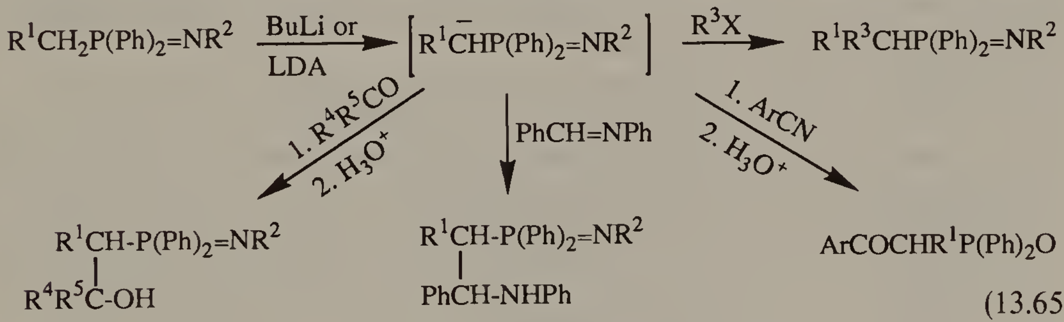
$$(Y = Si, Ge, Sn)$$

Wittig used N-tosyliminophosphoranes as precursors to pentaarylphosphoranes through reaction with aryllithiums, the imine group being expelled by the aryl anion. Pentaphenylphosphorane was prepared via this route,[355] but the same reaction was unsuccessful with the N-phenylimine.[308] However, when the N-phenylimine first was methylated to the aminophosphonium salt, the reaction with phenyllithium was successful.[356] Phenyl-bis-biphenylenephosphorane was prepared by both routes, from the N-tosylimine and from the aminophosphonium salt (Eq. 13.64).[308, 357] Stuckwish[358] found that N-phenyliminotriphenylphosphorane was deprotonated by phenyllithium at the ortho position of a P-phenyl ring.



(13.64)

N-Substituted imino(alkyl)diphenylphosphoranes were deprotonated with organolithium reagents, or with lithium amides, to form iminoylides which could be trapped in normal ylide-type reactions. Thus, the iminoylides were alkylated,[359, 360] acylated,[339] added to imines[213] and nitriles,[359] complexed with rhodium salts,[361] and reacted with aldehydes[362] and ketones[360] (Eq. 13.65). In the latter case, however, Wittig reactions did not occur, the initial betaine adduct instead being isolated as its conjugate acid or trapped as a silyl ether. Oxygen transfer to phosphorus as required for alkene formation did not occur, probably because of higher than normal electron density on phosphorus caused by the presence of the imine group. Interestingly, all of these reactions involved carbon as the nucleophilic center, rather than the also available imine nitrogen, undoubtedly reflecting differences in nucleophilicity.

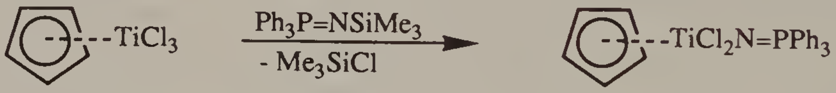


(13.65)

***13.4.4.2 Formation of N-Metalloiminotriphenylphosphoranes.*** Just as the anion of iminotriphenylphosphorane, prepared as described above, displaced halide from silicon, phosphorus, and sulfur to produce N-silyl, N-phosphinyl, and N-thio imines (see Sections 13.4.2.4–13.4.2.6), displacements also occurred with metallic halides. N-Germanyl and N-stannyl imines were prepared by this transmetallation process.[316, 351] However, this approach has not been successfully applied with transition metal halides. Dilworth et al.[363] were unable to obtain product using $CpTiCl_3$, but Cramer et al.[364] converted $Cp_3UCl$ to $Cp_3U(N{=}PPH_3)$ and $Cp_3ThCl$ to $Cp_3Th(NPPh_3)$. Interestingly, the P–N bond length was 1.612 Å, about normal for iminophosphoranes (see Section 13.2.1), but the U–N bond was very short (2.07 Å), leading to a proposal for considerable triple-bond character.

An alternate process for forming metal imides has been the reaction of metallic azides with phosphines in a Staudinger reaction.[32, 33] For example, azidopentachloroniobium and -tantalum with triphenylphosphine produced $Cl_5M{-}N{=}PPh_3$ (M = Nb or Ta).[365] However, N-trichlorotelluriumiminotriphenylphosphorane was not obtainable with azidotrichlorotellurium.[366]

The most widely used process for forming imine–metal bonds has been the well known (see Section 13.4.2.4) displacement of the trimethylsilyl group from N-trimethylsilyliminotriphenylphosphorane, but now using metal halides. An early report employed halodialkyl- or halodiarylboranes to produce N-diorganoboronyliminophosphoranes.[367] Use of $CpTiCl_3$ also was straightforward[363] (Eq. 13.66), whereas the transmetallation route had failed, and other



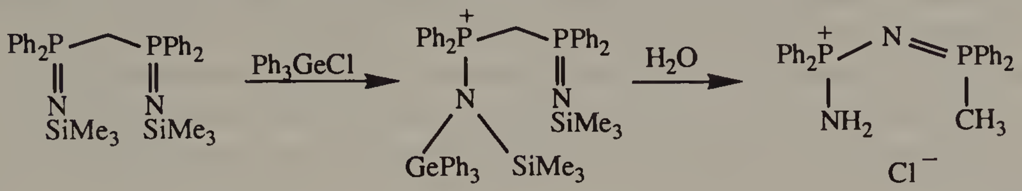
(13.66)

P-substituted imines reacted similarly with $CpTiCl_3$.[150, 368] The trimethylsilyl replacement reaction has been employed with numerous metal halides to produce N-metal imines as follows:

$VOCl_3 \rightarrow VOCl_2\ (N{=}PPh_2NS(O)Me_2)$[368]
$CpTaCl_4 \rightarrow CpTaCl_3(N{=}PPh_2NS(O)Me_2)$[368]
$Re_2O_7 \rightarrow ReO_3(N{=}PPh_3)$[369, 370]
$TcO_4 \rightarrow TcO_3(N{=}PPh_3)$[370]
$WF_6 \rightarrow WF_5(N{=}PPh_3)$[371]
$WF_5(NPPh_3) \rightarrow WF_4(N{=}PPh_3)_2$[371]
$WF_6 \rightarrow WF_4(N{=}PPh_2)_2FeCp_2$[372]
$WOCl_4 \rightarrow (WCl_3)_2(N_2PPh_2)_2$[373]
$OsO_4 \rightarrow OsO_2(OSiMe_3)_2(N{=}PPh_2)_2CH_2$[374]
$MoCl_6 \rightarrow MoCl_4(N{=}PPh_3)_2$[375, 376]
$TeCl_4 \rightarrow [TeCl_3(N{=}PPh_3)]_2$[377]

Dehnicke and Strahle have reviewed this chemistry recently.[378]

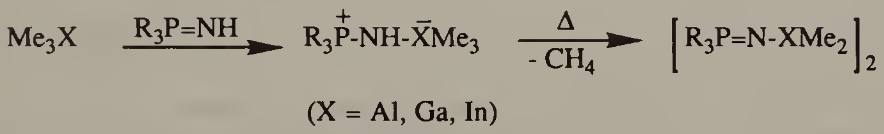
A recent example of this reaction used a bis-imine with triphenylgermanyl chloride, but resulted in the rearrangement of the product upon hydrolysis, probably via protonated N-unsubstituted bis-imine (Eq. 13.67).[379]



(13.67)

*13.4.4.3* ***Iminophosphorane–Metal Complexes.*** Iminophosphoranes form complexes with a wide variety of metal compounds, and some of this chemistry has been reviewed.[3] Noncarbonyl complexes are discussed first.

Imines formed donor–acceptor complexes with boron trifluoride and with triphenylboron.[306,335] The N-trimethylsilyl imine formed stable and isolable complexes with trimethylaluminum, -gallium, and -indium,[380] with triphenylaluminum,[381] and with tribromoaluminum.[382] The same reaction, but using the unsubstituted imine, afforded isolable complexes with trimethylaluminum, -gallium, and -indium, but on heating they evolved methane to afford dimers of $Me_2X–N{=}PPh_3$ (X = Al, Ga, In) (Eq. 13.68).[30,383]



$$\mathrm{Me_3X} \xrightarrow{\mathrm{R_3P{=}NH}} \mathrm{R_3\overset{+}{P}\text{-}NH\text{-}\overset{-}{X}Me_3} \xrightarrow[-\,\mathrm{CH_4}]{\Delta} \left[\mathrm{R_3P{=}N\text{-}XMe_2}\right]_2$$

(X = Al, Ga, In)

(13.68)

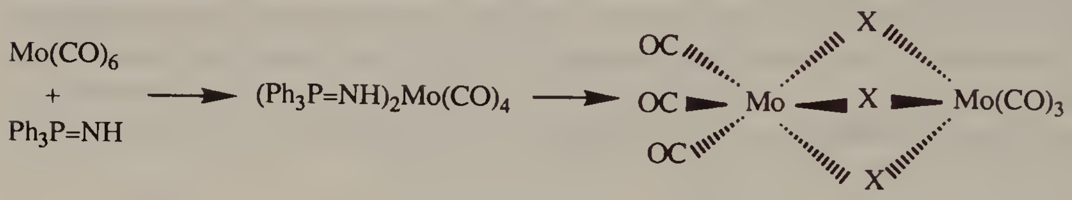
N-Unsubstituted imines (L) reacted with cadmium and mercuric dihalides to afford dimeric complexes tetrahedral about the metal, $MX_2L_2$.[384–386] Seidel reported that the same metal halides complexed with only one molecule of the N-phenyl imine.[387] The unsubstituted imine $Me_3P{=}NH$ reacted with dimethylzinc and dimethyl cadmium to probably initially form a complex which then eliminated methane, affording $MeX–N{=}PMe_3$ (X = Zn, Cd) as tetramers.[30]

The unsubstituted[388] and N-trimethylsilyl[389] imines (L) complexed with cupric chloride, the former as an $L_2CuCl_2$ monomer complex and the latter as an $LCuCl_2$ dimer with chloride bridging. A 1:1 monomeric complex was formed between $PhN{=}PPh_3$ and CuCl.[390] With N-phenyl imine and gold(I) iodide in toluene a complex between gold (II) iodide and the protonated imine $[(Ph_3P–NHPh)^+AuI_2^-]$ resulted by an unknown process.[391]

With nickel and cobalt dihalides, imines (L) formed monomeric complexes $L_2MCl_2$ containing tetrahedral metal atoms.[384,388] Platinum and palladium halides formed square planar complexes with imines, with the P–N bond lengths being longer than for iminophosphoranes in the former (1.64 Å),[392] but of normal length (1.60 Å)[220,393,394] in the latter complexes. With a bis-imine (L) rhodium formed a monomeric square planar complex $LRhCl_2$.[395]

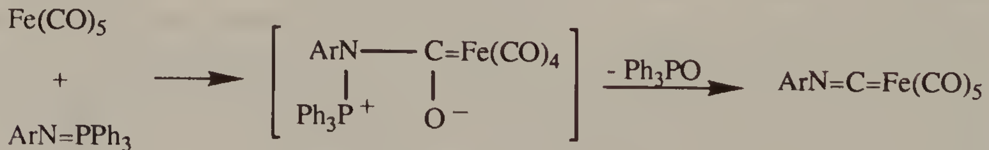
Interestingly, several complexes mentioned in the preceding paragraphs were formed with N-trimethylsilyl imines in which the trimethylsilyl group was not lost in the course of complex formation.[363, 393, 394] In other words the imines did not effect a nucleophilic displacement of halide from the metal, because the resulting halide would surely have attacked the $Me_3Si$ group, and instead simply served as a two-electron donor and filled the coordination shell of the metal.

A number of complexes have been formed by reaction between metal carbonyls and iminophosphoranes. N-Substituted and -unsubstituted imines (L) reacted with $Cr(CO)_5THF$,[171] $Mo(CO)_6$,[171, 396] $W(CO)_6$,[396, 397] and $W(CO)_5THF$[398] to form pentacarbonyls [e.g., $LCr(CO)_5$] in the case of chromium[171] and tungsten,[396] and tetracarbonyls [$L_2M(CO)_4$] in the case of molybdenum[171, 396] and tungsten.[396] In these structures the imine group simply replaced one or more CO groups with retention of the usual metal geometries. Further reaction led to the formation of $L_3$ complexes with Mo and Cr,[171] and heating of $L_2Mo(CO)_4$ produced the dinuclear octahedral complex $L_3Mo_2(CO)_6$ (Eq. 13.69).[396, 399] As mentioned earlier, a phosphazide has been shown to form a unique seven-coordinate complex with tungsten, $WBr_2(CO)_3(ArN{=}N{-}N{=}PPh_3)$.[49] Reaction of $Ph_3P{=}NH$ with $V(CO)_6$ resulted in a redox reaction to produce a tetracoordinate vanadium II cation, $V(HN{=}PPh_3)_4[V(CO)_6]_2$.[400]



X = $Ph_3P{=}NH$ (13.69)

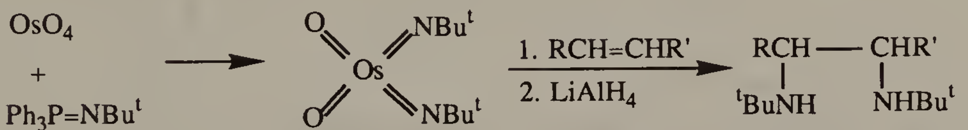
Reaction of imines with iron carbonyls have afforded two unusual reactions. The N-tolylimine did not displace CO in reaction with $Fe(CO)_5$, as had occurred with Cr, Mo, and W carbonyls, but instead the imine nitrogen attacked the CO group in an Aza–Wittig reaction, eliminating triphenylphosphine oxide and producing $Fe(CO)_4(CN\text{-tolyl})$ (Eq. 13.70).[221] Use of $Fe_2(CO)_9$ afforded a tricarbonyl with two isocyanide ligands, $Fe(CO)_3(CN\text{-tolyl})_2$. Reaction of the imine $(CF_3)_2P{-}N{=}PPh_3$ (L) with $Fe_2(CO)_9$ afforded a mixture of $LFe(CO)_4$ and $L_2Fe(CO)_3$ in which the iron retained its trigonal bipyramidal shape, but the ligand was bound through the tertiary phosphorus, not through the imine nitrogen.[401] Presumably the strong delocalization effects of the trifluoromethyl



(13.70)

groups diminished the electron density on nitrogen, and in fact the two P–N bond lengths were almost identical in the complexes (1.568 and 1.560 Å). Weinberger[88] reported complex formation between imines and Mo, Cr, and W carbonyls in which N substituents of the imines served as the coordination sites.

Imines have on occasion been found to react with the carbonyl groups of metal carbonyls in an Aza–Wittig reaction. Such was the case with $Fe(CO)_5$ (Eq. 13.70)[221] and also has been reported between $Cr(CO)_5THF$ and $Me_3P{=}NPh$.[171] Reaction of -ene complexes of $PdCl_2$ with two equivalents of $Ph_3P{=}NPh$ (L) in the presence of carbon monoxide resulted in a similar process, affording $LPdCl_2(CNPh)$.[220] Along a similar line an Aza–Wittig type reaction, rather than coordination, resulted when imines were treated with some metal oxy-complexes. By this means a rhenium–nitrogen bond was formed from $ReCl_3O(PPh_3)_2$ with elimination of triphenylphosphine oxide.[296, 402] Similarly, osmium tetroxide was converted to mono-,bis-, or tris-imine by one-to-three equivalents of N-*t*-butyl imine, and such products have found use as vicinal cis-diaminating reagents, much as $OsO_4$ has served as an hydroxylating reagent (Eq. 13.71).[403]



(13.71)

## 13.5 RELATED IMINOPHOSPHORANES

### 13.5.1 Bis-Iminophosphoranes

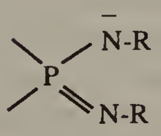
It is possible to incorporate more than one imine group in molecules and thereby create five different classes of bis-imines. These may be viewed as (1) derived from di-amines (**18**), (2) derived from di-phosphines (**19**), (3) iminoimines (**20**), (4) bis-iminoheteroatom compounds (**21**), and (5) N-triphenylphosphonio-iminotriphenylphosphorane (PNP) (**22**). Each of these will be discussed briefly with more attention paid to PNP in the next subsection. In general bis-imines of the first four classes exhibit chemistry characteristic of ordinary monoimines.

$Ph_3P{=}N{-}X{-}N{=}PPh_3$

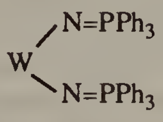
**18**

$RN{=}P(Ph)_2{-}Y{-}P(Ph)_2{=}NR$

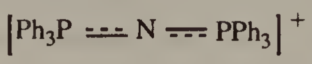
**19**



**20**

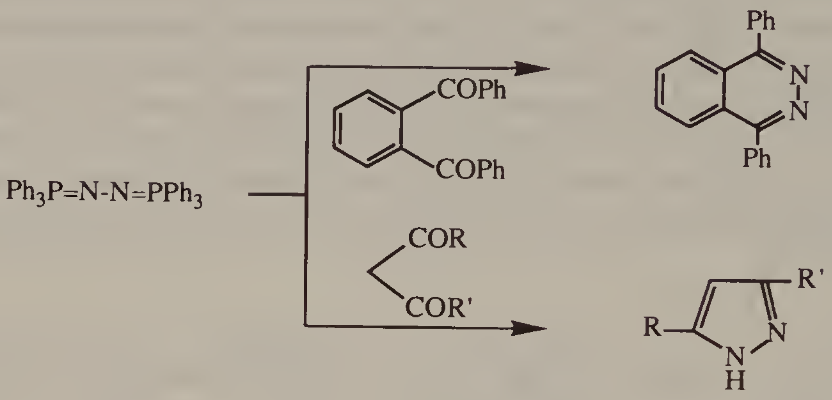


**21**



**22**

Many diamines ($H_2N$–X–$NH_2$) have been converted to the corresponding bis-imines (**18**) by standard synthetic processes (see Section 13.1). Two equivalents of triphenylphosphine dichloride reacted with hydrazine to afford, after deprotonation with sodium amide, the bis-imine $Ph_3P{=}N{-}N{=}PPh_3$.[194] It was stable under normal conditions, but dissociated to nitrogen and triphenylphosphine under heating. It reacted normally with alkylating agents and with aldehydes, the latter resulting in a bis-Aza–Wittig reaction.[404] With *o*-benzoylbenzophenone and with 1,3-ketones heteroaromatic compounds were formed (Eq. 13.72).[192,404] The imine derived formally from ethylenediamine,



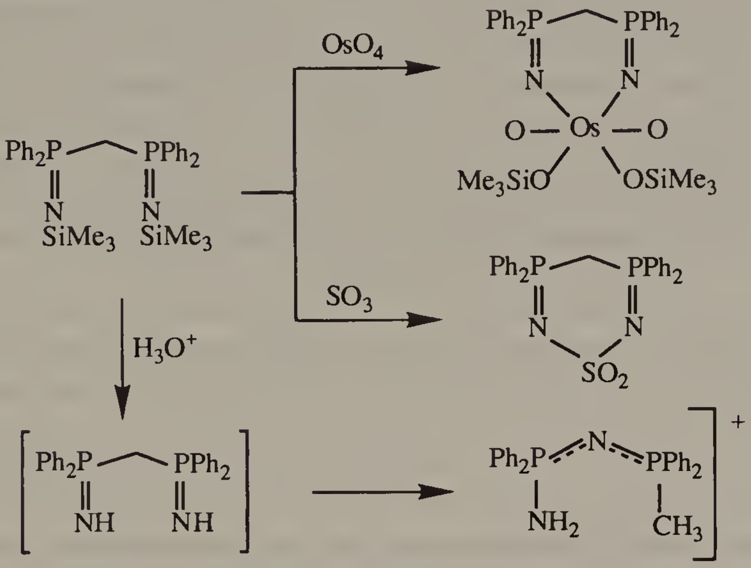
(13.72)

$Ph_3P{=}N\,(CH_2)_2N{=}PPh_3$, afforded a dihydropyrazine in reaction with benzil[192] and also found use as a bidentate ligand in reaction with Co, Ni, Hg, and Cd dihalides.[404] The imine from propane-1,3-diamine also has been isolated.[87]

Many bis-imines formally derived from aryl diamines have been prepared, usually from the aryl diazide and triphenylphosphine or from the diamine and triphenylphosphine dihalides, and many have been listed by Bestmann and Zimmerman.[405] Included were those derived from *o*-phenylenediamine,[55,57] *m*-phenylenediamine,[406] *p*-phenylenediamine,[57,407] 2,3-naphthylenediamine,[57] and 2,3-diamino-1,4-naphthoquinone.[55] N-Methyl-2,3-diazidomaleimide was converted to its corresponding bis-imine, whose structure has been determined.[391]

Diphosphines of general structure $Ph_2P$–Y–$PPh_2$ have been converted into bis-imines (**19**), usually by using an azide such as phenyl azide or trimethylsilyl azide. The simplest case with no Y group ($Ph_3SiN{=}PPh_2{-}Ph_2P{=}NSiPh_3$) has been known for many years.[408] Those with Y = *p*-phenylene[407] and Y = ferrocenyl[372] also have been obtained. However, with Y = *o*-phenylene or *cis*-ethenylene groups only a monoimine is known, while with Y = *trans*-ethenylene this bis-imine has been obtained[409].

Bis-imines have been prepared where Y = $(CH_2)_n$ and n = 1–4 (**19**). Bis(diphenylphosphino)methane (**19**, Y = $CH_2$) was converted to bis-N-arylimines,[410,411] to bis-N-trimethylsilylimines,[412] and with dimethyldiazidosilane to the 3,5-diphospha-2,6-diazasilacyclohexane derivatives.[412] The structures of the N-aryl bis-imines have been determined.[411] There were no significant differences in the P–N bond lengths or the angles about P and N between the two imine groups. The bis-imines underwent mono- or dimethylation,[191] would hydrolyze only at one P–N bond,[411] and reacted with two equivalents of carbonyl compound or carbon dioxide in Aza–Wittig reactions.[191,411] The N-trimethylsilyl bis-imines served as bidentate ligands with rhodium dicarbonyl dichloride,[395] sulfur trioxide,[330] and osmium tetroxide[374] (Eq. 13.73). In reactions involving hydrochloric acid, a skeletal rearrangement of the bis-N-silylimines occurred, converting a P–C–P system to a P–N–P system [379,412,413] (Eq. 13.73).

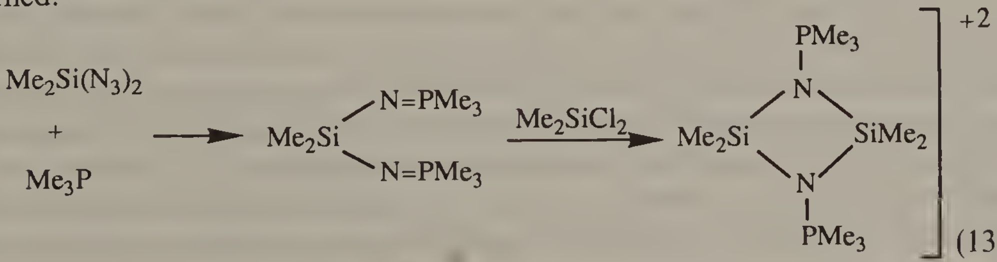


(13.73)

Bis-imines [**19**, $Y = (CH_2)_n$] where n = 2–4 also have been prepared.[87,331,412,413] Their chemistry appeared unexceptional with alkylation, hydrolysis, and protonation reactions reported.

Iminoimines (**20**), also called diazadiylides, are counterparts of bis-ylides (see Section 3.4.4) and iminóylides (see Section 13.4.4.1). They have been prepared as reactive intermediates in solution[414] and also have been isolated as dimeric lithium salts.[354,415] These dianions underwent mono- and bis-alkylation with group IV mono- and dihalides (Si, Ge, Sn),[319,416] and with tosylates.[354]

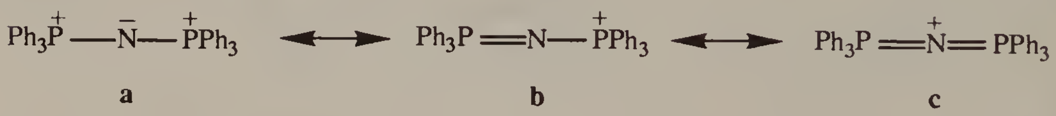
Many compounds with two triphenylphosphoranylimino groups attached to a heteroatom have been prepared (**21**). The connecting heteroatom groups represented by W have included sulfonyl,[327,417] methylphosphinyl,[322] $WF_4$,[371] $MoCl_4$,[375,376] diphenylsilyl,[418] and dimethylsilyl.[317] The latter bis-imine was silylated with dimethyldichlorosilane to effect closure of a four-membered ring (Eq. 13.74).[317] Where W = PhN or MeN only monoimines could be obtained.[409]



(13.74)

*13.5.1.1 N-Triphenylphosphonioiminotriphenylphosphorane (PNP).* The PNP cation (**22**) has the advantageous property of forming readily isolable salts of complex anions which also are soluble in organic solvents, making them widely useful in inorganic chemistry. Appel et al. first prepared PNP, also called bis(triphenylphosphine)iminium cation,[3] by brominating iminotriphenylphosphorane, and reacting the resulting N-bromoimine with triphenylphosphine.[301] Later the unsubstituted imine was found to react with triphenylphosphine dibromide,[196] or with nitrogen trichloride,[410] to afford the same cation. Heating aminotriphenylphosphonium azide,[77,420] or reacting triphenylphosphine dibromide with ammonia in the presence of triethylamine[234] also produced the cation. The two best syntheses seem to be $Ph_3PCl_2 + Ph_3P + H_2NOH{\cdot}HCl$[421] for large scale and $Br_2 + Ph_3P + H_2NOH{\cdot}HCl$[422] for smaller scale production of the PNP cation.

At least three major resonance contributing forms can be drawn for PNP (**23**). Swartz et al.[168] favored the totally polarized form (**23a**) on the basis of ESCA



$$\underset{\textbf{a}}{\mathrm{Ph_3\overset{+}{P}{-}\overset{-}{N}{-}\overset{+}{P}Ph_3}} \longleftrightarrow \underset{\textbf{b}}{\mathrm{Ph_3P{=}N{-}\overset{+}{P}Ph_3}} \longleftrightarrow \underset{\textbf{c}}{\mathrm{Ph_3P{=}\overset{+}{N}{=}PPh_3}}$$

**23**

studies which revealed the nitrogen having the lowest electron binding energy then known, and therefore with a higher electron density even than azide ion, and phosphorus with a very high binding energy, indicating a large positive charge on the equivalent phosphorus atoms.

X-Ray crystallographic analyses have been reported for a large number of PNP salts, including metal complexes of iron,[423–425] chromium,[426,427] molybdenum,[426–429] and tungsten.[397,428] The chloride salt of the PNP–boric acid complex,[430] the iodide salt of a PNP–TCNQ complex,[431] and the chloride salt of $Ph_2(NH_2)P{=}N{-}P(CH_3)Ph_2$ cation[379] also have been studied. In all of these instances the P–N bond distances fell within the very narrow range of 1.56–1.59 Å, and the molecules were bent at nitrogen, the P–N–P angles falling within the range of 134–143°. Of all the PNP complexes studied, only three differed from the generalizations made above regarding the P–N–P bond angle and the P–N bond length, and in those three instances the P–N bond was shorter (1.53–1.55 Å) and the P–N–P bond was approximately linear. These occurred in complexes of nickel,[432] gold,[433] and vanadium.[124] In one molybdenum carbonyl cluster ion there were two PNP cations, one bent and one linear. In all of these cases it appeared that the linear P–N–P bonds uniformly were the shortest. It was concluded that the energy difference between the linear and bent forms of PNP was not great. Glidewell[434] applied second order Jahn–Teller effect calculations to predicting bent versus linear structures, concluding that the relative atomic orbital binding energies of P and N were so close that structural effects could dictate the geometry. On the basis of contributing structure **23a**, it was predicted that more electronegative substituents on phosphorus should lead to more tightly-bound 3*p* electrons, and therefore a bent geometry.

### 13.5.2 Phosphazines

Phosphazines, also called phosphinazines ($RR'C{=}N{-}N{=}PR''_3$), could be considered simply as iminophosphoranes carrying a conjugating imino group, similar to N-vinyliminophosphoranes, and with the possibility of nucleophilicity being exhibited at the positions $\alpha$ and $\gamma$ to the phosphorus atom (see Section 13.1.5.1). However, most of their chemistry is identical to that of iminophosphoranes, the conjugated $N{=}CR_2$ group having virtually no effect. A large number of phosphazines have been tabulated by Bestmann and Zimmerman.[405]

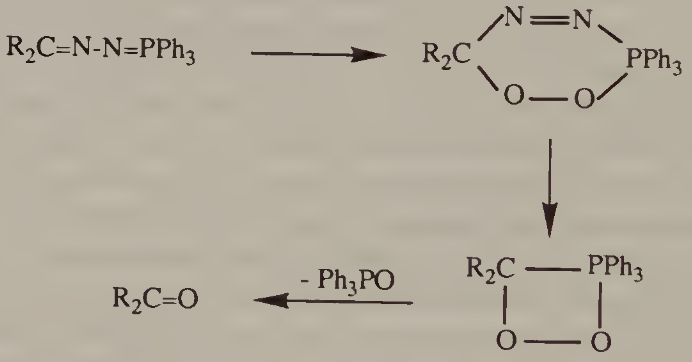
The most widely used synthesis of phosphazines has been 1:1 adduct formation between diazo compounds and triphenylphosphine. First discovered by Staudinger et al.[435,436] with diazofluorene, diphenyldiazomethane, diazomalonic ester, and diazoacetic ester, this high yield reaction since has been expanded to include diazocyclopentadienes,[437,438] diazoketones,[439] diazomethane,[440] and a variety of other diazomethanes usually carrying stabilizing groups.[441–443] On rare occasions other phosphines have been employed, such as trialkylphosphines,[435] trisaminophosphines (e.g., dimethylamino,[444] morpholino[445]), and trialkylphosphites.[445] Two kinetic studies on the reaction have been completed,[446,447] showing it to be first order in each reactant with relatively small ranges of reactivities resulting from structural variation and solvent changes. Electron donating phosphorus substituents enhanced the reaction rate,[446] and in substituted diphenyldiazomethanes the rate was enhanced, though by less than a factor of 10, by both electron withdrawing and electron donating substituents.[447] Energies of activation were 11–14 kcal/mol and entropies of activation were $-29$ to $-34$ cal/deg/mol.[447] Earlier workers[446] concluded the reaction involved nucleophilic attack of phosphine on the terminal nitrogen as for the Staudinger reaction. Later workers[447] unsuccessfully attempted to explain the reaction using a biphilic mechanism.

Phosphazines also have been prepared from hydrazones by two different routes. The first involved oxidation of the hydrazones to diazo compounds, which then were reacted as above with phosphines. Hypochlorite[448] and lead tetraacetate[449,450] have been used as oxidants. The second involved reaction with triphenylphosphine dibromide,[451] a variant of the Kirsanov reaction with amines (see Section 13.1.2). Alternatively, phosphine dibromide has been reacted first with hydrazine and then with sodium amide to afford the N-aminoiminophosphorane, which then was reacted with carbonyl compounds in a hydrazone-forming reaction, the end result being a phosphazine.[60,452]

The ultraviolet and infrared spectra,[453,454] as well as dipole moments,[453] of a variety of diarylphosphazines have been reported. The major electronic transition was $\pi$–$\pi^*$. The large dipole moments (3–9 D) and the effect of substituents on both ends of the $P{=}N{-}N{=}C$ conjugated system indicated considerable polarization along the conjugated system, the carbon being the negative end, and substituent interaction with the conjugated system was more effective from the carbon end than from the phosphorus end. The $^{31}P$ NMR peaks for phosphazines were at about 20 ppm, the same region as for iminophosphoranes, as would be expected,[142,444] with very small variations with the nature of carbon substituents. Protonation or methylation of phosphazines apparently occurred on the nitrogen adjacent to phosphorus since the $^{31}P$ peak then was shifted about 25 ppm downfield. The $^{13}C$ NMR peaks were nearly identical for the $CH_2$ groups of $Ph_3P{=}N{-}N{=}CH_2$ and $Ph_3P^+{-}N(CH_3)N{=}CH_2$, indicating little delocalization of negative charge to the $CH_2$ group of the former.[155]

Phosphazines generally are thermally stable. The original observation that diphenylmethylenetriphenylphosphorane was formed by loss of nitrogen from the corresponding azine by heating[7] spurred interest in phosphazines as possible precursors to ylides. However, this reaction failed with virtually all other phosphazines.[436,437,444,455] The dissociation of a phosphazine to reactants (phosphine and diazo compound) in solution has been demonstrated by $^{31}P$ NMR spectroscopy,[142] by a $^{14}C$ labelling experiment,[456] by ESR spectroscopy,[457] and by actual isolation of a diazo compound.[458]

Phosphazines have been photolyzed in the presence of oxygen to extrude nitrogen and form triphenylphosphine oxide and a ketone,[459] but in the absence of oxygen dimers of the carbon entity resulted.[457] Chemiluminescent highly shielded oxaphosphorane intermediates have been detected, believed to be formed from singlet oxygen[460,461] (Eq. 13.75). Thermal reaction with sulfur or selenium converted phosphazines into thio- or selenocarbonyls and phosphine sulfides or selenides.[462]

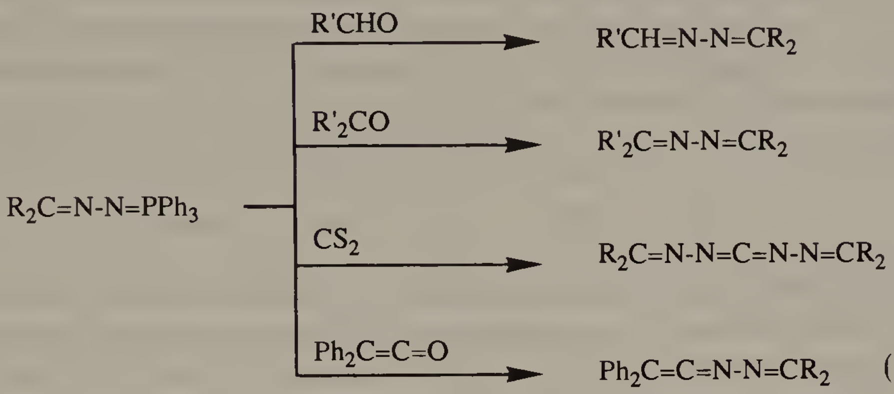


(13.75)

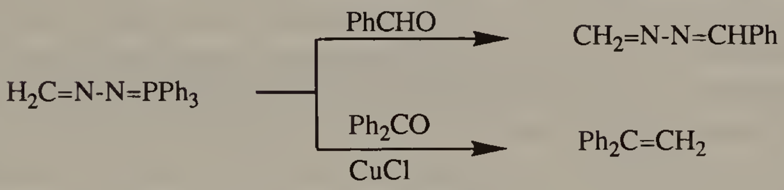
Phosphazines are stable in aqueous media, but have been hydrolyzed in acid or base solution to hydrazones and phosphine oxides,[435,436,439,444,463] similar to the hydrolysis reaction of iminophosphoranes (see Section 13.4.1.1). However, highly stabilized phosphazines, such as that from diazocyclopentadiene,[437] were inert to hydrolysis.

Phosphazines were protonated by mineral acids on the nitrogen adjacent to phosphorus, there being no evidence for conjugate protonation on carbon.[142,435,444,456] Likewise, alkylation of phosphazines occurred on nitrogen,[445] and not on carbon, as evidenced by $^{31}P$ and proton NMR spectra,[63,142,464] and hydrolysis to N-alkylhydrazones.[456] In a few instances, methylation of phosphazines afforded methylphosphonium salts resulting from dissociation of phosphazine to phosphine which then was quaternized.[439,456] *p*-Benzoquinotriphenylphosphazine was protonated on oxygen rather than nitrogen, thereby enabling aromatization of the ring.[465,466]

Phosphazines reacted with aldehydes,[451] ketones,[451] ketenes,[451] and carbon disulfide[467] in a manner analogous to iminophosphoranes (Aza–Wittig reaction), eliminating triphenylphosphine oxide or sulfide, and producing bisketenimines (Eq. 13.76). Wittig and Schlosser[440] found that in the presence of cuprous chloride a phosphazine and ketone produced an alkene, nitrogen having been lost perhaps to first form the ylide which then reacted with the ketone (Eq. 13.77). Nitrosobenzene and benzophenone phosphazine afforded benzophenone anil, probably also by initial transformation of phosphazine to ylide.[468]

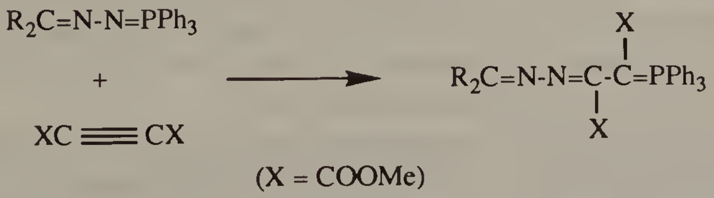


(13.76)



(13.77)

Phosphazines reacted with alkynes exactly as did iminophosphoranes (Section 13.4.3.1), the P=N group adding across the triple bond to afford ylides [463,469] (Eq. 13.78). In a similar manner phosphazines added across the triple bond of cyanogen and trifluoroacetonitrile,[347] as had iminophosphoranes.



$$R_2C=N\text{-}N=PPh_3 + XC\equiv CX \longrightarrow R_2C=N\text{-}N=\underset{\displaystyle X}{\underset{|}{C}}\text{-}\overset{\displaystyle X}{\overset{|}{C}}=PPh_3 \qquad (X = COOMe) \tag{13.78}$$

For all of the reactions listed above for phosphazines in which there was the possibility of nucleophilicity being exhibited at the conjugated carbon site, the reaction site instead was the nitrogen atom. In this respect phosphazines were different than vinyl-conjugated iminophosphoranes which exhibited some reactivity at the conjugated site (see Section 13.1.5.1).

### 13.5.3 P-Halo Iminophosphoranes

Although most iminophosphorane chemistry has involved alkyl- and arylphosphonio groups, imines have been prepared with one or more halogens on phosphorus. The most common have been those with the $=PCl_3$ group, but those with $=PBr_3$ and $=PF_3$ groups also have been prepared, as have those containing only one or two halogens.

P,P,P-Trichloroiminophosphoranes have been prepared directly by heating amines or amides with $PCl_5$, a variant of the Kirsanov reaction (see Section 13.1.2), examples including arylamines,[470–474] methylamine,[475,476] benzylamine,[477,478] alkylamines,[472,478,479] acylamides,[480] sulfonamides,[64,481] and amino acids[482,483] (Eq. 13.79). In a similar manner $Ph_2PCl_3$ reacted with

$$RNH_2 + PCl_5 \longrightarrow RN{=}PCl_3 \qquad (13.79)$$

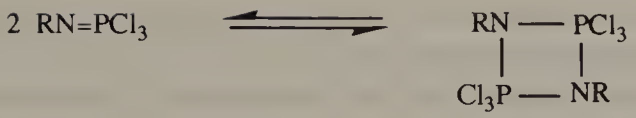
arylamines[484,485] and sulfonamides,[485–487] and $PhPCl_4$ reacted with arylamines,[488] alkylamines,[489] and sulfonamides.[490] On rare occasions groups other than phenyl were on phosphorus along with the chlorines.[489,491]

The alternate means of preparing P-haloimines was to employ the Staudinger reaction (see Section 13.1.1) with halophosphines. Thus, phenyl azide reacted with phosphorus trichloride,[492] dichlorophenylphosphine,[492] and chlorodiphenylphosphine[492,493] to produce the corresponding N-phenylimino-P-chlorophosphoranes (Eq. 13.80). The latter two phosphines also produced isolable imines with hydrazoic acid, but with $PCl_3$ only polymer was obtained, perhaps from $HN{=}PCl_3$.[492] The Staudinger reaction recently was employed as a means of obtaining P-fluoro imines, substituted phenyl azides being reacted with monofluorophosphines ($R_2PF$) and difluorophosphines ($RPF_2$) with R = alkyl, aryl, alkoxy, and dialkylamino[494,495] (Eq. 13.80). Phosphorus trifluoride would not form imines by this route.

$$R_nPX_{3\text{-}n} + ArN_3 \longrightarrow ArN{=}PR_nX_{3\text{-}n} \qquad (13.80)$$

The displacement of the trimethylsilyl group from amines by phosphorus-bound halogen has been employed to prepare P-haloimines,[496] including $F_3P{=}NMe$ (as a dimer).[497] Reaction of $PBr_3$ with chloramine-T produced N-tosylimino-P,P,P-tribromophosphorane.[498]

A unique feature of some P-haloiminophosphoranes is their ability to dimerize to diazadiphosphetidines (Eq. 13.81). It has become clear that dimerization is influenced by electronic and steric factors.[499,500] The presence of strong electron withdrawing groups on phosphorus and electron donating groups on nitrogen resulted in only the dimeric forms being known. Increasing the steric



(13.81)

requirements around nitrogen inhibited dimerization,[473, 478] Table 13.6 reports examples of related imines, some of which were dimeric, some monomeric, and some in which both forms existed in solution. It can be seen that most trichloro and all trifluoro derivatives were dimeric, and that gradual replacement of halogen with other groups, or the attachment of electron withdrawing groups on the imino nitrogen, resulted in a shift to the monomeric form. As an example, N-phenyliminotrichlorophosphorane was a dimer, whereas the N-(2,4-dinitrophenyl)imino analog was a monomer.[470] Similarly, trifluoro imines all were dimeric, whereas monofluoro imines all were monomeric.[494]

X-Ray crystallographic analyses have been completed for five P-haloimines, with four being dimeric and having the diazadiphosphetidine structure: $(Cl_3P{=}NMe)_2$;[501, 502] $(F_3P{=}NMe)_2$;[503] $(F_2PhP{=}NMe)_2$;[504, 505] $(F_2(CCl_3)P{=}NMe)_2$.[506] The fifth imine examined, $FPh_2P{=}NMe$, existed in a monomeric monoclinic form[507] and in a dimeric triclinic form.[508] All of the dimeric forms had nearly planar rings, approximately trigonal bipyramidal phosphorus, internal angles at phosphorus of about 80°, internal angles at nitrogen of about 100°, axial P–N bonds of about 1.73 Å, and equatorial P–N bonds of about 1.63 Å, and generally were centrosymmetric. The single monomeric example had a

**TABLE 13.6 Monomeric and Dimeric P-Haloiminophosphoranes**[a]

| Monomeric | Both | Dimeric |
|---|---|---|
| | **$Cl_3P$ Imines** | |
| $Cl_3P{=}NCH_2Bu^t$ (478) | $Cl_3P{=}NC_6H_4X$ (470, 472, 473, 474) | $Cl_3P{=}NMe$ (476, 501, 502) |
| $Cl_3P{=}NCOR$ (480) | | $Cl_3P{=}N$-alkyl (472, 479) |
| $Cl_3P{=}NSO_2Ph$ (481) | | $Cl_3P{=}N\text{-}CH_2C_6H_5$ (477, 478) |
| | | $Cl_3P{=}N(CH_2)_2\ Bu^t$ (478) |
| | **$Cl_nR_{3-n}P$ Imines** | |
| $Cl(Ph)_2P{=}NC_6H_5$ (474) | $Cl(o\text{-}C_6H_4O_2)P{=}NC_6H_5$ (509) | |
| $Cl_2(Ph)P{=}NC_6H_5$ (474, 488, 572) | | |
| | **$F_nR_{3-n}P$ Imines** | |
| $F(Ph)_2P{=}NC_6H_5$ (494, 495, 497) | $F(Ph)_2P{=}NMe$ (507, 508) | $F_3P{=}NMe$ (503) |
| | $FR_2P{=}NC_6H_4X$ (494, 495) | $F_2PhP{=}NMe$ (497, 504, 505) |
| | | $F_2(Cl_3C)P{=}NMe$ (506) |

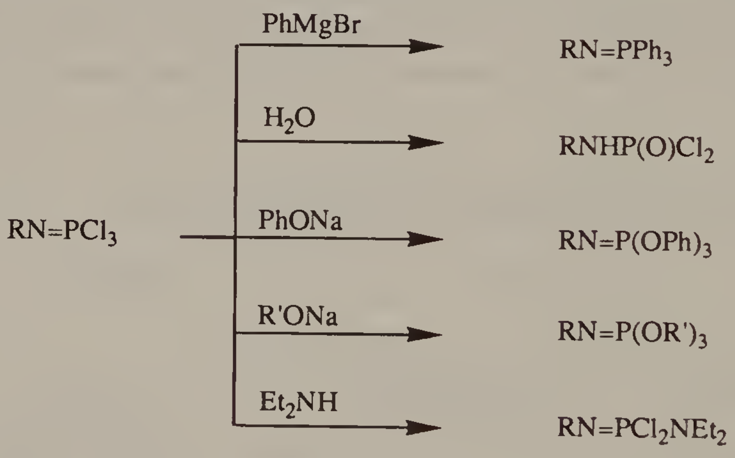
[a] Reference numbers are given in parentheses.

slightly longer than usual P=N bond (1.64 Å), a nitrogen bond angle of 119°, and a tetrahedral phosphorus atom.[507]

$^{31}$P NMR spectroscopy has been employed to detect the presence and determine the concentrations of dimeric and monomeric forms of P-haloimines in solution, the dimeric forms absorbing at higher fields. For example, for a series of imines $ArN=PCl_3$, the monomer peaks were at $-30$ to $-50$ ppm, but the dimer peaks were at $-72$ to $-86$ ppm.[473,474,509] For $ClPh_2P=NPh$ the monomer peak was at $+14$ ppm and the dimer peak was at $-22.3$ ppm.[510] Similarly, for the P-fluoro imines the monomer peaks were in the region $+47$ to $-17$ ppm and the dimer peaks were from $-48$ to $-78$ ppm.[494,495,511]

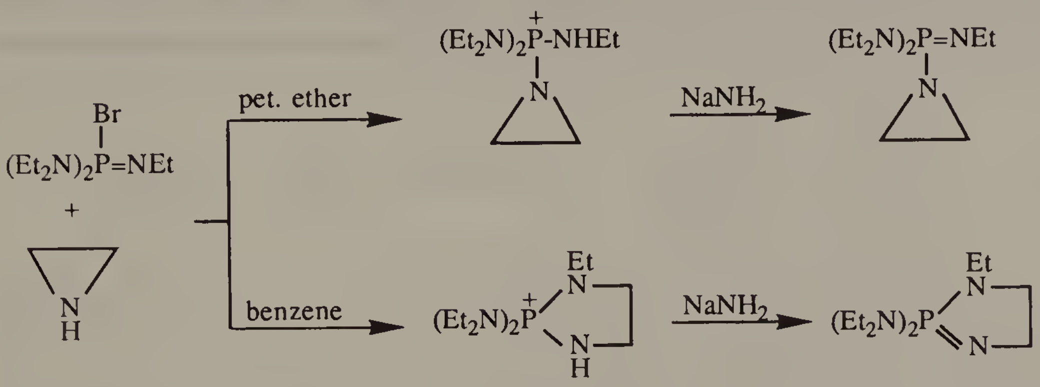
The P–N bond dissociation energies have been calculated for monomeric iminophosphoranes ($Ph_3P=NEt = 126$ kcal/mol; $Me_3P=NEt = 97$ kcal/mol)[173] and for a single dimeric iminophosphorane [$(Cl_3P=NMe)_2 = 74$ kcal/mol],[476] but the differences may not be significant in view of the major structural discontinuities. Heating dimeric forms of the P-haloimines usually increased the dissociation to monomer[474,512] and permitted subsequent reactions.

The halogens in P,P,P-trichloroimines are reactive and susceptible to displacement by nucleophiles (Eq. 13.82). Similar reactions occurred when one or two chlorines were present on phosphorus, as often has been the case with P-halocyclophosphazines (P-halophosphonitriles).[2] Water displaced one chloride followed by prototropy to produce a phosphoramide[493,513,514] and methanol did likewise.[514,515] Alkoxides[516–518] and phenoxides[519] also displaced chloride, producing phosphiteimines (see Section 13.5.4), a reaction that also has been employed with P-chloropolyphosphazines.[520] Phenyl Grignard reagent converted P,P,P-trichloroimines into iminotriphenylphosphoranes.[66] Azide also displaced chloride, with the product then being used in a Staudinger reaction to produce a bis-imine.[485]

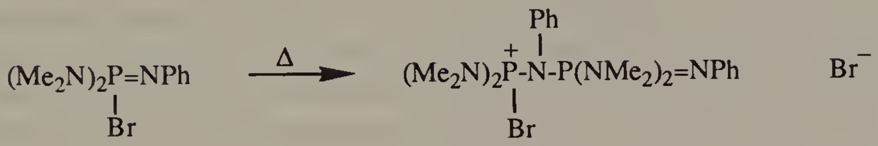


(13.82)

Amines also displaced chloride, with the reaction being controllable to effect stepwise mono-,[115,138,489,498,521,522] di-,[521–523] or in some cases, trisubstitution.[522] In an interesting reaction with aziridine, a P-monobromo imine underwent simple displacement in petroleum ether solvent, but a ring opening occurred in benzene solution providing access to diazaphospholines[115] (Eq. 13.83). Marchenko et al.[524] recently reported that a P-monobromo imine would effect an intermolecular displacement, a kind of "acyclic dimerization," which was suggested as a possible first step toward full dimerization (Eq. 13.84).

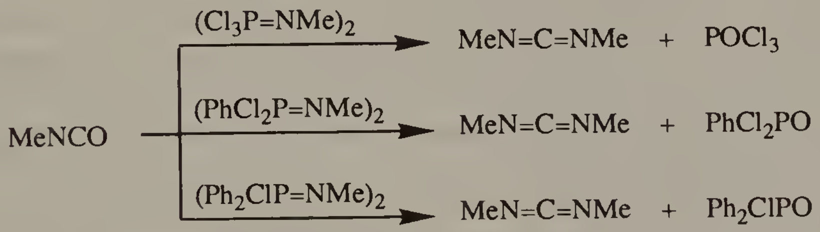


(13.83)



$$(Me_2N)_2P(Br){=}NPh \xrightarrow{\Delta} (Me_2N)_2\overset{+}{P}(Br)\text{-}N(Ph)\text{-}P(NMe_2)_2{=}NPh \quad Br^- \qquad (13.84)$$

A few examples of Aza–Wittig reactions have been reported using P-halo imines. N-Methyl-P-haloimines carrying one, two, or three chlorines reacted with methyl isocyanate to afford the carbodiimide and the expected phosphoryl chloride[230, 512] (Eq. 13.85). Reaction also was reported with carbon dioxide and



$$MeNCO \xrightarrow{(Cl_3P{=}NMe)_2} MeN{=}C{=}NMe + POCl_3$$
$$MeNCO \xrightarrow{(PhCl_2P{=}NMe)_2} MeN{=}C{=}NMe + PhCl_2PO \qquad (13.85)$$
$$MeNCO \xrightarrow{(Ph_2ClP{=}NMe)_2} MeN{=}C{=}NMe + Ph_2ClPO$$

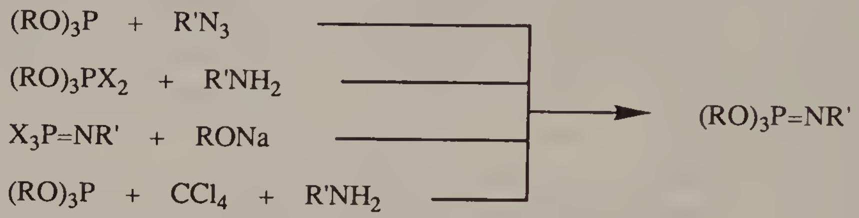
carbon disulfide, both stopping at the isocyanate stage.[512] Several instances have been reported of N-acylimino P-haloimines undergoing thermal elimination of a chlorophosphoryl entity to afford nitriles, in effect an intramolecular Aza–Wittig reaction of the enolate form of the imine[477, 491, 525] (see also Section 13.4.1.5).

### 13.5.4 Phosphiteimines

Phosphiteimines [$(RO)_3P{=}NR'$], also called phosphorimidates (derivatives of imidophosphoric acid $(HO)_3P{=}NH$) or iminotrialkoxyphosphoranes, occasionally have been used in place of iminotriphenylphosphoranes [$R_3P{=}NR'$]

because of the ready and economic availability of phosphites to replace phosphines as starting materials. Related compounds in which there were one or two alkoxy groups on phosphorus also have been prepared, but have found no unique synthetic use.

Phosphiteimines first were prepared in excellent yield by the Staudinger reaction of phosphites with azides[526] (Eq. 13.86), and this procedure remains the



(13.86)

method of choice.[527–529] Trimethyl and triethyl phosphite have been most widely employed[276], but triphenylphosphite[528, 529] other alkylphosphites,[530] thiophosphites,[530, 531] cyclic phosphites,[44, 532] and bicyclic phosphites[533] also have been used. The reaction was second order, with rates increased by nucleophilic phosphites and electrophilic azides.[44, 532] The reactivity sequences generally were alkyl phosphites > aryl phosphites; phosphites > thiophosphites; acyclic phosphites > bicyclic phosphites. Azides employed included hydrazoic acid,[534] alkyl azides,[527, 529] aryl azides,[44, 526, 527, 532] trimethylsilyl azide,[533, 535] sulfonyl azides,[528, 530, 531] phosphonyl azides,[533, 536] and acyl azides.[528, 533]

Phosphiteimines also have been prepared by the Kirsanov reaction of phosphite dihalides with amines[537, 538] (Eq. 13.86). Imino-P,P,P-trihalophosphoranes were converted into phosphiteimines using alkoxides[516, 517] or phenoxides [520] (Eq. 13.86), although the process occasionally was incomplete[515] or failed altogether.[539] The Atherton–Todd reaction[86] between a phosphite, $CCl_4$, and an amine also afforded phosphiteimines[540, 541] (Eq. 13.86). A single report exists of a reaction between aromatic nitro compounds and phosphites to afford the phosphiteimines directly.[542]

Infrared absorption for the P=N group was in the range 1280–1350 cm$^{-1}$.[527, 539] Monomeric phosphiteimines showed $^{31}$P NMR peaks in the same general range as other iminophosphoranes, about − 18 to + 21 ppm.[44, 278, 527, 532, 539, 540, 543] The rotational barrier about the P=N group must have been low because of the inability to detect diastereotopic methyl absorption for $(MeO)_3P{=}NMe$.[527] Dimeric phosphiteimines showed $^{31}$P NMR peaks from − 58 to − 62 ppm,[44, 543] consistent with the expected peak position for pentavalent phosphorus.

Most phosphiteimines were monomeric. However, those derived from 2-alkoxy-1,3,2-dioxaphospholanes existed as dimers if the N substituent was phenyl or a group less electron withdrawing,[44] and provided the five-membered ring did not carry substituents.[44] Replacement of the five-membered ring with two ethoxy groups, or replacement of ring oxygens with nitrogen, both led to monomeric imines.[532, 543] Once again it was apparent that incorporation of phosphorus in a five-membered ring favored a pentavalent phosphorus, the "phospholane effect." The structure of one dimer has been determined.[543]

Phosphiteimines are normally stable in the presence of water, those with strong electron withdrawing groups being very resistant to hydrolysis,[516] but others upon heating hydrolyzed to phosphoramidates with the loss of an alkoxy group[519, 537, 544] (Eq. 13.87). With acid catalysis the hydrolysis proceeded more

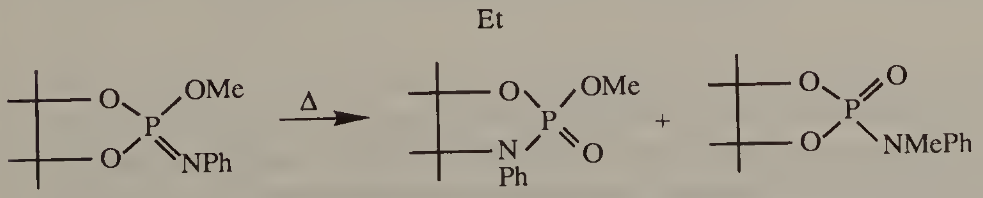
$$RN{=}P(OEt)_3 \xrightarrow{H_2O} RNHP(O)(OEt)_2 \xrightarrow[-\,(EtO)_2PO_2H]{H_3O^+} R\overset{+}{N}H_3 \qquad (13.87)$$

readily, and in most instances continued further to afford the amine and dialkylphosphate.[526, 539, 545] Zwierzak et al.[278, 529, 546, 547] developed an alternative to the Gabriel synthesis of primary amines by converting an alkyl halide to its azide, then to the phosphiteimine, and then hydrolyzing with gaseous hydrogen chloride to produce overall yields of 60–80% of amine. The mechanism of the hydrolyses probably involved protonation of the basic nitrogen, then attack of water at phosphorus to produce a tetraoxyaminophosphorane, and finally displacement on an alkyl group by a nucleophile such as water. The nature of the final step varied with the pH.[548] In a somewhat related reaction it was noted that some N-phenyl phosphiteimines added methanol across the P=N bond and then underwent displacement of aniline to form a pentaoxyphosphorane, detectable by $^{31}P$ NMR in solution.[532]

Phosphiteimines undergo a 1,3-thermal rearrangement to amidophosphates, involving conversion of an alkoxy oxygen to a phosphoryl oxygen and migration of an alkyl group from oxygen to nitrogen (Eq. 13.88), a so-called

$$RN{=}P(OEt)_3 \xrightarrow{\Delta} \underset{\displaystyle Et}{RN}{-}P(O)(OEt)_2 \qquad (13.88)$$

imide–amide arrangement[8b] which has been reviewed.[549] The rearrangements occurred virtually regardless of the nature of the substituent on nitrogen, including hydrogen,[534] alkyl,[527] aryl,[532, 550] trimethylsilyl,[278, 535] acyl[540] cyano,[530] carboxymethyl,[22] and sulfonyl.[551, 552] The nature of the migrating group varied widely, including methyl,[527, 534, 535] ethyl, [534, 552] higher alkyl,[278] phenyl,[550] and allyl.[550] In the case of a methoxy dioxaphospholane imine, both possible products were obtained[532] (Eq. 13.89). In all of these reactions it



(13.89)

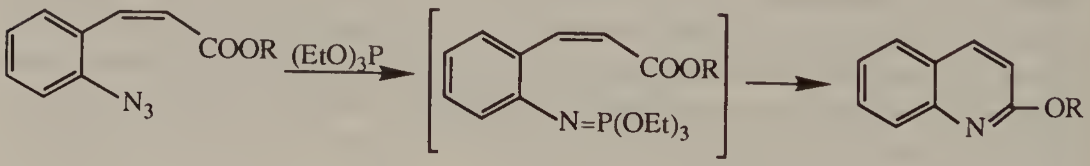
appears that an intramolecular $S_N2$ reaction has been effected by the nucleophilic imine nitrogen on the O-alkyl group,[527] and further credence was provided by the observation that rearrangement of O-allylic imines resulted in inversion of the allyl group.[550] In these rearrangements, as well as in the hydrolyses discussed previously and the alkylation reaction to be discussed subsequently, the driving force probably is the formation of the phosphoryl group. Two groups took advantage of the ability to lose a trifluoroethoxy group from an N-trimethylsilyl imine in forming linear polymeric phosphazenes.[1,553,554] Reaction of triethyl phosphite with azidoacetic acid produced diethyl N-carbethoxymethyl phosphoramidate, presumably by initial imine formation followed by rearrangement with ethyl migrating from oxygen to the carboxy group.[22]

Phosphiteimines underwent alkylation on nitrogen with alkyl halides, but subsequently a P-alkoxy group was lost, presumably by attack of halide, to afford a phosphoramidate[526,541,545] (Eq. 13.90). The alkylation was first order

$$\mathrm{RN{=}P(OEt)_3} \xrightarrow{\mathrm{R'X}} \mathrm{RR'N\text{-}\overset{+}{P}(OEt)_3} \xrightarrow{\mathrm{-\ EtX}} \mathrm{RR'N\text{-}P(O)(OEt)_2} \qquad (13.90)$$

in each reactant, with the rates being accelerated by electron donating groups on phosphorus and decelerated by electron withdrawing groups on nitrogen.[545,555] The reaction failed with stabilized imines such as $(EtO)_3P{=}NCOPh$.[539] The alkylation reaction, when followed by a hydrolysis, has been applied by Zwierzak and Koziara[529] to the synthesis of secondary amines. Triethylphosphiteimines were similarly acylated[526] and phosphorylated[556] to N-acyl- or N-phosphoryl phosphoramidates, in each case losing an ethoxy group.

Phosphiteimines reacted with carbonyl compounds in an Aza–Wittig reaction to expel phosphate and form imines. The first such report was reaction of N-phenyliminotriethoxyphosphorane with carbon disulfide to produce phenyl isothiocyanate.[526] More recently reactions have been reported between phosphiteimines and aldehydes,[557,558] ketones,[270,538,557] esters,[258,559] and imides.[270,538] Of particular use have been intramolecular Aza–Wittig reactions, including with derivatives of carboxylic acids, using triethylphosphite in place of triphenylphosphine[270,258,559–561] (Eq. 13.91).



(13.91)

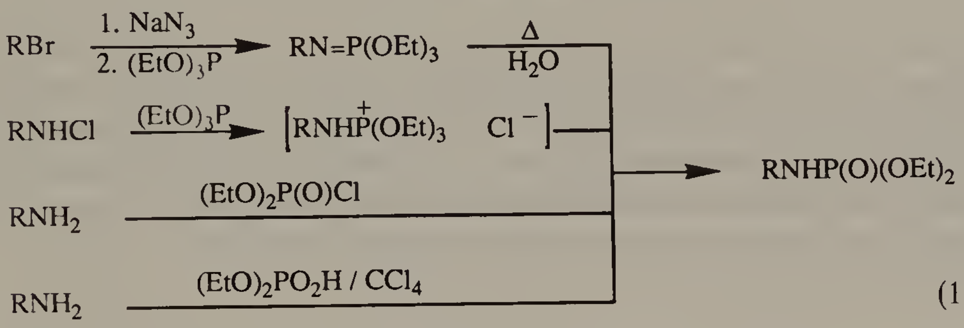
Triethylphosphite could replace triphenylphosphine in the formation of imines which reacted with nitrile oxides[350] (Eq. 13.62). Trialkyl phosphites also effectively replaced triphenylphosphine in reaction with diazo compounds to form P,P,P-trialkoxyphosphazines, but little of their chemistry has been explored.[562,563]

Similar chemistry has been reported for imines of general structure $R_n(R'O)_{3-n}P{=}NR''$ when $n = 1$ or 2, in which instances the imines have properties characteristic of both phosphiteimines and iminophosphoranes.[289, 564] In addition, similar chemistry has been discovered for iminophosphoranes carrying one or more amino groups on phosphorus.[130, 532]

### 13.5.5 Phosphoramidate Anions

Phosphoramidate anions are related to phosphonate carbanions as iminophosphoranes are related to phosphonium ylides, and as such would be expected to reflect chemistry similar both to ylides and to iminophosphoranes.

Phosphoramidate anions are obtained by proton removal from phosphoramidates, and the latter have been prepared by several routes (Eq. 13.92).



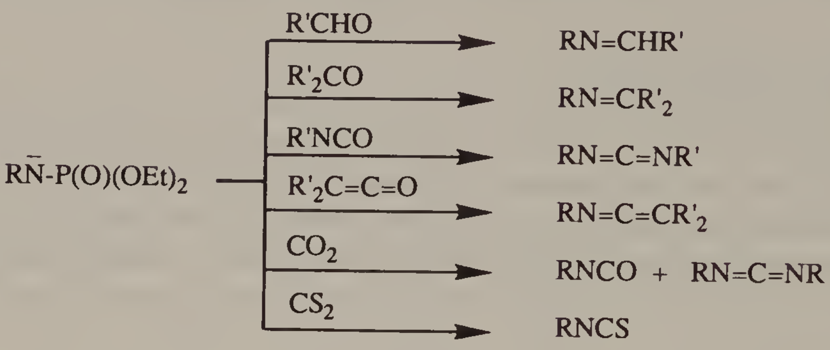
(13.92)

Conversion of alkyl halides to azides, then reaction with triethylphosphite to form the phosphiteimines, followed by hydrolysis of the imine, afforded good yields of phosphoramidates.[544] Reaction of N-haloamides with triethylphosphite[79] or reaction of amines with diethyl chlorophosphate also produced phosphoramidates.[245] Finally, the Atherton–Todd[86] sequence has been adapted to preparation of phosphoramidates in good yield.[565, 566]

Phosphoramidate anions exhibited normal nucleophilic behavior. They could be alkylated in good yield, and hydrolysis of the resulting N,N-disubstituted amides provided an overall effective route from primary amine or halide to secondary amine[566] (Eq. 13.93). Reaction with trimethylsilyl chloride produced an 89:11 mixture of N-silyl and O-silyl products, the latter presumably from silyl migration from nitrogen to oxygen.[567] Phosphoramidate anions also opened oxirane rings to afford aziridines.[348]

$$\mathrm{RBr}\ \xrightarrow[\substack{2.\ (\mathrm{EtO})_3\mathrm{P}\\ 3.\ \mathrm{H_2O}}]{1.\ \mathrm{NaN_3}}\ \mathrm{RNHP(O)(OEt)_2}\ \xrightarrow[\substack{2.\ \mathrm{R'Br}\\ 3.\ \mathrm{H_3O^+}}]{1.\ \mathrm{NaH}}\ \mathrm{RR'NH} \qquad (13.93)$$

Phosphoramidate anions reacted with a wide variety of carbonyl compounds in an Aza–Wittig type reaction, producing carbon imines and diethylphosphate. Discovered by Wadsworth and Emmons[568] only a year after their development of the reaction of phosphonate carbanions with carbonyls (the Wadsworth–Emmons reaction, see Chapter 10), the reaction provided an alternative to the use of iminophosphoranes. Phosphoramidate anions, formed using sodium hydride in benzene, reacted with aldehydes,[569] ketones,[568, 570] ketenes,[568] and isocyanates[568] (Eq. 13.94). Reaction with carbon dioxide produced a mixture of



(13.94)

isocyanate and carbodiimide,[568–570] the latter from reaction of isocyanate with additional phosphoramidate anion. However, reaction with carbon disulfide stopped at the isothiocyanate stage.[568, 569, 571] There were no particular advantages of phosphoramidate anions over iminophosphoranes in reaction with carbonyls, although the former probably are more nucleophilic. Reactivity with carboxylic acid derivatives has not been reported.

## REVIEWS

**1966** Johnson, A. Wm. *Ylid Chemistry*, Academic: New York, A review of iminophosphorane chemistry.

**1967** Singh, G.; Zimmer, H. *Organomet. Chem. Rev. 2*, 279–348. A review of phosphinimines and phosphazines.

**1972** Bestmann, H. J.; Zimmerman, R. In *Organic Phosphorus Compounds*; Kosolapoff, G. M. and Maier, L., Eds.; Wiley-Interscience: Vol. 3, Chapter 5A. A review of phosphinimines and phosphazines.

**1972** Allcock, H. R. *Phosphorus–Nitrogen Compounds:* Academic: New York, Preparation, properties, and reactions of phosphazenes, especially linear and cyclic polymers.

**1978** Shaw, R. A. *Phosphorus Sulfur 4*, 101–121. A review of phosphazanes and phosphazenes, especially cyclic oligomers.

**1978** Gilyarov, V. A. *Russ. Chem. Revs. 47*, 870–879. A review of the imide–amide and imide–imide rearrangements of imidophosphorus compounds.

**1981** Gololobov, Y. G.; Zhmurova, I. N.; Kasukhin, L. F. *Tetrahedron 37*, 437–472. A review of the Staudinger reaction.

**1981** Abel, S. W.; Mucklejohn, S. A. *Phosphorus Sulfur 9*, 235–266. A review of phosphinimines.

**1986** Tarasevich, A. S.; Boldeskul, I. E.; Kukhar, V. P. *Russ. Chem. Revs. 55*, 758–767. A review of the dimerization of iminophosphoranes.

**1988** Neilson, R. H.; Wisian-Neilson, P. *Chem. Revs. 88*, 541–562. A review of polyphosphazenes.

**1988** Shaw, R. A. *J. Organomet. Chem. 341*, 357–361. A review of migration rearrangements in cyclic polyphosphazenes.

**1988** Scriven, E. F. V.; Turnbull, K. *Chem. Revs. 88*, 298–368. A review of the role of azides in the Staudinger reaction.

**1989** Dehnicke, K.; Strahle, J. *Polyhedron 8*, 707–726. A review of phosphorane iminato complexes of transition metals.

**1991** Gusar, N. I. *Russ. Chem. Revs. 60*, 146–161. A review of the use of the Aza–Wittig reaction in heterocycle syntheses.

**1992** Gololobov, Y. G.; Kasukhin, L. F. *Tetrahedron 48*, 1353–1406. A review of the Staudinger reaction.

## REFERENCES

[1] Nielson, R. H.; Wisian-Nielson, P. *Chem. Rev.* **1988**, *88*, 541.

[2] Allcock, H. R. *Phosphorous–Nitrogen compounds*; Academic: New York, 1972.

[3] Abel, E. W.; Mucklejohn, S. A. *Phosphorus Sulfur* **1981**, *9*, 235.

[4] Niecke, E. In *Multiple Bonds and Low Coordination in Phosphorus Chemistry*; Regitz, M.; Scherer, O. J., Eds.; Georg Thieme Verlag: Stuttgart, Germany, 1990; Chapter D.8.

[5] Niecke, E.; Gudat, D. In *Multiple Bonds and Low Coordination in Phosphorus Chemistry*; Regitz, M.; Scherer, O. J., Eds., George Thieme Verlag: Stuttgart, Germany, 1990; Chapter E.3.

[6] Allcock, H. R. *Chem. Eng. News* **1968**, *63*, 68; *Science* **1992**, *255*, 1106.

[7] Staudinger, H.; Meyer, J. *Helv. Chim. Acta* **1919**, *2*, 635.

[8] (a) Gololobov, Y. G.; Zhmurova, I. N.; Kasukhin, L. F. *Tetrahedron* **1981**, *37*, 437. (b) Gololobov, Y. G.; Kasukhin, L. F. *Tetrahedron* **1992**, *48*, 1353.

[9] Scriven, E. F. V.; Turnbull, K. *Chem. Revs.* **1988**, *88*, 298.

[10] Birkofer, L.; Kim, S. M. *Chem. Ber.* **1964**, *97*, 2100.

[11] Urpi, F.; Vilarrasa, J. *Tetrahedron Lett.* **1986**, *27*, 4623.

[12] Wilson, S. R.; Pasternak, A. *Synlett.* **1990**, 199.

[13] Baechler, R. D.; Blohm, M.; Rocco, K. *Tetrahedron Lett.* **1988**, *29*, 5353.

[14] Vetter, H. J.; Noth, H. *Chem. Ber.* **1963**, *96*, 1308

[15] Wilburn, J. C.; Nielson, R. H. *Inorg. Chem.* **1977**, *16*, 2519.

[16] Baccolini G.; Todesco, P. E.; Bartoli, G. *Phosphorus Sulfur* **1981**, *10*, 387.

[17] Quin, L. D.; Keglevich, G.; Caster, K. C. *Phosphorus Sulfur* **1987**, *31*, 133.

[18] Takeishi, M.; Tadano, M.; Hayama, S. *Makromol. Chem. Rapid Comm.* **1983**, *3*, 871.

[19] Molina, P.; Alajarin, M.; Vidal, A. *Tetrahedron Lett*, **1988**, *29*, 3849.

[20] Baum, K.; Berkowitz, P. T.; Grakauskas, V.; Archibald, T. G. *J. Org. Chem.* **1983**, *48*, 2953.

[21] Tsuge, O.; Kanemasa, S.; Matsuda, K. *J. Org. Chem.* **1984**, *49*, 2688.
[22] Gololobov, Y. G.; Gusar, N. I.; Chaus, M. P. *Tetrahedron* **1985**, *41*, 793.
[23] Molina, P.; Arques, A.; Vinader, M. V. *Synthesis* **1990**, 469.
[24] Iino, Y.; Nitta, M. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 2235.
[25] Molina, P.; Alajarin, M.; Lopez-Leonardo, C. *Tetrahedron Lett*, **1991**, *32*, 4041.
[26] Lo, Y. S.; Sheehan, J. C. *J. Org. Chem.* **1975**, *40*, 191.
[27] Kricheldorf, H. R. *Synthesis* **1972**, 695.
[28] Derkach, G. I.; Narbut, A. V. *J. Gen. Chem.* **1965**, *35*, 1011.
[29] Heesing, A.; Steinkamp, H. *Chem. Ber.* **1982**, *115*, 2854.
[30] Schmidbaur, H.; Jonas, G. *Angew. Chem.* **1967**, *6*, 449; *Chem. Ber.* **1968**, *101*, 1271.
[31] Edelman, T. G.; Stenaov, B. I. *J. Gen. Chem.* **1969**, *39*, 678.
[32] Thayer, J. S.; West, R. *Inorg. Chem.* **1964**, *3*, 406.
[33] Lehn, W. L. *Inorg. Chem.* **1967**, *6*, 1061.
[34] Bergmann, E.; Wolff, H. A. *Chem. Ber.* **1930**, *63*, 1176.
[35] Leffler, J. E.; Honsberg, U.; Tsuno, Y.; Forsblad, I. *J. Org. Chem.* **1961**, *26*, 4810.
[36] Franz, J. E.; Osuch, C. *Tetrahedron Lett.* **1963**, 841.
[37] Bock, H.; Wiegrabe, W. *Angew. Chem.* **1963**, *2*, 484.
[38] Molina, P.; Arques, A.; Cartagena, I.; Obon, R. *Tetrahedron Lett.* **1991**, *32*, 2521.
[39] Kroshefsky, R. D.; Verkade, J. G. *Inorg, Chem.* **1975**, *14*, 3090.
[40] Onysko, P. P.; Proklina, N. V.; Prokopenko, V. P.; Gololobov, Y. G. *J. Gen. Chem.* **1984**, *54*, 289.
[41] Leffler, J. E.; Tsuno, Y. *J. Org. Chem.* **1963**, *28*, 902.
[42] Leffler, J. E.; Temple, R. D. *J. Am. Chem. Soc.* **1967**, *89*, 5235.
[43] Gololobov, Y. G.; Kasukhin, L. F. *J. Gen. Chem.* **1979**, *49*, 831.
[44] Kukhar, V. P.; Kasheva, T. N.; Kasukhin, L. F.; Ponomarchuk, M. P. *J. Gen. Chem.* **1984**, *54*, 1360.
[45] Horner, L.; Gross, A. *Liebigs Ann. Chem.* **1955**, *591*, 117.
[46] Gololobov, Y. G.; Kasukhin, L. F.; Ponomarchuk, M.; Klepa, T.; Yurchencko, R. *Phosphorus Sulfur* **1981**, *10*, 339.
[47] Ponomarchuk, M. P.; Sologub, L. S.; Kasukhin, L. F.; Kukhar, V. P. *J. Gen. Chem.* **1985**, *55*, 1532.
[48] Bock, H.; Schnoller, M. *Angew. Chem.* **1968**, *7*, 636.
[49] Hillhouse, G. L.; Goeden, G. V.; Haymore, B. L. *Inorg. Chem.* **1982**, *21*, 2064.
[50] Chernega, A. N.; Antipin, M. Y.; Struchkov, Y. T.; Boldeskul, I. E.; Ponomarchuk, M. P.; Kasukhin, L. F.; Kukhar, V. P. *J. Gen. Chem.* **1984**, *54*, 1766.
[51] Chidester, C. G.; Szmuszkovicz, J.; Duchamp, D. J.; Laurian, L. G.; Freeman, J. P. *Acta Cryst.* **1988**, *44C*, 1080.
[52] Chernega, A. N.; Antipin, M. Y.; Struchkov, Y. T.; Ponomarchuk, M. P.; Kasukhin, L. F.; Kukhar, V. P. *J. Gen. Chem.* **1989**, *59*, 1133.
[53] Goldwhitc, H.; Gysegem, P.; Schow, S.; Swyke, C. *J. Chem. Soc. Dalton* **1975**, *16*.
[54] Bellan, J.; Marre, M. R.; Sanchez, M.; Wolf, R. *Phosphorus Sulfur* **1981**, *12*, 11.
[55] Mosby, W. L.; Silva, M. L. *J. Chem. Soc.* **1965**, 1003.

56 Molina, P.; Arques, A.; Vinader. M. V. *Tetrahedron Lett.*, **1989**, *30*, 6237.

57 Horner, L.; Oediger, H. *Liebigs Ann. Chem.* **1959**, *627*, 142.

58 Zimmer, H.; Singh, G. *J. Org. Chem.* **1963**, *28*, 483.

59 Koidan, G. N.; Marchenko, A. P.; Kudryavtsev, A. A.; Pinchuk, A. M. *J. Gen. Chem.* **1982**, *52*, 1779.

60 Koidan, G. N.; Kulish, V. P.; Filonenko, L. P.; Krasovskii, A. N.; Pinchuk, A. M. *J. Gen. Chem.* **1987**, *57*, 677.

61 Zimmer, H.; Singh, G. *J. Org. Chem.* **1964**, *29*, 1579.

62 Walker, C. C.; Schechter, H. *J. Am. Chem. Soc.* **1968**, *90*, 5626.

63 Singh, G.; Zimmer, H. *J. Org. Chem.* **1965**, *30*, 417.

64 Shevchenko, V. I.; Stratienko, V. T.; Pinchuk, A. M. *Zh. Obshch. Khim.* **1964**, *34*, 3954; *Chem. Abstr.* **1965**, *62*, 9167.

65 Kirsanov, A. V., *Isv. Akad. Nauk SSSR* **1950**, 426; *Chem. Abstr.* **1951**, *45*, 1503; *Zh. Obshch. Khim.* **1952**, *22*, 269; *Chem. Abstr.* **1952**, *46*, 11135.

66 Kirsanov, A. V.; Nebrasova, Z. D. *Zh. Obshch. Khim.* **1956**, *26*, 903; *Chem. Abstr.* **1956**, *50*, 14631.

67 Hiraoka, T.; Sugimura, Y.; Saito, T.; Kobayashi, T. *Heterocycles* **1977**, *8*, 719.

68 Lee, K. W.; Singer, L. A. *J. Org. Chem.* **1974**, *39*, 3780.

69 Molina, P.; Lorenzo, A.; Aller, E. *Synthesis* **1992**, 297.

70 Stegmann, H. B.; Wax, G.; Peinelt, S.; Scheffler, K. *Phosphorus Sulfur* **1983**, *16*, 277.

71 Mann, F.; Chaplin, E. J. *J. Chem. Soc.* **1937**, 527.

72 Stratienko, V. T.; Shevchenko, V. I. *J. Gen. Chem.* **1964**, *34*, 1467.

73 Shevchenko, V. I., Puchkin, A. M.; Kirsanov, A. V. *Zh. Obshch. Khim.* **1965**, *35*. 1488; *Chem. Abstr.* **1965**, *63*, 14899.

74 Ferguson, G.; Lough, A. J.; Glidewell, C. *J. Chem. Soc. Perkin Trans. (2)* **1989**, 2065.

75 Appel, R.; Guth, E. *Z. Naturforsch.* **1960**, *15b*, 57.

76 Appel, R.; Hauss, A. *Chem. Ber.* **1960**, *93*, 405.

77 Appel, R.; Kohnlein, G.; Schollhorn, R. *Chem. Ber.* **1965**, *98*, 1355.

78 Sisler, H. H.; Ahuja, H. S.; Smith, N. L. *J. Org., Chem.* **1961**, *26*, 1819.

79 Wiesboeck, R. A. *J. Org. Chem.* **1965**, *30*, 3161.

80 Gotsmann, G.; Schwarzmann, M. *Liebigs Ann. Chem.* **1969**, *729*, 106.

81 Kirsanov, A. V.; Shtepanek, A. S.; Shevchenko, V. I. *Dopovodi Akad. Nauk Ukr. RSR* **1962**, *1*, 63; *Chem. Abstr.* **1962**, *57*, 11229.

82 Schonberg, A.; Singer, E. *Chem. Ber.* **1969**, *102*, 2557.

83 Niclas, H. J.; Martin, D. *Tetrahedron Lett.* **1978**, 4031.

84 Bittner, S.; Assaf, Y.; Krief, P.; Pomerantz, M.; Ziemnicka, B. T.; Smith, C. G. *J. Org. Chem.* **1985**, *50*, 1712.

85 Bittner, S.; Pomerantz, M.; Assaf, Y.; Krief, P.; Xi, S.; Witczak, M. K. *J. Org, Chem.* **1988**, *53*, 1.

86 Atherton, F. R.; Openshaw, H. T.; Todd, A. R. *J. Chem. Soc.* **1945**, 660.

87 Appel, R.; Blaser, B.; Kleinstuck, R.; Ziehn, K. D. *Chem. Ber.* **1971**, *104*, 1847.

88 Weinberger, B.; Fehlhammer, W. P. *Angew. Chem.* **1980**, *19*, 480.

89 Reference 4, pp. 303–304.

90 Romanenko, V. D.; Ruban, A. V.; Iksanova, S. V.; Markovskii, L. N. *J. Gen. Chem.* **1984**, *54*, 278.

91 Hoffmann, H. *Chem. Ber.* **1962**, *95*, 2563.

92 Bestmann, H. J.; Seng, F. *Tetrahedron* **1965**, *21*, 1373.

93 Wanner, M. J.; Koomen, G. J. *Tetrahedron Lett.* **1992**, *33*, 1513.

94 Campbell, T. W.; Monagle, J. J.; Foldi, V. S. *J. Am. Chem. Soc.* **1962**, *84*, 3673.

95 Monagle, J. J.; Mengenhauser, J. V. *J. Org. Chem.* **1966**, *31*, 2321.

96 Aksnes, G.; Froyen, P. *Acta Chem. Scand.* **1969**, *23*, 2697.

97 Hall, C. R.; Smith, D. J. H. *J. Chem. Soc. Perkin Trans. (2)* **1977**, 1373.

98 Senning, A. *Acta Chem. Scand.* **1965**, *19*, 1755.

99 Nitta, M.; Soeda, H.; Koyama, S.; Iino, Y. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 1325.

100 Barluenga, J.; Ferrero, M.; Palacios, F. *Tetrahedron Lett.* **1988**, *29*, 4863.

101 Iino Y.; Kobayashi, T.; Nitta, M. *Heterocycles* **1986**, *24*, 2437.

102 Nitta, M.; Soeda, H.; Iino, Y. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 932.

103 Kobayashi, T.; Nitta, M. *Chem. Lett.* **1986**, 1549.

104 Kanomata, N.; Nitta, M. *Tetrahedron Lett.* **1988**, *29*, 5957; *J. Chem. Soc. Perkin Trans. (1)* **1990**, 1119.

105 Nitta, M.; Kobayashi, T. *Chem. Lett.* **1986**, 463.

106 Nitta, M.; Iino. Y.; Mari, S. *Tetrahedron Lett.* **1991**, *32*, 6727.

107 Nitta, M.; Iino, Y. *J. Chem. Soc. Perkin Trans. (1)* **1990**, 435.

108 Iino, Y.; Hara, E.; Nitta, M. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 1913.

109 Schmidpeter, A.; Luber, J. *Phosphorus* **1974**, *5*, 55.

110 Kabachnik, M. I.; Gilyarov, V. A.; Tikhonina, N. A.; Kalinen, A. E.; Adrianov, V. G.; Struchkov, Y. T.; Timofeeva, G. I. *Phosphorus* **1974**, *5*, 65.

111 Tautz, H.; Schmidpeter, A. *Chem. Ber.* **1981**, *114*, 825.

112 Day, R. O.; Holmes, R. R.; Tautz, H.; Weinmaier, J. H.; Schmidpeter, A. *Inorg. Chem.* **1981**, *20*, 1222.

113 Schmidpeter, A.; Gross, J.; Schrenk, E.; Sheldrick, W. S. *Phosphorus Sulfur* **1982**, *14*, 49.

114 Sheldrick, W. S.; Schomburg, D.; Schmidpeter, A.; von Criegern, T. *Chem. Ber.* **1980**, *113*, 55.

115 Zaltsman, I. S.; Marchencko, A. P.; Pinchuk, A. M. *J. Gen. Chem.* **1987**, *57*, 2025.

116 Schmidpeter, A.; Zeiss, W. *Angew. Chem.* **1971**, *10*, 396.

117 Barleunga, J.; Lopez, F.; Palacios, F. *Tetrahedron Lett.* **1987**, *28*, 2875.

118 Bedel, C.; Foucaud, A. *Tetrahedron Lett.* **1991**, *32*, 2619.

119 Pauling, L. *Nature of the Chemical Bond*, 3rd ed.; Cornell University Press; Ithaca, NY, 1960; pp. 224 and 228.

120 Kaiser, J.; Hartung, H.; Richter, R. *Z. Anorg. Allg. Chem.* **1980**, *469*, 188.

121 Bart, J. C. J.; Bassi, I. W.; Calcaterra, M. *Acta Cryst.* **1982**, *38B*, 1932.

122 Hursthouse, M. B.; Walker, N. P. C.; Warrens, C. P.; Woolins, J. D. *J. Chem. Soc. Dalton* **1985**, 1043.

123 Llamas-Saiz, A. L.; Foces-Foces, C.; Elguero, J.; Molina, P.; Alajarin, M.; Vidal, A. *J. Chem. Soc. Perkin Trans. (2)* **1991**, 1667.

124 Wilson, R. D.; Bau, R. *J. Am. Chem. Soc.* **1974**, *96*, 7601.

125 Bar, I.; Bernstein, J. *Acta Cryst.* **1980**, *36B*, 1962.

126 Nerstad, G. O.; Romming, C.; Songstad, J. *Acta Chem. Scand.* **1985**, *39A*, 691.

127 Astrup, E. E.; Bouzga, A. M.; Starzewski, K. A. O. *J. Mol. Struct.* **1979**, *51*, 51.

128 Schmidbaur, H.; Bowmaker, G. A.; Kumberger, O.; Muller, G.; Wolfsberger, W. *Z. Naturforsch.* **1990**, *45B*, 476.

129 Antipin, M. Y.; Struchkov, Y. T.; Tikhonina, N. A.; Gilyarov, V. A.; Kabachnik, M. I. *Zh. Strukt. Khim.* **1981**, *22*, 93; *Chem. Abstr.* **1981**, *95*, 81124.

130 Marre, M. R.; Sanchez, M.; Wolf, R.; Jaud, J.; Galy, J. *Can. J. Chem.* **1984**, *62*, 2186.

131 Litvinov, I. A.; Struchkov, Y. T.; Dianova, E. N.; Arbuzov, B. A. *Bull. Acad. Sci. USSR* **1972**, *31*, 2408.

132 Llamas-Saiz, A. L.; Foces-Foces, C.; Elguero, J.; Molina, P.; Alajarin, M.; Vidal, A. *J. Chem. Soc. Perkin Trans. (2)* **1991**, 2033.

133 Johnson, A. Wm.; Wong, S. C. K., *Can. J. Chem.* **1966**, *44*, 2793.

134 Kukhar, V. P.; Petrashenko, A. A.; Zhmurova, I. N.; Tukhar, A. A.; Solodushenkov, S. N. *J. Gen. Chem.* **1970**, *40*, 1682.

135 Edelman, T. G.; Stepanov, B. I. *Zh. Obsbch. Khim.* **1967**, *37*, 963; *Chem. Abstr.* **1967**, *67*, 111875.

136 Ivanova, N. A.; Bulgarevich, S. B.; Morshovich, D. Y.; Kogan, V. A.; Osipov, O. A. *J. Gen. Chem.* **1979**, *49*, 659.

137 Edelman, T. G.; Stepanov, B. I. *J. Gen. Chem.* **1969**, *39*, 679.

138 Schwesinger, R. *Chimia* **1985**, *39*, 269.

139 Schwesinger, R.; Schlemper, H. *Angew. Chem.* **1987**, *26*, 1167; Link, R.; Schwesinger, R. *Angew. Chem.* **1992**, *31*, 850.

140 Kolodiazhnyi, O. I. *J. Gen. Chem.* **1975**, *45*, 539.

141 Wannagat, U.; Munstedt, R. *Phosphorus Sulfur* **1987**, *29*, 233.

142 Albright, T. A.; Freeman, W. J.; Schweizer, E. E. *J. Org. Chem.* **1976**, *41*, 2716.

143 Briggs, E. M.; Brown, G. W.; Cairns, P. M.; Jiricny, J.; Meidine, M. F. *Org. Mag. Res.* **1980**, *13*, 306.

144 Bodeker, J.; Kockritz, P.; Koppel, H.; Radeglia, R. *J. Prakt. Chem.* **1980**, *322*, 735.

145 Pomerantz, M.; Marynick, D. S.; Rajeshwar, K.; Chou, W. N.; Throckmorton, L.; Tsai, S. W.; Chen, P. C. Y.; Cain, T. *J. Org. Chem.* **1986**, *51*, 1223.

146 Pomerantz, M.; Ziemnicke, B. T.; Merchant, Z. M.; Chou, W. N.; Perkins, W. B.; Bittner, S. *J. Org. Chem.* **1985**, *50*, 1757.

147 Chou, W. N.; Pomerantz, M.; Witczak, M. K. *J. Org. Chem.* **1990**, *55*, 716.

148 Pomerantz, M.; Chou, W. N.; Witczak, M. K.; Smith, C. G. *J. Org. Chem.* **1987**, *52*, 159.

149 Bragin, J.; Chan, S.; Mazzola, E.; Goldwhite, H. *J. Phys. Chem.* **1973**, *77*, 1506.

150 Katti, K. V.; Cavell, R. G. *Inorg. Chem.* **1989**, *28*, 413.

151 Tarasevich, A. S.; Egorov, Y. P. *Teor. Eksp. Khim.* **1971**, *7*, 828; *Chem. Abstr.* **1972**, *76*, 106144.

152 Power, W. P.; Wasylishen, R. E.; Curtis, R. D. *Can. J. Chem.* **1989**, *67*, 454.

153 Chou, W. N.; Pomerantz, M. *J. Org. Chem.* **1991**, *56*, 2763.

[154] Martin, G. J.; Sanchez. M.; Marre, M. R. *Tetrahedron Lett.* **1983**, *24*, 4989.

[155] Albright, T. A.; Freeman, W. J.; Schweizer, E. E. *J. Am. Chem. Soc.* **1975**, *97*, 940.

[156] Yolles, S.; Woodland, J. H. R. *J. Organomet. Chem.* **1975**, *93*, 297.

[157] Schuster, I. *Tetrahedron* **1977**, *33*, 1075.

[158] Lutskii, A. E.; Samarai, L. I.; Kochergina, A. V.; Shepel, A.V.; Shevchenko, Z. A.; Derkach, G. I.; Kozlov, E. Z.; Drach, B. S. *Zh. Obshch. Khim.* **1967**, *37*, 2042; *Chem. Abstr.* **1968**, *68*, 34387.

[159] Phillips, G. M.; Hunter, J. S.; Sutton, L. E. *J. Chem. Soc.* **1945**, 146.

[160] Goetz, H.; Probst, D. *Liebigs Ann. Chem.* **1968**, *715*, 1.

[161] Borovikov, Y. Y.; Egorov, Y. P.; Zhmurova, I. N.; Kukhar, V. P.; Tukhar, A. A.; Yurchenko, R. I. *Teor. Eksp. Khim.* **1974**, *10*, 207; *Chem. Abstr.* **1974**, *81*, 12895.

[162] Zhmurova, I. N.; Kisilenko, A. A.; Kirsanov, A. V. *Zh. Obshch. Khim.* **1962**, *32*, 2580; *Chem. Abstr.* **1963**, *63*, 10877.

[163] Wiegraße, W.; Bock, H.; Luttke, W. *Chem. Ber.* **1966**, *99*, 3737.

[164] Wiegraße, W.; Bock, H. *Chem. Ber.* **1968**, *101*, 1414.

[165] Lutskii, A. E.; Shevchenko, Z. A.; Samarai, L. I.; Pinchuk, A. M. *Zh. Obshch. Khim.* **1967**, *37*, 2034; *Chem. Abstr.* **1968**, *68*, 34386.

[166] Stepanov, B. I.; Edelman. T. G. *J. Gen. Chem.* **1969**, *39*, 1518.

[167] Zhmurova, I. N.; Yurchenko, R. I.; Kirsanov, A. V. *J. Gen. Chem.* **1971**, *41*, 783.

[168] Swartz, W. E.; Ruff, J. K.; Hercules, D. M. *J. Am. Chem. Soc.* **1972**, *94*, 5227.

[169] Perry, W. B.; Schaaf, T. F.; Jolly, W. L. *J. Am. Chem. Soc.* **1975**, *97*, 4899.

[170] Widelov, A.; Folkesson, B.; Andersson C. *Spectrosc. Lett.* **1989**, *22*, 1101.

[171] Starzewski, K. A. O.; Dieck, H. t. *Inorg. Chem.* **1979**, *18*, 3307.

[172] Buchner, W.; Wolfsberger, W. *Z. Naturforsch.* **1974**, *29B*, 328.

[173] Claydon, A. P.; Fowell, P. A.; Mortimer, C. T. *J. Chem. Soc.* **1960**, 3284.

[174] Gonbeau, D.; Pfister-Guillouzo, G.; Mazieres, M.; Sanchez, M. *Can. J. Chem.* **1985**, *63*. 3242.

[175] Nguyen, M. T.; Hegarty, A. F. *J. Chem. Soc. Perkin Trans. (2)* **1987**, 47.

[176] (a) Molina, P.; Alajarin, M.; Leonardo, C. L.; Claramunt, R. M.; Foces-Foces, C.; Cano, F. H.; Catalan, J.; de Paz, J. L. G.; Elguero, J. *J. Am. Chem. Soc.* **1989**, *111*, 355. (b) Sudhakar, P. V.; Lammertsma, K. *J. Am. Chem. Soc.* **1991**, *113*, 1899.

[177] Schuster, P. *Monatsh. Chem.* **1967**, *98*, 1310.

[178] Goetz, H.; Klabuhn, B. *Liebigs Ann. Chem.* **1969**. *724*, 18.

[179] Trinquier, G. *J. Am. Chem. Soc.* **1986**, *108*. 568.

[180] Staudinger, H.; Hauser, E. *Helv. Chim. Acta* **1921**, *4*, 861.

[181] Nomura, Y.; Kikuchi, Y.; Takeuchi, Y. *Chem. Lett.* **1974**, 575.

[182] Bachi. M. D.; Vaya, J. *J. Org. Chem.* **1979**, *44*, 4393.

[183] Aubert, T.; Farnier, M.; Hanquet, B.; Guilard, R. *Synth. Comm.* **1987**, *17*, 1831.

[184] Nesterov, L. V.; Krepysheva, N. E. *Bull. Acad. Sci. USSR* **1975**, *24*, 2738.

[185] Boev, V. I. *J. Gen. Chem.* **1978**, *48*, 1459.

[186] Aubert, T.; Tabyaoui, B.; Farnier, M.; Guilard, R. *Synthesis* **1988**, 742.

[187] Molina, P.; Fresneda, P. M.; Canovas, M. *Tetrahedron Lett.* **1992**, *33*, 2891.

[188] Kloek, J. A.; Leschinsky, K. L. *J. Org. Chem.* **1983**, *43*, 1460.

189 Zbiral, E.; Stroh, J. *Liebigs Ann. Chem.* **1969**, *725*, 29.

190 Yagupolskii, Y. L.; Kondvatenko, N. V.; Yagupolskii, L. M. *Zh. Org. Khim.* **1972**, *8*, 1253; *Chem. Abstr.* **1972**, *77*, 100962.

191 Kovtun, V. Y.; Gilyarov, V. A.; Kabachnik M. I. *Izv. Akad. Nauk SSSR* **1971**, *10*, 2217; *Chem Abstr.* **1972**, *76*, 46254.

192 Appel, R.; Volz, P. *Chem. Ber.* **1975**, *108*, 623.

193 Cohen, H. L. *J. Polym. Sci., Polym. Chem. Ed.* **1983**, *23*, 1671.

194 Appel, R.; Schollhorn, R. *Angew. Chem.* **1964**, *3*, 805.

195 Messmer, A.; Pinter, I.; Szego, F. *Angew. Chem.* **1964**, *3*, 228.

196 Appel, R.; Hauss, A. *Z. Anorg. Allg. Chem.* **1961**, *311*, 290.

197 Pailer, M.; Haslinger, E. *Monatsh. Chem.* **1970**, *101*, 508.

198 Ohler, E.; Schmidt, U. *Chem. Ber.* **1975**, *108*, 2907.

199 Khoukhi, M.; Vaultier, M.; Carrie, R. *Tetrahedron Lett*, **1986**, *27*, 1031.

200 Lambert, P. H.; Vaultier, M.; Carrie, R. *J. Chem. Soc. Chem. Commun.* **1982**, 1224; *J. Org. Chem.* **1985**, *50*, 5352.

201 Vaultier, M.; Lambert, P. H.; Carrie, R. *Bull. Soc. Chem. Fr.* **1986**, 83.

202 Ackrell, J.; Galeazzi, E.; Muchowski, J. M.; Tokes, L. *Can. J. Chem.* **1979**, *57*, 2696.

203 Flitsch, W.; Mukidjam, E. *Chem. Ber.* **1979**, *112*, 3577.

204 Pfaendler, H. R.; Straßer, R. *Liebigs Ann. Chem.* **1987**, 911.

205 Sasaki, T.; Eguchi, S.; Okano, T. *J. Am. Chem. Soc.* **1983**, *105*, 5912.

206 Zbiral, E.; Stroh, J. *Liebigs Ann. Chem.* **1969**, *727*, 231.

207 Froyen, P. *Phosphorus Sulfur* **1991**, *63*, 283.

208 Tabyaoui, B.; Aubert, T.; Farnier, M.; Guilard, R. *Synth. Comm.* **1988**, *18*, 1475.

209 Froyen, P. *Acta Chem. Scand.* **1972**, *26*, 1777.

210 Wong, S. C. K.; Johnson, A. Wm. *J. Org. Chem.* **1972**, *37*, 1850.

211 Schmidpeter, A.; von Criegern, T. *Angew. Chem.* **1978**, *17*, 55.

212 Eguchi, S.; Takeuchi, H.; Watanabe, N. *Nippon Kagaku Kaishi* **1987**, *7*, 1280; *Chem. Abstr.* **1988**, *108*, 149952.

213 Barluenga, J.; Lopez, F.; Palacios, F. *Synthesis* **1989**, 298.

214 Kovacs, J.; Pinter, I.; Messmer. A.; Toth, G. *Carbohydr. Res.* **1983**, *3*, 871.

215 Molina, P.; Alajarin, M.; Vidal, A.; Foces-Foces, M. C.; Cano, F. H. *Tetrahedron* **1989**, *45*, 4263.

216 Molina, P.; Arques, A.; Vinader, M. V.; Becher, J.; Brondum, K. *J. Org. Chem.* **1988**, *53*, 4654.

217 Molina, P.; Arques, A.; Vinader, M. V. *J. Org. Chem.* **1990**, *55*, 4724.

218 Molina, P.; Arques, A.; Fresneda, P. M.; Vinader, M. V.; Foces–Foces, M. C.; Cano, F. H. *Chem. Ber.* **1989**, *122*, 307.

219 Molina, P.; Fresneda, P. M. *Synthesis* **1989**, 878.

220 Kiji, J.; Matsumura, A.; Okazaki, T.; Haishi, T.; Furukawa, J. *J. Chem. Soc. Chem. Commun.* **1975**, 751.

221 Alper, H.; Partis, J. *J. Organomet. Chem.* **1972**, *35*, C40.

222 Mirkin, C. J.; Lu, K. L.; Snead, T. E.; Geoffroy, G. L.; Rheingold, A. L. *J. Am. Chem. Soc.* **1990**, *112*, 2809.

223 Mirkin, C. J.; Lu, K. L.; Geoffroy, G. L.; Rheingold, A. L.; Staley, D. L. *J. Am. Chem. Soc.* **1989**, *111*, 7279.

224 Itoh, K.; Okamura, M.; Ishii, Y. *J. Organomet. Chem.* **1974**, *65*, 327.

225 Froyen, P. *Phosphorus Sulfur* **1991**, *57*, 11.

226 Molina, P.; Fresneda, P. M. *J. Chem. Soc. Perkin Trans. (1)* **1988**, 1819.

227 Molina, P.; Aller, E.; Lorenzo, A. *Tetrahedron* **1991**, *47*, 6737.

228 Taylor, E. C.; Patel, M. *J. Heterocycl. Chem.* **1991**, *28*, 1857.

229 Saito, T.; Nakane, M.; Erdo, M.; Yamashita, H.; Oyamada, Y.; Motoki, S. *Chem. Lett.* **1986**, 135.

230 Hormuth, P. B.; Latscha, H. P. *Z. Anorg. Allg. Chem.* **1969**, *365*, 26.

231 Froyen, P. *Phosphorus Sulfur* **1991**, *60*, 81.

232 Zhmurova, I. N.; Mortynyuk, A. P. *Zh. Obshch. Khim.* **1968**, *38*, 876; *Chem. Abstr.* **1968**, *69*, 59346.

233 Shtepanek, A. S.; Doroshenko, V. V.; Zasorina, V. A.; Tochilkina, L. M.; Kirsanov, A. V. *J. Gen. Chem.* **1974**, *44*, 2092.

234 Yamada, K.; Inamoto, N. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 1559.

235 Burson, W. C.; Jones, D. R.; Turnbull, K.; Preston, P. N. *Synthesis* **1991**, 745.

236 Gusar, N. I. *Russ. Chem. Revs.* **1991**, *60*, 146.

237 Molina, P.; Fresneda, P. M.; Alarcon, P. *Tetrahedron Lett.* **1988**, *29*, 379.

238 Molina, P.; Fresneda. P. M.; Almendros, P. *Tetrahedron* **1991**, *47*, 4175.

239 Molina, P.; Lorenzo, A.; Aller, E. *Tetrahedron* **1992,** *48*, 4601.

240 Molina, P.; Vilaplana, M. J. V. *Synthesis* **1990**, 476.

241 Molina, P.; Alajarin, M.; Vidal, A. *J. Org. Chem.* **1990**, *55*, 6140.

242 Molina, P.; Vilaplana, M. J. V.; Perez, J. *Tetrahedron* **1990**, *46*, 7855.

243 Molina, P.; Arques, A.; Molina, A. *Synthesis* **1991**, 21.

244 Molina, P.; Alajarin, M.; Lopez-Leonardo, C.; Cano. F.; Llamas-Saiz, A. L.; Foces-Foces, C.; Claramunt, R. M.; Elguero, J. *J. Chem. Soc. Perkin Trans. (1)* **1992**, 199.

245 Monagle J. J.; Campbell, T. W.; McShane, H. F. *J. Am. Chem. Soc.* **1962**, *84*, 4288.

246 Capuana, L.; Braun, C.; Kuhn, F. *Liebigs Ann. Chem.* **1992**, 15.

247 Cristau, H. J.; Chiche, L.; Kadoura, J.; Torreilles, E. *Tetrahedron Lett.* **1989**, *29*, 3931.

248 Appel, R.; Hauss, A. *Angew. Chem.* **1959**, *71*, 626.

249 Shtepanek, A. S.; Tkachenko, E. N.; Kirsanov, A. V. *J. Gen. Chem.* **1969**, *39*, 1445.

250 Biddlestone, M.; Shaw, R. A. *J. Chem. Soc. Dalton* **1975**, 2527.

251 Zbiral, E.; Bauer, E. *Phosphorus* **1972**, *2*, 35.

252 Zbiral, E.; Stroh, J. *Liebigs Ann. Chem.* **1969**, *725*, 29.

253 Zbiral, E. *Synthesis* **1974**, 775.

254 Aubert, T.; Farnier, M.; Guilard, R. *Synthesis* **1990**, 149; *Tetrahedron* **1991**, *47*, 53.

255 Bruche, L.; Garanti, L.; Zecchi, G. *J. Chem. Res. Synopses* **1989**, 16; *Chem. Abstr.* **1989**, *111*, 77919.

256 Garcia, J.; Vilarassa, J.; Bordas, X.; Banaszek, A. *Tetrahedron Lett.* **1986**, *27*, 639.

257 Montforts, F. P.; Schwartz, U. M.; Maib, P.; Mai, G. *Liebigs Ann. Chem.* **1990**, 1037.

[258] Takeuchi, H.; Yanagida, S. I.; Ozaki, T.; Hagiwara, S.; Eguchi, S. *J. Org. Chem.* **1989**, *54*, 431.

[259] Molina, P.; Alajarin, M.; Ferao, A. *Synthesis* **1986**, 843.

[260] Stegmann, H. B.; Stocker, F.; Wax, G. *Synthesis* **1981**, 816.

[261] Stegmann, H. B.; Klotz, D.; Weiß, J. E. *Chem. Ber.* **1985**, *118*, 4632.

[262] Barbin, P.; Clin, B.; Dunogues, J. *Bull. Soc. Chem. Fr.* **1987**, 997.

[263] Aubert, T.; Tabyaoui, B.; Farnier, M.; Guilard, R. *J. Chem. Soc. Perkin Trans. (1)* **1989**, 1369.

[264] Kurita, J.; Iwata, T.; Yasuike, S.; Tsuchiya, T. *J. Chem. Soc. Chem. Commun.* **1992**, 81.

[265] Eguchi, S.; Yamashita, K.; Matsushita, Y. *Synlett.* **1992**, 295.

[266] Muchowski, J. M. *Can. J. Chem.* **1974**, *52*, 2255.

[267] Takeuchi, H.; Hagiwara, S.; Eguchi, S. *Tetrahedron* **1989**, *45*, 6375.

[268] Eguchi, S.; Takeuchi, H. *J. Chem. Soc. Chem. Commun.* **1989**, 602.

[269] Zimmer, H.; Al-Khathlan, H. *Abstracts of Papers*, 197th National Meeting of the American Chemical Society, Dallas, TX; American Chemical Society: Washington, DC, 1989; ORGN 228.

[270] Luheshi, A. B.; Salem, S. M.; Smalley, R. K.; Kennewell, P. D.; Westwood, R. *Tetrahedron Lett.* **1990**, *31*, 6561.

[271] Wolfsberger, W. *Z. Naturforsch.* **1978**, *33b*, 1452.

[272] Shtepanek, A. S.; Tochilkina, L. M.; Kirsanov, A. V. *Zh. Obshch. Khim.* **1975**, *45*, 2117; *Chem. Abstr.* **1976**, *84*, 44271.

[273] Horner, L.; Winkler, H. *Tetrahedron Lett*, **1964**, 175.

[274] Mungall, W. S.; Greene, G. L.; Heavner, G. A.; Letsinger, R. L. *J. Org. Chem.* **1975**, *40*, 1659.

[275] Vaultier, M.; Knouzi, N.; Carrie, R. *Tetrahedron Lett.* **1983**, *24*, 763.

[276] Koziara, A.; Pacewicka, K. O.; Zawadzki, S.; Zweirak, A. *Synthesis* **1985**, 202.

[277] Katritzky, A. R.; Jiang, J.; Urogdi, L. *Tetrahedron Lett.* **1989**, *30*, 3303.

[278] Flindt, E. P.; Rose, H.; Marsmann. H. C. *Z. Anorg. Allg. Chem.* **1977**, *430*, 155.

[279] Stegmann, H. B.; Bauer, G.; Breitmaier, E.; Herrman, E.; Scheffler, K. *Phosphorus* **1975**, *5*, 207.

[280] Stegmann, H. B.; Haller, R.; Scheffler, K. *Chem. Ber.* **1977**, *110*, 3817.

[281] Cadogan, J. I. G.; Stewart, N. J.; Tweddle, N. J. *J. Chem. Soc. Chem. Commun.* **1978**, 182.

[282] Sanchez, M.; Brazier, J. F.; Havalla, D.; Munoz, A.; Wolf, R. *J. Chem. Soc. Chem. Commun.* **1976**, 730.

[283] Cadogan, J. I. G.; Gosney, I.; Henry, E.; Naisby, T.; Nay, B.; Stewart, N. J.; Tweddle, N. J. *J. Chem. Soc. Chem. Commun.* **1979**, 189.

[284] Cadogan, J. I. G.; Stewart, N. J.; Tweddle, N. J.; *J. Chem. Soc. Chem. Commun.* **1979**, 191.

[285] Szmuszkovics, J.; Kane, M. P.; Laurian, L. G.; Chidester, C. G.; Scahill, T. A. *J. Org. Chem.* **1981**, *46*, 3562.

[286] Ittah, Y.; Sasson, Y.; Shahak, I.; Tsaroom, S.; Blum, J. *J. Org. Chem.* **1978**, *43*, 4271.

[287] Rutkovskii, E. K.; Kostina, V. G. Feshchenko, N. G. *J. Gen. Chem.* **1988**, *58*, 1117.

[288] Garcia, J.; Urpi, F.; Vilarrasa, J. *Tetrahedron Lett.* **1984**, *25*, 4841.

289 Zaloom, J.; Calandra, M.; Roberts, D. C. *J. Org. Chem.* **1985**, *50*, 2601.

290 Yim, A. S.; Akhtar, M. H.; Unrau, A. M.; Oehlschlager, A. C. *Can. J. Chem.* **1978**, *56*, 289.

291 Zimmer, H.; Jayawant, M. *Tetrahedron Lett.* **1966**, 5061.

292 Trippett, S.; Walker, D. M. *J. Chem. Soc.* **1960**, 2976.

293 Partos, R. D.; Speziale, A. J. *J. Am. Chem. Soc.* **1965**, *87*, 5068.

294 Derkach, G. I.; Gubnitskaya, E. S.; Kirsanov, A. V. *Zh. Obshch. Khim.* **1961**, *31*, 3679; *Chem. Abstr.* **1962**, *57*, 9876.

295 Corey, E. J.; Samuelsson, B.; Luzzio, F. A. *J. Am. Chem. Soc.* **1984**, *106*, 3682.

296 Maata, E. C.; Kim, C. *Inorg. Chem.* **1989**, *28*, 623.

297 Tsai, E. W.; Witczak, M.; Rajeshwar, K.; Pomerantz, M. *J. Electroanal. Chem.* **1987**, *236*, 219.

298 Hassner, A.; Galle, J. E. *J. Am. Chem. Soc.* **1970**, *92*, 3733.

299 Penkovskii, V. V.; Egorov, Y. P.; Shapoval, G. S. *J. Gen. Chem.* **1971**, *41*, 742.

300 Pak, C. M.; Gulick, W. M. *J. Korean. Chem. Soc.* **1974**, *18*, 341; *Chem. Abstr.* **1975**, *82*, 49224.

301 Appel, R.; Hauss, A.; Buchler, G. *Z. Naturforsch.* **1961**, *16b*, 405.

302 Kostina, V. G.; Feshchenko, N. G.; Rutkovskii, E. K. *J. Gen. Chem.* **1983**, *53*, 1223.

303 Zbiral, E. *Tetrahedron Lett.* **1966**, 2005.

304 Gutsch, P. A. *Diss. Abstr.* **1971**, *31B*, 5259.

305 Martynov, I. V.; Gafurov, R. G.; Ustinov, A. K.; Aleinikov, N. N.; Kashtanov, S. A. *Bull. Acad. Sci. USSR* **1987**, *36*, 1332.

306 Appel, R.; Vogt, F. *Chem. Ber.* **1962**, *95*, 2225.

307 Cameron, T. S.; Mannan, K.; Biddlestone, M.; Shaw, R. A. *Z. Naturforsch.* **1975**, *30b*, 973.

308 Wittig, G.; Kochendoerfer, E. *Chem. Ber.* **1964**, *97*, 741.

309 Fukui, K.; Sudo, R. *Bull. Chem. Soc. Jpn.* **1970**, *43*, 1160.

310 Bryce, M. R.; Moore, A. J.; Kim, Y. H.; Liu, Z. X.; Nowak, M. J. *Tetrahedron Lett.* **1987**, *28*, 4465.

311 Zhmurova, I. N.; Martynyuk, A. V.; Kirsanov, A. V. *J. Gen. Chem.* **1971**, *41*, 787.

312 Zimmer, H.; Jayawant, M.; Gutsch, P. *J. Org. Chem.* **1970**, *35*, 2826.

313 Katritzky, A. R.; Jiang, J.; Urogdi, L. *Synthesis* **1990**, 565.

314 Wamhoff, H.; Haffmanns, G.; Schmidt, H. *Chem. Ber.* **1983**, *116*, 1691.

315 Jochims, J. C.; Rahman, M. A.; Zsolnai. L.; Herzberger, S.; Huttner, G. *Chem. Ber.* **1983**, *116*, 3692.

316 Schmidbaur, H.; Jonas, G. *Chem. Ber.* **1967**, *100*, 1120.

317 Wolfsberger, W.; Schmidbaur, H. *J. Organomet. Chem.* **1971**, *28*, 301.

318 Wolfsberger, W. *J. Organomet. Chem.* **1979**, *173*, 277.

319 Scherer, O.; Schieder, G. *J. Organomet. Chem.* **1969**, *19*, 315.

320 Riesel, L.; Friebe, R. *Z. Anorg. Allg. Chem.* **1991**, *604*, 85.

321 Appel, R.; Buchler, G. *Z. Anorg. Allg. Chem.* **1963**, *320*, 3.

322 Wolfsberger, W.; Pickel, H. H.; Schmidbaur, H. *Z. Naturforsch.* **1971**, *26b*, 979.

[323] Marchenko, P. P.; Koidan, G. N.; Pinchuk, A. M.; Kirsanov, A. V. *J. Gen. Chem.* **1984**, *54*, 1581.

[324] Noth, H.; Meinel, L.; Madersteig, H. *Angew. Chem.* **1965**, *4*, 709.

[325] Bartsch, R.; Stelzer, O.; Schmutzler, R. *Z. Naturforsch.* **1991**, *46b*, 495.

[326] Shtepanek, A. S.; Zasorina, V. A.; Kirsanov, A. V. *J. Gen. Chem.* **1973**, *43*, 21.

[327] Kirsanov, A. V.; Shtepanek, A. S.; Pinchuk, A. M. *Ukr. Khim. Zh.* **1987**, *53*, 395; *Chem. Abstr.* **1988**, *109*, 110502.

[328] Zhmurova, I. N.; Martynyuk, A. P. *Zh. Obshch. Khim.* **1967**, *37*, 2706; *Chem. Abstr.* **1968**, *69*, 67491.

[329] Senning, A.; Kelly, P. *Naturwissenschaften* **1968**, *55*, 543.

[330] Appel, R.; Ruppert, I.; Montenarh, M. *Chem. Ber.* **1976**, *109*, 71.

[331] Ruppert, I.; Appel, R. *Chem. Ber.* **1978**, *111*, 751.

[332] Zimmer, H.; Singh, G. *Angew. Chem.* **1963**, *2*, 395.

[333] Takeishi, M.; Shiozawa, N. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 4063.

[334] Hawthorne, M. F. *J. Am. Chem. Soc.* **1961**, *83*, 367.

[335] Zimmer, H.; Singh, G. *J. Org. Chem.* **1964**, *29*, 3412.

[336] Brown, G. W.; Cookson, R. C.; Stevens, I. D. R.; Mak, T. C. W.; Trotter, J. *Proc. Chem. Soc.* **1964**, 87.

[337] Briggs, E. M.; Brown, G. W.; Dawson, W. T.; Jircny, J. *J. Chem. Soc. Chem. Commun.* **1975**, 641.

[338] Mak, T. C. W.; Trotter, *J. Acta Cryst.* **1965**, *18*, 81.

[339] Barluenga, J.; Lopez, F.; Palacios, F. *J. Chem. Soc. Chem. Commun.* **1985**, 1681.

[340] Barluenga, J.; Lopez, F.; Palacios, F. *J. Chem. Soc. Chem. Commun.* **1986**, 1574.

[341] Barluenga, J.; Marino, I.; Palacios, F. *J. Chem. Soc. Perkin Trans. (1)* **1991**, 341; *Tetrahedron Lett.* **1989**, *30*, 5493.

[342] Kobayashi, T.; Nitta, M. *Chem. Lett.* **1985**, 1459.

[343] Soliman, F. M.; Said, M. M. *Phosphorus Sulfur* **1991**, *61*, 335.

[344] Nitta, M.; Kanomata, N. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 2401.

[345] Nitta, M.; Ohnuma, M.; Iino, Y. *J. Chem. Soc. Perkin Trans. (1)* **1991**, 1115.

[346] Kanomata, N.; Kawaji, H.; Nitta, M. *J. Org. Chem.* **1992**, *57*, 618.

[347] Ciganek, E. *J. Org. Chem.* **1970**, *35*, 3631.

[348] Appel, R.; Halstenberg, M. *Chem. Ber.* **1976**, *109*, 814.

[349] Shahak, I.; Ittah, Y.; Blum, J. *Tetrahedron Lett.* **1976**, *17*, 4003.

[350] Huisgen, R.; Wulff, J. *Chem. Ber.* **1969**, *102*, 1848; *Tetrahedron Lett.* **1967**, 921.

[351] Schmidbaur, H.; Wolfsberger, W. *Chem. Ber.* **1968**, *101*, 1664.

[352] Cristau, H. J.; Manginot, E.; Torreilles, E. *Synthesis* **1991**, 382.

[353] Cristau, H. J.; Kadoura, J.; Chiche, L.; Torreilles, E. *Bull. Soc. Chem. Fr.* **1989**, 515.

[354] Cristau, H. J.; Garcia, C.; Kadoura, J.; Torreilles, E. *Phosphorus Sulfur* **1990**, *49/50*, 151; Cristau, H. J.; Manginot, E.; Perraud, A.; Torreilles, E. *Abstracts of Lectures*, 12th International Conference on Phosphorus Chemistry. Toulouse, Fr.; **1992**, 9.

[355] Wittig, G.; Hellwinkel, D. *Angew. Chem.* **1962**, *1*, 53.

[356] Wittig, G.; Kochendorfer, E. *Angew. Chem. (Ger.).* **1958**, *70*, 506.

[357] Wittig, G.; Maercker, A. *Chem. Ber.* **1964**, *97*, 749.

[358] Stuckwish, C. G. *J. Org. Chem.* **1976**, *41*, 1173.

[359] Barluenga, J.; Lopez, F.; Palacios, F. *J. Chem. Res.* (*S*) **1985**, 211; *Chem. Abstr.* **1986**, *104*, 34141.

[360] Roy, A. K.; Wettermark, U. G.; Scheide, G. M.; Wissian-Neilson, P.; Neilson, R. H. *Phosphorus Sulfur* **1987**, *33*, 147.

[361] Grim, S. O.; Kettler, P. B. *J. Chem. Soc. Chem. Commun.* **1991**, 979.

[362] Barluenga, J.; Lopez, F.; Palacios, F. *Synthesis* **1988**, 562.

[363] Dilworth, J. R.; de Leifde-Meijer, H. J.; Teuben, J. H. *J. Organomet. Chem.* **1978**, *159*, 47.

[364] Cramer, R. E.; Edelmann, F.; Mori, A. L.; Roth, S.; Gilje, J. W.; Tatsumi, K.; Nakamura, A. *Organometallics* **1988**, *7*, 841.

[365] Dubgen, R.; Muller, U.; Weller, F.; Dehnicke, K. *Z. Anorg. Allg. Chem.* **1980**, *471*, 89.

[366] Wiberg, N.; Schwenk, G.; Schmid, K. H. *Chem. Ber.* **1972**, *105*, 1209.

[367] Marringgele, W.; Meller, A.; Noth, H.; Schroen, R. *Z. Naturforsch.* **1978**, *33b*, 673.

[368] Roesky, H. W.; Schrumpf, F.; Noltemeyer, M. *Z. Naturforsch.* **1989**, *44b*, 35.

[369] Roesky, H. W.; Hesse, D.; Rietzel, M.; Noltemeyer, M. *Z. Naturforsch.* **1990**, *45b*, 72.

[370] Katti, K. V.; Singh, P. R.; Katti, K. K.; Barnes, C. L.; Kopicka, K.; Ketring, A. R.; Volkert, W. A. *Abstracts of Lectures*, 12th International Conference on Phosphorus Chemistry, Toulouse, Fr.; **1992**, 147.

[371] Roesky, H. W.; Seseke, U.; Noltemeyer, M.; Jones, P. G.; Sheldrick, G. M. *J. Chem. Soc. Dalton* **1986**, 1309.

[372] Roesky, H. W.; Swarat, K.; Edelmann, F. *Z. Naturforsch.* **1988**, *43b*, 231.

[373] Roesky, H. W.; Raubold, T.; Noltemeyer, M.; Witt, M.; Bohra, R. *Z. Naturforsch.* **1992**, *47b*, 171.

[374] Katti, K. V.; Roesky, H. W.; Rietzel, M. *Z. Anorg. Allg. Chem.* **1987**, *553*, 123.

[375] Hosler, K.; Weller, F.; Dehnicke, K. *Z. Naturforsch.* **1987**, *42b*, 1563.

[376] Volp, K.; Weller, F.; Dehnicke, K. *Z. Naturforsch.* **1987**, *42b*, 947.

[377] Munzenberg, J.; Noltemeyer, M.; Roesky, H. W. *Chem. Ber.* **1989**, *122*, 1915.

[378] Dehnicke, K.; Strahle, J. *Polyhedron* **1989**, *8*, 707.

[379] Katti, K. V.; Pinkerton, A. A.; Carell, R. G. *Inorg. Chem.* **1991**, *30*, 2631.

[380] Schmidbaur, H.; Wolfsberger, W. *Angew. Chem.* **1966**, *5*, 312; *Chem. Ber.* **1967**, *100*, 1000.

[381] Schmidbaur, H.; Wolfsberger, W. *Chem. Ber.* **1967**, *100*, 1016.

[382] Schmidbaur, H.; Wolfsberger, W. *Chem. Ber.* **1967**, *100*, 1023.

[383] Schmidbaur, H.; Kuhn, G.; Kruger, U. *Angew. Chem.* **1965**, *4*, 877.

[384] Appel, R.; Volz, P. *Z. Anorg. Allg. Chem.* **1975**, *413*, 45.

[385] Abel, E. W.; Mucklejohn, S. A.; Cameron, T. S.; Cordes, R. E. *Z. Naturforsch.* **1978**, *33b*, 339.

[386] Abel, E. W.; Mucklejohn, S. A. *Inorg. Chim. Acta* **1979**, *37*, 107.

[387] Seidel, W. *Angew. Chem.* **1965**, *4*, 785.

[388] Appel, R.; Schaaff, R. *Z. Naturforsch.* **1961**, *16b*, 405.

389 Fenske, D.; Bohm, E.; Dehnicke, K.; Strahle, J. *Z. Naturforsch.* **1988**, *43b*, 1.

390 Maurer, A.; Fenske, D.; Beck, J.; Hiller, W.; Strahle, J.; Bohm, E.; Dehnicke, K. *Z. Naturforsch.* **1988**, *43b*, 5.

391 Bohm, E.; Dehnicke, K.; Beck, J.; Hiller, W.; Strahle, J.; Maurer, A.; Fenske, D. *Z. Naturforsch.* **1988**, *43b*, 138.

392 Vicente, J.; Chicote, M. T.; Baeza, J. F.; Lahoz, F. J.; Lopez, J. A. *Inorg. Chem.* **1991**, *30*, 3617.

393 Katti, K. V.; Batchelor, R. J.; Einstein, F. W.; Cavell, R. G. *Inorg. Chem.* **1990**, *29*, 808.

394 Fukui, M.; Itoh, K.; Ishii, Y. *Bull. Chem. Soc. Jpn.* **1975**, *48*, 2044.

395 Imhoff, P.; Elsevier, C. J. *J. Organomet. Chem.* **1989**, *361*, C61.

396 Bock, H.; tom Dieck, H. *Z. Naturforsch.* **1966**, *21b*, 739.

397 Darensbourg, D. J.; Pala, M.; Simmons, D.; Rheingold, A. L. *Inorg. Chem.* **1986**, *25*, 3537.

398 Sleiman, H. F.; Mercer, S.; McElwee-White, L. *J. Am. Chem. Soc.* **1989**, *111*, 8007.

399 Miller, J. S.; Visscher, M. O.; Caulton, K. G. *Inorg. Chem.* **1974**, *13*, 1632.

400 Heiber, W.; Winter, E.; Schubert, E. *Chem. Ber.* **1962**, *95*, 3070.

401 Ang, H. G.; Cai, Y. M.; Koh, L. L.; Kwik, W. L. *J. Chem. Soc. Chem. Commun.* **1991**, 850.

402 Chatt, J.; Dilworth, J. R. *J. Chem. Soc. Chem. Commun.* **1972**, 549.

403 Chong, O. A.; Oshima, K.; Sharpless, K. B. *J. Am. Chem. Soc.* **1977**, *99*, 3420.

404 Appel, R.; Siegemund, G. *Z. Anorg. Allg. Chem.* **1968**, *363*, 183.

405 Bestmann, H. J.; Zimmerman, R. In *Organophosphorus Compounds*; Kosolapoff, G. M. and Maier, L., Eds.; Wiley Interscience: New York, 1972; Chapter 5A, pp. 142–145.

406 Zhmurova, I. N.; Yurchenko, R. I. *Zh. Obshch. Khim.* **1968**, *38*, 613; *Chem. Abstr.* **1968**, *69*, 107589.

407 Herring, D. L. *J. Org. Chem.* **1961**, *26*, 3998.

408 Paciorek, K. L.; Kratzer, R. H. *J. Org. Chem.* **1966**, *31*, 2426.

409 Cavell, R. G.; Reed, R. W.; Katti, K. V.; Balakrishna, M. S.; Collins, P. W.; Mozol, V.; Bartz, I. *Abstracts of Lectures*, 12th International Conference on Phosphorus Chemistry, Toulouse, Fr.; **1992**, 13.

410 Kovtun, V. Y.; Gilyarov, V. A.; Kabachnik, M. I. *Izv. Akad. Nauk SSSR* **1972**, *11*, 2612; *Chem. Abstr.* **1973**, *78*, 58542.

411 Imhoff, P.; van Asselt, R.; Elsevier, C. J.; Vrieze, K.; Goubitz, K.; van Molssen, K. F.; Stam, C. H. *Phosphorus Sulfur* **1990**, *47*, 401.

412 Appel, R.; Ruppert, I. *Z. Anorg. Allg. Chem.* **1974**, *406*, 131.

413 Appel, R.; Ruppert, I. *Chem. Ber.* **1975**, *108*, 919.

414 Kabachnik, M. I.; Gilyarov, V. A.; Koudriavtsev, R. V. *Tetrahedron Lett.* **1965**, 2691.

415 Scherer, O. J.; Klusman, P. *Angew. Chem.* **1968**, *7*, 541.

416 Scherer, O. J.; Schnabl, G. *Inorg. Chim. Acta* **1976**, *19*, L38.

417 Moeller, T.; Vandi, A. *J. Org. Chem.* **1962**, *27*, 3511.

418 Wiberg, N.; Raschig, F. *Angew. Chem.* **1962**, *1*, 335.

419 Appel, R.; Buchler, G. *Z. Naturforsch.* **1962**, *17b*. 422.

420 Cookson, R. C.; Hughes, A. N. *J. Chem. Soc.* **1963**, 6061.

421 Ruff, J. K.; Schlientz, J. S. *Inorg. Synth.* **1974**, *15*, 84.

422 Lalor, F. J.; Chaona, S. *J. Organomet. Chem.* **1988**, *344*, 163.

423 Chin, H. B.; Smith, M. B.; Wilson, R. D.; Bau, R. *J. Am. Chem. Soc.* **1974**, *96*, 5285.

424 Goldfield, S. A.; Raymond, K. N. *Inorg. Chem.* **1974**, *13*, 770.

425 Farrugia, L. J.; Howard, J. A. K.; Mitrprachachon, P.; Stone, F. G. A.; Woodward, P. *J. Chem. Soc. Dalton* **1981**, 1134.

426 Cotton, F. A.; Darensbourg, D. J.; Kolthammer, B. W. S. *J. Am. Chem. Soc.* **1981**, *103*, 398.

427 Handy, L. B.; Ruff, J. K.; Dahl, L. F. *J. Am. Chem. Soc.* **1970**, *92*, 7312, 7327.

428 Ruff, J. K.; White, R. P.; Dahl. L. F.; *J. Am. Chem. Soc.* **1971**, *93*, 2159.

429 Kirtley, S. W.; Andrews, M. A.; Bau, R.; Grynkewich, G. W.; Marks, T. J.; Tipton, D. L.; Whittlesey, B. R. *J. Am. Chem. Soc.* **1977**, *99*, 7154.

430 Andrews, S. J.; Robb, D. A.; Welch, A. J. *Acta Cryst.* **1983**, *39C*, 880.

431 Ahmad, M. M.; Brya, M. R.; Halfpenny, J.; Weiler, L. *Tetrahedron Lett.* **1984**, *25*, 4275.

432 Longoni, L.; Manassero, M.; Sansoni, M. *J. Organomet. Chem.* **1979**, *174*, C41.

433 Uson, R.; Laguna, A.; Laguna, M.; Jones, P. G.; Sheldrick, G. M.; *J. Chem. Soc. Dalton* **1981**, 366.

434 Glidewell, C. *J. Organomet. Chem.* **1978**, *159*, 23.

435 Staudinger, H.; Meyer, J. *Helv. Chim. Acta* **1919**, *2*, 619.

436 Staudinger, H.; Luscher, G. *Helv. Chim. Acta* **1922**, *5*, 75.

437 Ramirez, F.; Levy, S. *J. Org. Chem.* **1958**, *23*, 2037.

438 Webster, O. W. *J. Am. Chem. Soc.* **1966**, *88*, 4055.

439 Bestmann, H. J.; Buckschewski, H.; Leube, H. *Chem. Ber.* **1959**, *92*, 1345.

440 Wittig, G.; Schlosser, M. *Tetrahedron* **1962**, *18*, 1023.

441 Diekmann, J. *J. Org. Chem.* **1963**, *28*, 2933.

442 Khokhlov, P. S.;Kashemirov, B. A.; Mikityuk, A. D.; Strepikheev, Y. A.; Chimishkyan, A. L. *J. Gen. Chem.* **1984**, *54*, 2495.

443 Moderhack, D.; Peru, L. *J. Chem. Soc. Chem. Commun.* **1988**, 1144.

444 Arbuzov, B. A.; Polozov, A. M.; Polezhaeva, N. A. *J. Gen. Chem.* **1984**, *54*, 1755.

445 Reid, W.; Hersek, S.; Trummlitz, H. *Liebigs Ann. Chem.* **1966**, *692*, 105.

446 Goetz, H.; Juds, H. *Leibigs Ann. Chem.* **1964**, *678*, 1.

447 Bethell, D.; Dunn, S. F. C.; Khodaei, M. M.; Newall, A. R. *J. Chem. Soc. Perkin Trans. (2)* **1989**, 1829.

448 Disselnkotter, H. *Angew. Chem.* **1964**, *3*, 379.

449 Ciganek, E. *J. Am. Chem. Soc.* **1965**, *87*, 652.

450 Gale, D. M.; Middleton, W. J.; Krespan, C. G. *J. Am. Chem. Soc.* **1965**, *87*, 657.

451 Bestmann, H. J.; Fritzche, H. *Chem. Ber.* **1961**, *94*, 2477.

452 Walker, C. C.; Schechter, H. *Tetrahedron Lett.* **1965**, 1447.

453 Goetz, H.; Juds, H. *Liebigs Ann. Chem.* **1966**, *698*, 1.

454 Goetz, H.; Klabuhn, B.; Juds, H. *Liebigs Ann. Chem.* **1970**, *735*, 88.

455 Horner, L.; Lingnau, E. *Liebigs Ann. Chem.* **1955**, *591*, 135.

456 Bestmann, H. J.; Gothlich, L. *Liebigs Ann. Chem.* **1962**, *655*, 1.

457 Dalton, D. R.; Liebman, S. A. *Tetrahedron* **1969**, *25*, 3321.

458 Wittig, G.; Schwarzenbach, K. *Liebigs Ann. Chem.* **1961**, *650*, 1.

459 Suzuki, N.; Wakatsaki, S.; Izawa, Y. *Tetrahedron Lett.* **1980**, *21*, 2313.

460 Akasaka, T.; Sato, R.; Miyama, Y.; Ando, W. *Tetrahedron Lett.* **1985**, *26*, 843.

461 Akasaka, T.; Sato, R.; Ando, W. *J. Am. Chem. Soc.* **1985**, *107*, 5539.

462 Murphy, C. J.; San Filippo, L. J.; Guziec, F. S. *Abstracts of Papers*, 191st National Meeting of the American Chemical Society, New York; American Chemical Society: Washington, DC, 1986; ORGN 31.

463 Miyamoto, T.; Matsumoto, J. I. *Chem. Pharm. Bull.* **1988**, *36*, 1321.

464 Bellan, J.; Marre-Mazieres, M. R.; Sanchez, M.; Songstad, J. *C. R. Seances Acad. Sci.* **1985**, *301*, 785.

465 Horner, L.; Schmelzer, H. G. *Chem. Ber.* **1961**, *94*, 1326.

466 Ried, W.; Appel, H. *Liebigs Ann. Chem.* **1961**, *646*, 82.

467 Braunholtz, W. *J. Chem. Soc.* **1922**, *121*, 300.

468 Schonberg. A.; Brosowski, K. H. *Chem. Ber.* **1959**, *92*, 2602.

469 Brown, G. W.; Cookson, R. C.; Stevens, I. D. R. *Tetrahedron Lett.* **1964**, 1263.

470 Zhmurova, I. N.; Kirsanov, A. V. *J. Gen. Chem.* **1960**, *30*, 3018.

471 Zhmurova, I. N.; Kirsanov, A. V. *J. Gen. Chem.* **1962**, *32*, 2540.

472 Zhmurova, I. N.; Drach, B. S. *Zh. Obshch. Khim.* **1964**, *34*, 1441; *Chem. Abstr.* **1964**. *61*, 5499.

473 Bermann, M.; Utvary, K. *Monatsh. Chem.* **1969**, *100*, 1041.

474 Fluck, E.; Wachtler, D. *Liebigs Ann. Chem.* **1980**, 1651.

475 Latscha, H. P.; Hormuth, P. B. *Z. Anorg. Allg. Chem.* **1968**, *359*, 81.

476 Chapman, A. C.; Holmes, W. S.; Paddock, N. L.; Searle, H. T. *J. Chem. Soc.* **1961**, 1825.

477 Glidewell, C. *Angew. Chem.* **1975**, *14*, 826.

478 Zhmurova, I. N.; Drach, B. S. *J. Gen. Chem.* **1964**, *34*, 3091.

479 Becke-Goering, M.; Leichner, L.; Schorf, B. *Z. Anorg. Allg. Chem.* **1966**, *343*, 154.

480 Kirsanov, A. V.; Derkach, G. I. *J. Gen. Chem.* **1956**, *26*, 2245.

481 Kirsanov, A. V. *J. Gen. Chem.* **1952**, *22*, 329.

482 Zhmurova, I. N.; Drach, B. S.; Kirsanov, A. V. *J. Gen. Chem.* **1965**, *35*, 344.

483 Gurarii, L. I.; Mukmenev, E. T. *J. Gen. Chem.* **1987**, *56*, 2346.

484 Zhmurova, I. N.; Kirsanov, A. V. *Zh. Obshch. Khim.* **1963**, *33*, 1015; *Chem. Abstr.* **1963**, *59*, 8782.

485 Bock, H.; Wiegraße, W. *Chem. Ber.* **1966**, *99*, 1068.

486 Shevchenko, V. I.; Stratienko, V. T.; Pinchuk, A. M. *Zh. Obshch. Khim.* **1960**, *30*, 1566; *Chem. Abstr.* **1961**, *55*, 1490.

487 Shevchenko, V. I.; Stratienko, V. T.; Pinchuk, A. M. *J. Gen. Chem.* **1965**, *35*, 362.

488 Zhmurova, I. N.; Kirsanov, A. V. *Zh. Obshch. Khim.* **1961**, *31*, 3685; *Chem. Abstr.* **1962**, *57*, 13795.

489 Bodnarchuk, N. D.; Gavrilenko, B. B.; Derkach, G. I. *J. Gen. Chem.* **1970**, *40*, 1455.

490 Shevchenko, V. I.; Merkulova, Z. V. *Zh. Obshch. Khim.* **1959**, *29*, 1005; *Chem. Abstr.* **1960**, *54*, 1371.

491 Shokol, V. A.; Gamaleya, V. F.; Kukhar, V. P. *J. Gen. Chem.* **1970**, *40*, 420.

492 Bunting, R. K.; Schmulbach, C. D. *Inorg. Chem.* **1966**, *5*, 533.

493 Hoffmann, H.; Grunewald, R.; Horner, L. *Chem. Ber.* **1960**, *93*, 861.

494 Riesel, L.; Sturm, D,; Nagel, A.; Taudien, S.; Beuster, A.; Karwatski, A. *Z. Anorg. Allg. Chem.* **1986**, *542*, 157.

495 Singer, R.; Storzer, W.; Schmutzler, R. *Z. Anorg. Allg. Chem.* **1987**, *555*, 154.

496 Roesky, H. W.; Grimm, L. F. *Angew. Chem.* **1970**, *9*, 244.

497 Schmutzler, R. *J. Chem. Soc. Chem. Commun.* **1965**, 19.

498 Roesky, H. W.; Remmes, G. *Z. Naturforsch.* **1971**, *26b*, 75.

499 Tarasevich, A. S.; Boldeskuhl, I. E.; Kukhar, V. P. *Russ. Chem. Revs.* **1986**, *55*, 758.

500 Tsvetkov, E. N.; Korkin, A. A. *J. Gen. Chem.* **1989**, *59*, 849.

501 Hoard, J. L.; Jacobson, R. A. *J. Chem Soc. (A)* **1966**, 1203.

502 Hess, H.; Forst, D. *Z. Anorg. Allg. Chem.* **1966**, *342*, 240.

503 Almenningen, A.; Anderson, B.; Astrup, E. E. *Acta Chem. Scand.* **1969**, *23*, 2179.

504 Cox, J. W.; Corey, E. R. *J. Chem. Soc. Chem. Commun.* **1967**, 123.

505 Fild, M.; Sheldrick, W. S.; Stankiewicz, T. *Z. Anorg. Allg. Chem.* **1975**, *415*, 43.

506 Sheldrick, W. S.; Hewson, M. J. C. *Acta Cryst.* **1975**, *31B*, 1209.

507 Adamson, G. W.; Bart, J. C. J. *J. Chem. Soc. (A)* **1970**, 1452; *J. Chem. Soc. Chem. Commun.* **1969**, 1036.

508 Harris, R. K.; Wazeer, M. I. M.; Schlack, O.; Schmutzler, R.; Sheldrick, W. S. *J. Chem. Soc. Dalton* **1977**, 517.

509 Kukhar, V. P.; Grishkun, E. V.; Kalibabchuk. N. N. *J. Gen. Chem.* **1982**, *52*, 1982.

510 Haubold, W.; Becke-Goering, M. *Z. Anorg. Allg. Chem.* **1970**, *372*, 273.

511 Riesel, L.; Sturm, D.; Zschunke, A.; Thomas, B. *Z. Anorg. Allg. Chem.* **1987**, *544*, 225.

512 Ulrich, H.; Sayigh, A. A. *Angew. Chem.* **1962**, *1*, 595.

513 Zhmurova, I. N.; Drach, B. S.; Kirsanov, A. V. *Zh. Obshch. Khim.* **1965**, *35*, 1018; *Chem. Abstr.* **1965**, *63*, 9796.

514 Heukel, J.; Hammontou, Y.; de Jaeger, R. *Phosphorus Sulfur* **1991**, *63*, 19.

515 Riesel, L. *Z. Chem.* **1983**, *23*, 344.

516 Kirsanov, A. V.; Shevchenko, V. I. *J. Gen. Chem.* **1954**, *24*, 483.

517 Shevchenko, V. I.; Tkach, V. P.; Kirsanov, A. V. *Zh. Obshch. Khim.* **1963**, *32*, 4047; *Chem. Abstr.* **1963**, *58*, 13832.

518 Shevchenko, V. I.; Stratienko, V. T. *Zh. Obshch. Khim.* **1960**, *30*, 1958; *Chem. Abstr.* **1961**, *55*, 6425.

519 Zhmurova, I. N.; Voitsekhouskaya, I. Y.; Kirsanov, A. V. *Zh. Obshch. Khim.* **1961**, *31*, 3741; *Chem. Abstr.* **1962**, *57*, 9702.

520 Blonsky, P. M.; Shriver, D. F.; Austin, P.; Allcock. H. R. *J. Am. Chem. Soc.* **1984**, *106*, 6854.

521 Bermann, M.; Utvary, K. *Monatsh. Chem.* **1969**, *100*, 1280.

522 Shevchenko, M. V.; Kukhar, V. P. *J. Gen. Chem.* **1986**, *56*, 73.

523 Shevchenko, V. I.; Stratienko, V. T. *Zh. Obshch. Khim.* **1959**, *29*, 3458; *Chem. Abstr.* **1960**, *54*, 15284.

524 Marchenko, A. P.; Miroshnichenko, V. V.; Pinchuk, A. M. *J. Gen. Chem.* **1984**, *54*, 1086.

525 Kirsanov, A. V.; Derkach, G. I. *Zh. Obsch. Khim.* **1956**, *26*, 2631; *Chem. Abstr.* **1956**, *51*, 1821.

526 Kabachnik, M. I.; Gilyarov, V. A. *Bull. Acad. Sci. USSR* **1956**, 809.

527 Goldwhite, H.; Gysegem, P.; Schow, S.; Swyke, C. *J. Chem. Soc. Dalton* **1975**, 12.

528 Laszlo, P.; Polla, E. *Tetrahedron Lett.* **1984**, *25*, 4651.

529 Zwierzak, A.; Koziara, A. *Phosphorus Sulfur* **1987**, *30*, 331.

530 Arrington, D. E. *J. Chem. Soc. Dalton* **1975**, 1221.

531 Goedler, J.; Ullmann, H. *Chem. Ber.* **1961**, *94*, 1067.

532 Marre. M. R.; Sanchez, M.; Brazier, J. F.; Wolf, R.; Bellan, J. *Can. J. Chem.* **1982**, *60*, 456.

533 Lei, G.; Xu, H.; Xu, X. *Phosphorus Sulfur* **1992**, *66*, 101.

534 Kabachnik, M. I.; Gilyarov. V. A. *Izv. Akad. Nauk SSSR* **1961**, 816; *Chem. Abstr.* **1961**, *55*, 27014.

535 Schlack, O.; Stadelmann, W.; Stelzer, O.; Schmutzler, R. *Z. Anorg. Allg. Chem.* **1976**, *419*, 275.

536 Kabachnik, M. I.; Gilyarov, V. A. *Izv. Akad. Nauk SSSR* **1961**, 819.

537 Zhmurova, I. N.; Kirsanov, A. V. *Zh. Obshch. Khim.* **1959**, *29*, 1687; *Chem. Abstr.* **1960**, *54*, 8688.

538 Al-khathlan, H. Z.; Al-Lohedan, H. A. *Phosphorus Sulfur* **1991**, *63*, 301.

539 Glidewell, C. *J. Organomet. Chem.* **1976**, *108*, 335.

540 Steinbach. J.; Hermann, E.; Riesel, L. *Z. Anorg. Allg. Chem.* **1984**, *511*, 51.

541 Albrecht, S.; Hermann, E.; John, A. *Z. Anorg. Allg. Chem.* **1987**, *552*, 132.

542 Sundberg. R. J. *J. Am. Chem. Soc.* **1966**, *88*, 3781.

543 Gilyarov, V. A.; Tikhonina, N. A.; Andrianov, V. G.; Struchkov, Y. T.; Kabachnik. M. I. *J. Gen. Chem.* **1978**, *48*, 670.

544 Koziara, A. *J. Prakt. Chem.* **1988**, *330*, 473.

545 Gilyarov, V. A.; Kudryavtsev, R. V.; Kabachnik, M. I. *Zh. Obshch. Khim.* **1966**, *36*, 708; *Chem. Abstr.* **1966**, *65*, 8798.

546 Koziara, A.; Zwierzak, A. *Tetrahedron Lett.* **1987**, *28*, 6513.

547 Zidani, A.; Carrie, R.; Vaultier, M. *Bull. Soc. Chim. Fr.* **1992**, 71.

548 Chaturvedi, R. K.; Pletcher, T. C.; Zioudron, C.; Schmir. G. C. *Tetrahedron Lett.* **1970**, 4339.

549 Gilyarov, V. A. *Russ. Chem. Revs.* **1978**, *47*, 870.

550 Pudovik, A. N.; Aladzheva, I. M.; Kotova, V. G.; Zinkovskii, A. F. *J. Gen. Chem.* **1969**, *39*, 1498.

551 Shevchenko, V. I.; Tkach, V. P.; Kirsanov, A. V. *Zh. Obshch. Khim.* **1965**, *35*, 1224; *Chem. Abstr.* **1965**, *63*, 11411.

552 Kay, I. T.; Snell, B. K. *Tetrahedron Lett.* **1967**, 2251.

553 Flindt, E.; Rose, H. *Z. Anorg. Allg. Chem.* **1977**, *428*, 204.

554 Wisian-Neilson, P.; Neilson, R. H. *J. Am. Chem. Soc.* **1980**, *102*, 2848.

555 Genkina, G. K.; Gilyarov, V. I.; Matrosov, E. I.; Kabachnik, M. I. *J. Gen. Chem.* **1970**, *40*, 1482.

556 Gilyarov, V. A.; Tikhonia, N. A.; Kabachnik, M. I. *Zh. Obshch. Khim.* **1971**, *41*, 2355; *Chem. Abstr.* **1972**, *76*, 113303.

557 Hickey, D. M. B.; MacKenzie, A. R.; Moody, C. J.; Rees, C. W. *J. Chem. Soc. Chem. Commun.* **1984**, 776; *J. Chem. Soc. Perkin Trans. (1)* **1987**, 921.

558 Gajda, T.; Koziara, A.; Osowska-Pacewicka, K.; Zawadzki, S.; Zwierzak, A. *Synth. Comm.* **1992**, *22*, 1929.

559 Foster, S. A.; Leyshon, L. J.; Saunders, D. G. *J. Chem. Soc. Chem. Commun.* **1973**, 29.

560 Lee, K. J.; Choi, D. O.; Kim, S.; Jeong, J. U.; Park, H. *Synthesis* **1990**, 455.

561 Leyshon, L.; Saunders, D. G. *J. Chem. Soc. Chem. Commun.* **1971**, 1608.

562 Kabachnik. M. I.; Gilyarov, V. A. *Dokl. Akad. Nauk USSR* **1956**, *106*, 473; *Chem. Abstr.* **1956**, *50*, 13723.

563 Poshkus, A. C.; Herweh, J. E. *J. Org. Chem.* **1962**, *27*, 2700.

564 Shokol, V. A.; Molyavko, L. I.; Derkach, G. I. *J. Gen. Chem.* **1970**, *40*, 983.

565 Appel, R.; Eirig, H. *Chem. Ber.* **1975**, *108*, 914.

566 Zwierzak, A. *Synthesis* **1984**, 332.

567 Hodgson, P. K. G.; Katz, R.; Zon, G. *J. Organomet. Chem.* **1976**, *117*, C63.

568 Wadsworth, W. S.; Emmons. W. D. *J. Am. Chem. Soc.* **1962**, *84*, 1316.

569 Wadsworth, W. S.; Emmons, W. D. *J. Org. Chem.* **1964**, *29*, 2816.

570 Major, R. T.; Hedrick, R. J. *J. Org. Chem.* **1965**, *30*, 1268.

571 Olejniczak, B.; Zwierzak, A. *Synthesis* **1989**, 300.

572 Zhmurova, I. N.; Kirsanov, A. V. *Zh. Obshch. Khim.* **1963**, *33*, 182; *Chem. Abstr.* **1963**, *59*, 657.

573 Hewlins, M. J. E. *J. Chem. Soc.* (*B*) **1971**, 942.

574 Llamas-Saiz, A. L.; Foces-Foces, C.; Molina, P.; Alajarin, M.; Vidal, A.; Claramunt, R. M.; Elguero, J. *J. Chem. Soc. Perkin Trans. (2)* **1991**, 1025.

575 Butterfield, P. J.; Tebby, J. C. *J. Chem. Soc. Perkin Trans. (1)* **1978**, 1237.

576 Chiu, K. W.; Fawcett, J.; Kemmitt, R. D. W.; Russell, D. R. *J. Chem. Soc. Dalton* **1986**, 457.

577 Cameron, A. F.; Hair, N. J.; Morris, D. G. *Acta Cryst.* **1974**, *30B*, 221.

578 Beck, R.; Zsolnai, L.; Huttner, G.; Herzberger, S.; Jochims, J. C. *Chem. Ber.* **1982**, *115*, 2981.

579 Holt, E. M.; Holt, S. L. *J. Chem. Soc. Dalton* **1974**, 1990.

580 Liblong, S. W.; Oakley, R. T.; Cordes, A. W.; Noble, M. C. *Can. J. Chem.* **1983**, *61*, 2062.

581 Babu, Y. S.; Manohar, H.; Cameron, T. S. *Acta Cryst.* **1979**, *35B*, 1410.

582 Cameron, T. S.; Prout, C. K. *J. Chem. Soc.* (*C*) **1969**, 2281.

583 Bodeker, J.; Kockritz, A.; Kockritz, P.; Radeglia, R. *J. Prakt. Chem.* **1985**, *327*, 723.

584 Schmidbaur, H.; Blaschke, G. *Z. Naturforsch.* **1978**, *33b*, 1556.

585 Wolfsberger, W. *Z. Naturforsch.* **1988**, *43b*, 295.

586 Kostina, V. G.; Rutkovskii, E. K.; Feshchenko, N. G. *J. Gen. Chem.* **1991**, *61*, 767.

587 Birkofer, L.; Ritter, A.; Kim, S. M. *Chem. Ber.* **1963**, *96*, 3099.

588 Yoshida, H.; Ogata, T.; Inokawa, S. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 1541.

589 Shevchenko, V. I.; Shtepanek, A. S.; Kirsanov, A. V. *Zh. Obshch. Khim.* **1962**, *32*, 2595; *Chem. Abstr.* **1963**, *58*, 9126.

590 Marsh, F. O.; Hermes, M. E. *J. Am. Chem. Soc.* **1964**, *86*, 4506.

591 Mitsch, R. A. *J. Am. Chem. Soc.* **1967**, *89*, 6297.

592 Zinner, G.; Beck, G.; Fehlhammer, W. P.; Wiberg, N. *J. Organomet. Chem.* **1989**, *368*, 23.

593 Senning, A.; Kelly, P. *Naturwissenchaften* **1968**, *55*, 543.

594 Westberg, D. S.; Arrington. D. E. *Synth. React. Inorg. Met.-Org. Chem.* **1988**, *18*, 301.

595 Baldwin, R. A.; Washburn, R. M. *J. Org. Chem.* **1965**, *30*, 2093.

596 Hiebl, J.; Zbiral, E. *Liebigs Ann. Chem.* **1988**, 765.

597 Kulpe, S.; Seidel, I. *Z. Chem.* **1984**, *24*, 110.

598 Ranganathan, R.; Larwood, D. *Tetrahedron Lett.* **1978**, 4341.

599 Mohan, T.; Day, R. O.; Holmes, R. R. *Inorg. Chem.* **1992**, *31*, 2271.

# 14

# TRANSITION METAL COMPLEXES WITH YLIDES

William C. Kaska and K. Alexander Ostoja Starzewski

## 14.1 INTRODUCTION

The charge distribution and energy levels of ylides can be conveniently viewed as the result of specific donor–acceptor interactions between phosphines and carbenes. These interactions resemble those of phosphines coordinated to metal fragments in a general topological and isolobal sense (Eq. 14.1). By extending

$$R_3P \dashrightarrow CR'R'' \qquad \text{vs} \qquad R_3P \dashrightarrow ML_n \tag{14.1}$$

Phosphorus carbon ylide — Phosphorus transition metal ylide

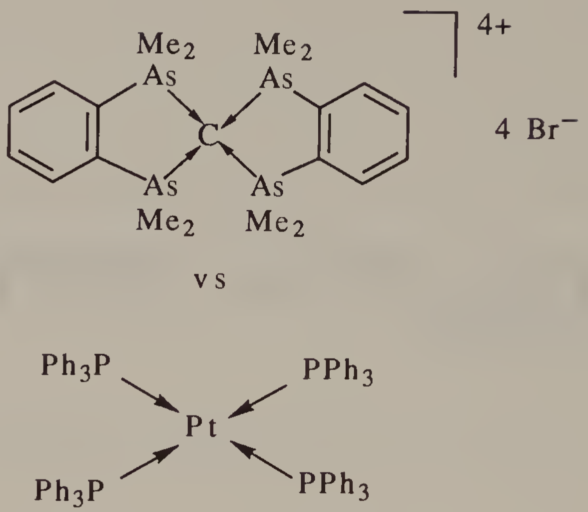
this analogy to other donor atoms like (1) nitrogen, arsenic, or sulfur in complexes with transition metals, (2) their counterparts with carbon (N, P, As, S ylides), (3) nitrogen (phosphine imines, etc.), and (4) oxygen (phosphine oxides, sulfoxides, etc.) several branches of chemistry can be related. By this logic a carbodiphosphorane, which can be viewed as two phosphine ligands complexed to a formally zerovalent carbon, resembles bis(phosphine)platinum(0) (Eq. 14.2).

$$R_3P \dashrightarrow C \dashleftarrow PR_3 \qquad R_3P \dashrightarrow Pt \dashleftarrow PR_3 \tag{14.2}$$

Even "coordination number expansion" by phosphorus or arsenic can be depicted by this analogy, so that a study of the ylide bond could add to an understanding of ylide-like transition metal complexes. The extreme resonance structure for the carbodiphosphorane and the analogy to transition metal complexes shown in equations 14.2 and 14.3 were originally suggested in 1973.[1–3]

---

*Ylides and Imines of Phosphorus*, Edited by A. William Johnson.
ISBN 0-471-52217-1 © 1993 John Wiley & Sons, Inc.



(14.3)

On the other hand, ylides themselves provide an outstanding ligand potential for synthetic, catalytic, and theoretical aspects of transition metal chemistry. The extreme bond system of phosphorus–carbon ylides is reflected in very low first ionization potentials (Table 14.1). Photoelectron spectroscopic data place this class of isolable energy rich compounds on the very top of an energy scale of ligands that do not have a net charge. The molecular property "$IE_1$" is a quantitative description for the energetic availability of an outermost valence electron and thus a prominent feature of reactivity. Within a molecular orbital approximation, the electron is ejected from the highest occupied molecular

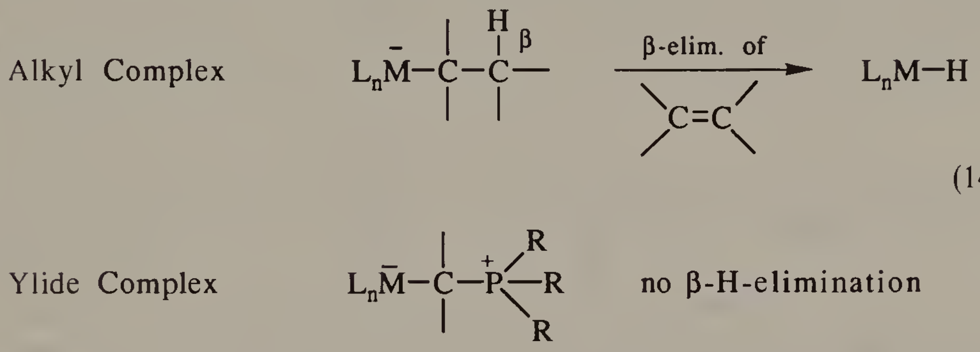
**TABLE 14.1 Gas-Phase UV–PES Vertical Ionization Potentials $IE_1$ (eV) of Ylides ("$n_c$-"), and Related Phosphines ($n_P$)**[a]

| | | R = Me | R = Ph | Ref |
|---|---|---|---|---|
| $R_3PCHCHCHMe$ | "$n_c^{\pi}$-" | 6.02 | 5.95 | 7 |
| $R_3PCHCHCHPh$ | "$n_c^{\pi}$-" | 6.20 | | 7 |
| $R_3PCHCHCH_2$ | "$n_c^{\pi}$-" | 6.20 | | 7 |
| $R_3PCHPh$ | "$n_c^{\pi}$-" | 6.19 | 6.01 | 7 |
| $R_3PCHMe$ | "$n_c^{\pi}$-" | | 6.15 | 7 |
| $R_3PCH_2$ | "$n_c^{\pi}$-" | 6.81 | 6.62 | 7 |
| $R_3PCHSiMe_3$ | "$n_c^{\pi}$-" | 6.81 | 6.71 | 6 |
| $R_3PC(SiMe_3)_2$ | "$n_c^{\pi}$-" | 6.92 | | 6 |
| $R_3AsCH_2$ | "$n_c^{\sigma}$-" | 6.72 | | 8 |
| $R_3AsCHSiMe_3$ | "$n_c^{\pi}$-" | 6.56 | | 8 |
| $R_3AsC(SiMe_3)_2$ | "$n_c^{\pi}$-" | 6.66 | | 8 |
| $R_3PCp$ | $\pi_{C=C}$/"$n_c^{\pi}$-" | 6.82/7.02 | 6.66/6.91 | 7, 9 |
| $R_3PC(CN)_2$ | "$n_c^{\pi}$-" | | 7.63 | 10 |
| $R_3P$ | $n_P$ | 8.60 | 7.80 | 7 |

[a] Abbreviations: Me = Methyl, Ph = Phenyl, Cp = Cyclopentadienide; "$n_c$" designates ionization from an orbital with largest coefficient on the ylidic carbon.

orbital (HOMO). Molecular orbital calculations at various levels of sophistication (EHMO, CNDO, MNDO, ab initio) describe the HOMOs of most ylides as being strongly localized on the ylidic carbon. Exceptions to this are found for cyclopentadienide derivatives, where the orbital of corresponding symmetry is the HOMO-1. In terms of reactivity, the low first ionization potentials of ylides reflect high oxidizability, high proton affinity, and basicity.

Chapter 2 of this monograph reviews studies of the electronic structure and bonding of ylides and an analysis of the electronic structure and reactivity of ylides and analogous iminophosphoranes also has been published by Ostoja Starzewski and tom Dieck[4] as well as Fackler.[5] These ylide characteristics, together with their ability to form ylide anions, and their ease of synthesis make them exciting and versatile ligands to transition metals. Thus ylides as ligands with practically no back-bonding characteristics offer a unique way of preparing carbon–metal bonded species. This is particularly so because a major kinetic pathway for the decomposition of transition metal alkyl moieties, the $\beta$-elimination, is blocked by the phosphonium group (Eq. 14.4). Accordingly, in the past two decades a variety of ylide-metal structural arrangements have been synthetically accomplished with, no doubt, many more to come (Fig. 14.1). The impressive range of organometallic ylide chemistry already covers most of the d-block and some f-block elements. Their structural variety may be grouped and rationalized in terms of ylide coordination modes designated **A**–**N** as shown in Figure 14.1. Throughout this chapter reference is made to these ylide bond-centered coordination modes by letter and number to indicate compound type and number. Many additional complex types exist which are based on remote ligating functions and are designated by **X**.



(14.4)

**A** represents the fundamental monodentate $\sigma$-complex. Its metal carbon bond may be described in a simplified manner as the result of a two electron/two orbital stabilizing interaction between the high lying carbon-centered ylide HOMO "$n_{c-}$" and a vacant metal orbital. For a given ylide, the amount of stabilization depends on the energy of the metal orbital, which can be tuned chemically with the other ligands attached to the metal. **B** and **C** represent linking of a $\pi$-system to the ylidic carbon which not only results in a delocalization of electron density, it also raises the energy levels of the $\pi$-substituent with respect to the unperturbed parent $\pi$-hydrocarbon [i.e., for the ligands in **B** and **C**

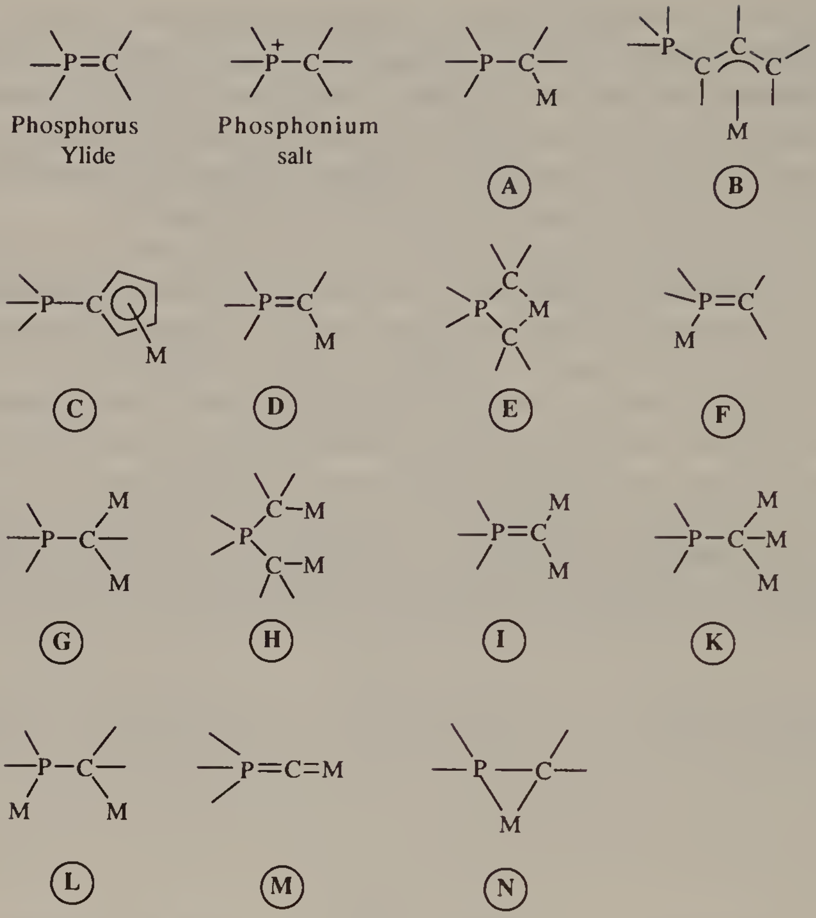


Figure 14.1 Ylide-metal coordination modes.

relative to ethylene and *cis*-butane respectively (Table 14.2)]. In the exceptional case of cyclopentadienylidenephosphoranes ($R_3PC_5H_4$) the extreme perturbation of the $\pi$-substituent pushes the corresponding *cis*-butadiene level even slightly above that of the ylide bond $n_c^-$ level. The enhanced energetic availability of the substituent $\pi$-electron makes it clear why strongly conjugated

**TABLE 14.2 (C=C)$\pi$ Vertical Ionization Potentials of Conjugated Ylides $IE_2$ and Related $\pi$-Hydrocarbons ($IE_1$)[a]**

| | $IE_2$ (Ylide) (eV) | $IE_1$ ($\pi$-Hydrocarbon) (eV) |
|---|---|---|
| $Me_3P{=}CH{-}CH{=}CH_2$ | 9.20 | Ethylene: 10.51 |
| $Me_3P{=}C_5H_4$ | 6.82 ($IE_1$) ! | Butadiene: 9.1 |
| $Me_3P{=}CH{-}C_6H_5$ | 8.32 | Benzene: 9.25 |

[a] For a discussion of the extreme perturbation of ylide substituents, see references 6–10 in Table 14.1; for hydrocarbon references see Turner, D. W.; Baker, C. ; Baker, A. D.; Brundle, C. R. In *Molecular Spectroscopy*, Wiley-Interscience: London, 1970.

ylides may act as polyhapto $\pi$-ligands when metal localized orbitals of appropriate symmetry are accessible.

The "activation" of an ylide carbon substituent, which is a general feature and not limited to $\pi$-systems, is reminiscent of the well-known activation of ligands and substrate molecules in metal-based organic reactions and transition metal catalysis, respectively (Eq. 14.5).

$$\begin{array}{l} R_3P \longrightarrow C \text{ —— Substituent(activated)} \\ \\ R_3P \longrightarrow M \text{ —— Ligand(activated)} \end{array} \tag{14.5}$$

**D** and **E** represent metal stabilized "ylide anions" and are formally derived from **A**, depending on the site of deprotonation. **D** reestablishes the ylide functionality with a metallo-substituted ylidic carbon. The structural counterpart with phosphorus carrying a transition metal substituent in **F** has been shown to exist in a few cases, requiring specific synthetic measures. When ylide bond formation involves a second phosphorus substituent, a bidentate $\sigma$-chelating ligand is formed in **E**. In **H** the same bis-methylide structure acts for two metal centers as bidentate bridging ligand.

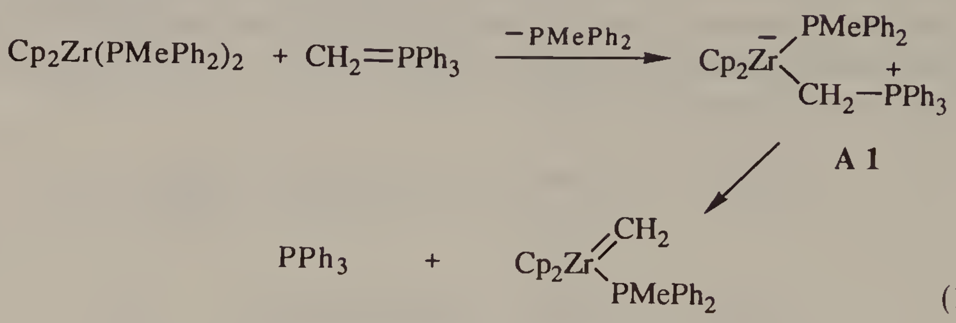
The bridging ligand in **L** may be looked upon as being derived from **F**, followed by an **A**-type coordination to a second metal center. If only one metal is involved, chelate coordination type **N** results (i.e., a three-membered metallocycle is formed).

The logical reaction sequence from an uncoordinated ylide $R_3P{=}CH_2$ via **A** to **D** may be repeated by starting from ylide **D**, complexing a second metal in **G** which again is deprotonated to ylide **I**. **K** finally completes and highlights the stepwise attaching and bridging of up to three metal centers based on a single ylidic carbon.

The ligand properties of simple deprotonated ylides $[R_3PCX]^-$ resemble those of carbodiphosphoranes ($R_3P{=}C{=}PR_3$) and of iminophosphoranes ($R_3PNX$). Each of the three structures provides *two* electron pairs in high-lying strongly C or N localized orbitals (HOMO, HOMO-1). In fact for $Me_3P{=}C{=}PMe_3$ and for $Me_3P{=}NSiMe_3$ no splitting of $IE_1$ and $IE_2$ is observable in photoelectron spectra [i.e., both electron pairs $n_C^\pi$, $n_C^\sigma$ (6.5 eV)[11] and $n_N^\pi$, $n_N^\sigma$ (8.30 eV)[4,7] are practically degenerate].

## 14.2 COMPLEXES WITH TITANIUM, ZIRCONIUM, AND HAFNIUM

The concept of a nonremovable $\beta$-onium group in ylide reactions is not without exception. Treatment of $Cp_2Zr(PPh_2Me)_2$ with $Ph_3P{=}CH_2$ displaced $Ph_2PMe$ to form a complex of type **A**.[12–14] This was not stable and $PPh_3$ was lost from the ylide to give a zirconium methylene complex. The triphenyl phosphine moiety did not complex to the metal, however, and the complex decomposed at room temperature (Eq. 14.6).



(14.6)

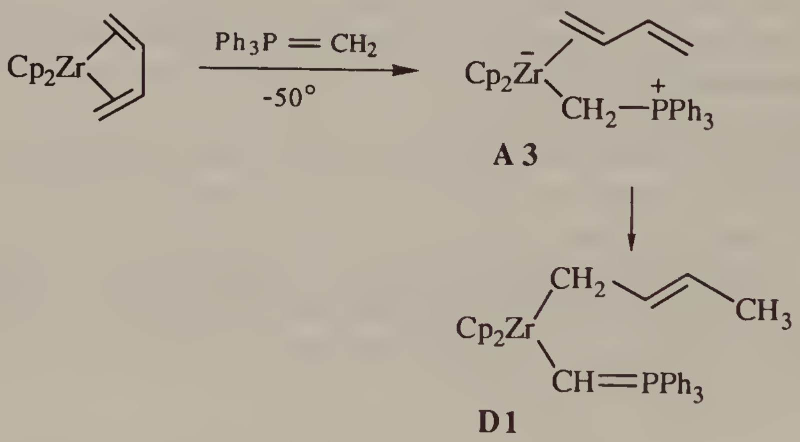
Type **A** complexes also formed when $Me_3P{=}CH_2$[15] was treated with $Cp_2ZrCl_2$ (Eq. 14.7), although other ylides gave **D** and **E** complexes. Interestingly the interaction of $Cp_2{}^*ZrCl_2$ and $Ph_3P{=}CH_2$ did not give identifiable **A** products, only recovery of starting materials.[16]

$$Cp_2MCl_2 \quad + \quad Me_3P{=}CH_2 \longrightarrow Cp_2M(CH_2\text{-}PMe_3)_2^+\ 2\ Cl^-$$

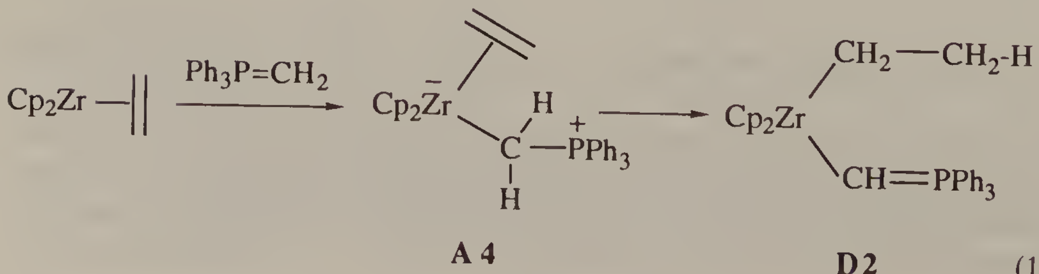
M = Ti, Zr **A 2**

(14.7)

Erker[17] has observed the displacement of butadiene from a divalent zirconocene complex in much the same way as a tricovalent phosphine is displaced to form an **A** complex alkylidene (Eq. 14.8). A similar reaction occurred with an ethylene derivative (Eq. 14.9).[18]

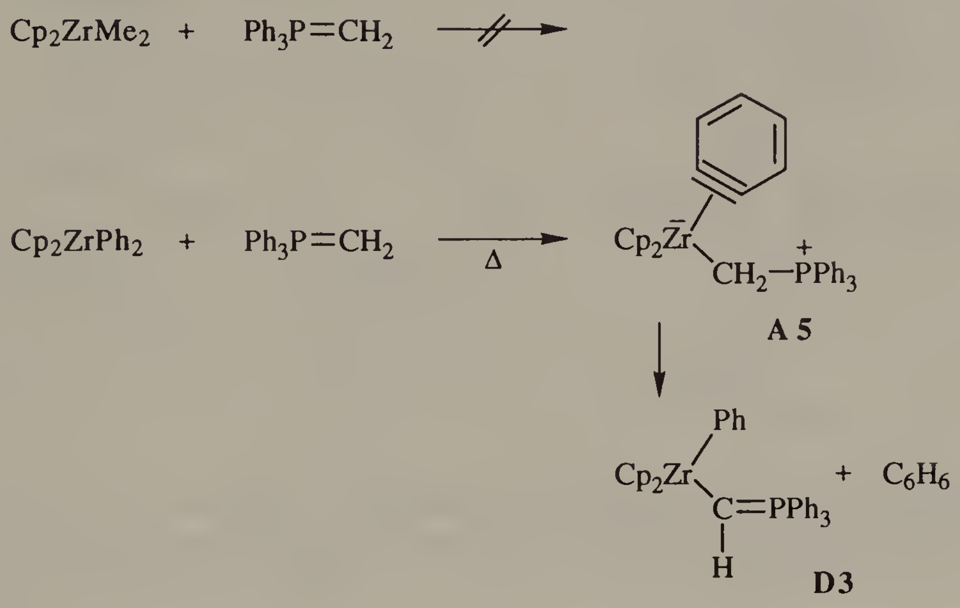


(14.8)



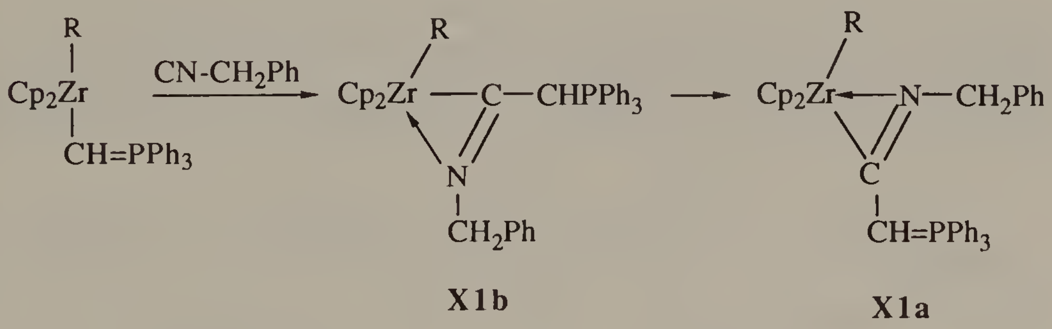
(14.9)

The formation of type **A** complexes can also begin by treating ylides with zirconocene aryl derivatives, as shown in Eq. 14.10,[17, 19–21] but not with the alkyl derivatives.



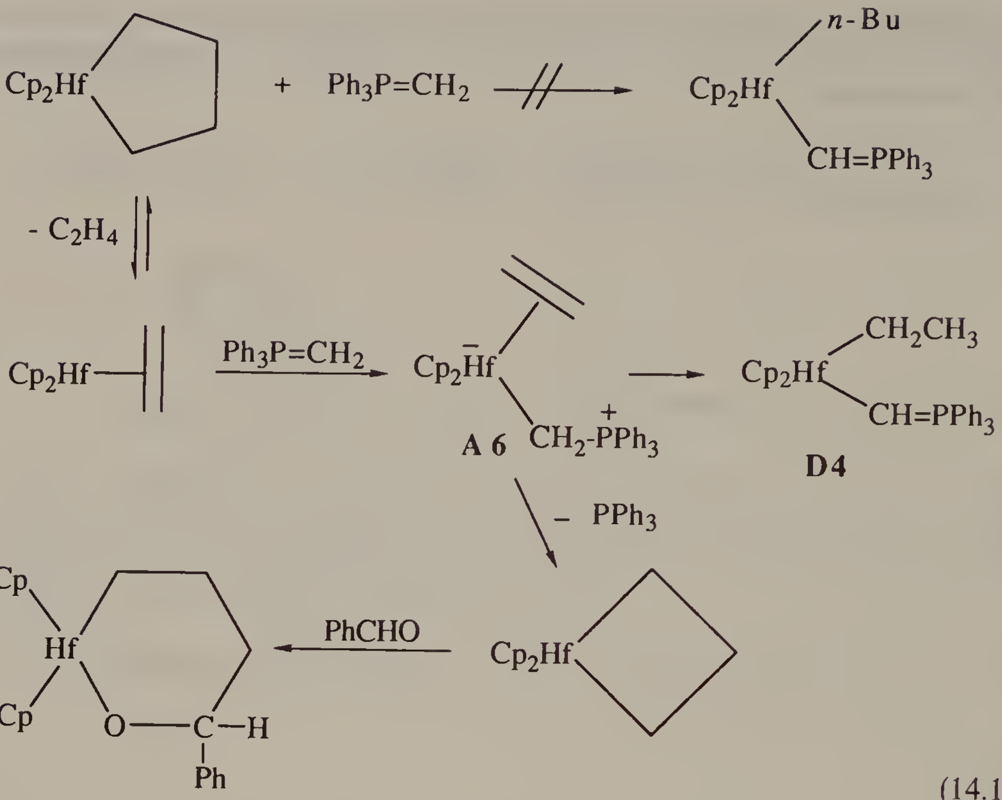
(14.10)

The metallocene ylides did not react with simple ketones and aldehydes to give Wittig reaction products (alkenes) but treatment with isonitriles gave insertion into the Zr–C (ylide) bond, as shown in Eq. 14.11. The products like **X1a** and **X1b** differed in their conformation, and may be viewed as metallated imino–stabilized ylides ($R_3P{=}CH{-}CH{=}X$, X = O, NR).[22–24]



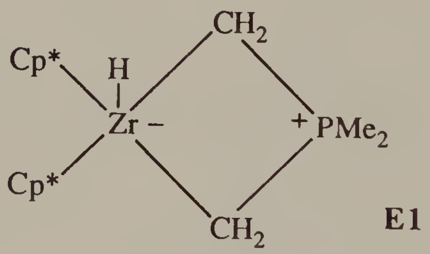
(14.11)

Erker has observed two competing reactions at 90°C for bis(cyclopentadienyl)hafnacyclopentane and $Ph_3P{=}CH_2$ (Eq. 14.12). Assuming a thermally generated (ethylene)hafnocene intermediate, there was a methylene transfer from the phosphorus atom to the metal which either formed a metallocyclobutane or a complex **D**.[24]

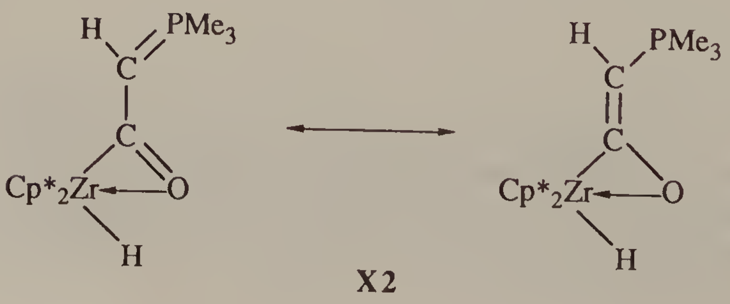


(14.12)

Interaction of permethylzirconocene dihydride with excess $Me_3P{=}CH_2$ gave a metallocycle (Eq. 14.13) that was described as a distorted trigonal bipyramid with one hydrogen atom and an ylidic carbon in the axial position.[25] The compound inserted CO to form β-metallated keto-stabilized ylides (Eq. 14.14).[26]

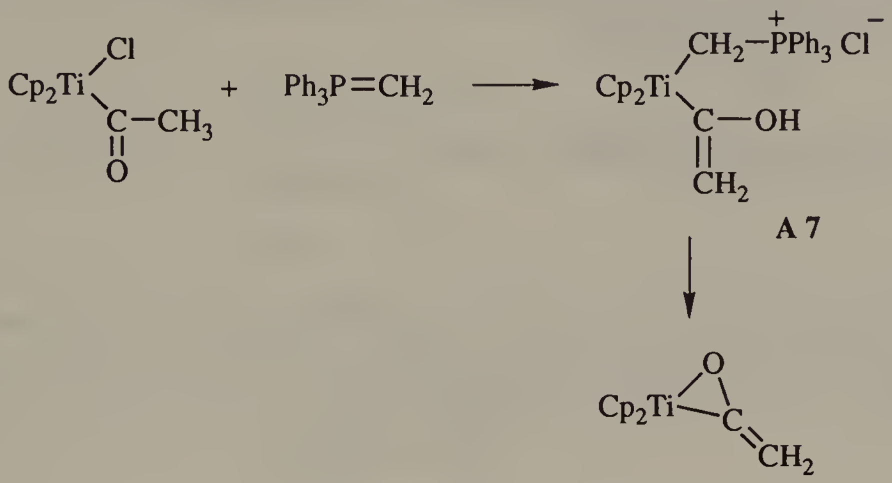


(14.13)



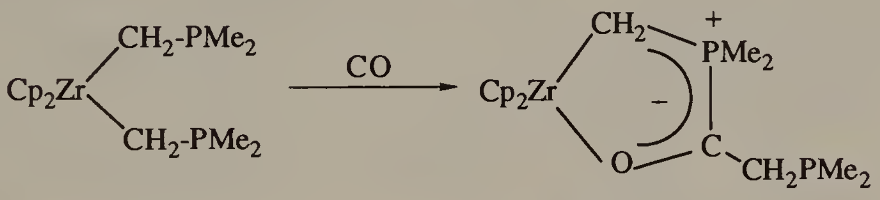
(14.14)

The metal-substituted keto complex in Eq. 14.15 did not undergo a Wittig reaction; a Type **A** complex was produced instead. This gave an oxirane metallocompound after displacement of phosphonium salt (Eq. 14.15).[27]


**A 7**

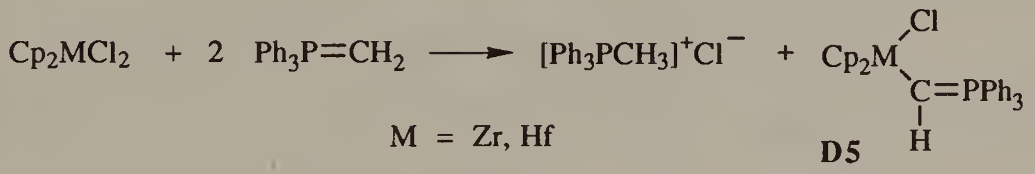
(14.15)

The Karsch[28] nonylide phosphine complex, $Cp_2Zr(CH_2PMe_2)_2$, reacted with CO to form the insertion product **A8X3** (Eq. 14.16). The complex also interacted with $Ni(COD)_2$ to form a zero-valent nickel complex **L**.


**A8X3**

(14.16)

Transylidation, which is the subsequent deprotonation of **A** type complexes, readily occurred when additional molar amounts of ylide were used. Treatment of $Cp_2MCl_2$ ($M = Zr, Hf$) with $Ph_3P{=}CH_2$[29] gave transylidated product **D** (Eq. 14.17). The X-ray molecular structure of the zirconium complex **D5** shows a short Zr–C bond which suggests carbon π overlap from zirconium to phosphorus. Although transition metal-substituted methylene triphenylphosphoranes were reported in 1974, via transylidation reactions (14.17), new results show that multiple α-triphenylphosphoniummethylidene complexes can be prepared $[W(NBu^t)_2(CHPPh_3)_2]$.[29] This process also occurred when two equivalents of

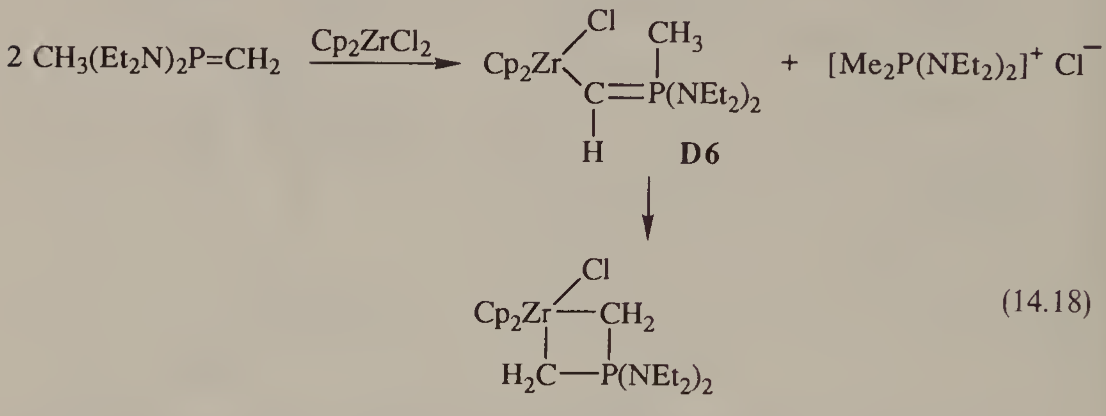

$$Cp_2MCl_2 + 2\ Ph_3P{=}CH_2 \longrightarrow [Ph_3PCH_3]^+Cl^- + Cp_2M(Cl)(CH{=}PPh_3)$$

$M = Zr, Hf$

**D5**

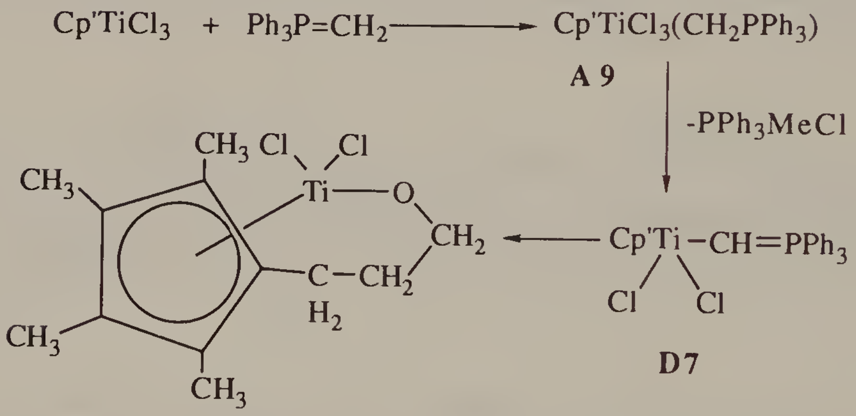
(14.17)

$Me(Et_2N)_2P{=}CH_2$ were treated with zirconocene dichloride and type **D** and **E** products were obtained (Eq. 14.18).[30] Transylidation also occurred with $Cp'TiCl_3$ when it was treated with $Ph_3P{=}CH_2$ (Eq. 14.19). The reaction presumably formed $Cp'TiCl_2CH{=}PPh_3$ which decomposed at 155°C to form $[\eta^5{:}\eta^1\text{-}C_5Me_4(CH_2)_3O]TiCl_2$.[31]



**E2**

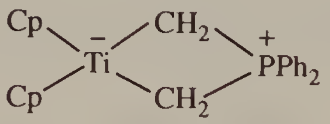
(14.18)



(14.19)

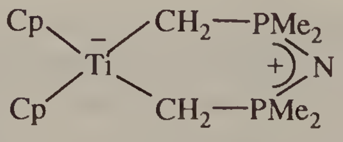
$Cp' = C_5H_4(CH_2)_3OMe$

Lithiated ylides are often favored in the synthesis of E-type complexes with the formation of chelate derivatives (Eqs. 14.20 and 14.21).[32, 33]



**E3**

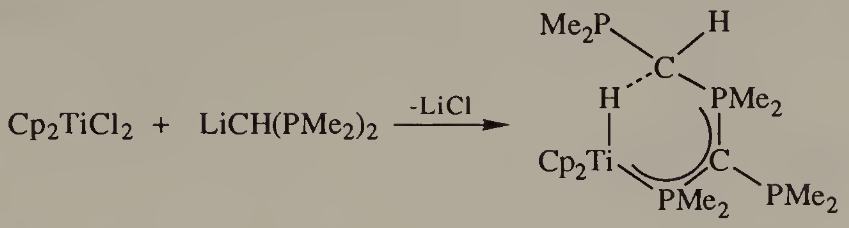
(14.20)



**A 10**

(14.21)

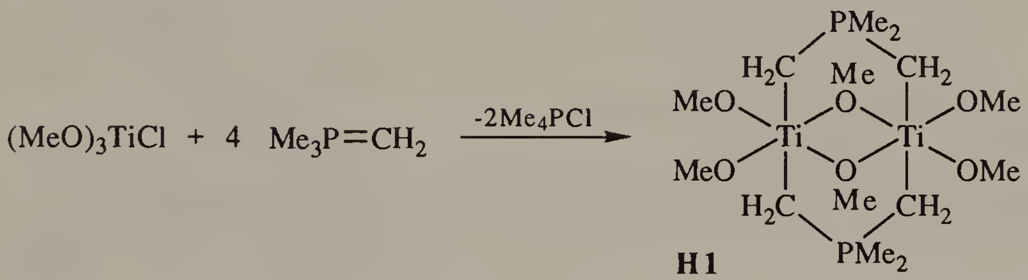
Karsch[34] observed an unusual rearrangement in the reaction of titanocene dichloride with lithiated phosphines which resulted in a ylide titanium complex (**X4**).



(14.22)

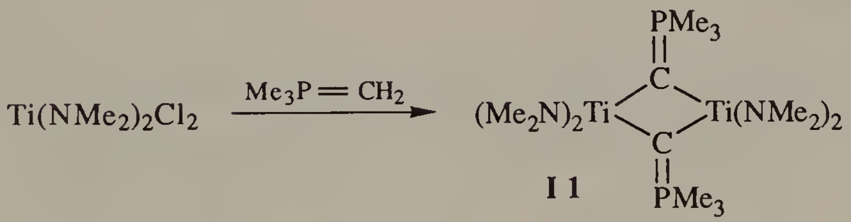
**X4**

The interaction of the perhalogenated halides of titanium did not give isolable products except when alkoxy or dialkyl amino derivatives were used. Bridging complex structures of type **H** and **I** were formed as shown in Eqs. 14.23 and 14.24.[35] However, perhalogenated zirconium compounds gave complexes of type **I**.[36]



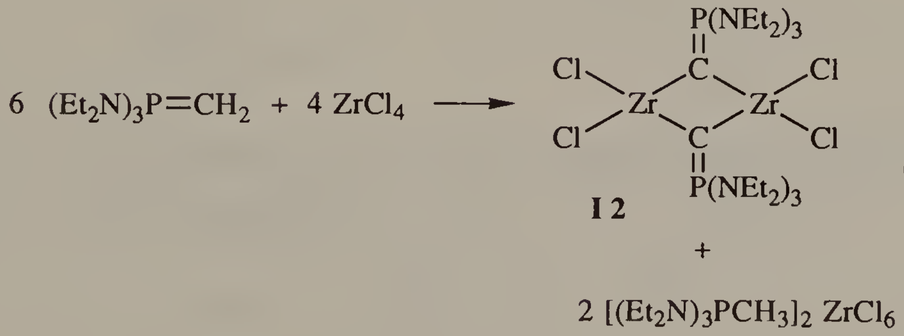
**H1**

(14.23)



**I1**

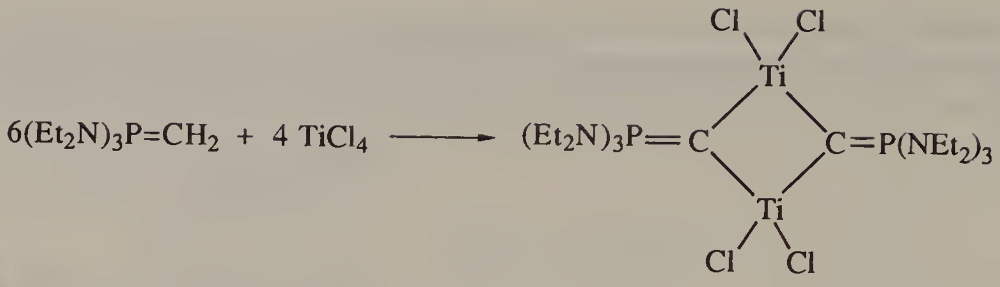
(14.24)



**I2**

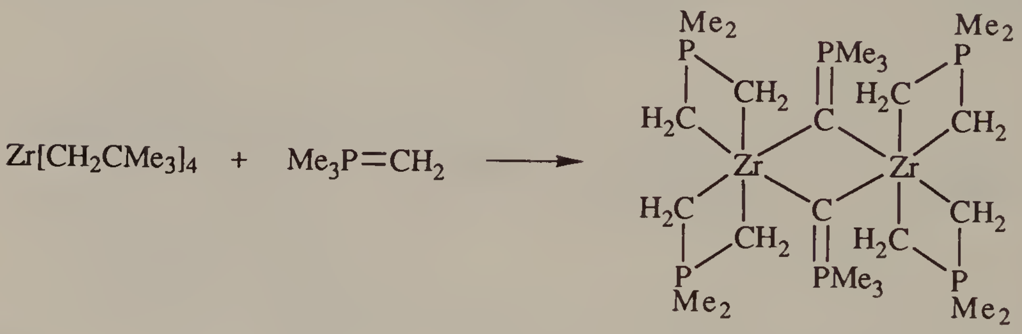
(14.25)

The introduction of bulky diethylamino groups on the phosphorus atom resulted in replacement of both ylidic hydrogen atoms with a transition metal (Eq. 14.26).[37] Likewise the peralkylated zirconium complex $Zr[CH_2CMe_3]_4$

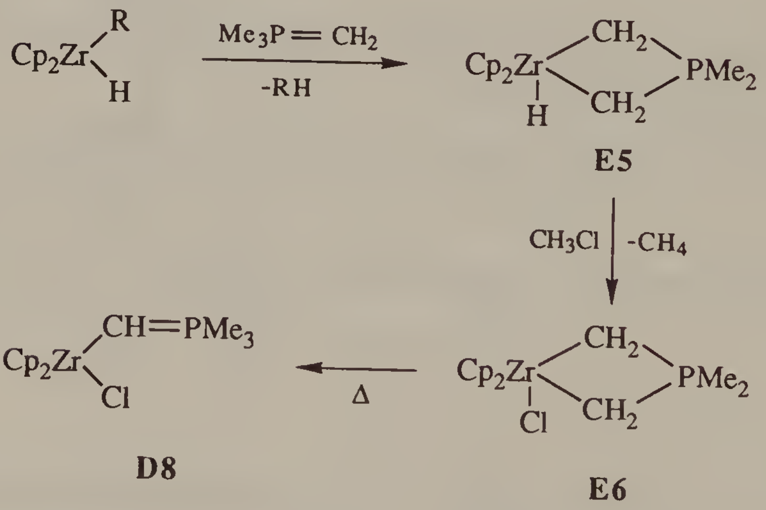


**I3** (14.26)

eliminated neopentane when treated with $Me_3P{=}CH_2$ (Eq. 14.27). The bridging carbon atoms have short Zr–C and P–C bonds, the latter, (1.688 Å) resembling those of the free ylide. This single complex incorporated both structures **E** and **I**.[38] Similar formation of type **E** structures occurred with $Cp_2ZrR(H)$ (Eq. 14.28).[39]

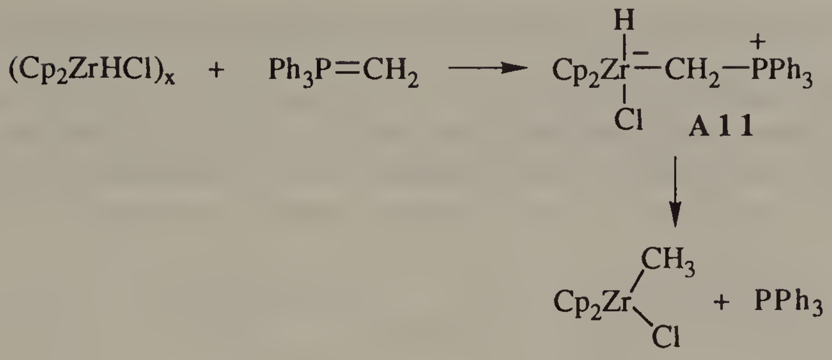


**E4I4** (14.27)



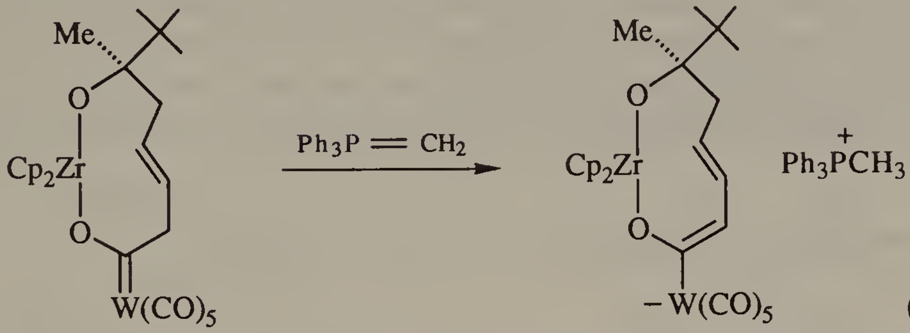
(14.28)

The initial addition product (**A11**) of triphenylphosphinemethylene to zirconocene hydrochloride loses triphenylphosphine. The net result was transfer of a carbene to the metal atom (Eq. 14.29).[19]



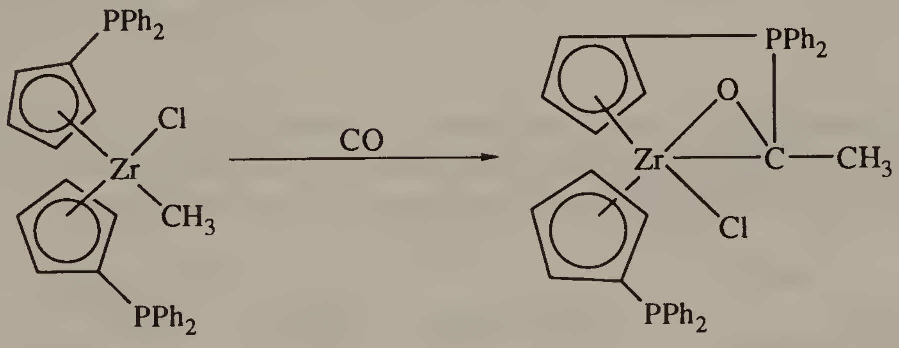
(14.29)

Phosphorus ylides have been used to deprotonate metal carbene compounds forming salts with large phosphonium cations, as shown in Eq. 14.30.[40]



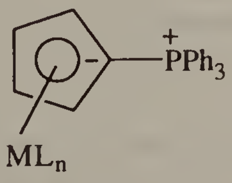
(14.30)

A phosphino-substituted zirconocene complex inserted a CO group into the $Zr{-}CH_3$ bond and formed an acetyl group which could be viewed as an ylide complex of type **C** (Eq. 14.31).[41]



**C1X5** (14.31)

There are reports of titanium complexes (Eq. 14.32) with the ylide triphenylphosphoniumcyclopentadienide, but no structural data are available.[42]

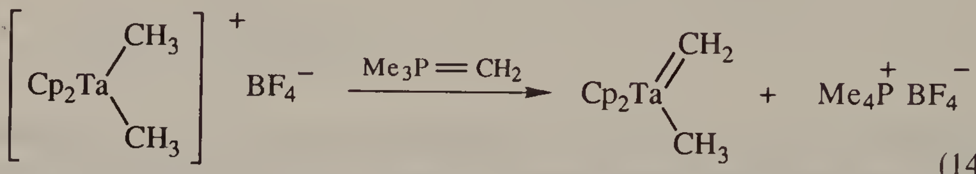


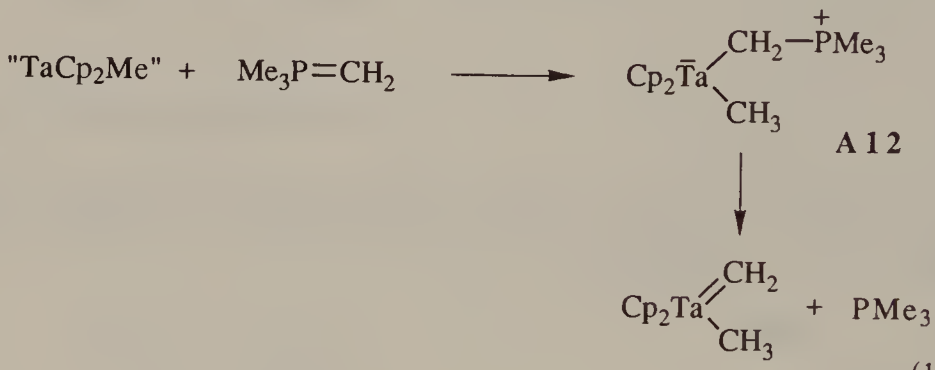
(14.32)

**C2**

## 14.3 COMPLEXES OF VANADIUM, NIOBIUM, AND TANTALUM

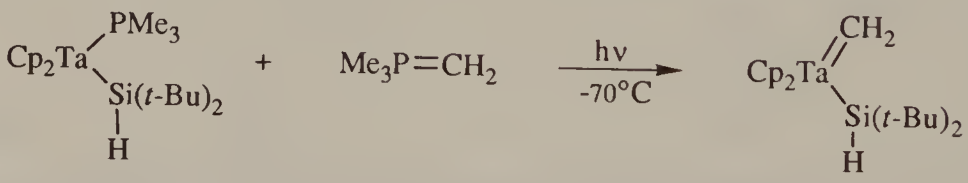
A chemical parallel between Group V transition metal complexes and Main Group V ylides became obvious when ylides were used to synthesize the first coordinated alkylidene by deprotonation of the coordinated alkyl groups (Eq. 14.33). Most likely an **A**-type complex formed first, followed by formation of the alkylidene.[43] However, alkylidene transfer also occurred with $TaCp_2Me$ which was generated from $TaCp_2LMe$ ($L = C_2H_4$ or $PMe_3$) (Eq. 14.34).[44] Alkylidene or carbene transfer has been observed with other transition metal systems although the generality has not been studied in a systematic fashion.


(14.33)


**A 12**

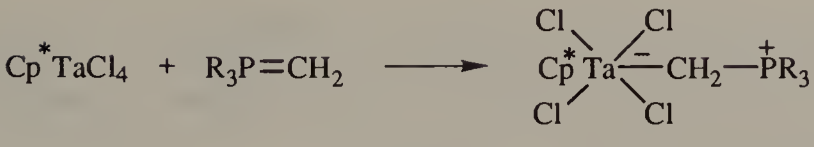
(14.34)

A silylmethylene complex was formed by photolysis of $Cp_2Ta(PMe_3)SiH(t\text{-}Bu)_2$ and methylide. Presumably this occurred by alkylidene transfer from an **A** complex to the tantalum, and is similar to the zirconium systems.[45]

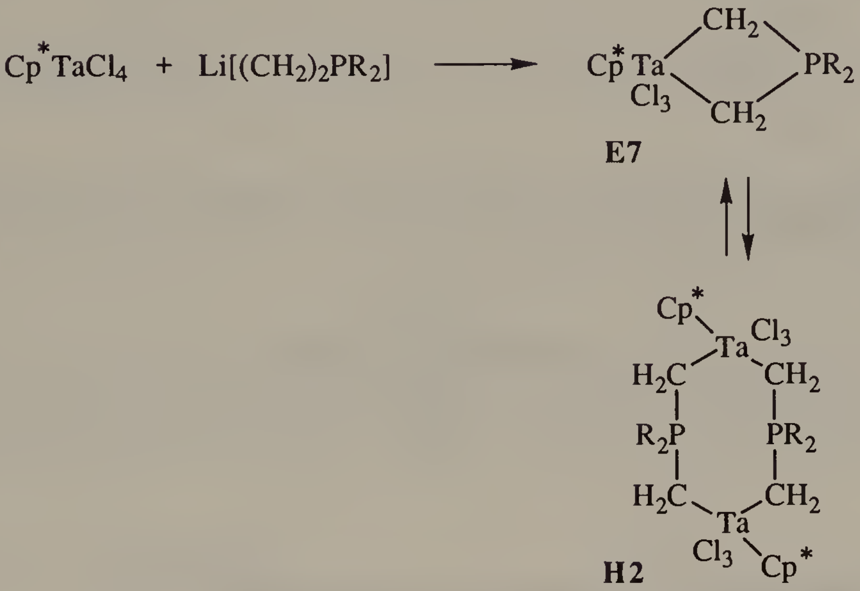

(14.35)

Treatment of vanadium hexacarbonyl with $Ph_3P{=}CH_2$ gave the first ylide transition metal complex, as reported by Hieber.[46] Instead of addition, displacement of the CO groups gave the disproportionated salt $[V(H_2C{-}PPh_3)_4][V(CO)_6]_2$ (**A13**).

Neutral type **A** complexes could be made by treating $Cp^*TaCl_4$ with $R_3P = CH_2$ (Eq. 14.36).[47] With lithiated phosphines, an **E**-type complex was formed directly and there was no need for transylidation to occur (Eq. 14.37).[48]


**A 14**

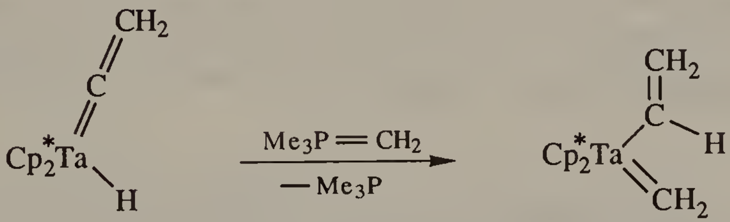
(14.36)

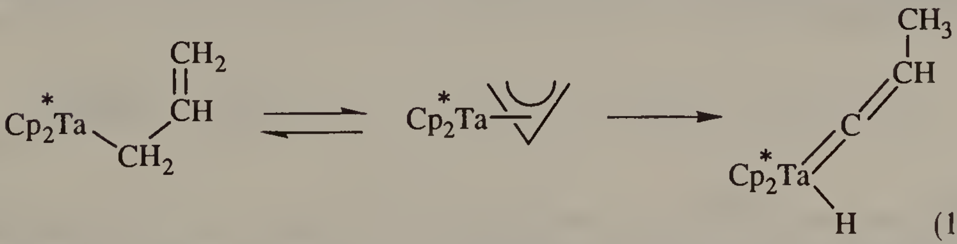

**E7**

**H2**

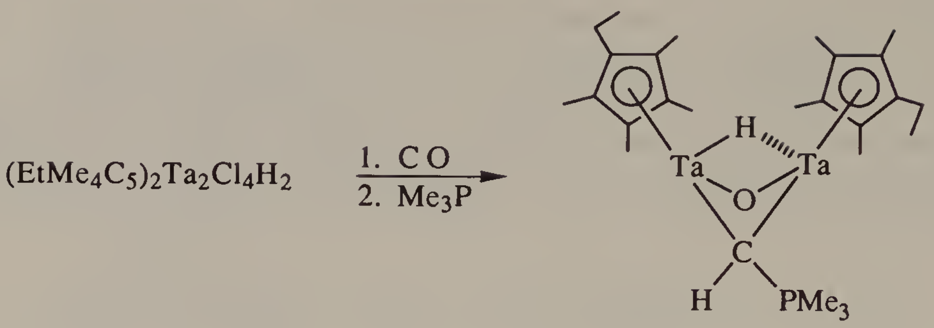
(14.37)

The role of metal vinylidenes in Fischer–Tropsch processes has led to the use of $Me_3P{=}CH_2$ to make higher vinylidene homologs. These processes are presumably initiated by the formation of **A**-type complexes (Eqs. 14.38 and 14.39).[49]


(14.38)


(14.39)

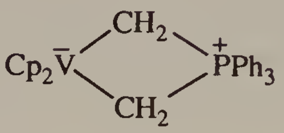
A binuclear complex could be obtained by treating a tantalum hydride with CO and $PMe_3$. The intermediate 2-formyl tantalum complex interacted with $PMe_3$ by disrupting the formyl ligand and forming a type **G** complex (Eq. 14.40).[50]



**G1**

(14.40)

A single type **E** vanadium complex has been characterized by ESR spectroscopy as **E8** (Eq. 14.41).[51]



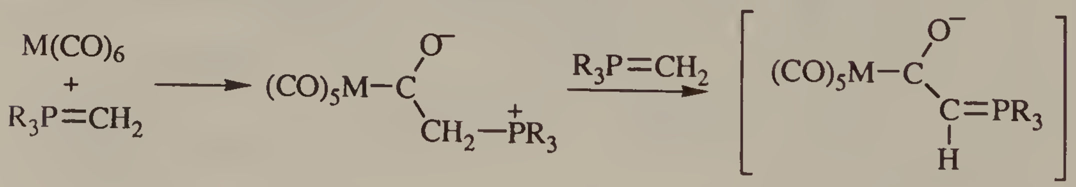
**E8**

(14.41)

## 14.4 COMPLEXES OF CHROMIUM, MOLYBDENUM, AND TUNGSTEN

### 14.4.1 Ylide Reactions with Carbonyl Compounds

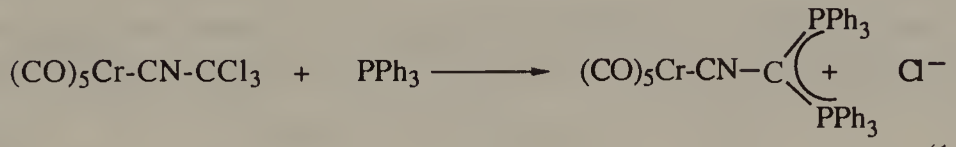
*14.4.1.1 Addition Reactions.* Phosphorus ylides that do not have electron-withdrawing groups on the alkylidene moiety are nucleophilic enough to add across the carbonyl group of $M(CO)_6$ complexes to give pseudo **D**-type complexes. In Eq. 14.42 a C–O group has been formally inserted between the ylide–metal bond. This is a potentially useful reaction for the synthesis of carbon–carbon bonds.[52] The product after alkylation is a carbene, but there is no loss of triphenylphosphine oxide which would convert the carbonyl group into a coordinated acetylide. This can be done with bis-ylides however, and certain iron carbonyl compounds. A measure of the electrophilicity of the carbonyl group is given by the force constant.[53]



**X6** $R_3\overset{+}{P}CH_3$

(14.42)

Fehlhammer[54] has approached the synthesis of Group VI metal carbonyl ylide complexes in a novel fashion by starting from isocyanide compounds. In nonaqueous solvents a carbodiphosphorane complex was formed (Eq. 14.43). When water was present the product was the monophosphonium ylide complex (Eq. 14.44).



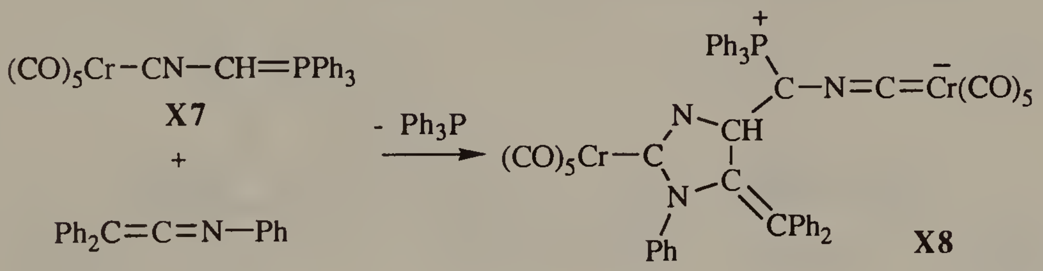
$$(CO)_5Cr\text{-}CN\text{-}CCl_3 + PPh_3 \longrightarrow (CO)_5Cr\text{-}CN\text{-}C(PPh_3)_2^{+}\ Cl^-$$

(14.43)

$$(CO)_5Cr\text{-}CN\text{-}CCl_3 + PPh_3 + H_2O \longrightarrow (CO)_5Cr\text{-}CN\text{-}CH_2\overset{+}{P}Ph_3\ Cl^-$$

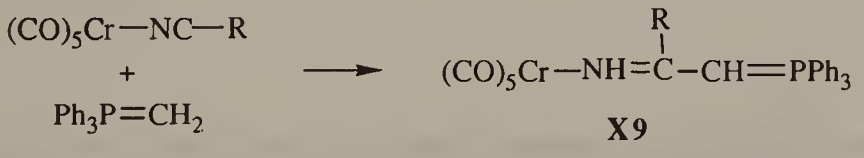
(14.44)

The chromium isonitrile ylide **X7** formed a cycloaddition product in reaction with a ketenimine as illustrated in Eq. 14.45.[55] Coordinated nitriles added ylides similarly (14.46), but the exploitation of these reactions in organic synthesis has not been reported.[56]



**X7** **X8**

(14.45)



$$(CO)_5Cr{-}NC{-}R + Ph_3P{=}CH_2 \longrightarrow (CO)_5Cr{-}NH{=}\overset{R}{\overset{|}{C}}{-}CH{=}PPh_3$$

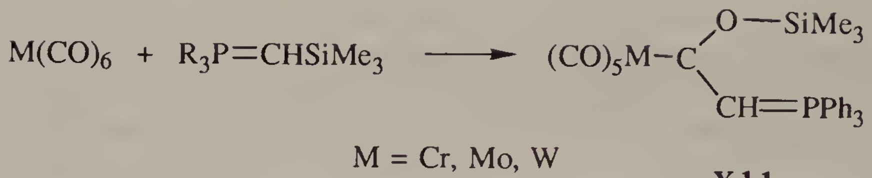
**X9** (14.46)

Photolysis of the carbodiphosphorane $(Ph_3P)_2C$ in the presence of $W(CO)_6$ gave a small yield of the acetylide (Eq. 14.47). Since triphenylphosphine oxide

$$W(CO)_6 + Ph_3P{=}\bar{C}{-}\overset{+}{P}Ph_3 \longrightarrow (CO)_5\bar{W}{-}C{\equiv}C{-}\overset{+}{P}Ph_3$$

**X10** (14.47)

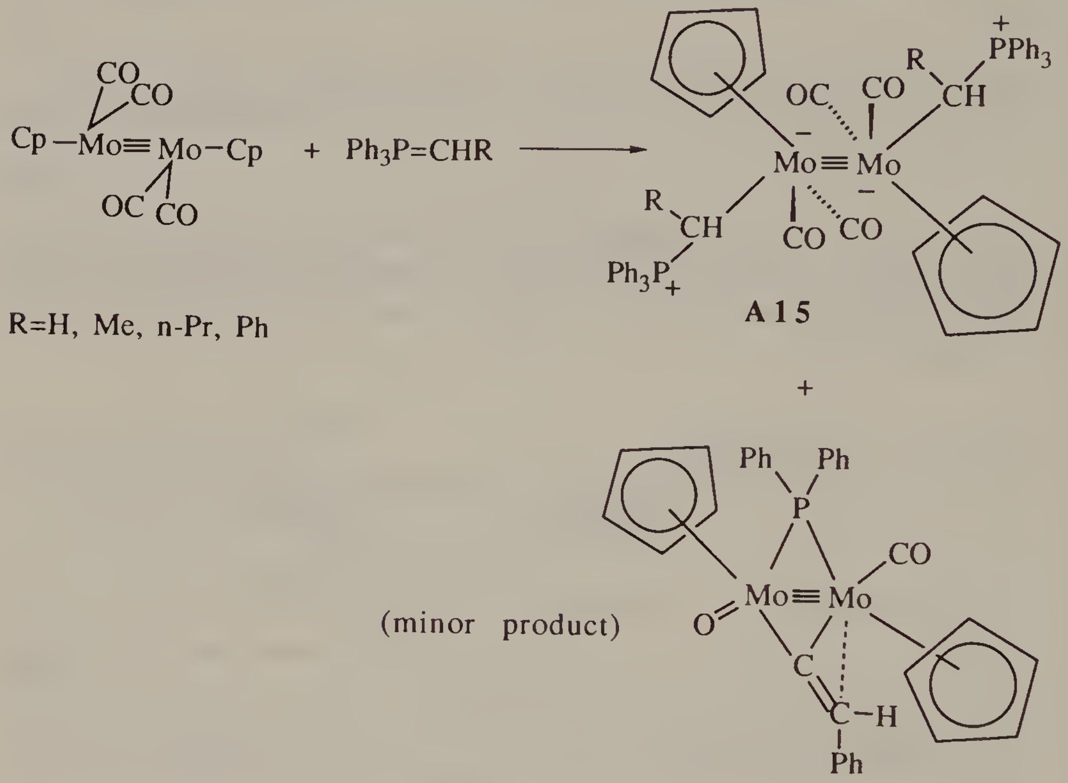
was isolated in the reaction mixture, this is an example of a Wittig reaction on a coordinated carbonyl group.[57] A similar reaction occurred with manganese and rhenium carbonyls (Eq. 14.86). Substituted phosphorus ylides that were sufficiently nucleophilic (i.e., without electron-withdrawing groups) effected addition to the carbonyl group (14.48).[58]



**X11**

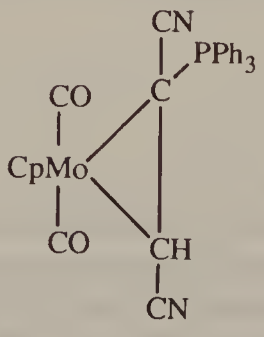
(14.48)

Treatment of $Ph_3P{=}CH_2$ with $Cp_2Mo_2(CO)_4$ gave mostly the **A**-type addition product and very little of the Wittig product was observed (Eq. 14.49).[59]



(14.49)

Cyanoacetylenes and dicyanoacetylenes interacted with $CpM(CO)_3H$ complexes to form $CpMo(CO)_3{-}C(R){=}CH(CN)$. When these were irradiated in the presence of triphenylphosphine, ylide complexes were formed (Eq. 14.50).[60]



(14.50)

**A16X12**

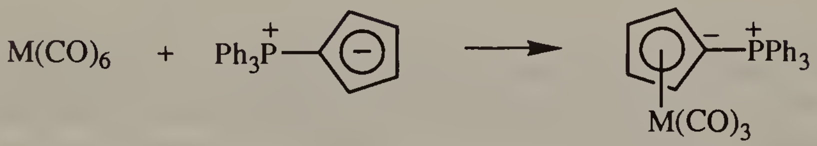
*14.4.1.2* ***Substitution Reactions.*** In some instances ylides do not add to the carbonyl group of metal carbonyls, but effect substitution reactions instead. The first Group VI ylide complex was synthesized by treating cycloheptatriene-molybdenumtricarbonyl with $Ph_3P{=}CHCH_3$ to form $(CO)_3Mo[Ph_3PCHCH_3]_3$.[61] Other examples of substitution are shown in Eqs. 14.51–14.54.

$$M(CO)_6 \xrightarrow[THF]{h\nu} M(CO)_5THF \xrightarrow{Ylide} M(CO)_5(Ylide) \qquad (14.51)$$

| Ylide: | |
|---|---|
| $Ph_3P{=}CH_2$ | **A 17** |
| $Me_3P{=}CH_2$ | **A 18** |
| $Me_3P{=}CHPh$ | **A 19** |
| $Me_3P{=}NH$ | **A 20** |
| $Me_3P{=}NPh$ | **A 21** |
| $Ph_3P{=}NSiMe_3$ | **A 22** |
| $Ph_3P{=}NH$ | **A 23** |

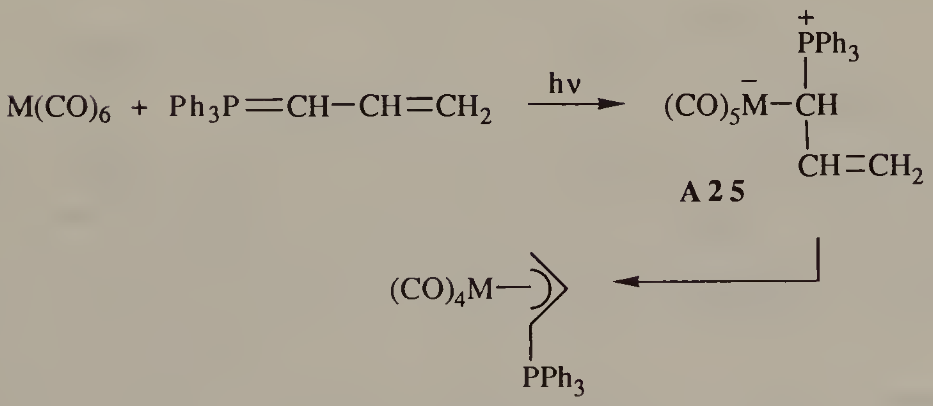
$$(CO)_5CrBr^- + Ph_3P{=}CRR' \longrightarrow (CO)_5\overset{-}{Cr}\text{-}CRR'\text{-}\overset{+}{P}Ph_3 + Br^- \qquad (14.52)$$

**A 24**



(14.53)

**C3**



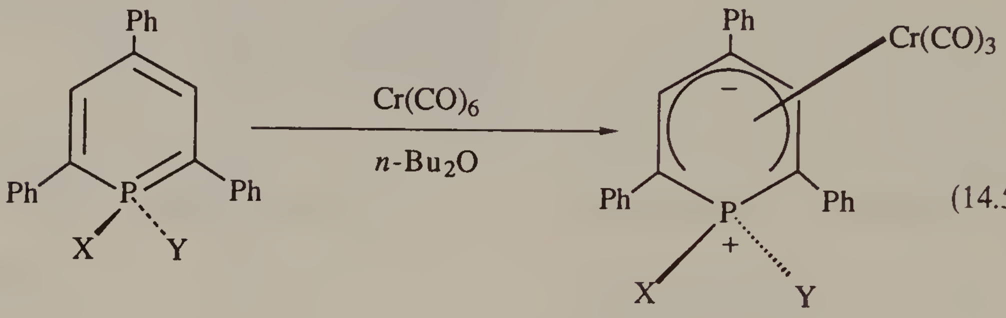
**A 25**

**B 1** (14.54)

Several ylide-Cr, Mo, and W tetracarbonyl and pentacarbonyl complexes have been prepared thermally or photochemically through direct substitution of carbon monoxide ligands. Alternatively, substitution of tetrahydrofuran from the photochemically prepared $M(CO)_5THF$ complexes is a method of general applicability.[62, 63]

The isoelectronic phosphineimine complexes, $R_3P{-}NX{-}ML_n$, can be considered as metal-stabilized ylides themselves (type **D**). The remaining nitrogen lone pairs are able to bind a second metal fragment. Subsequent heating resulted in binuclear tricarbonyl complexes of the type $(R_3PNX)_3[M(CO)_3]_2$ with bridging phosphineimine ligands.[63] In contrast, most sulfur ylides did not add to the carbonyl group of metal carbonyl compounds except for $Fe(CO)_5$.[64]

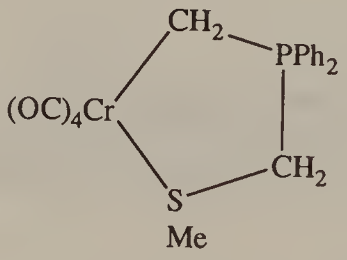
Type **C** ylide complexes with cyclopentadienyl rings can be extended to the phosphorins. Thus 2,4,6-triphenyl-$\lambda^5$-phosphorins added nucleophiles and electrophiles to the phosphorus atom to give phosphorin-ylide complexes as shown in Eq. 14.55.[65]



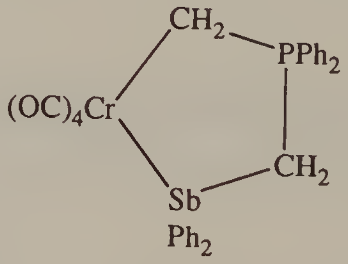
**C4**

(14.55)

Pentacarbonyl (dimethyloxosulfonio)methylidechromium(0)$[(OC)_5Cr\{CH_2S(O)Me_2\}]$ reacted with tertiary phosphines with displacement of dimethyl sulfoxide and generation of $[(OC)_5Cr(CH_2PR_3)]$, and bifunctional phosphines lead to ylidic metallocycles (Eq. 14.56).[66]



**A26X13**

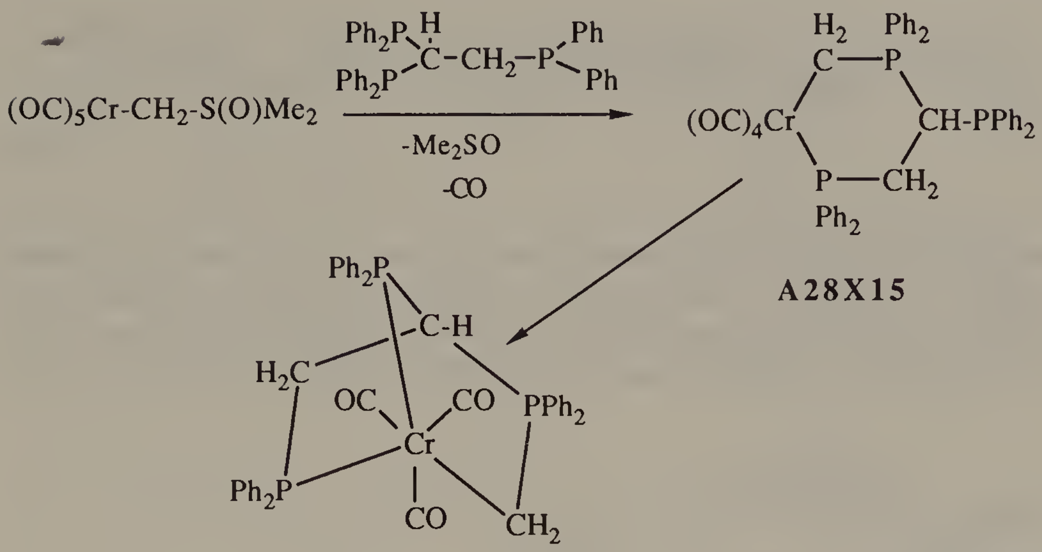


(14.56)

**A27X14**

Another example of the facile extrusion of dimethyl sulfoxide from sulfur ylides by phosphines is shown in Eq. 14.57.[67] The equilibrium shown in Eq. 14.58 depicts the different arrangements of the hydrogen atoms for the unstable ylide which resulted upon complexation with the chromium atom.

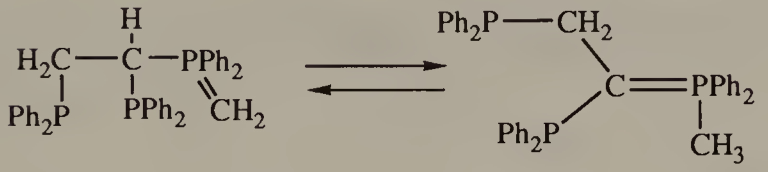
Substitution of the halide by triphenylphosphine in the complex $CpCr(NO)_2CH_2I$ gave a cationic ylide complex (Eq. 14.59).[68]



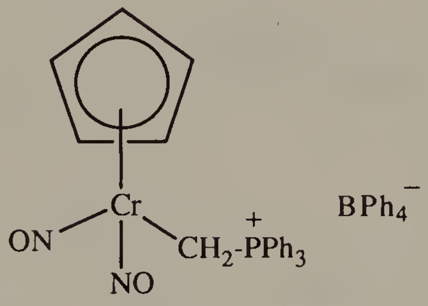
A28X15

A29X16

(14.57)



(14.58)



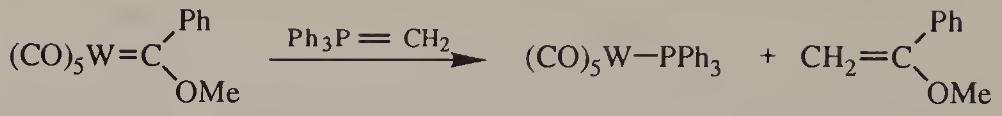
A30

(14.59)

The complex $[CpW(CO)_3]_2$ reacted with $Ph_3P{=}CH_2$ (L) by substituting two of the carbonyl groups to give $[CpW(CO)_2L_2]_2$ (**A31**). On the other hand $[Cp^*M(CO)_2]_2$ ($Cp^* = C_5Me_5$, M = Cr, W) did not appear to react with phosphorus ylides. The corresponding molybdenum compound, $[Cp^*Mo(CO)_2]_2$, did react, but the only complex that could be isolated was $Cp^*Mo(CO)_2(PPh_3)Cl$.[69]

### 14.4.2 Ylide Reactions with Carbene and Carbyne Complexes

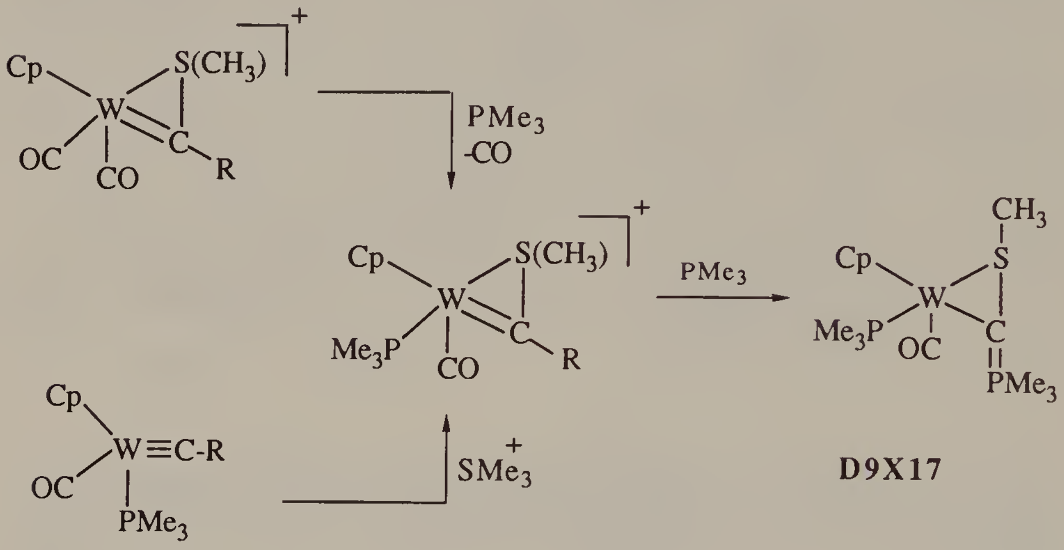
Carbene complexes reacted with ylides to form alkenes rather than incur addition across the carbonyl group (Eq. 14.60).[70] Treatment of carbene[71] or carbyne[72] complexes with phosphines gave ylide adducts when the reaction was



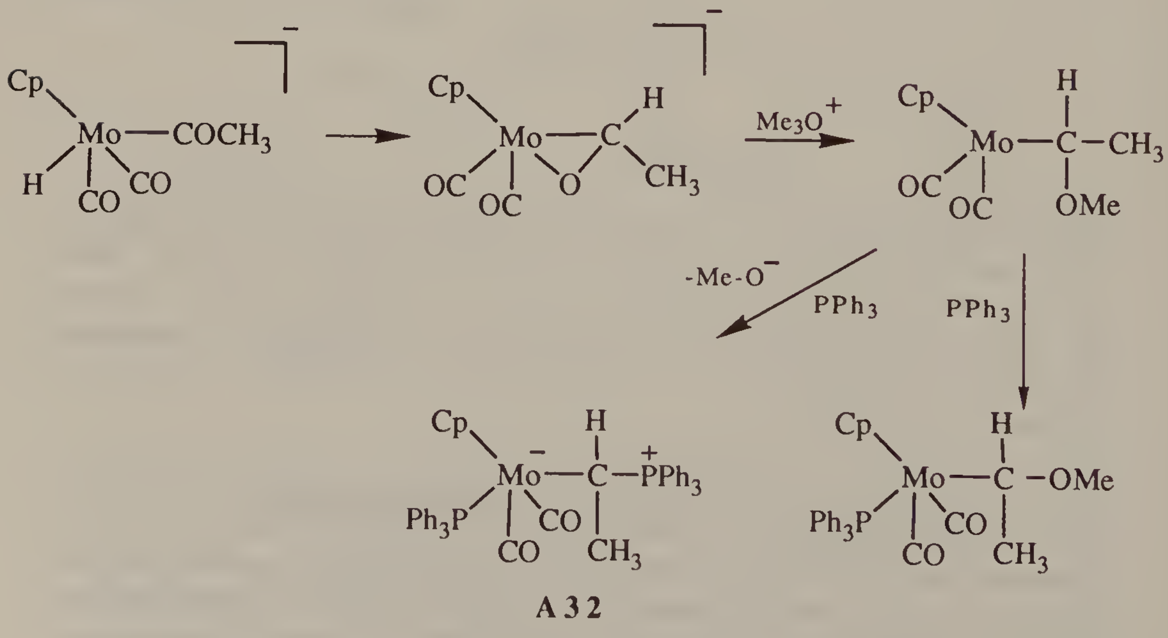
$$(CO)_5W=C(Ph)(OMe) \xrightarrow{Ph_3P=CH_2} (CO)_5W-PPh_3 + CH_2=C(Ph)(OMe)$$

(14.60)

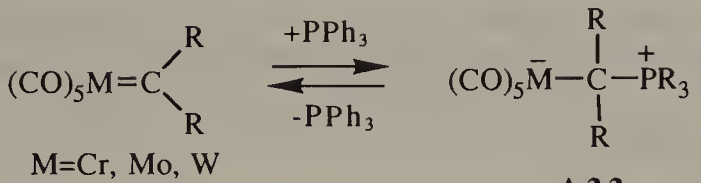
controlled so that complex formation occurred at the carbene carbon atom (Eqs. 14.61 and 14.62). This usually was the case with Fischer-type carbenes since they are electron deficient. If the carbene had bulky substituents like $(CO)_5W=C(Ph)_2$ treatment with $PPh_3$ gave the ylide as the cleavage product (Eq. 14.64), but when $PMe_3$ was used an adduct (**A34**) was formed (Eq. 14.65).[73]



(14.61)

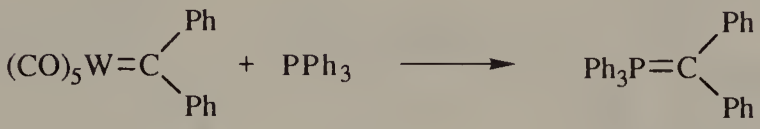


(14.62)

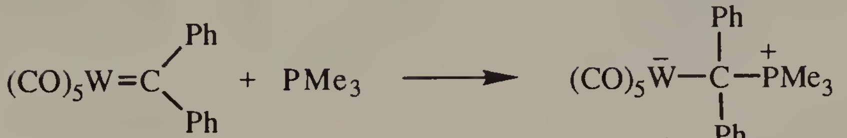


**A33**

(14.63)



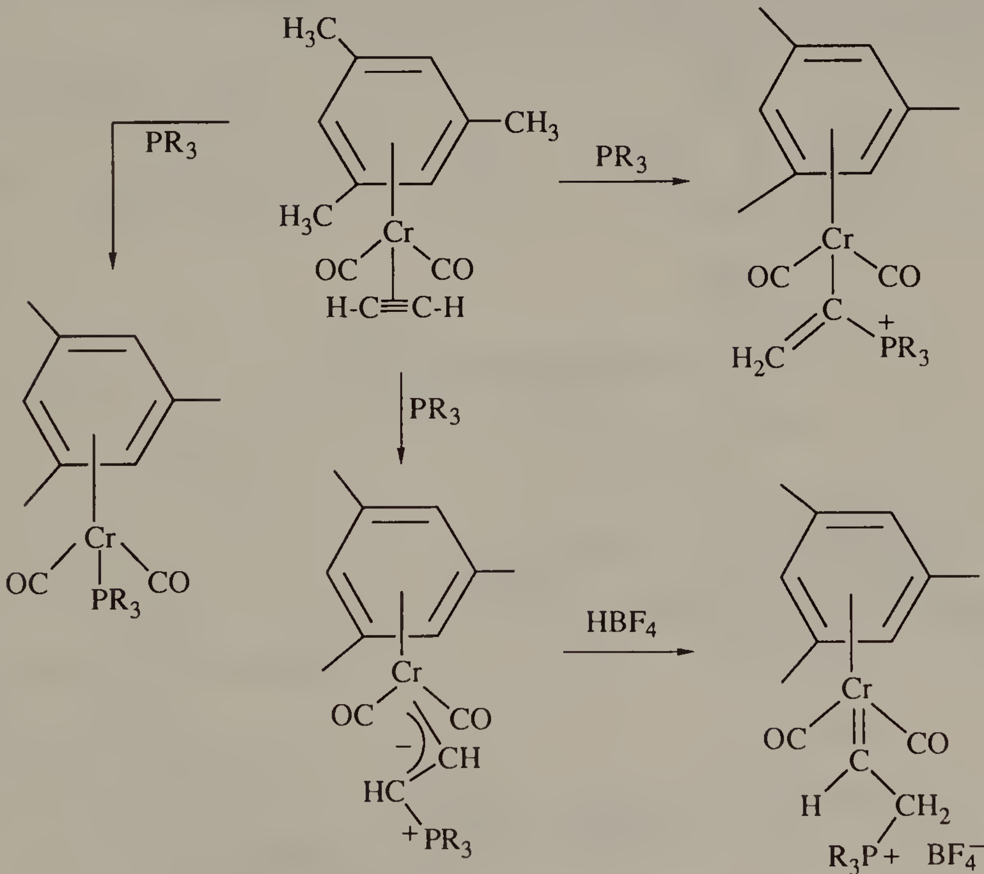
(14.64)



**A34**

(14.65)

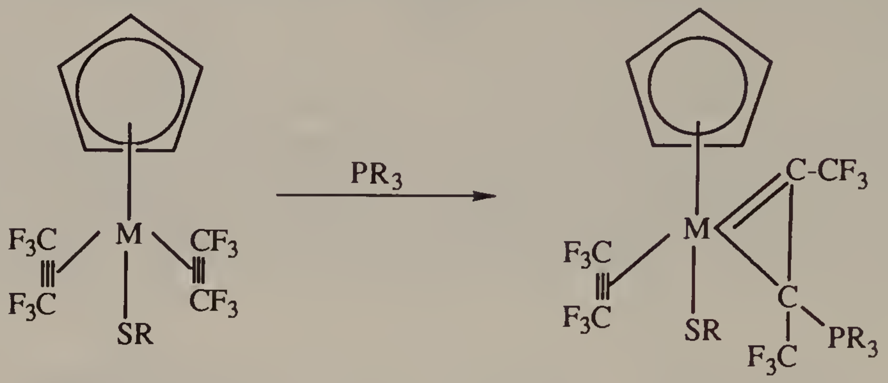
Treatment of an arene acetylene complex with phosphines yielded a variety of ylide complexes, including a carbene adduct as shown in Eq. 14.66.[74]



**X18**

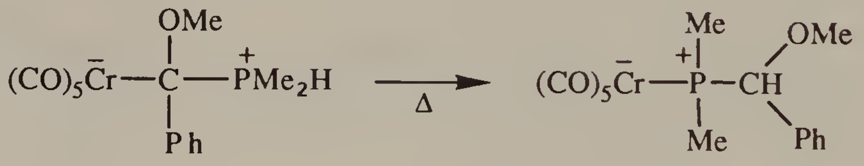
(14.66)

Another example illustrates ylide formation with hexafluorobutyne complexes of molybdenum and tungsten by treatment with phosphines (Eq. 14.67).[75]



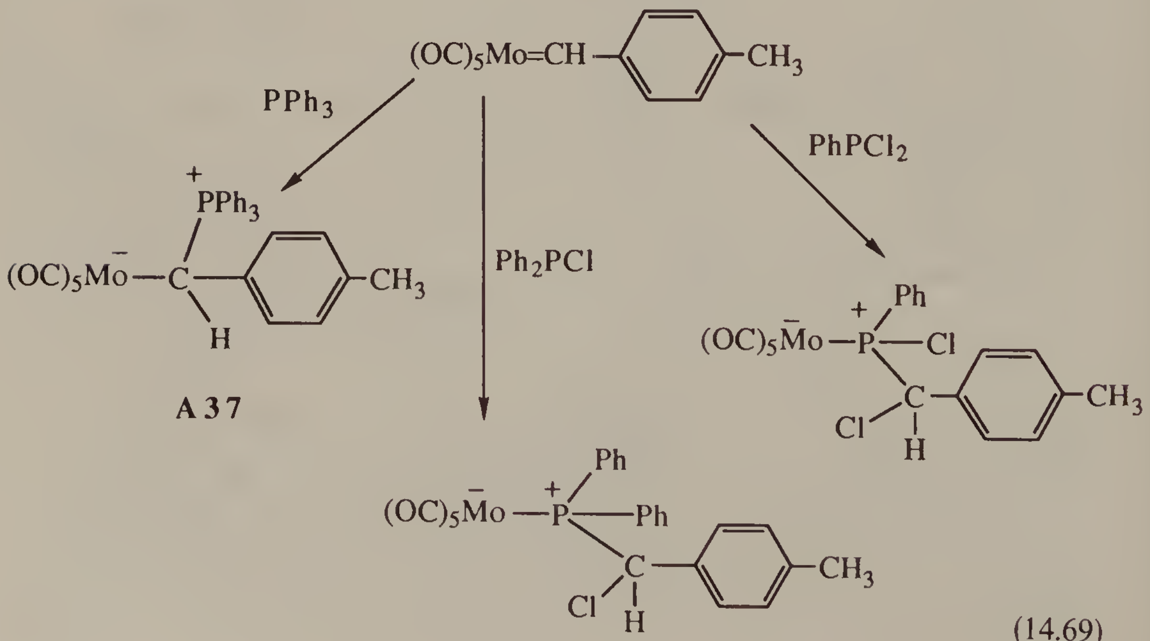
**A35X19** (14.67)

An ylide-to-phosphine rearrangement occurred with adducts that carried hydrogen on the phosphorus atom (Eq. 14.68).[76] Another interesting rearrangement was observed when *p*-substituted benzylidene molybdenum pentacarbonyl complexes interacted with different substituted organophosphines. Chloro groups on phosphines promoted a Stevens-type rearrangement which has also been noted in the nickel ylide series (Eq. 14.69).[77]



(14.68)

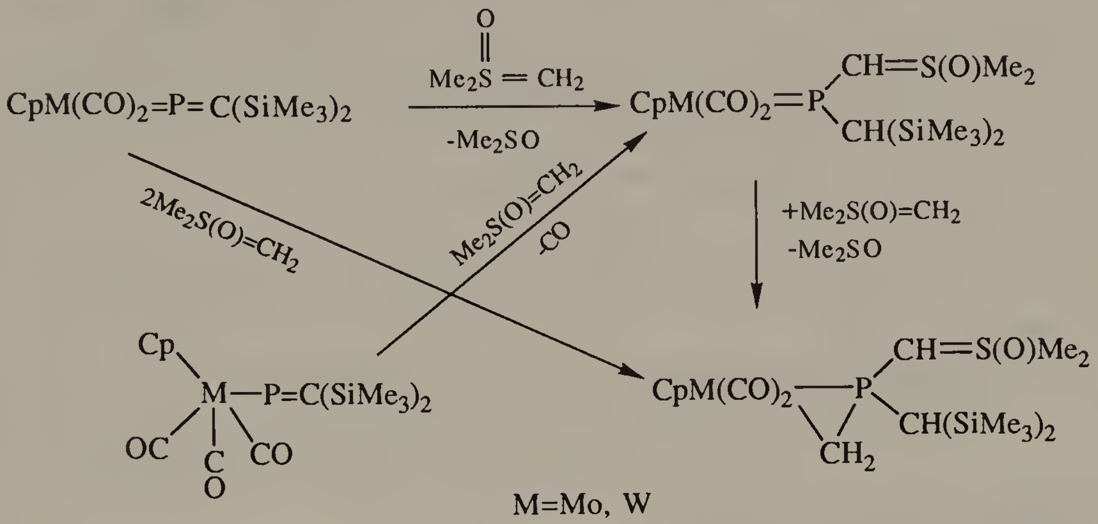
**A36**



**A37**

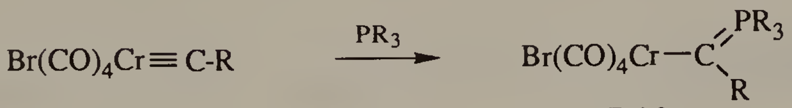
(14.69)

Weber has shown that incipient carbenes could be formed when sulfur ylides were treated with metal alkylidene phosphines, as illustrated by the complexes in Eq. 14.70.[78] Phospha-Wittig reagents [$M{-}P(R){=}PBu_3$; $R = W(CO)_5$] converted aldehydes into phosphaalkene complexes ($M{-}P(R){=}CHR^1$).[79]

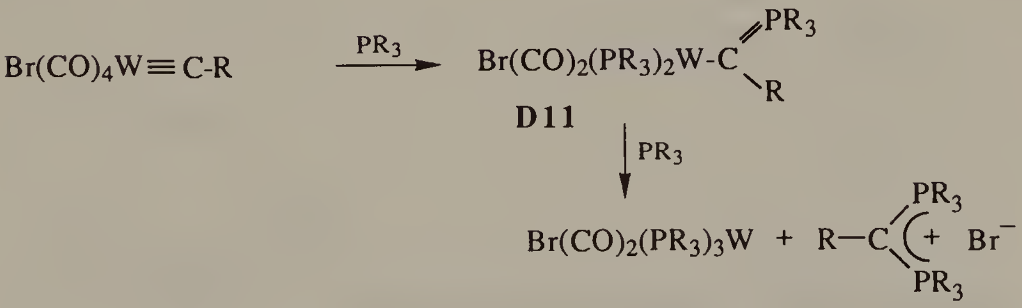


**F1N1** (14.70)

Carbyne complexes formed ylides with phosphines, as shown in Eqs. 14.71–14.73.[80]

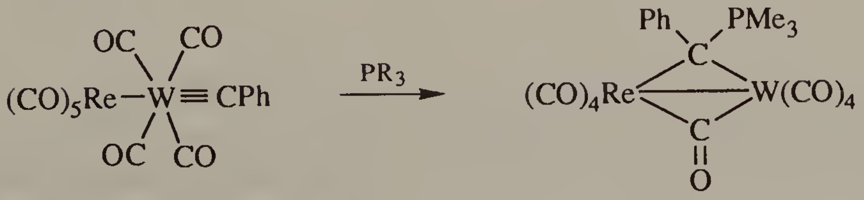


**D10** (14.71)



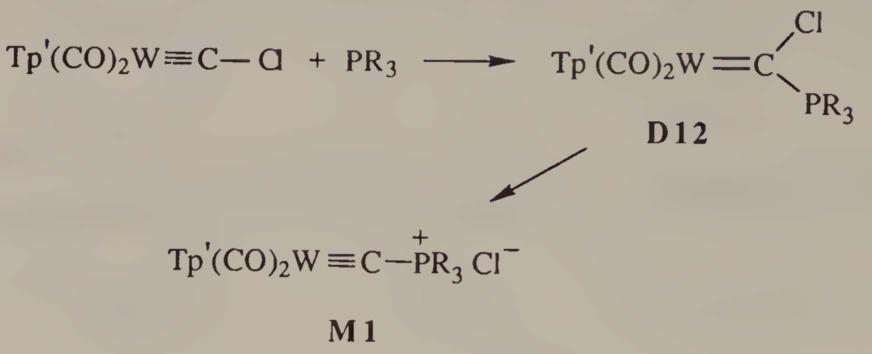
**D11**

(14.72)



**G2** (14.73)

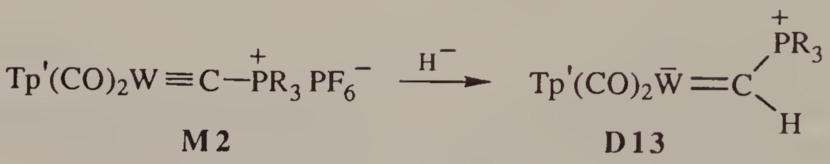
Templeton has synthesized some pseudo ylide complexes (Eqs. 14.74 and 14.75) from Tp′(CO)$_2$W≡C–Cl (Tp′ = 3,5-dimethylpyrazoylborate).[81]



**D12**

**M1**

(14.74)



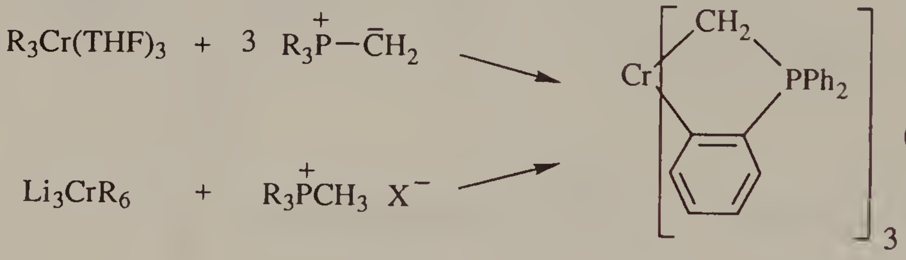
**M2**

**D13**

(14.75)

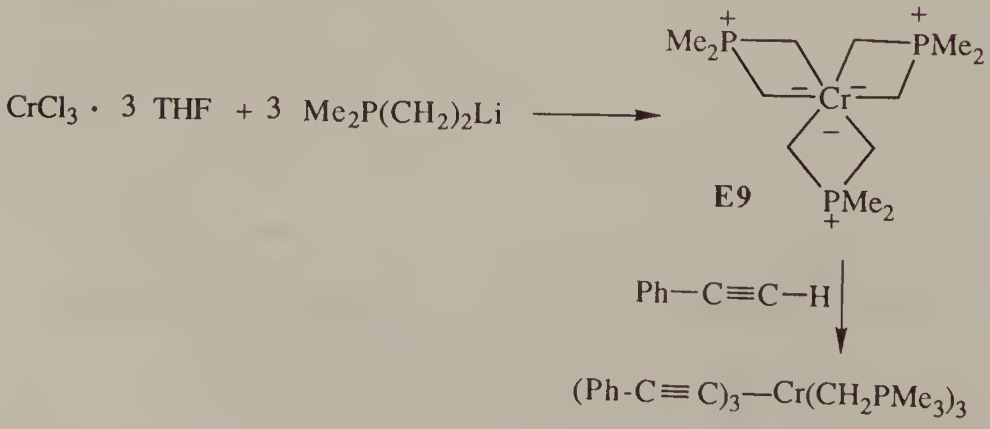
### 14.4.3 Homoleptic Complexes

Homoleptic complexes have been described (Eq. 14.76).[82] A most interesting reaction of the homoleptic ylides is treatment of Cr[(CH$_2$)$_2$P(CH$_3$)$_2$]$_3$ with phenylacetylene (Eq. 14.77). The reaction is in essence a carbon metallation



**A38 X 20**

(14.76)



**E9**

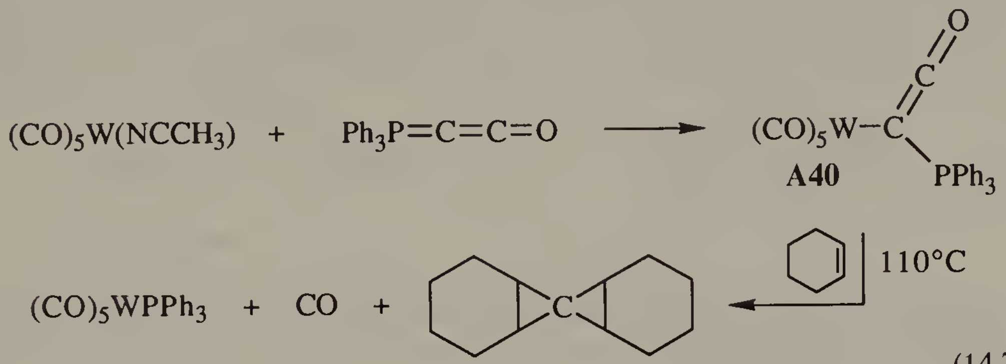
**A39**

(14.77)

reaction. The choice of the substrate is rather specific, in the sense that phenylacetylene has an acidic C–H bond. Moreover, this suggests that suitable ylide complexes can promote carbon–hydrogen activation reactions.[83]

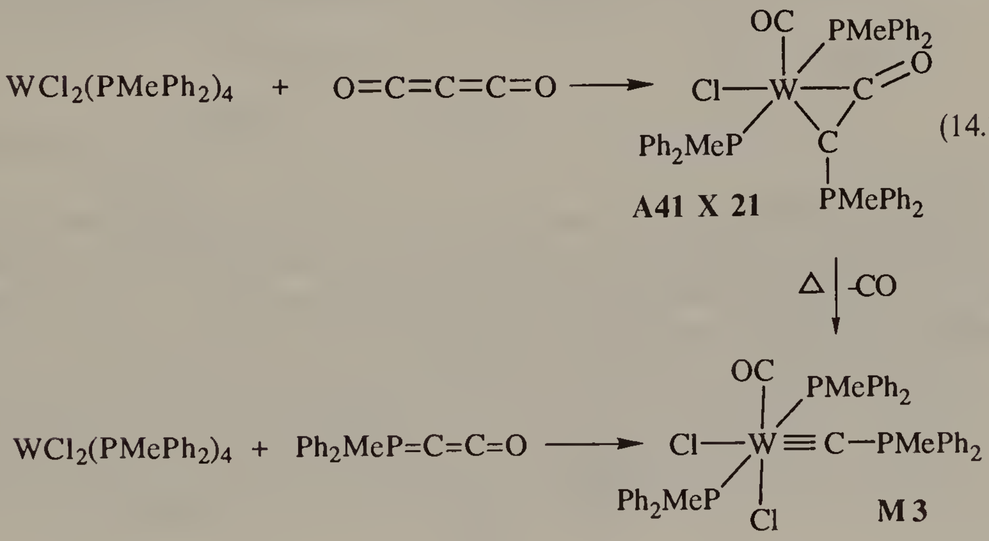
### 14.4.4 Rearrangements

An interesting series of rearrangements has been discovered using a ketene ylide which formed a complex with $(CO)_5W(NCCH_3)$ (Eq. 14.78).[84]



(14.78)

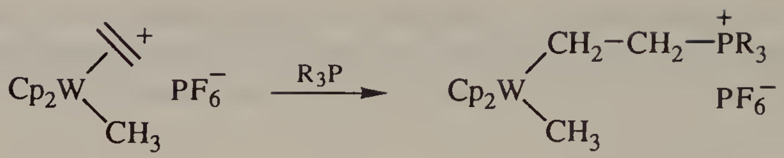
When $WCl_2(PMePh_2)_4$ was treated with carbon suboxide (O=C=C=C=O) a new ylide complex was obtained (Eq. 14.79), the same complex being obtainable from a ketene ylide (Eq. 14.80).[85]



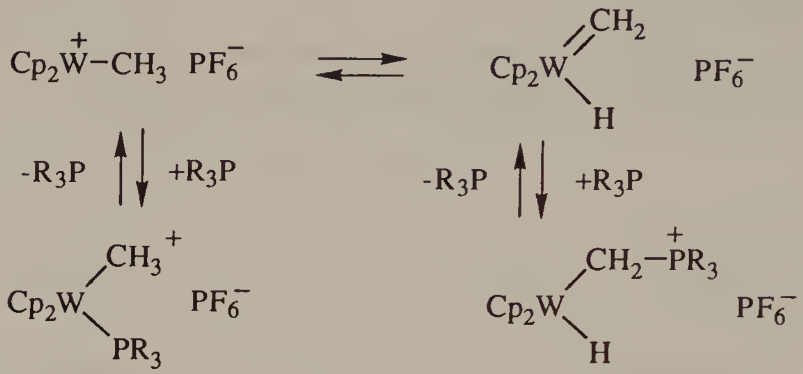
(14.79)

(14.80)

The bis(cyclopentadienyl)tungsten complexes illustrate some remarkable rearrangements. Treatment of an ethylene complex with a tertiary phosphine gave a phosphonium salt (Eq. 14.81).[86] When the ethylenic group was replaced with a methyl group, α-elimination gave a 16-electron complex cationic hydrido tungsten-ylide complex (Eq. 14.82).



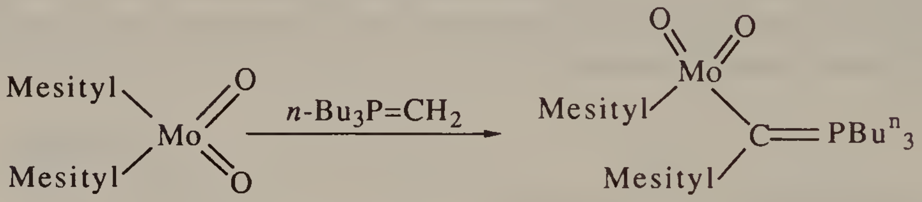
(14.81)



A 42

(14.82)

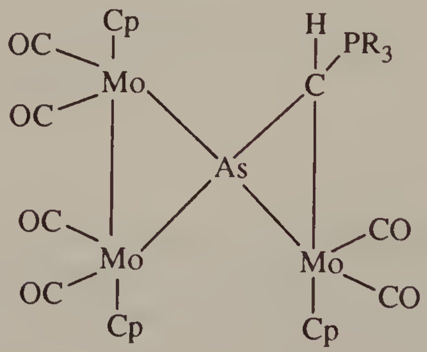
An attempt to transfer a methylene group to a metal-oxo complex in analogy to the Wittig transfer of methylene to a carbonyl group of an aldehyde or ketone has been tested (Eq. 14.83).[87]



**D14**

(14.83)

An ylide-based spiro cluster which is similar to those recently observed with iron group compounds has been prepared by Ziegler (Eq. 14.84).[88] The complex may be viewed as an **AX**-type, as an arsino-stabilized ylide, or as a **G**-type bridging the "metals" molybdenum and arsenic.

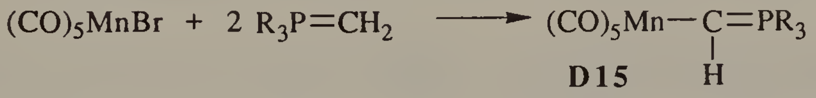


(14.84)

**A43 X 22**

## 14.5 COMPLEXES WITH MANGANESE AND RHENIUM

Almost all transition metal ylide chemistry with rhenium has been studied with substituted complexes rather than the homoleptic halides. Further, bromo(pentacarbonyl)manganese and bromo(pentacarbonyl)rhenium underwent transylidation-type reactions. Reaction of manganese or rhenium pentacarbonylbromide with methylenetriphenylphosphorane gave a type **D** complex after transylidation (Eq. 14.85). The bis-ylide hexaphenylcarbodiphosphorane gave an acetylide which could be considered a metalla-cumulene ylide, $Ph_3P{=}C{=}C{=}ML_n$, a homolog of type **M** in which a carbon atom has been formally inserted into the M=C bond (Eq. 14.86). The elimination of triphenylphosphine oxide in



$$(CO)_5MnBr + 2\,R_3P{=}CH_2 \longrightarrow (CO)_5Mn{-}\underset{H}{\underset{|}{C}}{=}PR_3$$

**D15**

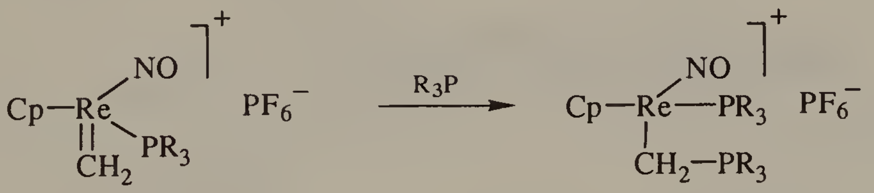
(14.85)

$$(CO)_5MnBr + (Ph_3P)_2C \longrightarrow (CO)_4\underset{Br}{\underset{|}{\overset{-}{Mn}}}{-}C{\equiv}C{-}\overset{+}{P}Ph_3$$

**X23**

(14.86)

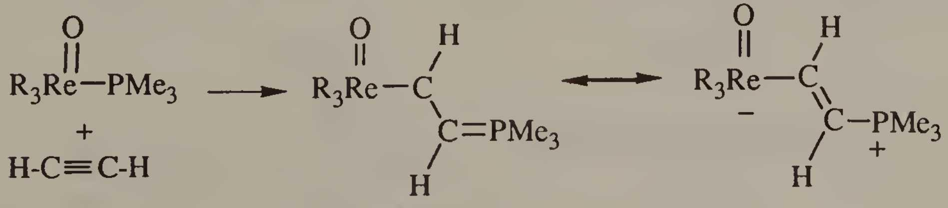
this reaction is an example of carbon–carbon bond formation via a Wittig-type reaction on a coordinated metal carbonyl.[52, 89] Reaction of a cationic methylene complex with triphenylphosphine gave an ylide derivative of form **A** (Eq. 14.87)[90] which was converted to its corresponding ylide and alkylated stereospecifically (Eq. 14.94).



(14.87)

**A44**

In a very unusual reaction $ReO(PMe_3)(CH_2SiMe_3)_3$ and acetylene gave a metallapropenide, another pseudo complex of type **X**, without direct use of a preformed ylide (Eq. 14.88).[91] The adducts of phosphines with $\eta^6$-arenetricarbonylmanganese cations gave $\eta^5$-cyclohexadienylphosphonium-tricarbonylmanganese cations. The phosphine added in the exo position.[92]



R = $CH_2SiMe_3$

**X24**

(14.88)

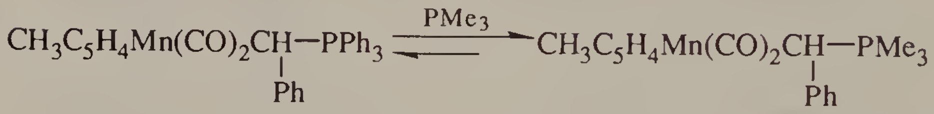
Treatment of $CpMn(CO)_2THF$ with $Me_3P{=}CH_2$ gave ylide adducts of type **A** (Eqs. 14.89 and 14.90).[93] Carbene splitting of the coordinated ylide, as indicated by phosphine exchange (alkylidene transfer), can occur with these manganese complexes, but the product has not been isolated (Eq. 14.91).[94]

$$CpMn(CO)_2THF \xrightarrow{Me_3P=CH_2} Cp\overset{-}{Mn}(CO)_2\text{-}CH_2\overset{+}{P}Me_3 \qquad (14.89)$$

**A45**

$$CpMn(CO)_2THF \xrightarrow{Ph_3P=CH_2} Cp\overset{-}{Mn}(CO)_2\text{-}CH_2\overset{+}{P}Ph_3 \qquad (14.90)$$

**A46**

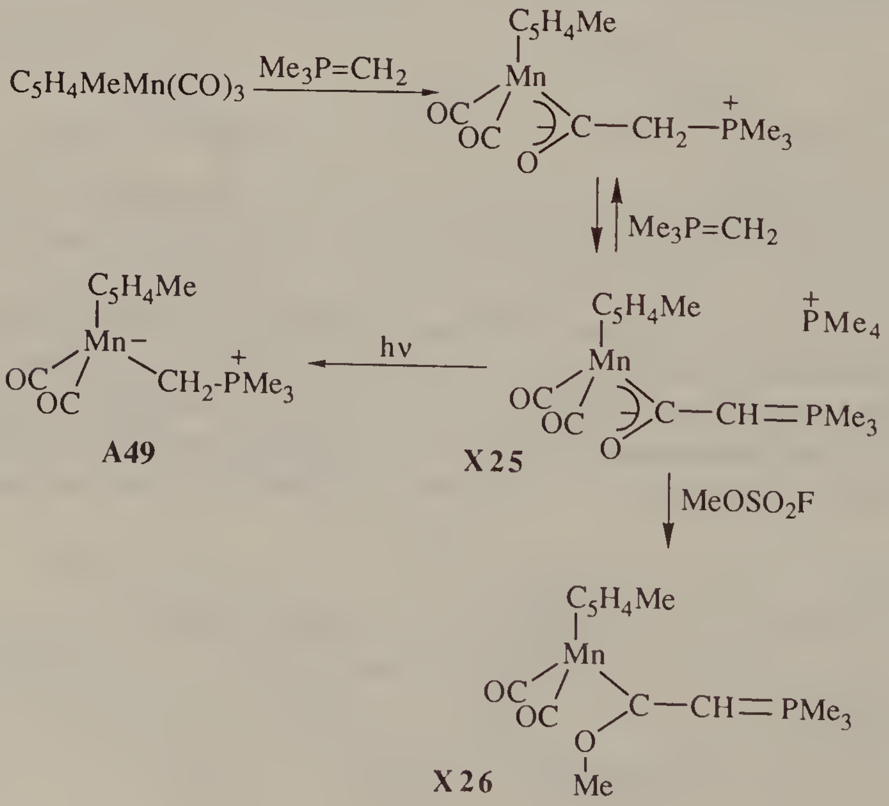


$$CH_3C_5H_4Mn(CO)_2\underset{\displaystyle Ph}{CH}{-}PPh_3 \overset{PMe_3}{\rightleftharpoons} CH_3C_5H_4Mn(CO)_2\underset{\displaystyle Ph}{CH}{-}PMe_3$$

**A47** **A48** (14.91)

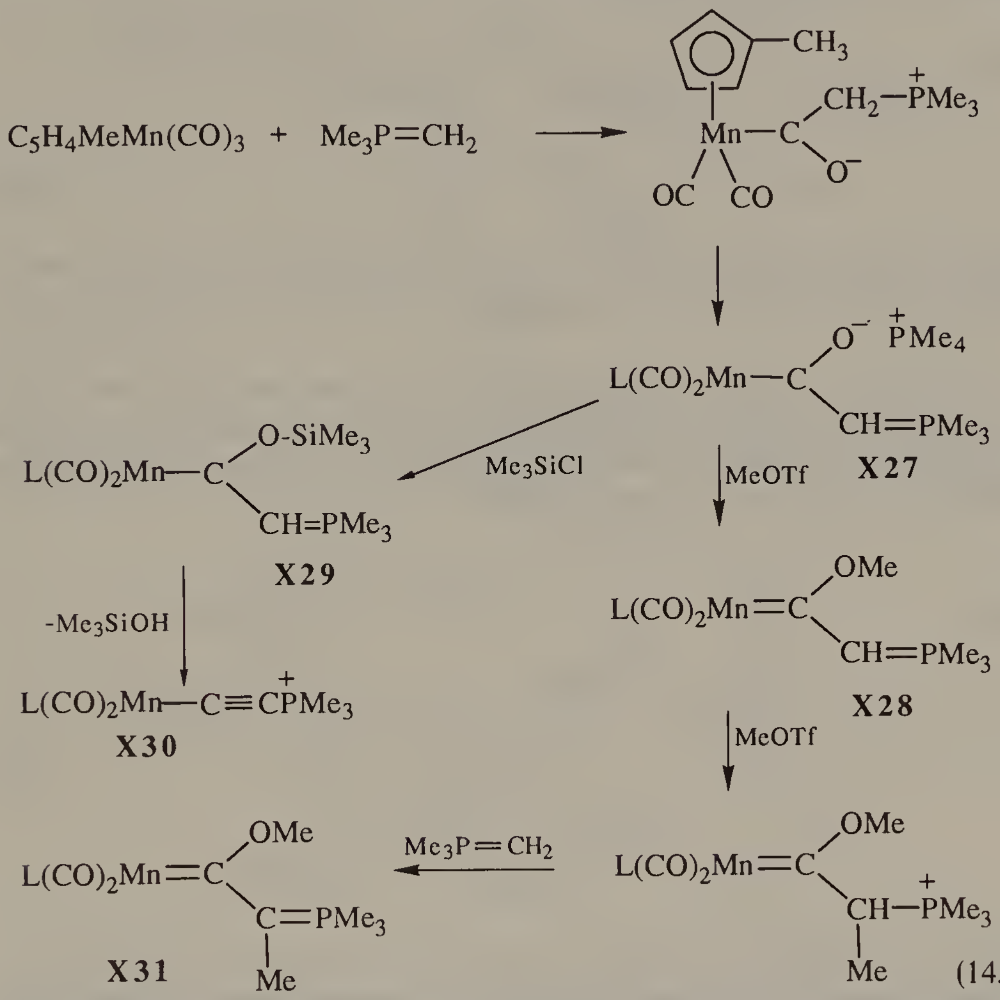
The ketene ylide, $Ph_3P{=}C{=}C{=}O$, was nucleophilic enough to displace $Et_2O$ from the photolyzed coordination sphere of $CpM(CO)_2Et_2O$ and a type **A** complex was obtained. Similar substitution was obtained with iron carbonyls.[95]

The work of Blau and Malisch with $CpMn(CO)_3$ and $Me_3P{=}CH_2$ is summarized in Eq. 14.92. Here addition of the ylide to the carbonyl group occurred,



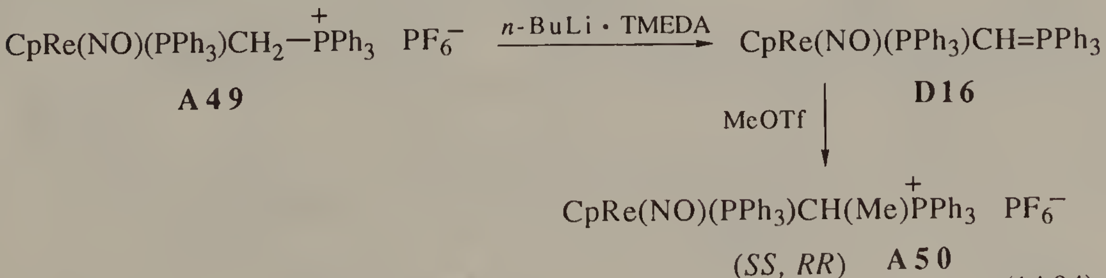
**A49** **X25** **X26** (14.92)

followed by transylidation.[96] Direct addition of a phosphorus ylide to the carbonyl group also occurred with $CH_3C_5H_4Mn(CO)_3$. With suitable alkylating agents carbene ylides could be obtained in which the carbon chain length has been increased by one unit (Eq. 14.93).[97] The synthesis of new carbon–carbon bonds is illustrated by the preparation of **X30**.[97]



(14.93)

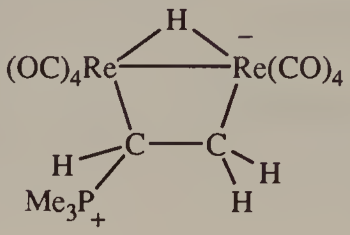
Transylidation or metallation to give substituted ylides has been studied with rhenium compounds.[98] A rhenium ylide complex (**A44**) was prepared by treatment of $CpRe(NO)(PPh_3)(CH_3)$ with $Ph_3C^+PF_6^-$ and a phosphine. The coordinated ylide was deprotonated with *n*-BuLi/TMEDA and the **D**-type complex was alkylated stereospecifically (Eq. 14.94).



$$CpRe(NO)(PPh_3)CH_2{-}\overset{+}{P}Ph_3\ PF_6^- \xrightarrow{n\text{-BuLi}\cdot\text{TMEDA}} CpRe(NO)(PPh_3)CH{=}PPh_3 \xrightarrow{MeOTf} CpRe(NO)(PPh_3)CH(Me)\overset{+}{P}Ph_3\ PF_6^-$$

(14.94)

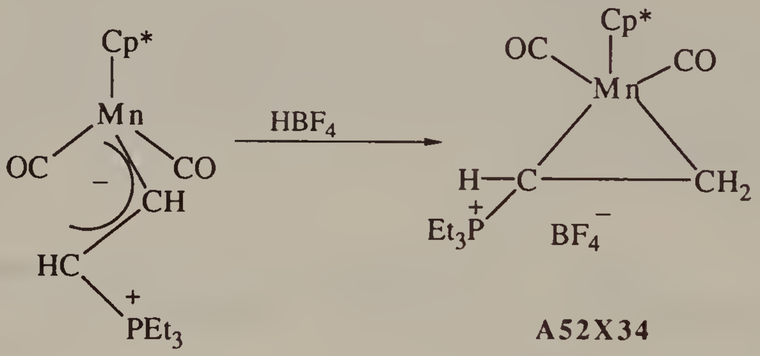
Ligands coordinated to the Group VII elements form ylide complexes in a variety of ways. For example ($\mu$-hydrido) ($\mu$-alkenyl) dirhenium octacarbonyl complexes, which were formed on photolysis of $Re_2(CO)_{10}$ in the presence of simple olefins like ethylene, reacted with trimethylphosphine to form bridging **AX**-type structures (Eq. 14.95).[99]



(14.95)

**A51X32**

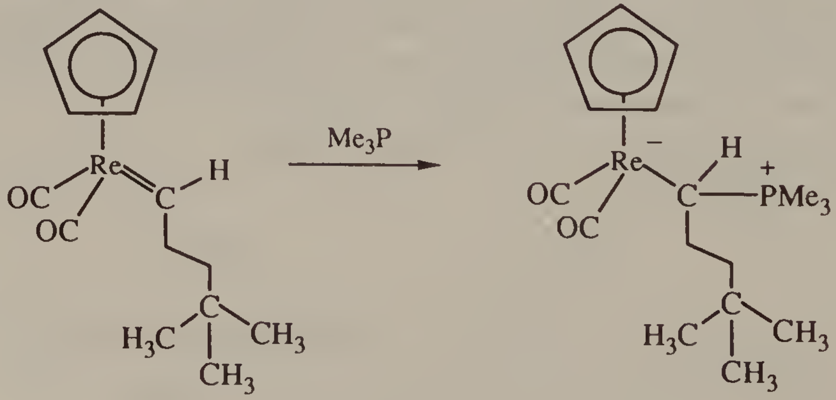
The acetylene complex $Cp^*Mn(CO)_2(C_2H_2)$ reacted with phosphines to give a $\beta$-metallated complex which could be protonated to give a metallocycle (Eq. 14.96).[100] Complexes also were formed from vinylidene and allenylidene $CpMn(CO)_2$ complexes and phosphines.[101]



(14.96)

**X33** **A52X34**

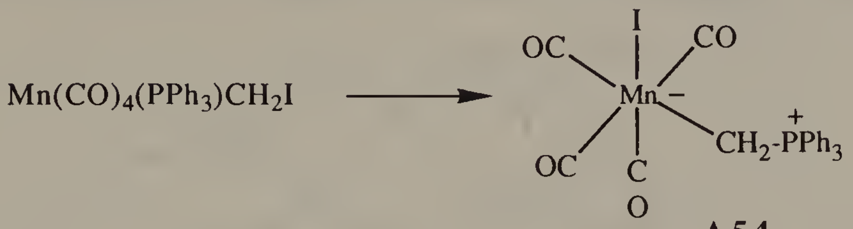
There are carbene rhenium complexes of the type $CpRe(CO)_2(CHR)$ which interacted with phosphines to give **A**-type ylide complexes (Eq. 14.97).[102]



(14.97)

**A53**

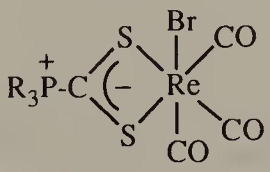
Equation 14.98 is an example of a rearrangement in solution at room temperature of an iodomethyl derivative to an ylide complex of type **A**. The corresponding rhenium complex did not undergo rearrangement.[103]



**A54**

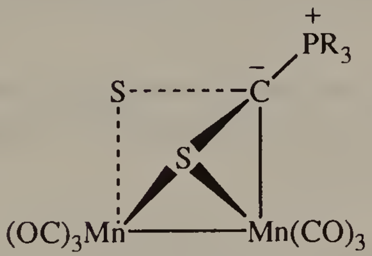
(14.98)

Bulky adducts of trialkylphosphines with carbon disulfide are special ligands with chelating and bridging capabilities which formed ylide complexes (Eq. 14.99).[104]



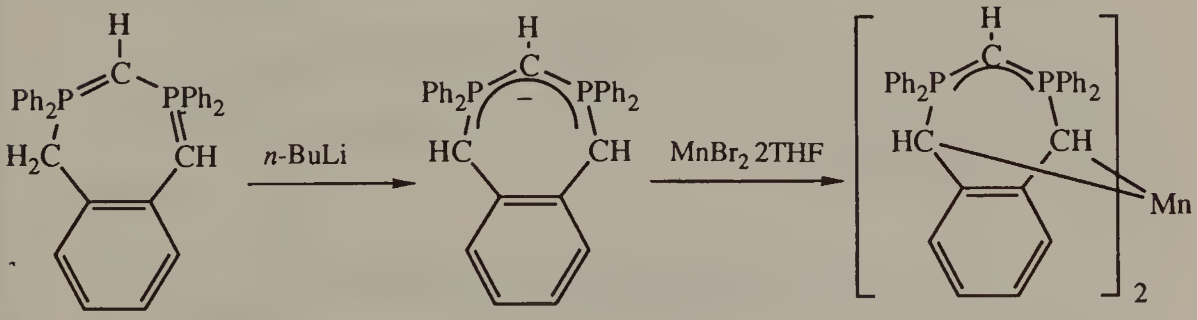
**X35**

(14.99)



**A55X36**

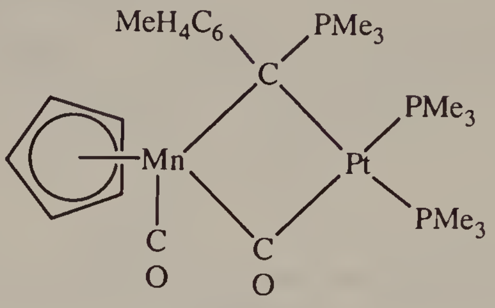
A paramagnetic tetrahedral manganese $d^5$ complex formed when a metallated cyclic bis-ylide was treated with manganese dibromide (Eq. 14.100). Iron and cobalt analogs could also be prepared.[105]



**A56**

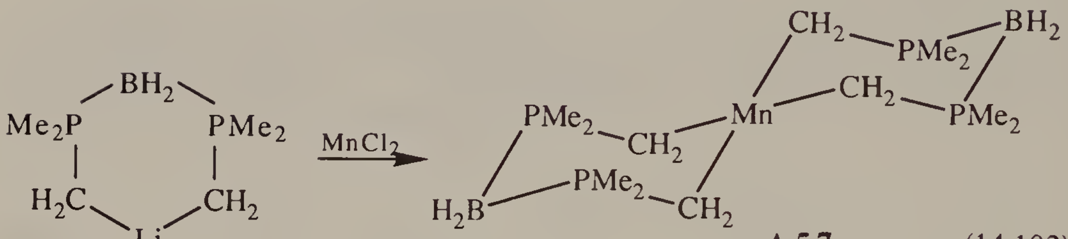
(14.100)

F. G. A. Stone has described a metallo-ylide cluster which contained manganese and platinum (Eq. 14.101).[106] An interesting example of a mixed ylide complex was formed from $MnCl_2 \cdot THF$ and bis(dimethylmethylenephosphoranyl)dihydroborate anion (Eq. 14.102).[107]



**G3**

(14.101)



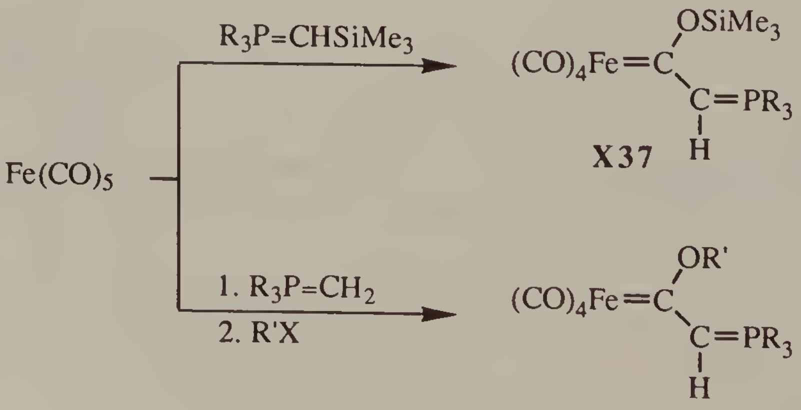
**A57**

(14.102)

C-type ylide complexes with dimethylsulfonium- and triphenylphosphonium-cyclopentadienide have been reported for manganese and rhenium $[(\text{ylide})M(CO)_3]^+PF_6^-$ (C5).[108]

## 14.6 IRON, RUTHENIUM, AND OSMIUM COMPLEXES

Interaction with coordinated ligands is the main feature of reactivity in this group of transition metals with ylides, often with concurrent transylidation (Eq. 14.103).[109]

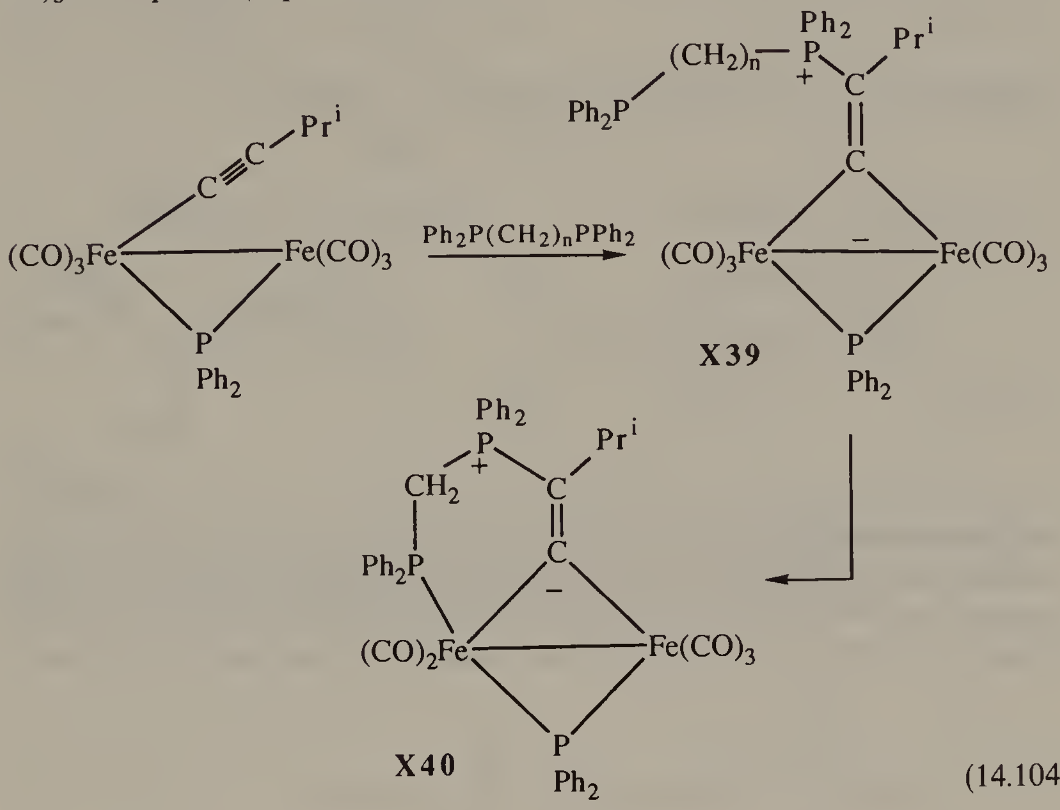


**X37**

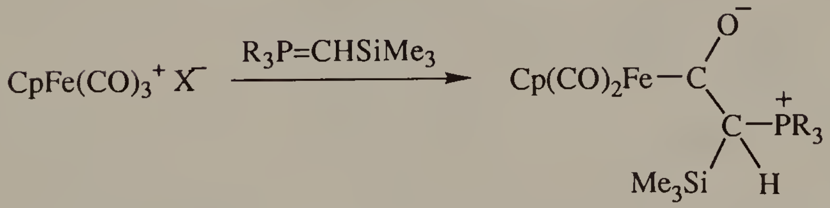
**X38**

(14.103)

Hydrocarbyl complexes such as those shown in Eq. 14.104 are highly activated to nucleophilic attack at the acetylenic ligand and gave phosphonium zwitterions of type **X**.[110] A similar set of reactions occurred with the CpFe $(CO)_3^+\ X^-$ species (Eq. 14.105).[111, 112]

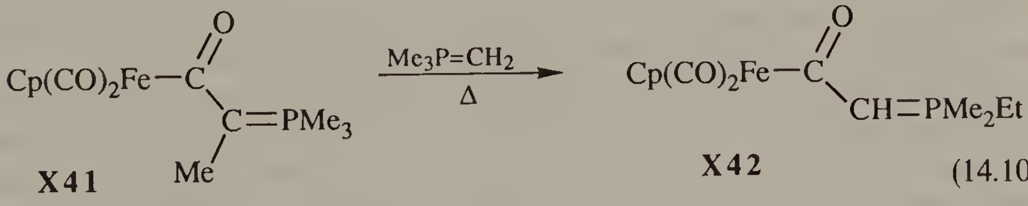


(14.104)

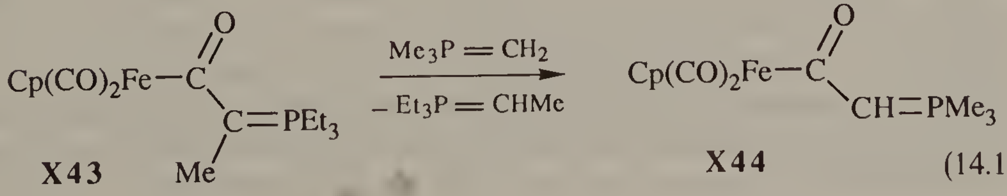


(14.105)

Rearrangement and substitution can occur as shown in Eqs. 14.106 and 14.107 with the cyclopentadienyl iron complexes.[111]

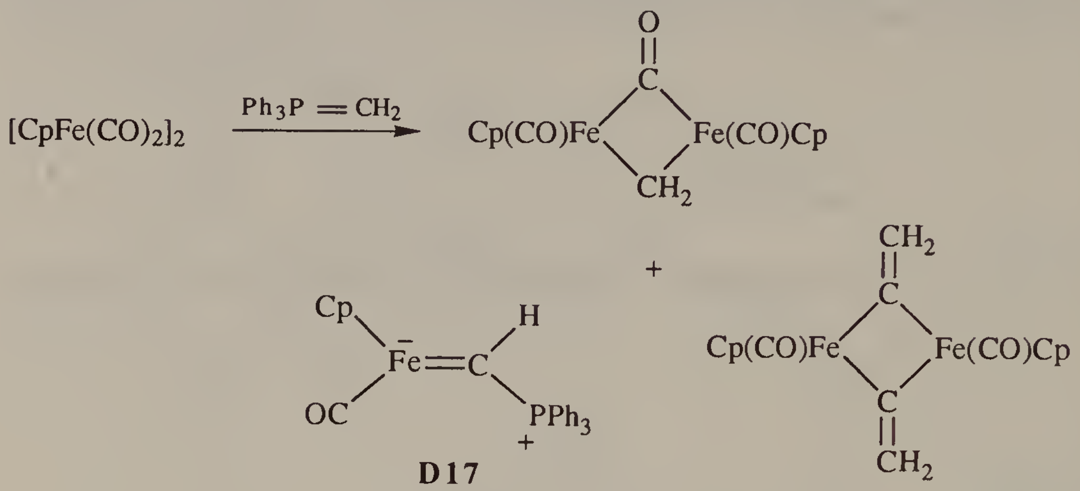


(14.106)



(14.107)

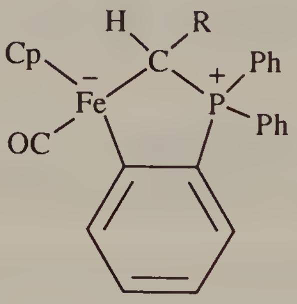
Actual transfer of a methylene group via a Wittig reaction to yield alkylidene complexes has been observed with the dimer $[CpFe(CO)_2]_2$ (Eq. 14.108).[113] The



**D17**

(14.108)

ready availability of this iron dimer makes this type of reaction easy to accomplish, but synthetic utility and extension of this reaction to other compounds has not been tested. $[CpFe(CO)_2]_2$ also reacted with ylides in the presence of *n*-BuLi to give mononuclear *o*-metallated complexes (Eq. 14.109).[114]

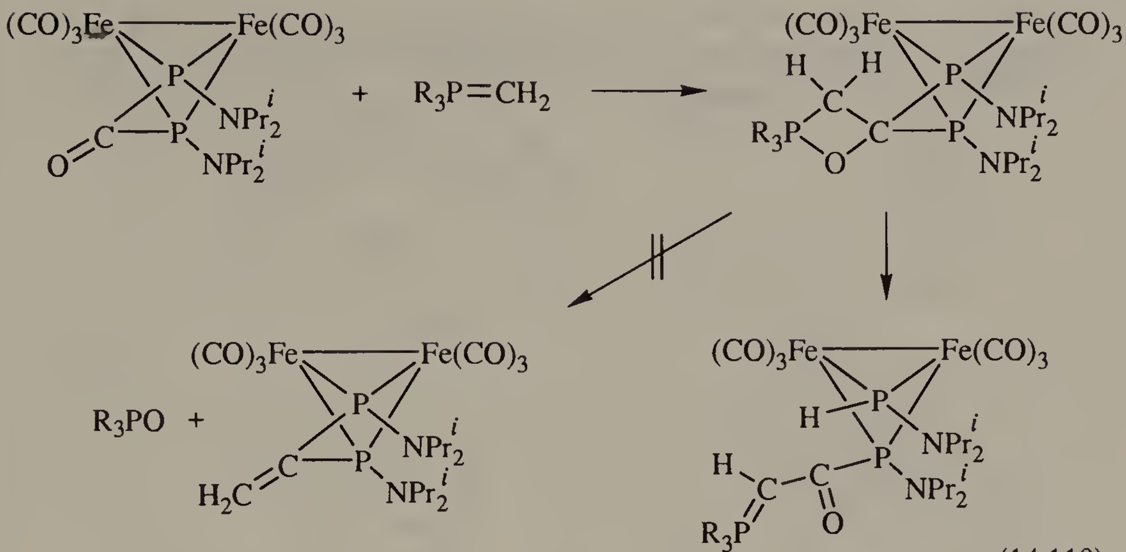


(14.109)

**A58X45**

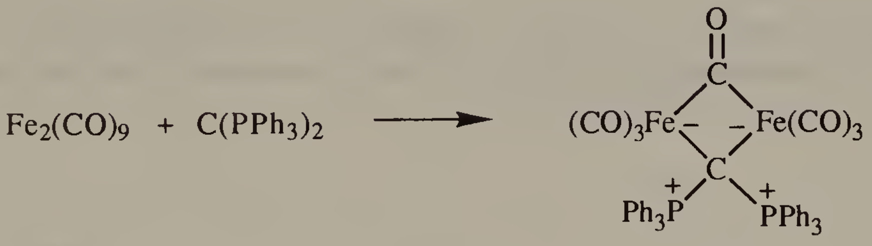
The cationic iron complex $[Cp^*Fe(CO)_2(CH_2)]BF_4$ when treated with $Ph_3P$ gave the ylide compound, $[Cp^*Fe(CO)_2(CH_2PPh_3)]BF_4$, **A59**.[115]

Another attempt to induce Wittig olefination with a metal carbonyl compound was the treatment of $R_3P{=}CH_2$ with the air-stable phosphorus-bridging carbonyl compound $(i\text{-}Pr_2NP)_2COFe_2(CO)_6$.[116] Oxetane formation did not result in phosphine oxide formation. Hydrogen migration to phosphorus occurred instead and a phosphoniumacylmethylide complex was formed (Eq. 14.110). Weber et al.[117] observed that treatment of the same carbonyl compound with $Me_2S(O){=}CH_2$ gave $[(i\text{-}Pr_2NPCH_2)_2CO]Fe_2(CO)_6$, which resulted from insertion of the methylene group into the phosphorus–carbon bond rather than Wittig olefination.

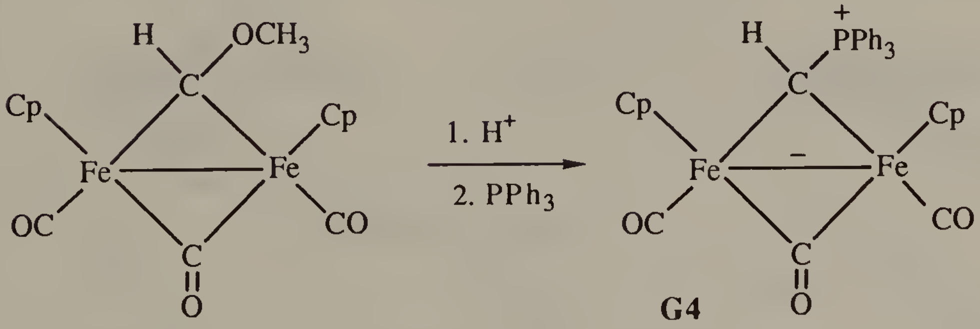


(14.110)

Substitution of CO by ylide occurred with carbodiphosphorane (Eq. 14.111).[118a] Both ylide electron pairs of the carbodiphosphorane formed an **A**-type complex with a bridging interaction that is reminescent of the coordination mode **G** of deprotonated ylides, $R_3PCH^-$ (Eq. 14.112).[118b]



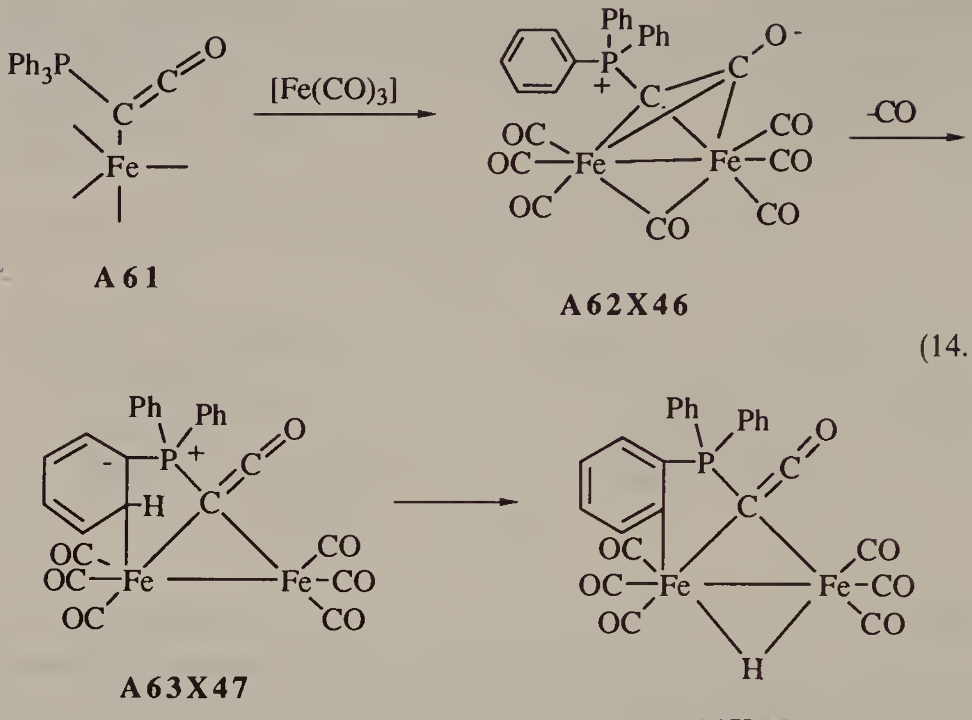
**A 60** (14.111)



**G4**

(14.112)

Substitution of CO was the rule when $Ph_3P{=}C{=}C{=}O$ was treated with the small iron cluster $Fe_3(CO)_{12}$ to give intermediate type **G** complexes (Eq. 14.113).[119] An allenylidene triphenylphosphorane complex was formed.



**A61**

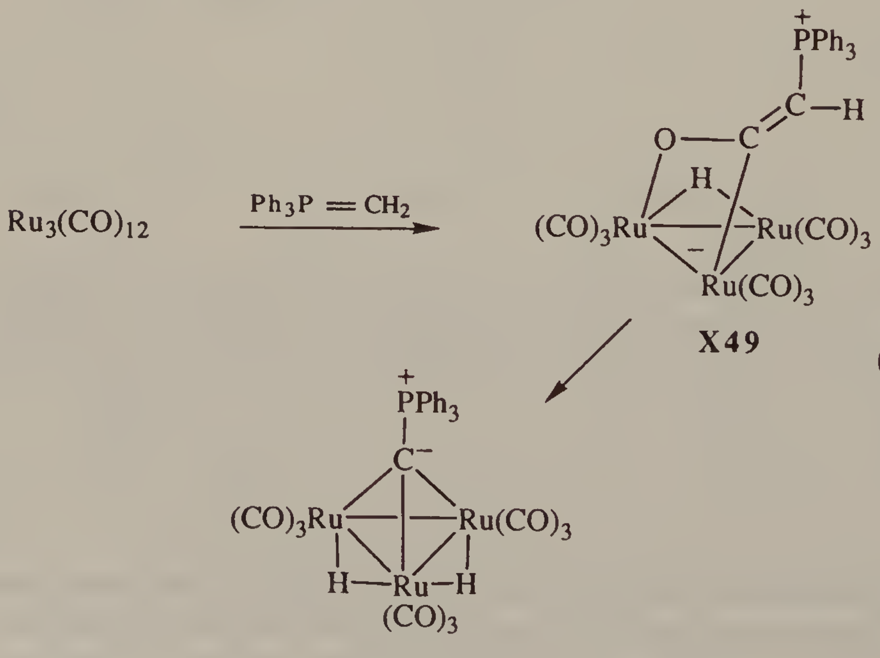
**A62X46**

**A63X47**

**A64X48**

(14.113)

The ylide chemistry of ruthenium clusters has been illustrated by the recent work of Vahrenkamp (Eq. 14.114),[120] which represents a possible route to designed carbon-containing metal clusters.

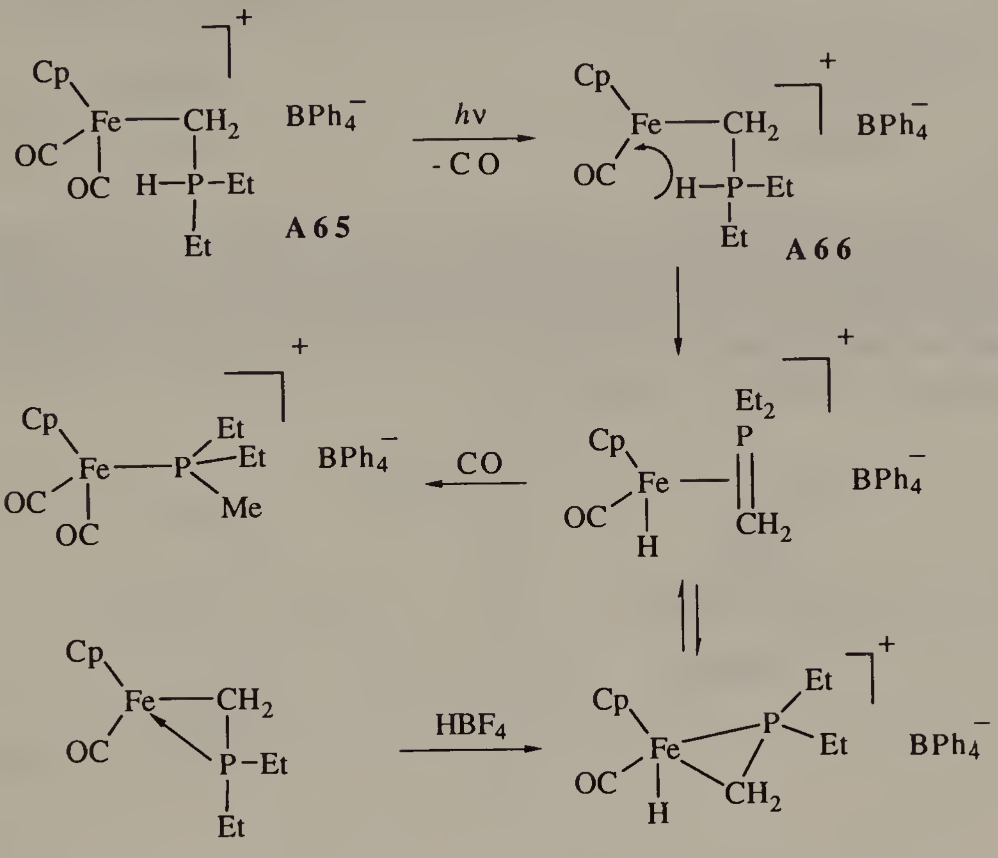


**X49**

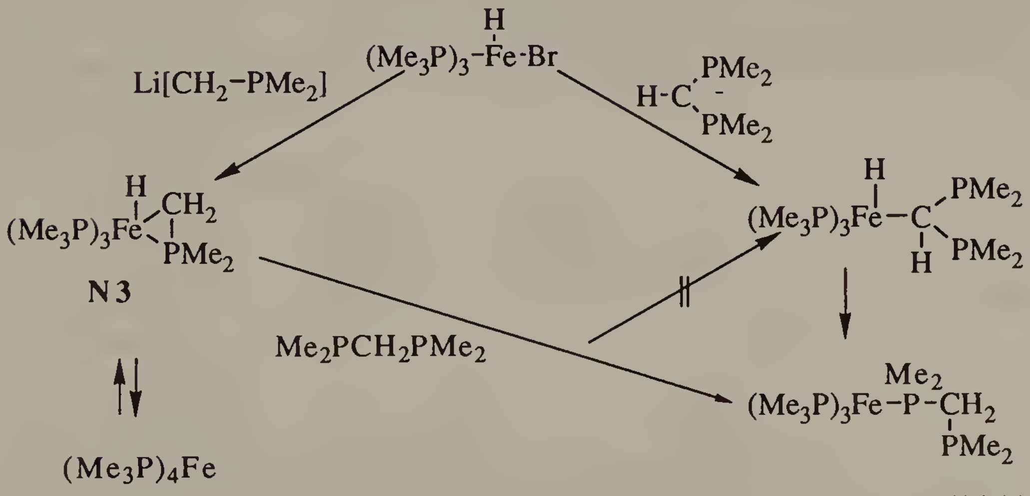
**K1**

(14.114)

The photolytic $\eta^1 \rightarrow \eta^2$ conversion of iron ylide complexes is shown in Eq. 14.115[121] and carbene scission (alkylidene transfer) is possible, as shown in Eq. 14.116.[122]

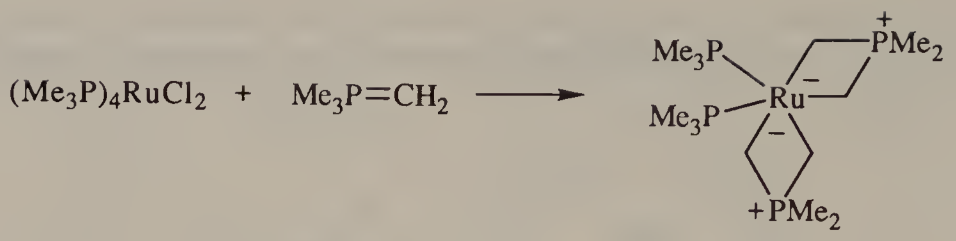


(14.115)



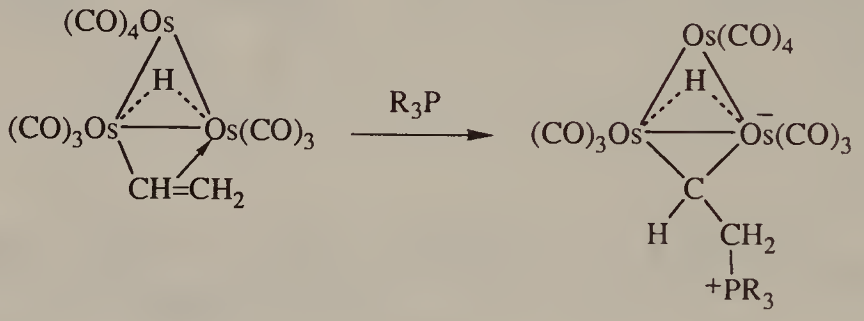
(14.116)

Ruthenium formed internally metallated materials with methylenetrimethylphosphorane (Eq. 14.117).[123]

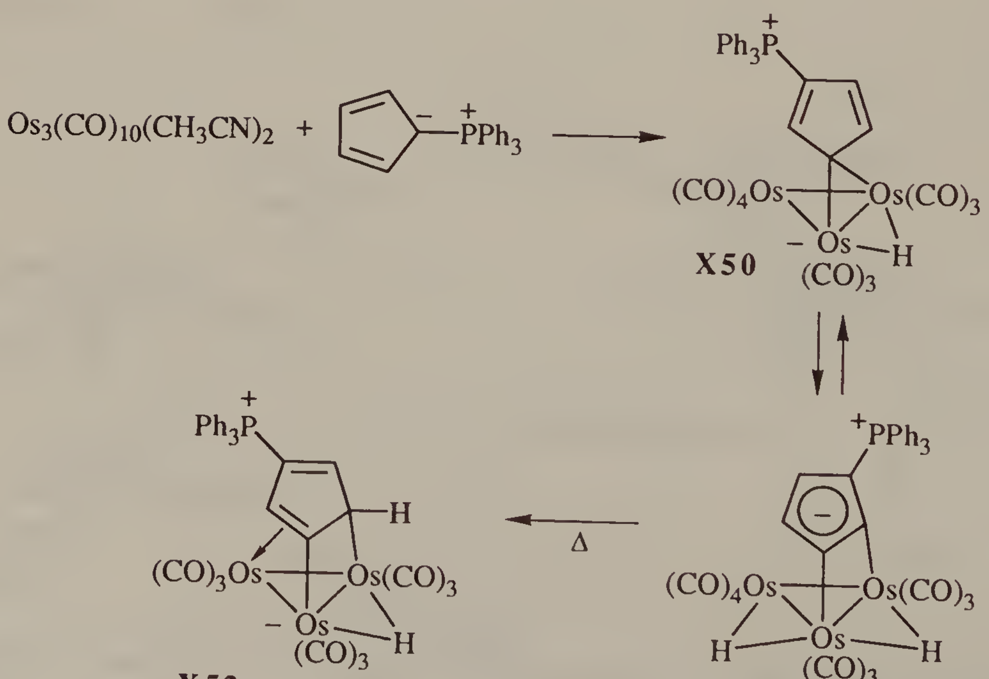


**E10** (14.117)

An internal metallated phosphonium salt was formed when the osmium cluster shown in Eq. 14.118 was treated with a phosphine.[124, 125] The oxidative addition of formylmethylenetriphenylphosphorane to osmium carbonyl clusters lead to related structures.[125] Equations 14.119 and 14.120 illustrate additional reactions of ylides with osmium clusters.



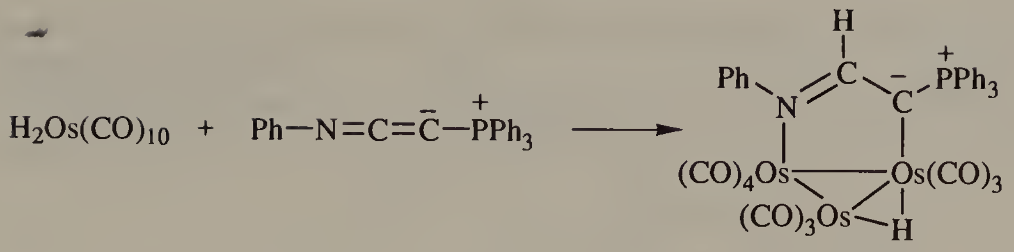
(14.118)



**X50**

**X52**

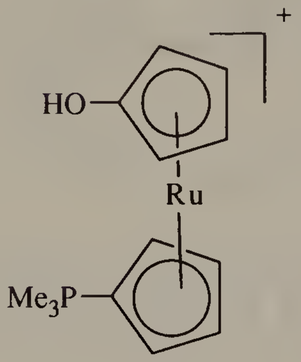
**X51** (14.119)



**A67X53**

(14.120)

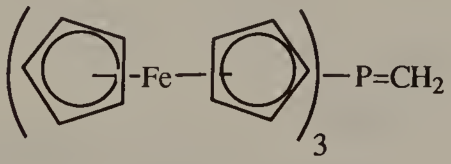
The **C**-type sandwich complex formed through nucleophilic substitution of trimethylphosphine on the cyclopentadienyl ring of a dimeric ruthenium cyclopentadienone complex (Eq. 14.121).[126]



(14.121)

**C6**

Triferrocenylphosphoniummethylide has been synthesized and its structure determined (**X54**).[127] This material could be a precursor for the synthesis of nonlinear optical materials. Ferrocene-like bis-phosphonium iron complexes are known (Eq. 14.123), but very little is known about their chemical reactivity.[128]

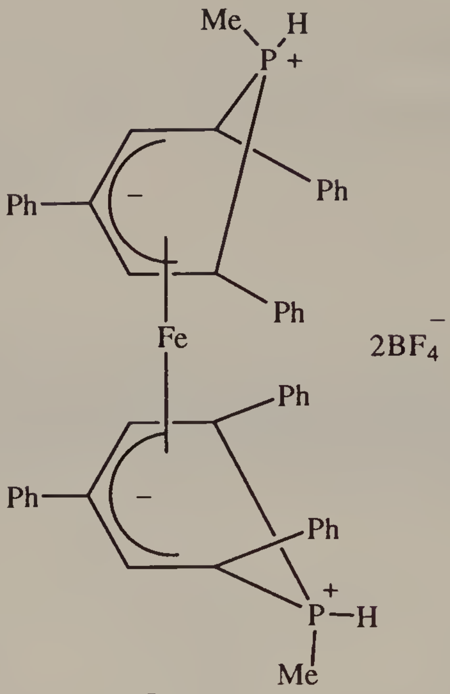


(14.122)

**X54**

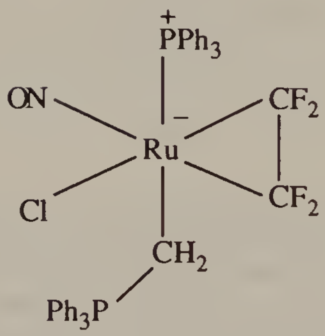
The ylide complex **A68** formed when $[Ru(CH_2)(Cl)(NO)(PPh_3)_2]$ was treated with tetrafluoroethylene (Eq. 14.124), although treatment with ethylene gave no ylide complex. The osmium ylide analog to **A68** formed similarly.[129]

Ylide iron tetracarbonyl complexes $[(Ph_3PCHR)Fe(CO)_4]$ were obtained from phosphines and germylated heterocycles (Eq. 14.125).[130] The same ylide



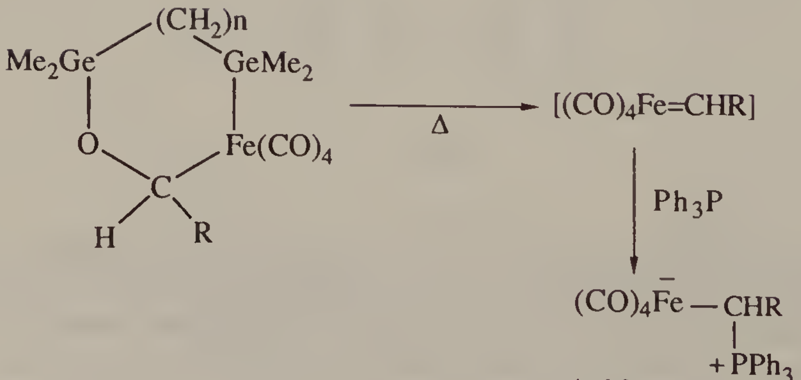
**C7**

(14.123)



**A 68**

(14.124)

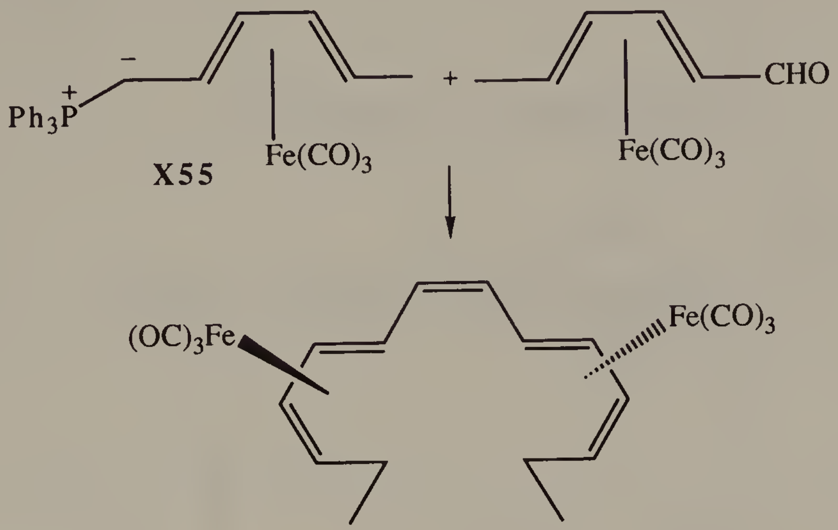


**A 69**

(14.125)

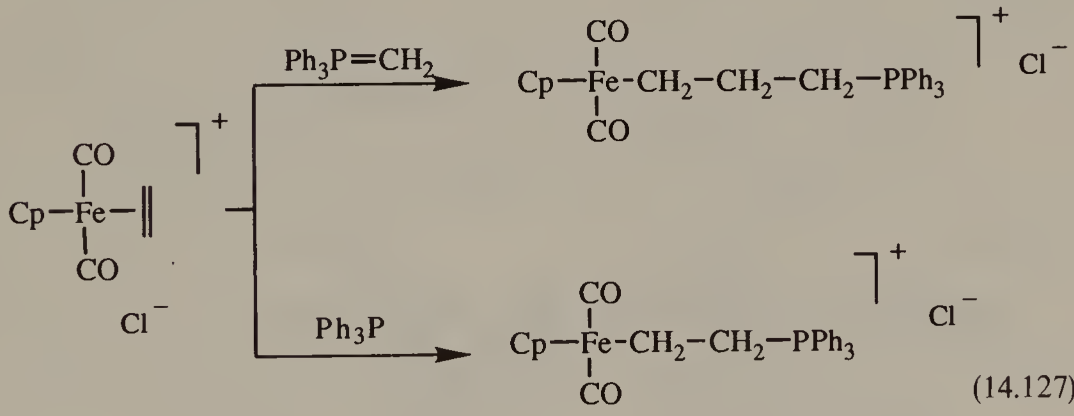
complexes were accessible from iron pentacarbonyl, methylene chloride and a phase-transfer catalysis.[131]

A Wittig reaction was performed with the conjugated ylide complex **X55** to produce a complexed pentaaene (Eq. 14.126).[132]



(14.126)

When olefins were coordinated to $CpFe(CO)_2^+$ followed by treatment with phosphorus ylides, or phosphines, the newly formed complexes resembled ethylene insertion products in a growing polymer chain (Eq. 14.127).[133]



$$\left[Cp{-}\overset{CO}{\underset{CO}{Fe}}{-}\|\right]^+ Cl^- \xrightarrow{Ph_3P{=}CH_2} \left[Cp{-}\overset{CO}{\underset{CO}{Fe}}{-}CH_2{-}CH_2{-}CH_2{-}PPh_3\right]^+ Cl^-$$

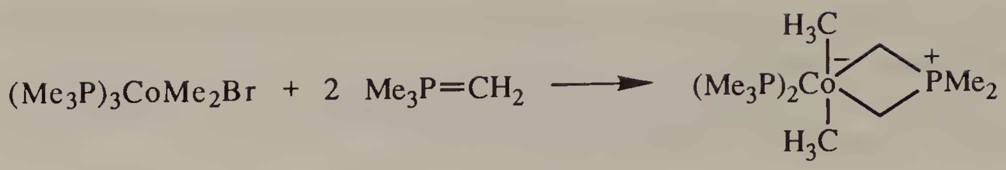
$$\left[Cp{-}\overset{CO}{\underset{CO}{Fe}}{-}\|\right]^+ Cl^- \xrightarrow{Ph_3P} \left[Cp{-}\overset{CO}{\underset{CO}{Fe}}{-}CH_2{-}CH_2{-}PPh_3\right]^+ Cl^-$$

(14.127)

## 14.7 COMPLEXES WITH COBALT, RHODIUM, AND IRIDIUM

Chelate complexes **E** with cobalt are common, especially with ylides that readily undergo transylidation (Eq. 14.128),[134] although some terminal complexes of type **A** are known as well (Eq. 14.129). Similar cobalt nitrosyl complexes also have been made (Eq. 14.130) but detailed studies have not been reported.[135]

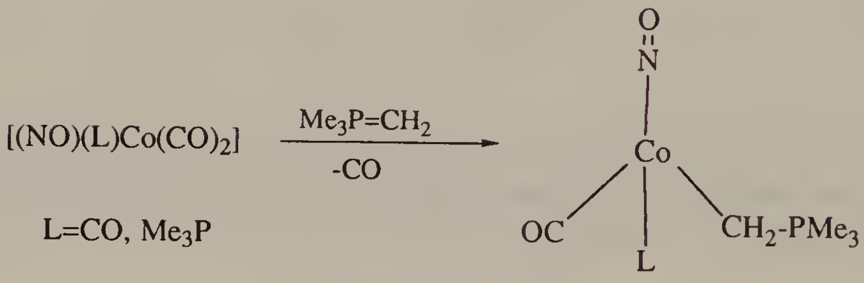
Treatment of tetrakis(trimethylphosphine)rhodium chloride with methylene chloride gave a cationic ylide complex (Eq. 14.131).[136]



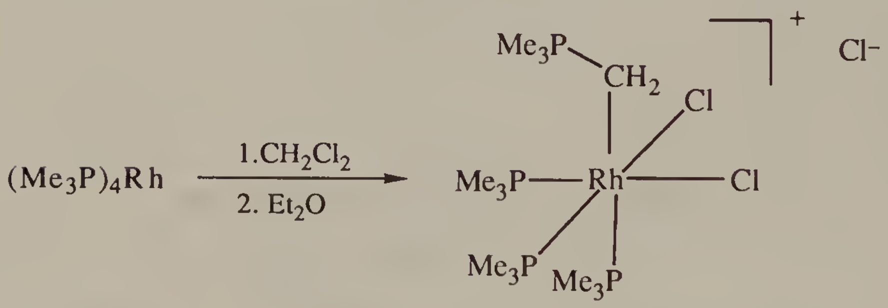
**E11**

(14.128)

$$2(Me_3P)_3CoCl + 2\ Me_3P{=}CH_2 \longrightarrow \underset{\textbf{A70}}{(Me_3PCH_2)_2CoCl_2} + (Me_3P)_4Co + 2\ Me_3P \qquad (14.129)$$



**A71** (14.130)

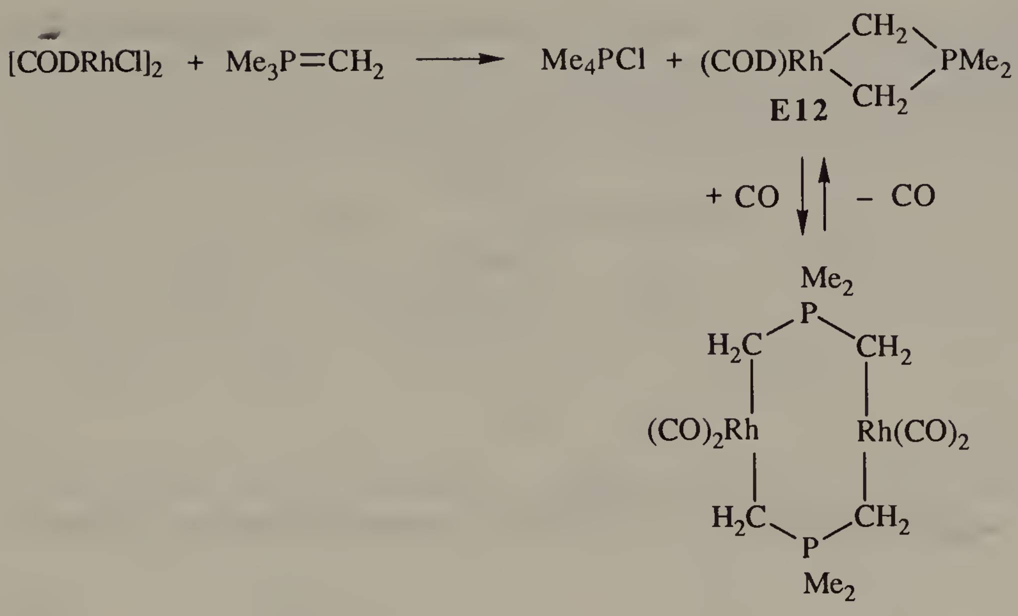


**A72** (14.131)

Displacement of neutral ligands from the coordination sphere of low valent complexes by ylides has been extended to rhodium and iridium (Eq. 14.132).[137]

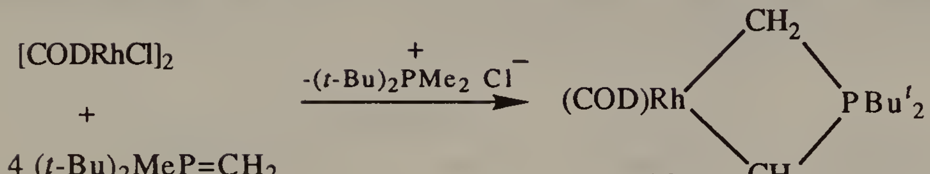
Sterically demanding ylides afforded metallocycles with rhodium (Eq. 14.133) and iridium (Eq. 14.134) complexes with no oligomerization of the ring system.[138]

A rhodium derivative with a chelating phosphine instead of COD is shown in Eq. 14.135.[139]

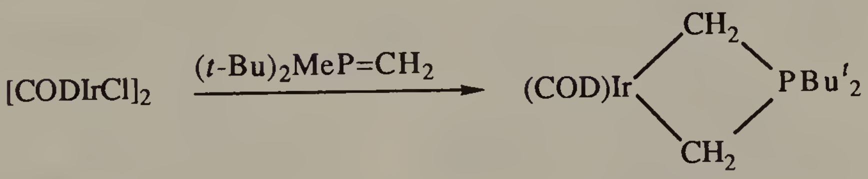


**E12**

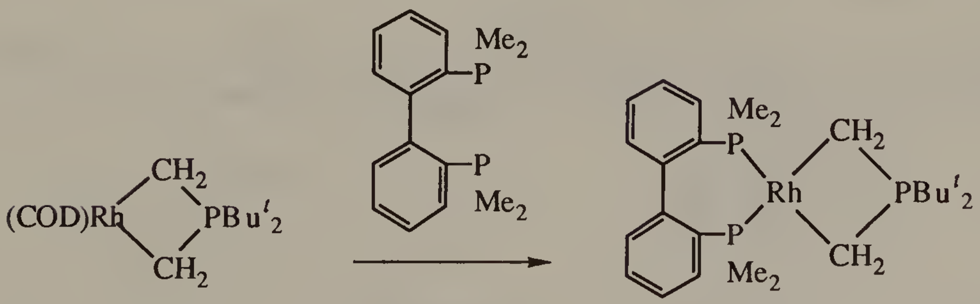
**H3** (14.132)



**E13** (14.133)



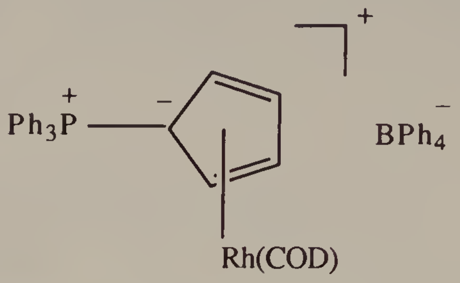
**E14** (14.134)



**E13**

**E15** (14.135)

Triphenylphosphoniumcyclopentadienide has a planar $C_5$ ring in a complex with rhodium (Eq. 14.136). Half-sandwich derivatives with CO and triphenylphosphine instead of COD also have been reported.[140] A related half-sandwich ylide complex **C9** was accessible by ring substitution with phosphines (Eq. 14.137).[141]



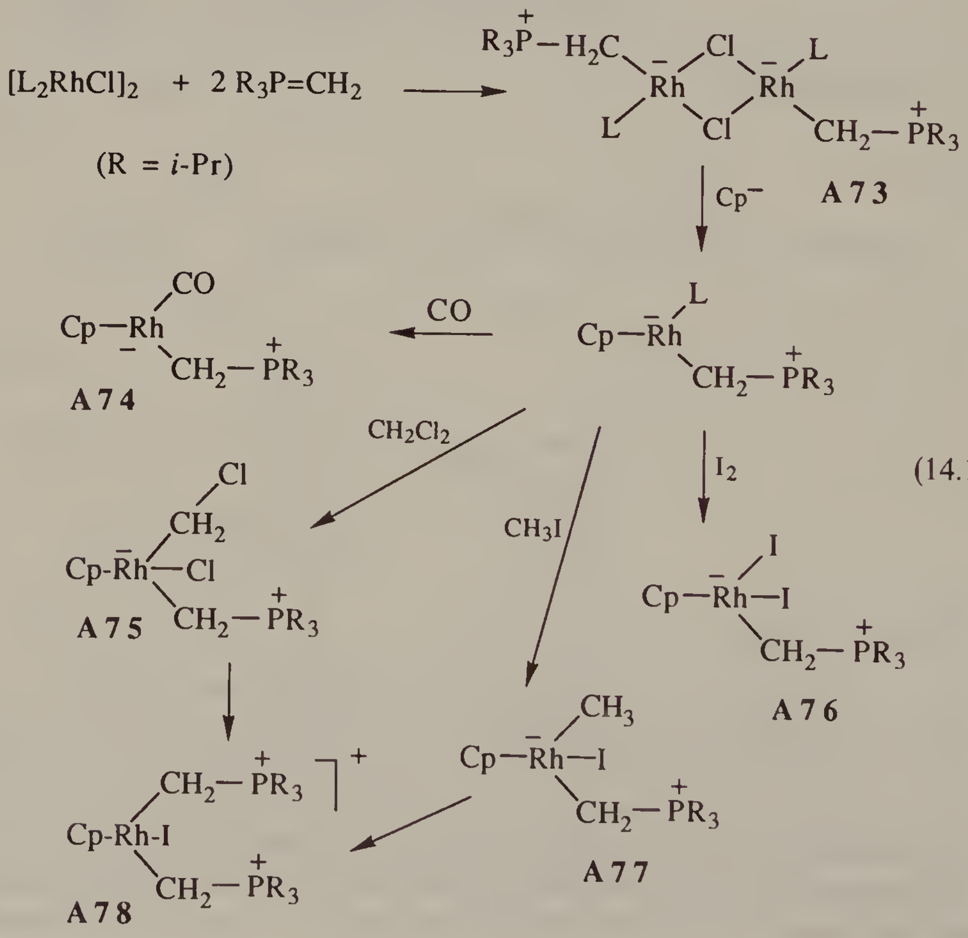
**C8**

(14.136)

$$[CpRh(PEt_3)_2]\,[BF_4]_2 \xrightarrow{Et_3P} [(Et_3PC_5H_4)RhH(PEt_3)_3]\,[BF_4]_2$$

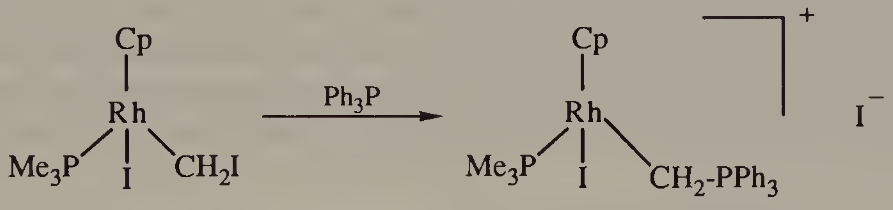
**C9** (14.137)

Treatment of $[L_2RhCl]_2$ with $R_3P{=}CH_2$ displaced only one ligand, and no transylidation occurred, although this aspect could be controlled by the amount of ylide used in the reaction (Eq. 14.138).[142]



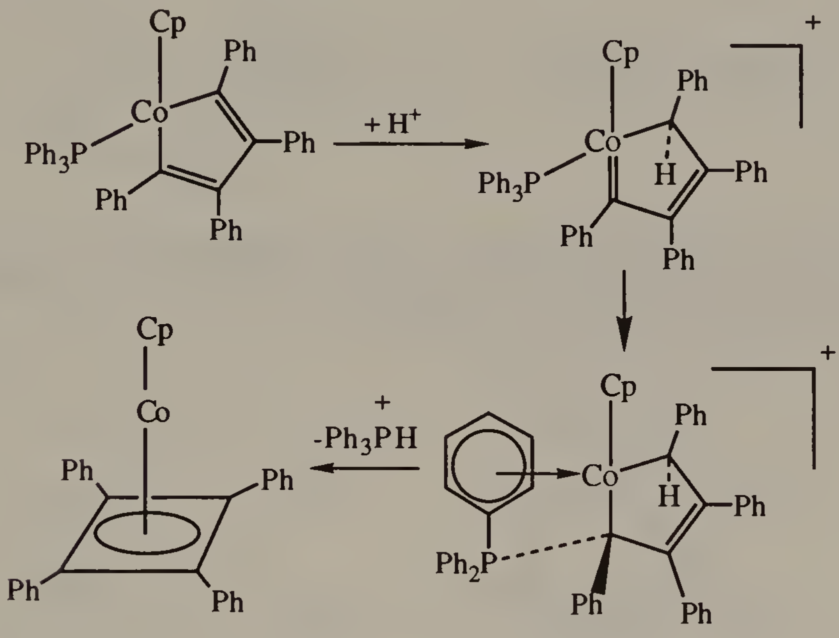
(14.138)

Reaction 14.139 is a synthetic approach to A-type ylides of rhodium complexes. The use of amines or sulfides instead of phosphines gave the analogous nitrogen, arsenic, or sulfur compounds.[143] Pentamethylcyclopentadienylrhodium complexes with chelating phosphino-ylide ligands have also been reported.[144]



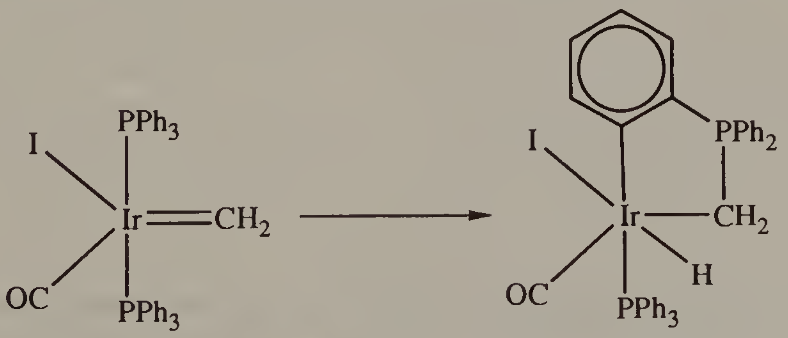
**A79** (14.139)

A protonated cobaltacyclopentadiene rearranged to form an ylide structure followed by the loss of a phosphonium ion, as shown in Eq. 14.140.[145]



**A80X56** (14.140)

An iridium carbene complex was found to undergo rearrangement to an ylide complex with intramolecular C–H activation by *o*-metallation (Eq. 14.141).[146]



**A81X57** (14.141)

## 14.8 COMPLEXES WITH NICKEL, PALLADIUM, AND PLATINUM

### 14.8.1 Ylide Reactions with Carbonyl, Perfluorinated, and Cyclopentadienyl Compounds.

The carbonyl groups in electron-rich transition metals are not sufficiently electropositive for ylide addition to occur at the carbonyl group. Substitution of the carbonyl groups occurs instead to give compounds of type **A** (Eq. 14.142).[147, 148] The reaction with hexaphenylcarbodiphosphorane proceeded likewise (Eq. 14.143).[149]

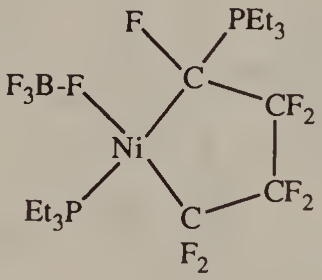
$$Ni(CO)_4 + R_3P{=}CH_2 \longrightarrow (CO)_3\overset{-}{Ni}\text{-}CH_2\text{-}\overset{+}{P}R_3 \qquad (14.142)$$

**A82**

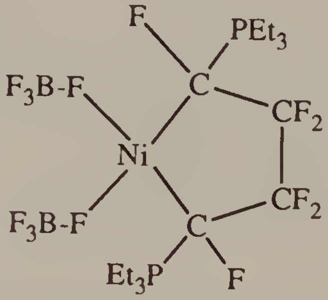
(14.143)

**A83**

The perfluorometallacyclopentane complex $[Ni(PEt_3)_2(CF_2)_4]$ interacted with strong Lewis acids like $BF_3$ to give ylide complexes after fluoride abstraction and phosphine migration (Eq. 14.144).[150]



**A84X58**



(14.144)

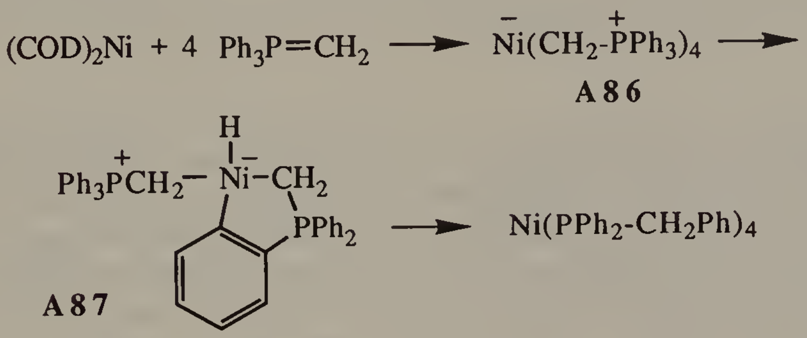
**A85X59**

The monoylide complexes $(R_3PCH_2)Ni(CDT)$ and $(R_3PCH_2)Ni(C_2H_4)$, prepared from $[Ni(CDT)]$ and $[Ni(C_2H_4)_3]$ at low temperature, decompose at room temperature by carbene splitting. The stability of the $CH_2$–Ni(0) bond decreases in the series ylide–$Ni(CO)_3$ > ylide–$Ni(C_2H_4)_2$ > ylide–Ni(COT) according to a declining Lewis acidity of the nickel atom. The carbene splitting seems to be correlated with a decreasing one bond P–C NMR coupling constant.[151]

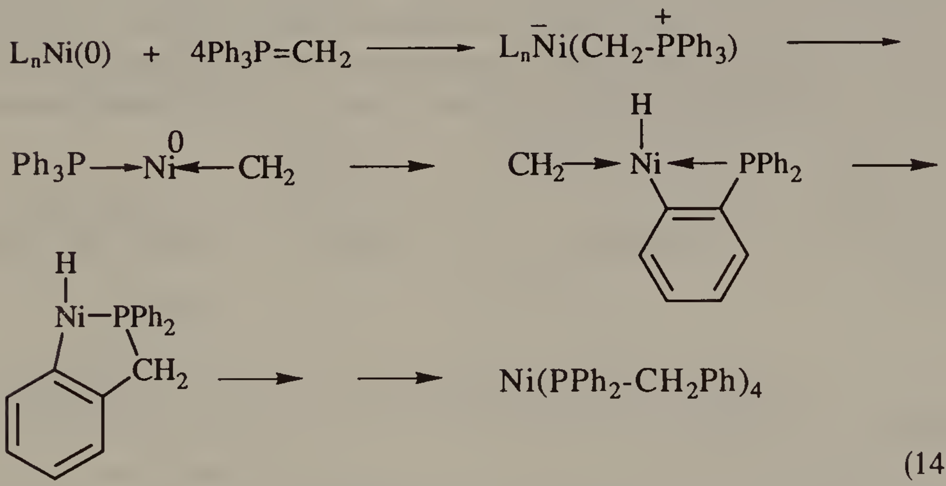
Nickel complexes of type **C** have been reported with one and two Cp–ylide ligands—$[Ni(Ph_3PC_5H_4)(PPh_3)_2]^{2+}\,2[PF_6]^-$ (**C10**) and $[Ni(Ph_3PC_5H_4)_2]^{2+}\,2[PF_6]^{2-}$ (**C11**).[152]

### 14.8.2 Homoleptic Compounds and Chelates

One of the first complexes of transition metals with ylides was reported in 1972 with the displacement of cyclooctadiene from $(COD)_2Ni$ by $Ph_3P{=}CH_2$, followed by a Stevens-type rearrangement (Eq. 14.145).[153] With $Me_3P{=}CH_2$ and $(COD)_2Ni$ the only isolable product was $Ni(PMe_3)_4$. It is possible that alkylidene transfer occurred, but no metal alkylidene was isolated as in the case of some of the early transition metals. This may be rationalized in terms of a zero-valent late transition metal where no empty *d* orbitals are available for formation of multiple bonds (Eq. 14.146).[154]



(14.145)

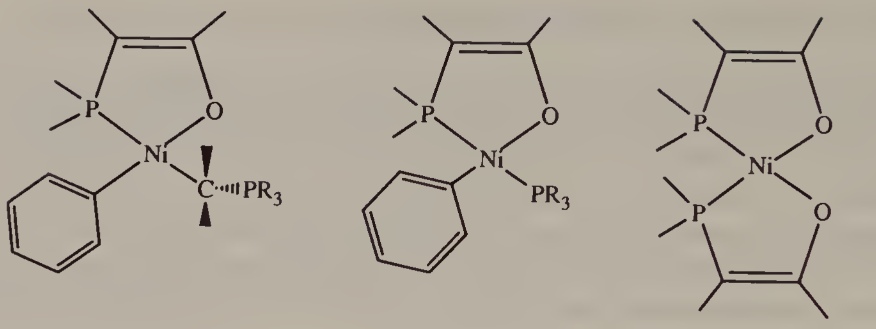


(14.146)

Treatment of bromo($\eta^5$-cyclopentadienyl)triphenylphosphine nickel with ylides gave cationic nickel complexes (Eq. 14.147).[155]

$$[NiBr(Cp)(PPh_3) \xrightarrow{\text{ylide}} \underset{\textbf{A88}}{[Ni(Cp)(PPh_3)(ylide)]^+\ Br^-} \qquad (14.147)$$

There is a growing relevance of ylide transition metal chemistry to polymerization catalysis, in particular using nickel complexes that have chelated ylide ligands. Three general structures which involve P-metallated ylide complexes are shown in Figure 14.2.[156, 157] The first two, which are formed through nickel

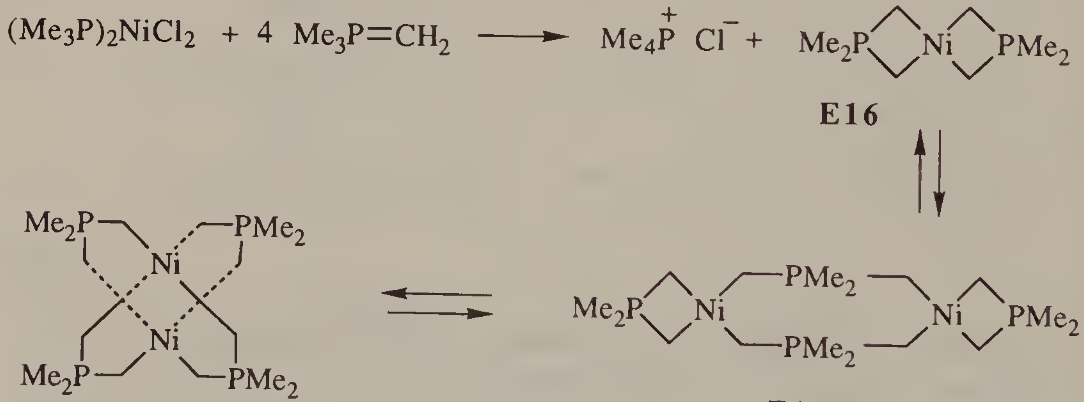


d(Ni-O)= 1.951 Å d(Ni-O)= 1.914 Å d(Ni-0)=1.885 Å

**Figure 14.2** Ylide–nickel chelates with nickel–oxygen bond lengths (refs. 156 and 157).

insertion into ylide (P-phenyl) bonds, are highly active oligomerization and polymerization catalysts. Derivatives of the third structural type are catalytically inactive. A comparison of the structural parameters for specific derivatives shows a dramatic increase of the Ni–O bond length from right to left.

A series of homoleptic complexes have been made using $Me_3P{=}CH_2$ and nickel halide complexes such as $(Me_3P)_2NiCl_2$ (Eq. 14.148). The structures of these materials are very similar to dimeric nickel complexes of diphenyltriazene.[158,159] When more bulky groups were on the phosphorus atoms, the product was **E18** (Eq. 14.149).[160] Analogous reactions with Pd and Pt occurred to give dimeric structures of type **E**.

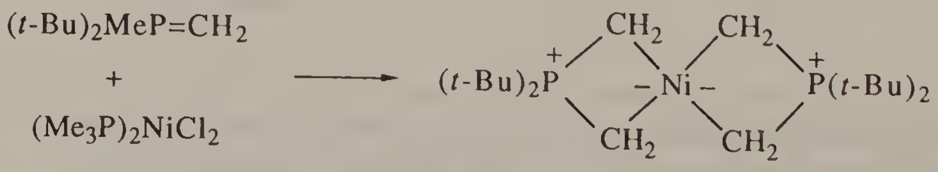


**E16**

**H5**

**E17H4**

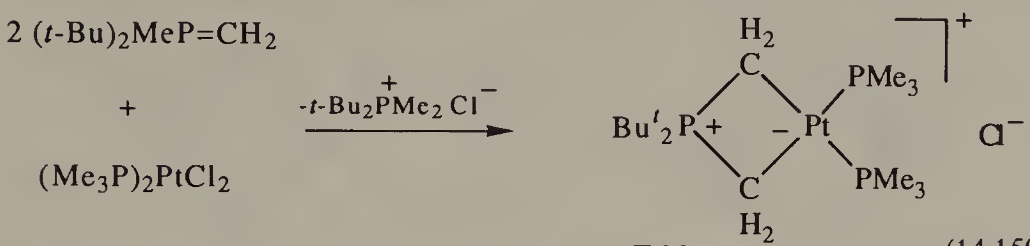
(14.148)



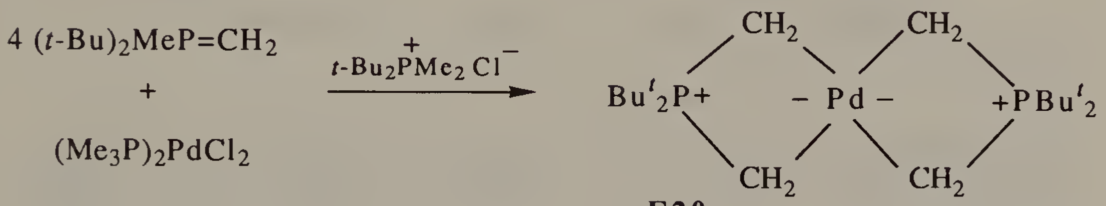
**E18**

(14.149)

Bis(trimethylphosphine)platinum dichloride and its palladium counterpart gave type **E** complexes (Eq. 14.150a and b).[161] When a lithiated bis-ylide was used a type **E** product also was obtained (Eq. 14.151).[161, 162]

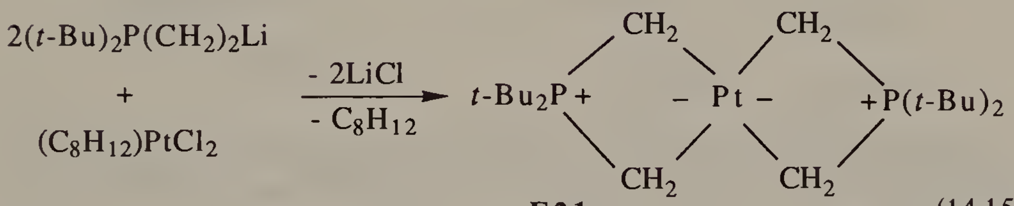


**E19** (14.150a)



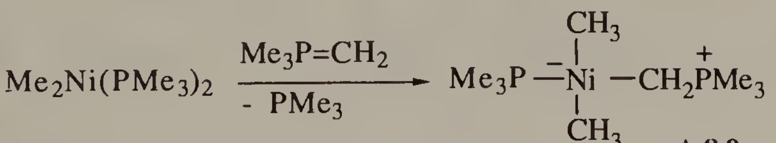
**E20**

(14.150b)



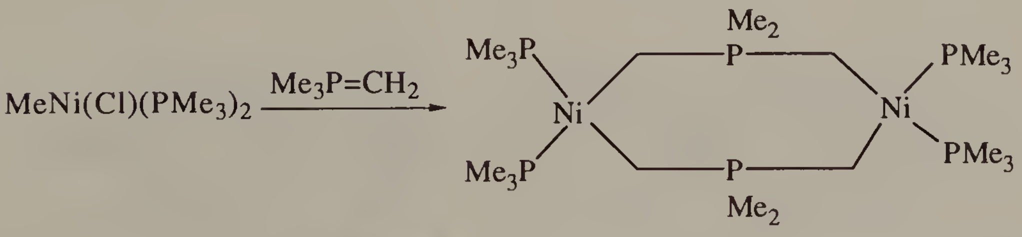
**E21** (14.151)

Alkyl compounds of the $d^8$ group often formed type **A** complexes before transylidation occurred, as shown in Eqs. 14.152 and 14.153.[163]



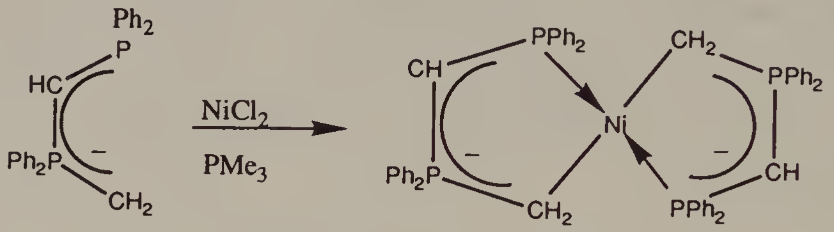
$$Me_2Ni(PMe_3)_2 \xrightarrow[-\ PMe_3]{Me_3P=CH_2} Me_3P-\overset{CH_3}{\underset{CH_3}{\overset{-}{Ni}}}-CH_2\overset{+}{P}Me_3 \qquad (14.152)$$

**A 89**



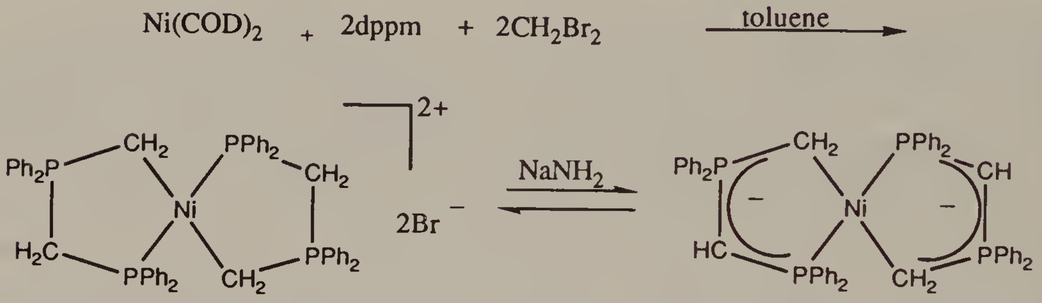
**H6** (14.153)

Ylides and metallated ylides can be made from bis-phosphines and these in turn can be used to make chelate ylide complexes as shown in Eq. 14.154.[164] A new synthesis of this chelated ylide reported by Kubiak et al.[165] formally involved a double oxidative addition of a methylene halide (Eq. 14.155).



(14.154)

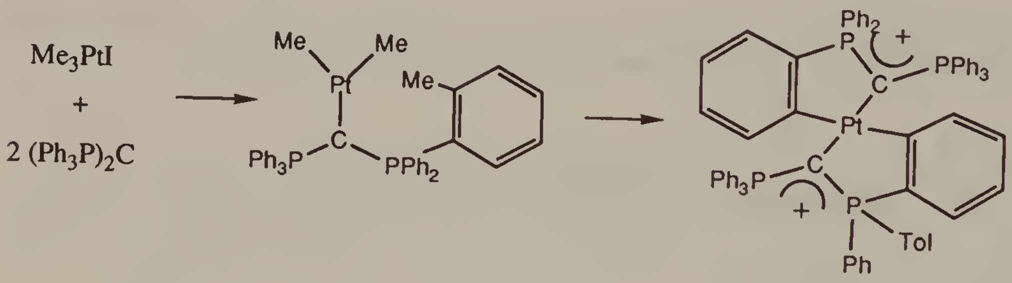
**A90F2**



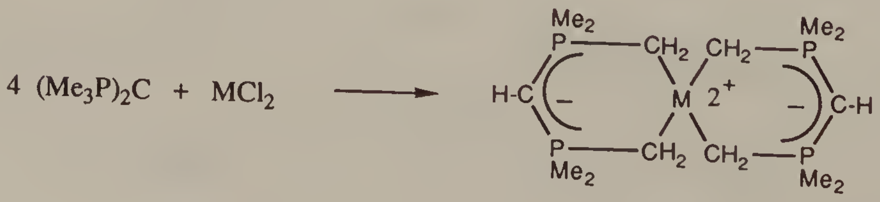
**A91X60** **A92F3**

+ NiBr$_2$(COD) + 3COD (14.155)

All of the alkyl groups in Me$_3$Pt–I could be removed with hexaphenylcarbodiphosphorane (Eq. 14.156)[166] but the hexamethylcarbodiphosphorane gave a chelate complex (Eq. 14.157).[167]

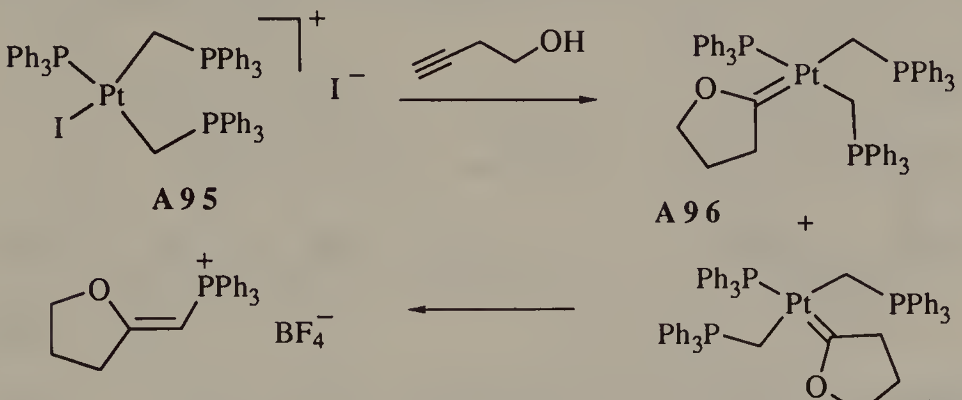


**A93X61** (14.156)



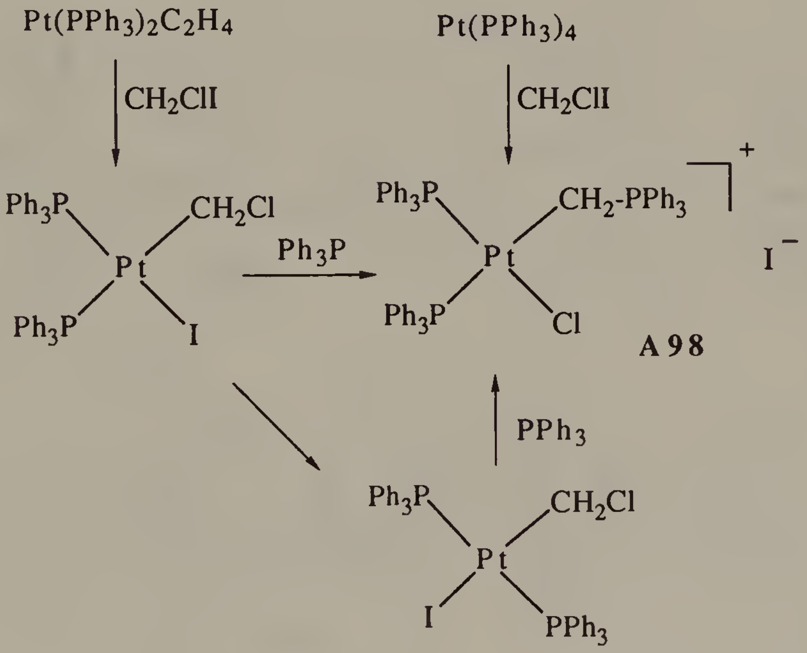
**A94** (14.157)

The reactivity of coordinated ylides has been studied by Stryker. An isolable 2-oxacyclopentylidene bis(phosphonium ylide) complex of platinum underwent a migratory insertion reaction (Eq. 14.158).[168]

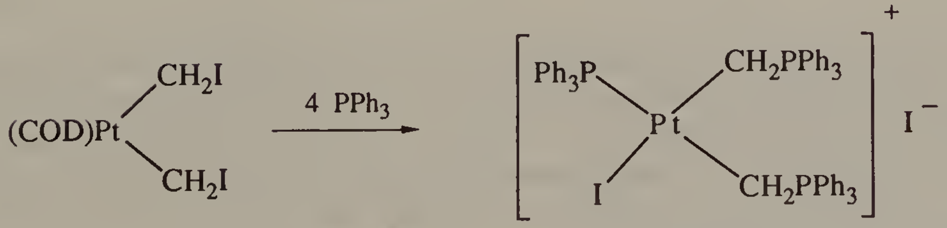


**A95** **A96** **A97** (14.158)

α-Halogenomethylplatinum(II) complexes interacted with tertiary phosphines to give cationic ylide–platinum complexes (Eq. 14.159).[169] The same synthetic principle was applicable for the preparation of platinum complexes which contained two ylide ligands (Eq. 14.160).[170]

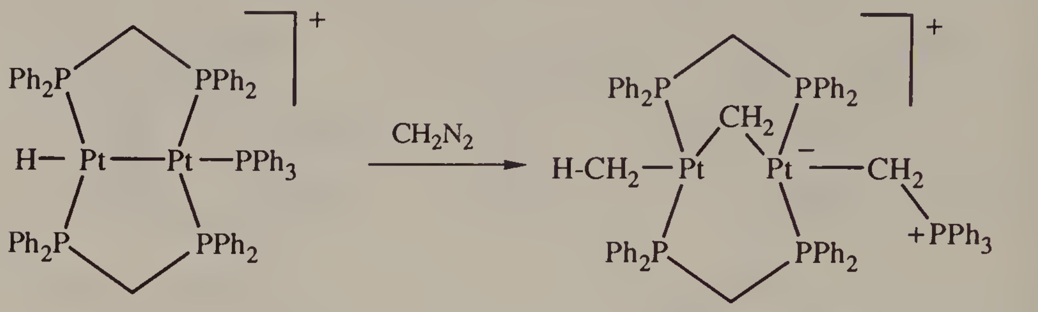


**A98** (14.159)



**A99** (14.160)

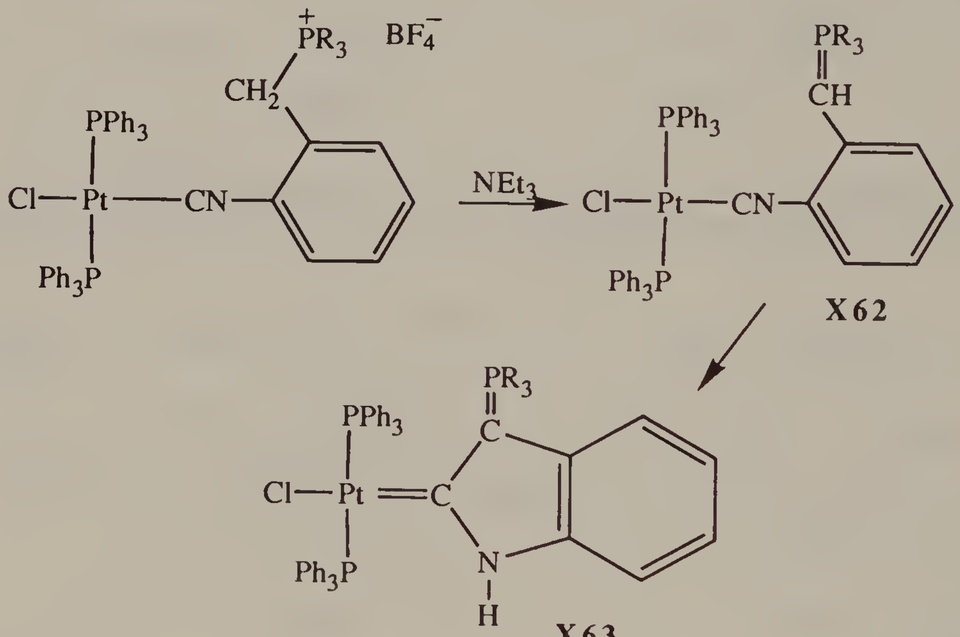
A triple methylene insertion has been discovered in the reaction of diazomethane with a dinuclear hydrido platinum complex. Methylene groups inserted into Pt–Pt, Pt–H, and Pt–P bonds (Eq. 14.161).[171]



**A100** (14.161)

Treatment of *cis*-$[(Ph_3PCH_2)(Ph_3P)PtCl_2$ (**A101**) with $AlCl_3$ in dichloromethane gave the 3-coordinate cationic complex $[(Ph_3PCH_2)(Ph_3P)PtCl]^+$ $[AlCl_4]^-$ (**A102**).[172] This reaction is useful for introducing various ligands (arsines, sulfides, etc.) in the coordination sphere of ylide platinum complexes.

Formation of an indole system occurred with an intramolecular cyclization of phosphonium-substituted platinum-coordinated isocyanide (Eq. 14.162).[173]



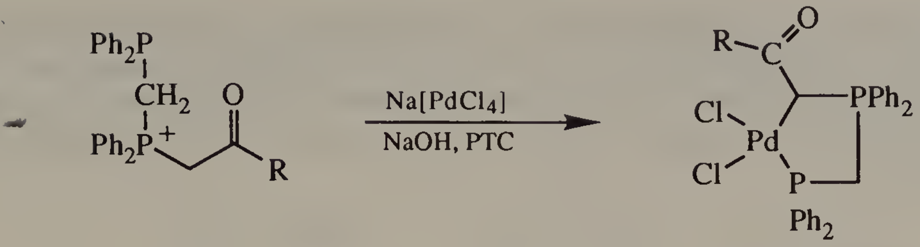
**X62**

**X63**

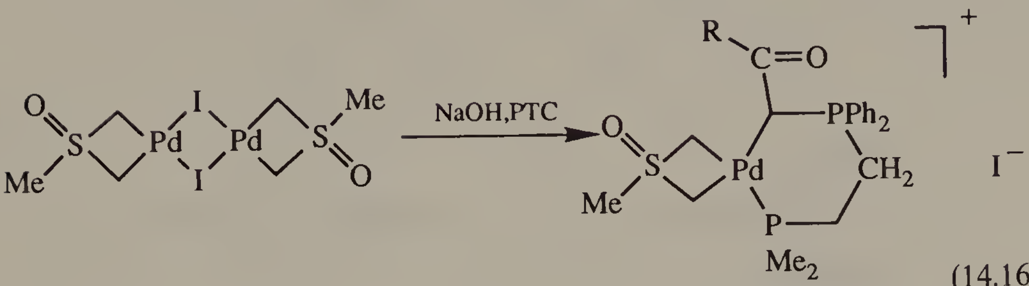
(14.162)

Phase transfer processes have been used with some success for the synthesis of some stable ylides of palladium (Eq. 14.163).[174] Platinum ylide complexes have been formed by substitution and 1,2-Wagner–Meerwein shifts (Eq. 14.164).[175]

The interaction of chlorobis(methylene)phosphoranes, which could be considered reverse bis-ylides, with platinum gave phosphaallene complexes as three-electron donors (Eq. 14.165).[176]

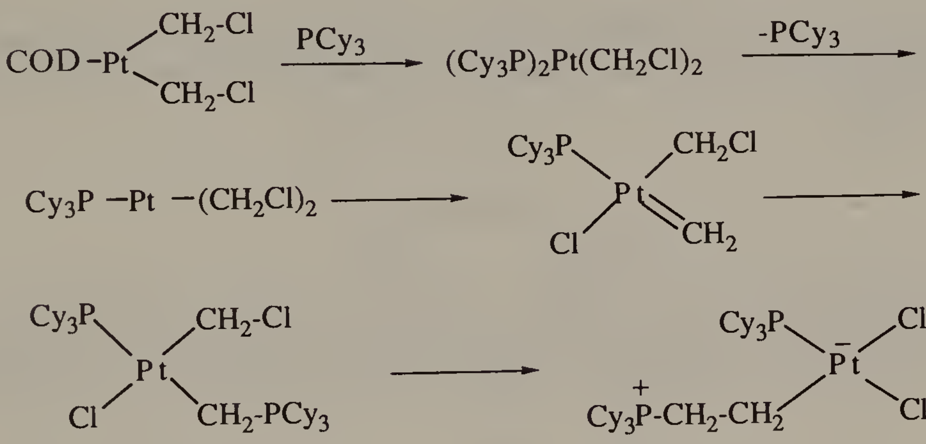


**A103X64**



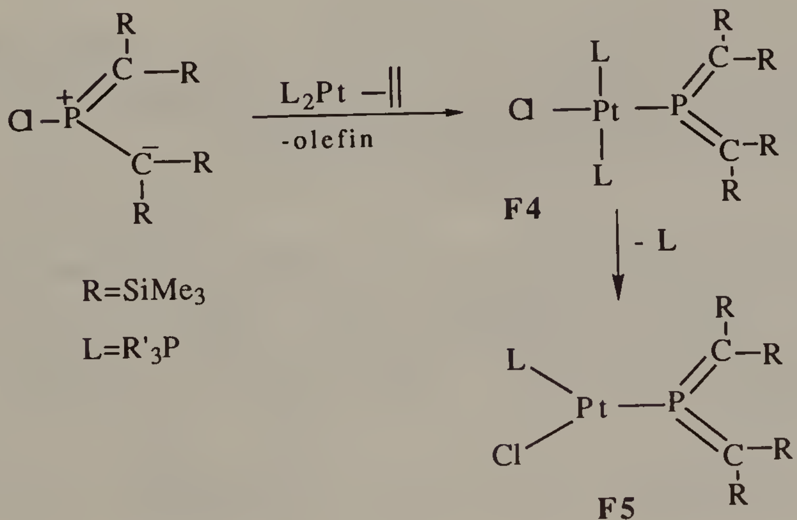
(14.163)

**A104X65**



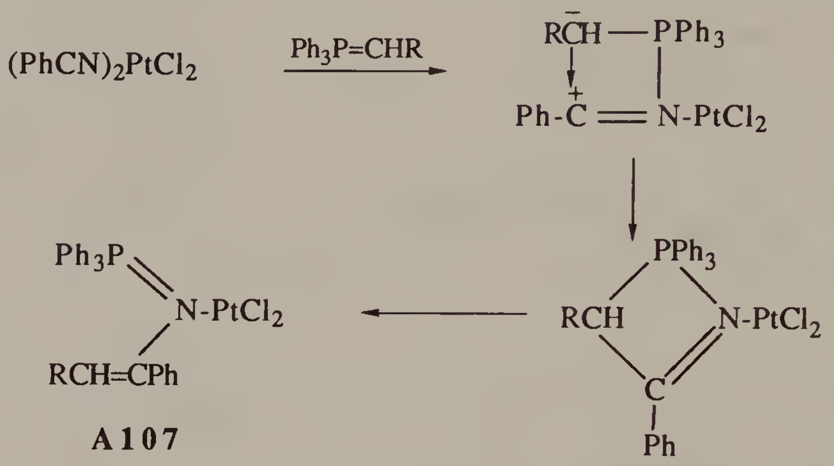
**A105**

(14.164)



(14.165)

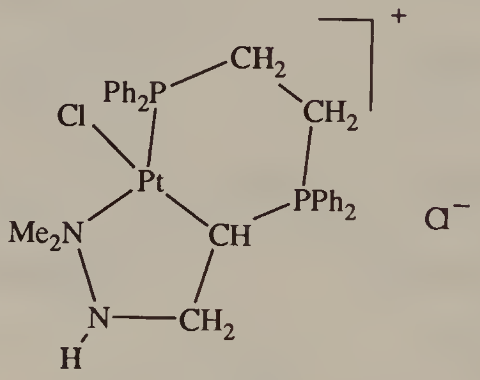
Normally the reaction of ylides with benzonitrile complexes of Pd and Pt resulted in displacement of the weakly coordinated benzonitrile [e.g., $(PhCN)_2PdCl_2$ + ylide → $Cl_2Pd\,(ylide)_2$] (**A106**). In other instances, however, ylides added to the nitrile bond to give an iminophosphorane complex (Eq. 14.166).[177]



**A107**

(14.166)

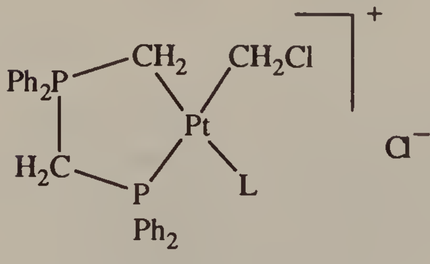
Treatment of *cis*-$[PtCl_2(PPh_2CH{=}CH_2)_2]$ with an excess of N, N-dimethylhydrazine in hot benzene gave a platinum complex with a tridentate ylide ligand (Eq. 14.167).[178]



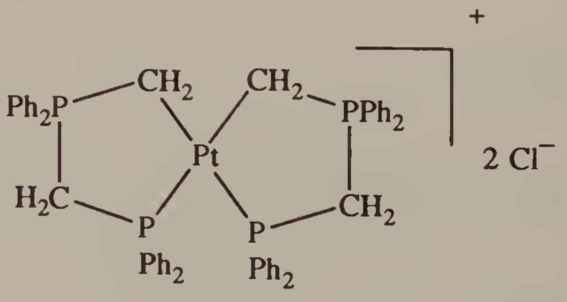
**A108X66**

(14.167)

Treatment of bis(halogenomethyl) platinum complexes with phosphines or pyridine gave ylide complexes. When bis(diphenylphosphino)methane was used, cyclic ylide compounds were formed (Eq. 14.168).[179]



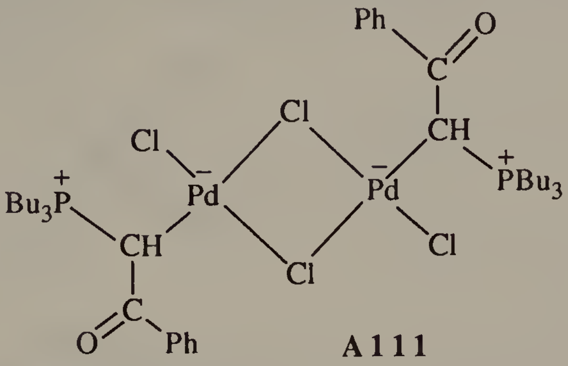
**A109X67**



**A110X68**

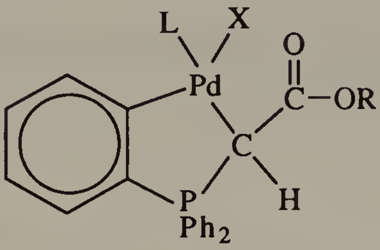
(14.168)

The dinuclear palladium complex **A111** is an example of a carbonyl-stabilized ylide which is **C**-coordinated (Eq. 14.169).[180] Other examples of **C**-bonding coupled with *o*-metallation of a phenyl ring are known for carbonyl-stabilized ylides (Eq. 14.170).[181]



**A111**

(14.169)



**A112X69**

(14.170)

It is noteworthy that *o*-coordination to palladium may occur. When acetylmethylenetriphenylphosphorane was treated in benzene with bis(triphenylphosphine)(pentachlorophenyl)(perchlorato)palladium, a cationic ylide complex formed in 99% yield (Eq. 14.171).[182]

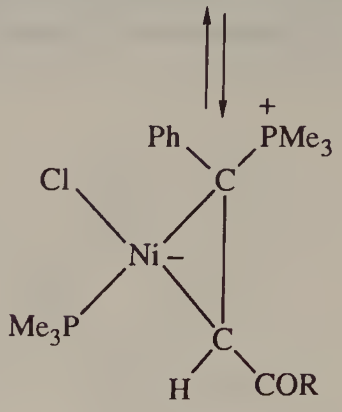
$$\begin{array}{c}[Pd(OClO_3)(C_6Cl_5)(L)_2] \\ + \\ Ph_3PCHCOMe\end{array} \longrightarrow \begin{array}{c}[Pd(C_6Cl_5)(L_2)(OCMeCHPPh_3)]^+ ClO_4^- \\ \textbf{X70}\end{array} \qquad (14.171)$$

Alkyne insertion into a nickel acyl complex gave a trans-(*Z*)-vinylketone derivative. Reversible trimethylphosphine migration produced a ylide–nickel complex which rearranged from *O*-coordination to $\eta^2$–carbon–carbon coordination (Eq. 14.172).[183]

Dicationic palladium or platinum ylide complexes in which the ylide was $\eta^5$-coordinated with diene ligands [e.g., $(Ph_3PC_5H_4)M(diene)^{+2}\ 2PF_6^-$] (**C12**) have been prepared by treating the corresponding acetone complexes $[M(Me_2CO)_2M(diene)]^{2+}2[PF_6^-]$ with cyclopentadienyltriphenylphosphorane.[184]

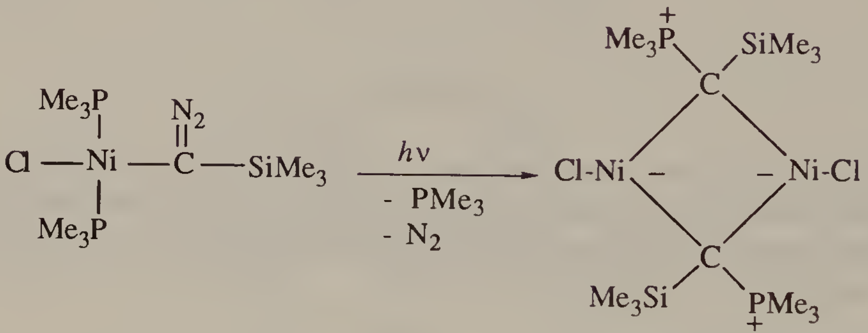
A new variant in ylide synthesis has been reported by Klein in which photoactivation of a diazosilylmethyl group gave an onium salt of type **G**

$$trans\text{-}[NiCl(COR)(PMe_3)] \xrightarrow{Ph\text{-}C\equiv C\text{-}H} trans\text{-}(Z)\text{-}[\overline{NiCl(CPh{=}CHCRO})(PMe_3)_2]$$

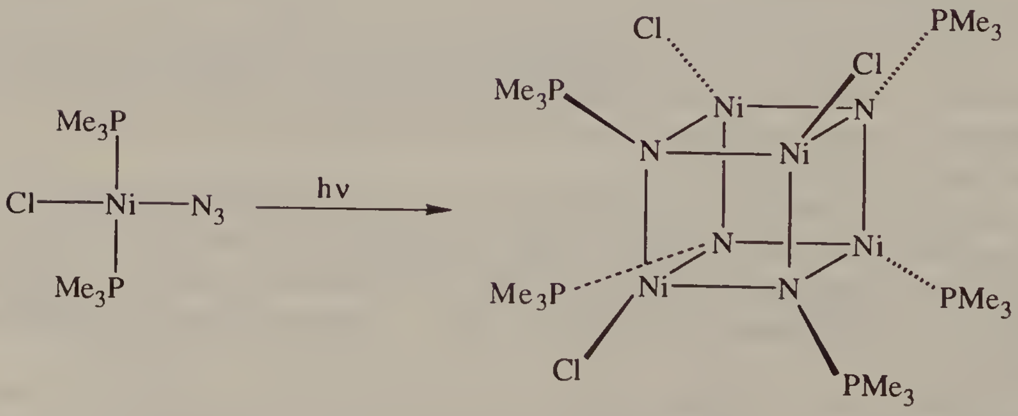


**A113X71** (14.172)

(Eq. 14.173).[185] In addition, this approach has been applied to the synthesis of nickel clusters (Eq. 14.174).[186]



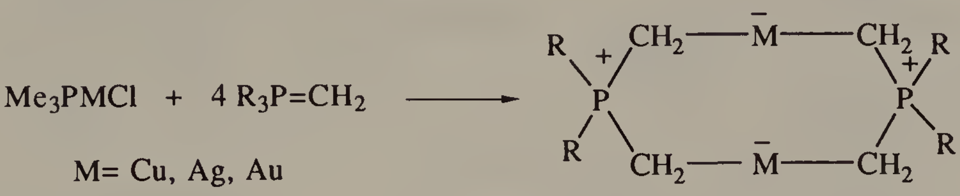
**G5** (14.173)



**K2** (14.174)

## 14.9 COMPLEXES OF COPPER, SILVER, AND GOLD

Copper, silver, and gold complexes with ylides are among the most stable ylide–metal complexes known. They generally fall into the bonding classification **H** shown in Figure 14.1. They have been prepared by transylidation-type reactions (Eq. 14.175).[187]

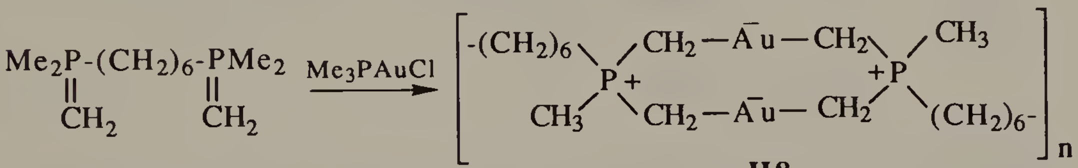


M= Cu, Ag, Au

R= Me, Et

**H7** (14.175)

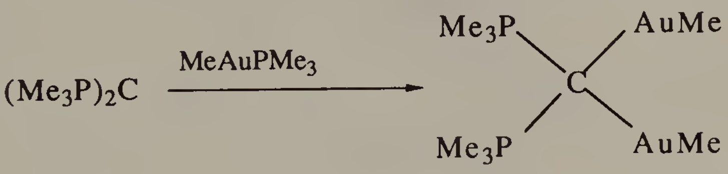
Spectroscopic data suggest that there is a transannular metal–metal interaction in these compounds, which in the case of the gold atoms makes them have a classical oxidation state of + 2.[188] Thus, oxidations occurred with electrophiles such as halogens and methyl iodide with the formation of metal–metal bonds. Gold–gold distances in such materials were 2.597 Å.[189] Polymeric materials also have been synthesized, as shown in Eq. 14.176.[190]



**H8**

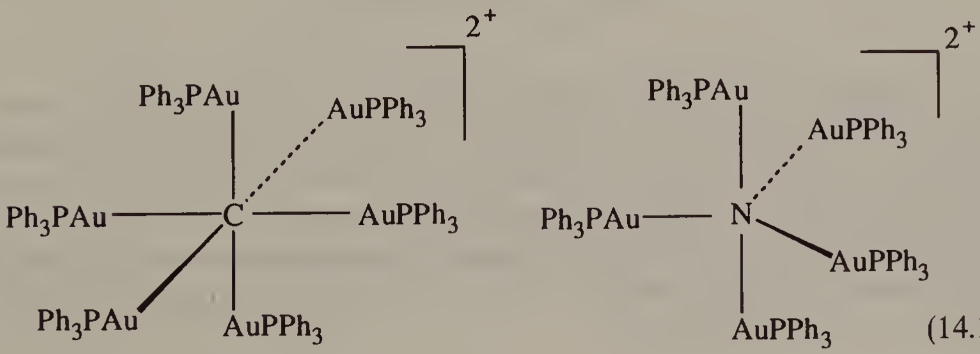
(14.176)

By considering the L–Au unit as an isolobal unit with hydrogen Schmidbaur has synthesized **A114**.[191] Extension of this approach has led to complexes with multiple gold atoms as ligands to carbon and nitrogen (Eq. 14.178).[192]



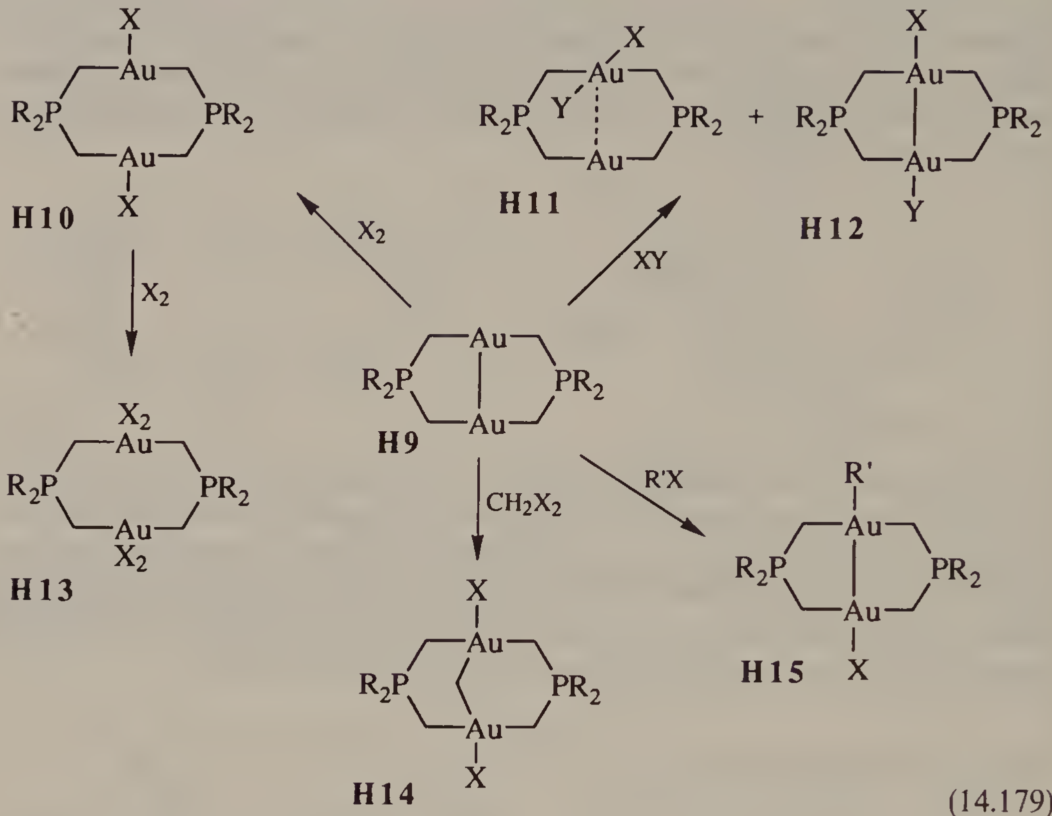
(14.177)

**A114**



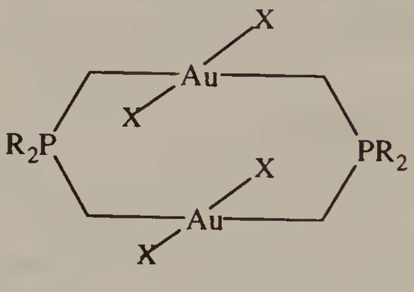
(14.178)

General reactions of the gold metallocycles are illustrated in Eq. 14.179.[193]



(14.179)

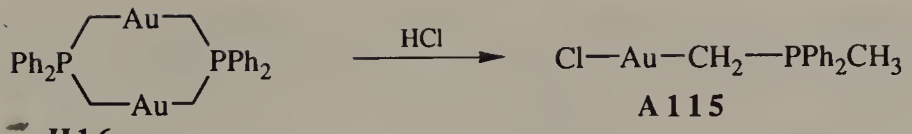
More detailed studies show that the complex $[Au(CH_2)_2PPh_2]_2$ underwent oxidation to give AuII and AuIII species (Eq. 14.180). Stereochemical isomers also could be isolated.[194]



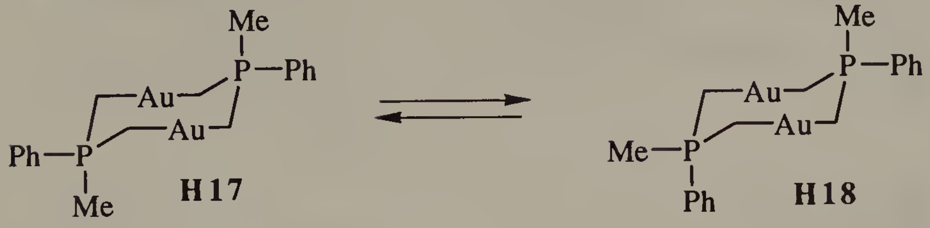
(14.180)

**H13** *trans/trans*

Four additional important reactions of ylide–gold complexes are shown in Eq. 14.181.[194] Treatment of **H**-type gold complexes with ylides led to halogen displacement and spiro-type ylide–gold complexes (Eq. 14.182).[195] Replacement of halogen atoms in gold–ylide complexes was very facile, as has been shown recently by Uson (Eq. 14.183).[196] A mixed-valence pentanuclear gold complex with a linear $Au_5^+$ chain and four bridging diphenylphosphoniumbismethylide ligands is known (Eq. 14.184).[197]



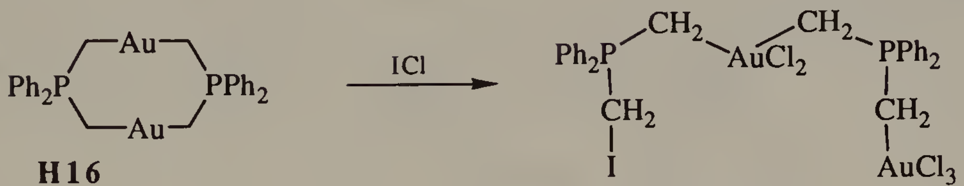
**H16** **A115**



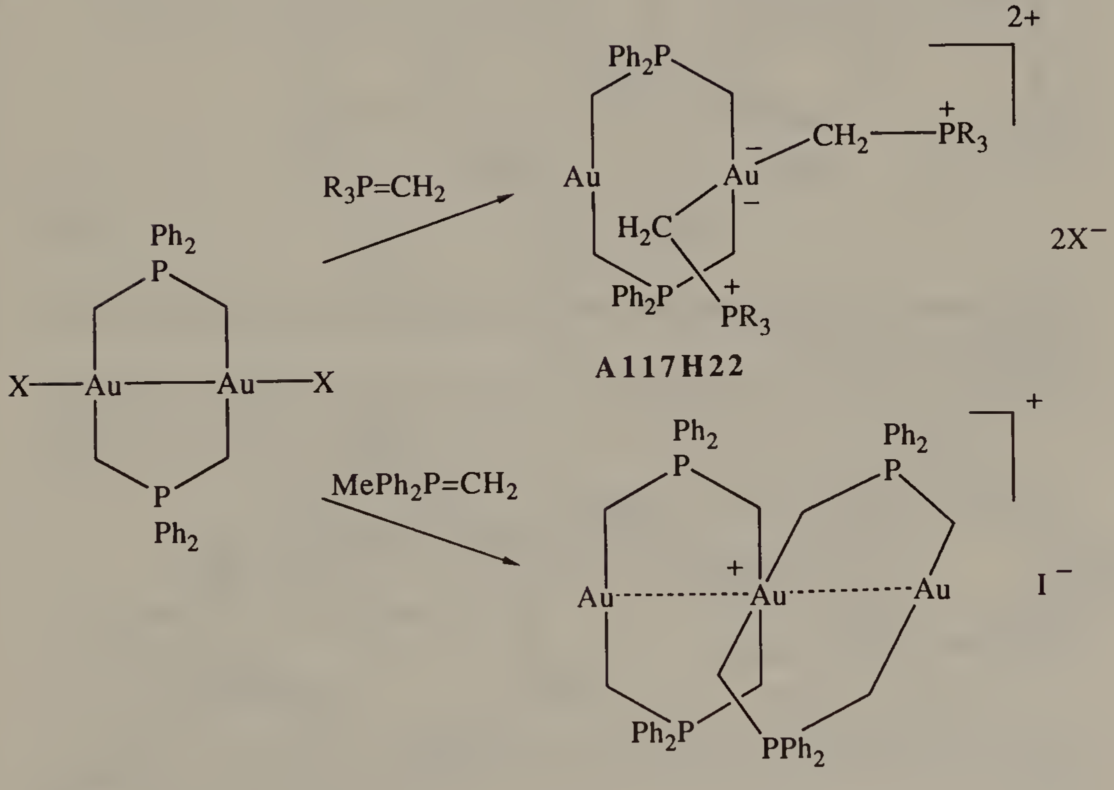
**H17** **H18**

(14.181)

**H19** **E21H20**



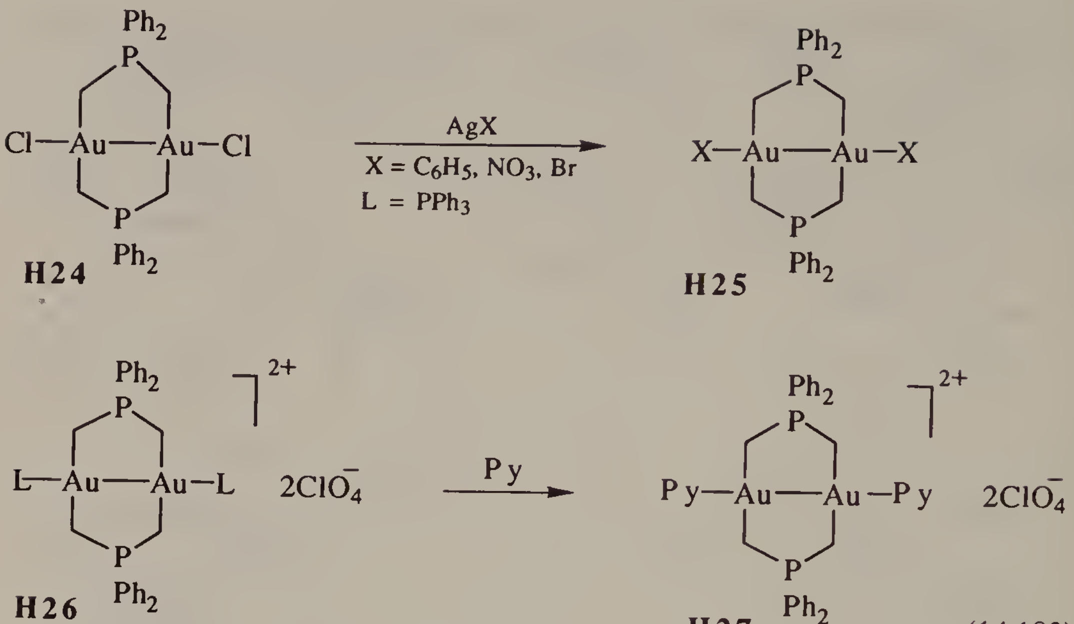
**H16** **A116H21**



**A117H22**

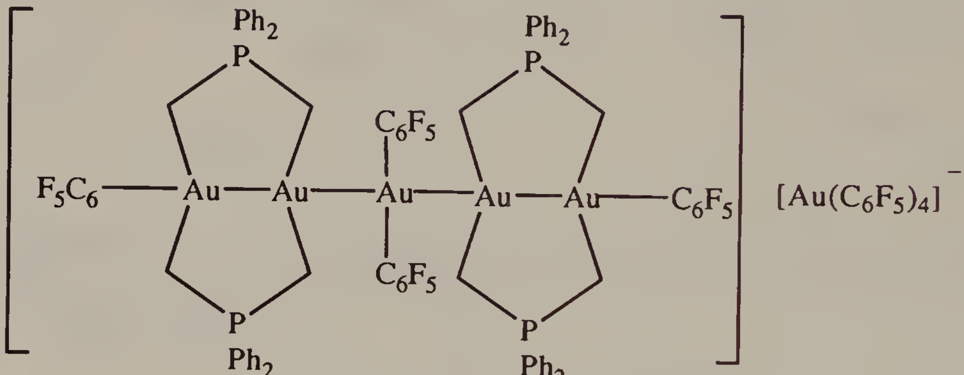
**H23**

(14.182)



**H24** **H25** **H26** **H27**

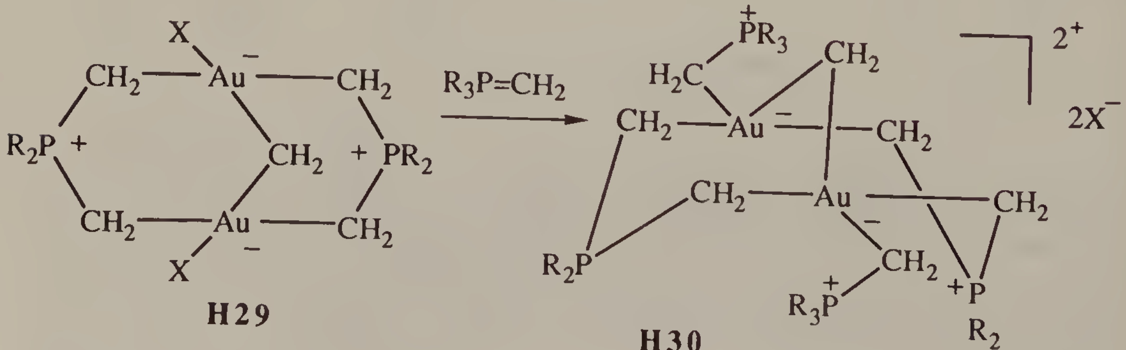
(14.183)



**H28**

(14.184)

Replacement of multiple halogen atoms with additional ylide ligands also was possible (Eq. 14.185).[198]

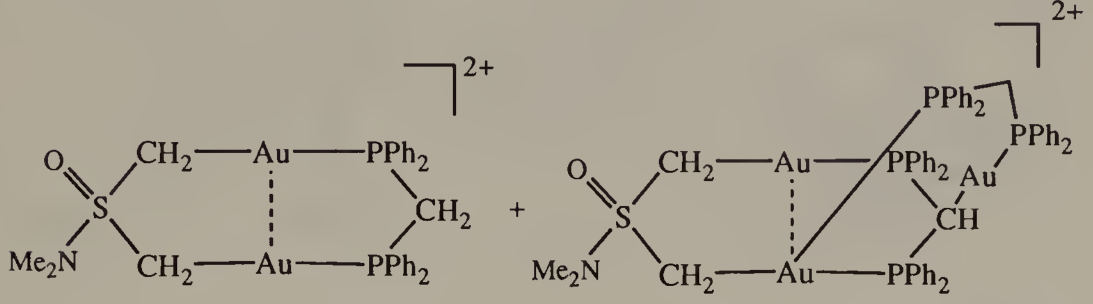


**H29** **H30**

(14.185)

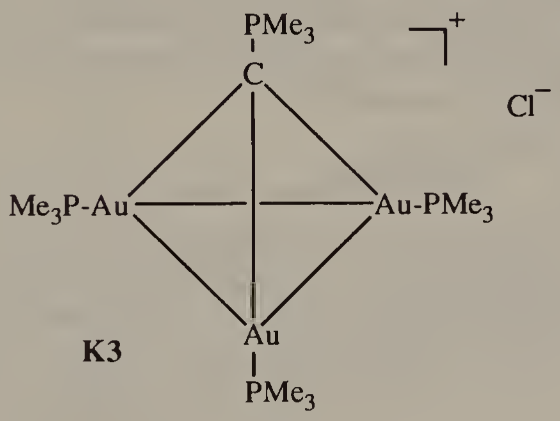
There are a few sulfur ylide complexes of gold with juxtaposed metal atoms. A recent phase transfer synthesis has been used to prepare luminescent gold compounds (Eq. 14.186). The internuclear separation between the gold atoms was 2.965 Å.[199]

$$Au_2(dppm)Cl_2 + [Me_2S(O)NMe_2]^+ BF_4^- \xrightarrow{PTC/OH^-}$$



(14.186)

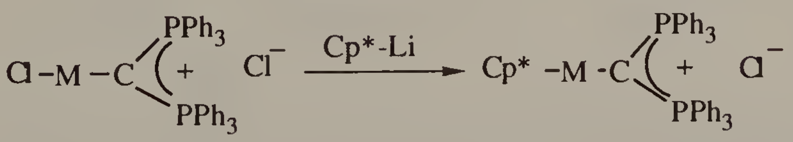
A gold cluster complex that is illustrative of ylide bonding mode **K** has been synthesized by Schmidbaur et al. (Eq. 14.187).[200] Here again the isolobal relationship with hydrogen is evident. The chemical properties of such clusters can be explained by relativistic effects of the gold atoms.



**K3**

(14.187)

Bis-ylides formed copper and silver complexes (Eq. 14.188) in which the metal–halogen bond could easily be substituted by nucleophilic reagents.[201]

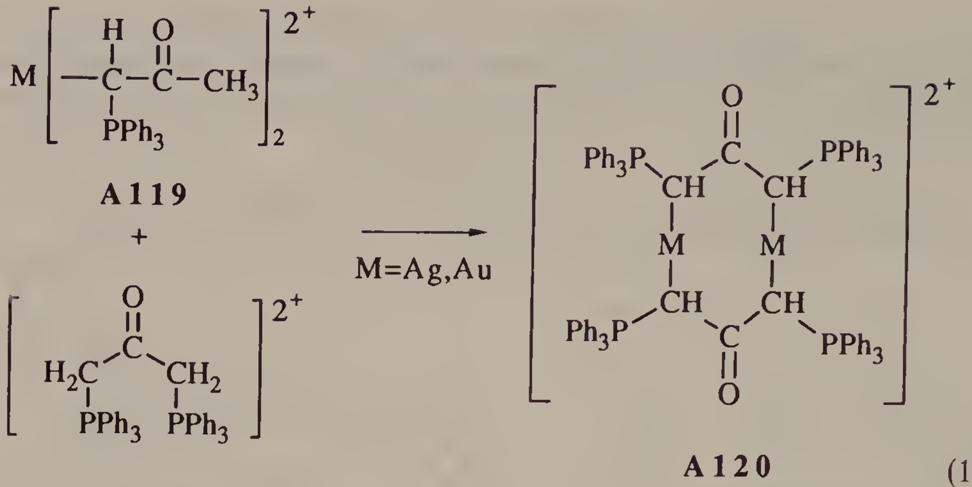


(14.188)

M= Cu, Ag

**A118**

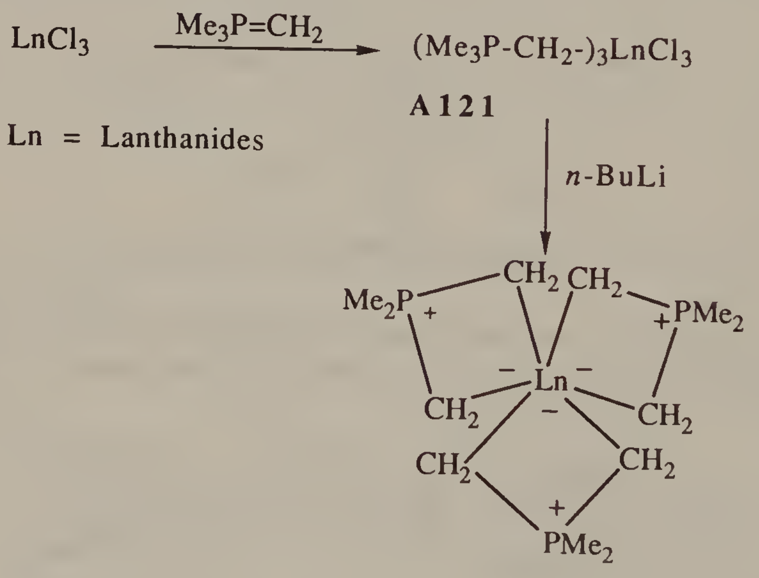
Some unusual silver and gold ylide complexes have been recently prepared by Vicente et al. (Eq. 14.189).[202]



**A119** + → M=Ag,Au **A120** (14.189)

## 14.10 COMPLEXES WITH THE LANTHANIDE AND ACTINIDE ELEMENTS

The anhydrous lanthanide elements interact with ylides in much the same way as the other transition element halides and give complexes of type **E** (Eq. 14.190).[203] With dicyclopentadienyl(*t*-butyl)lutetium and dicyclopentadienylchlorolutetium there was only adduct formation (Eq. 14.191). No transylidation reactions were observed.[204]



$$LnCl_3 \xrightarrow{Me_3P{=}CH_2} (Me_3P\text{-}CH_2\text{-})_3LnCl_3$$

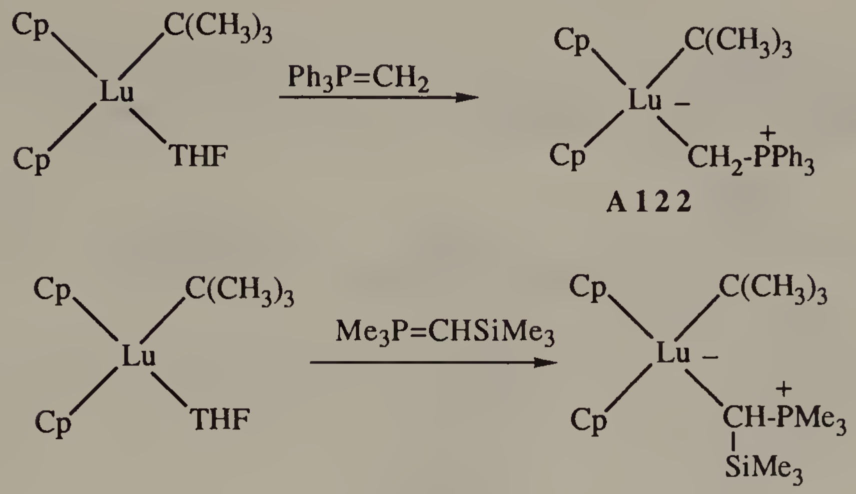
**A121**

Ln = Lanthanides

*n*-BuLi

**E22** (14.190)

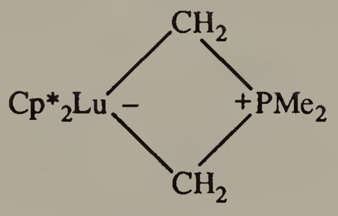
Mononuclear pentamethylcyclopentadienyllutetium complexes with one and two dimethylphosphonium bis-methylide chelating ligands are known (Eq. 14.192).[205]



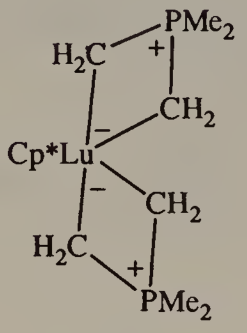
**A 1 2 2**

**A 1 2 3**

(14.191)



**E23**



**E24**

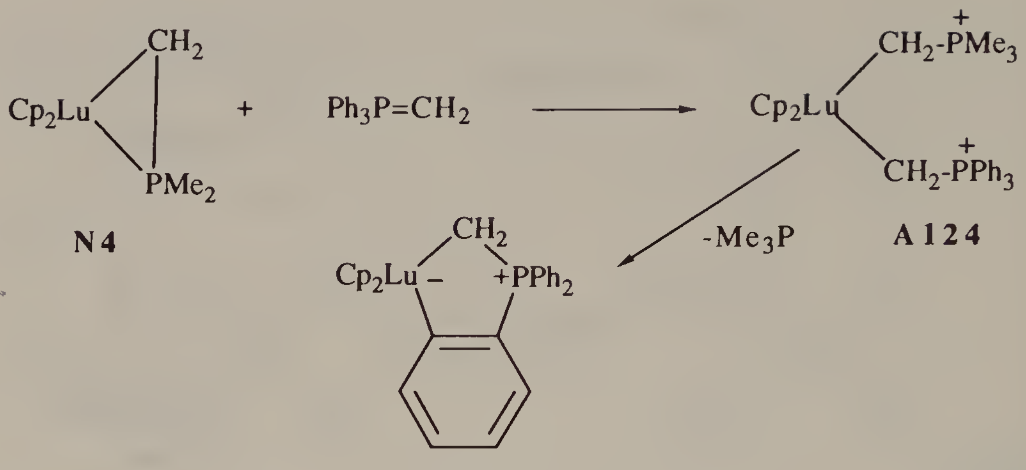
(14.192)

Pentamethylcyclopentadienyl neodymium and samarium complexes with dimethylphosphoniumbismethylide showed a rapid exchange of methylene and methyl protons at $-40°C$ in the $^1H$ NMR spectra. The fluxional behavior was discussed in terms of methyl–carbon bond breaking, rotation, and recombination processes of the ylide ligand (Eq. 14.193).[206]

$$[Na(Et_2O)_2][Cp_2^*MCl_2] + Li[(H_2C)_2PMe_2] \xrightarrow[M=Sm,\ Nd]{THF} [Cp^*_2M(H_2C)_2PMe_2]$$

**E23** (14.193)

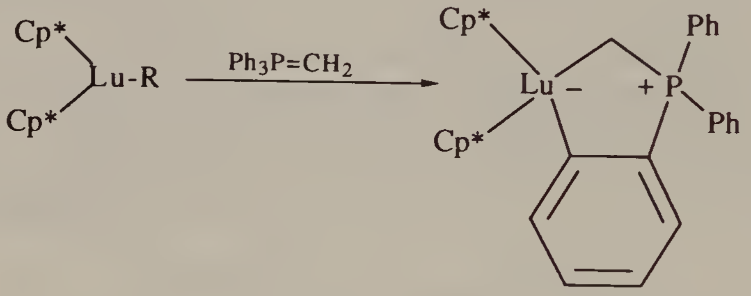
Dicyclopentadienyllutetium chloride reacted with dimethylphosphinomethyllithium in THF at $-30°C$ to form a metalloheterocyclic three-membered ring. The ylide complex ring structure (**N4**) was opened with methylenetriphenylphosphorane to give an A-type complex, which in turn lost trimethylphosphine through *o*-metallation and formed a new five-membered heterocyclic ylide complex (Eq. 14.194).[207]



**A125X72**

(14.194)

A similar C–H activation of methylenetriphenylphosphorane and other substrates was reported for pentamethylcyclopentadienyllutetium complexes (Eq. 14.195).[208]



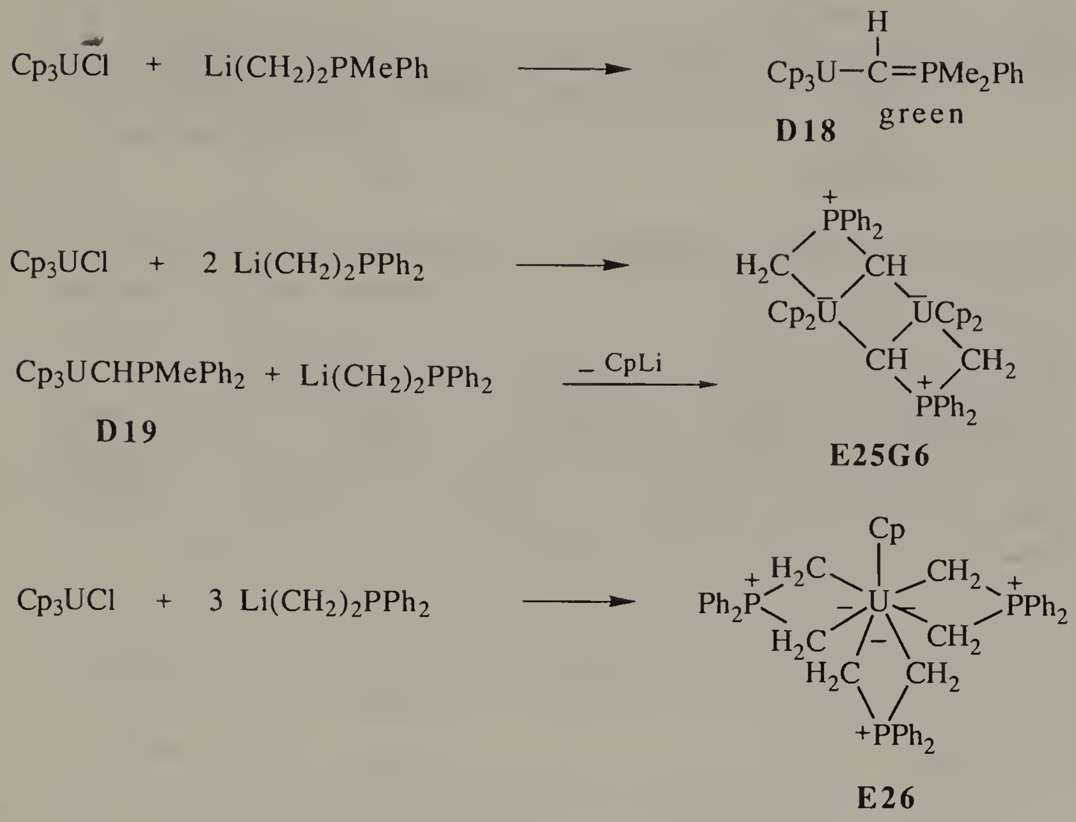
(14.195)

**A126X73**

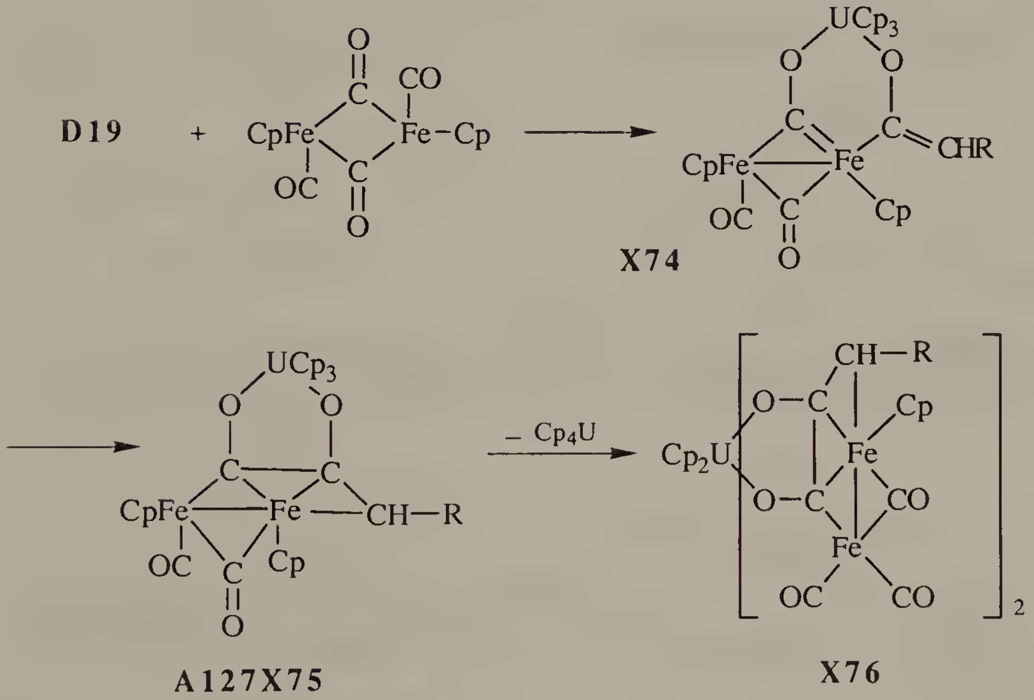
The actinide elements have been investigated mostly with uranium but similar observations would presumably occur with thorium. When uranium cyclopentadienyl complexes were treated with ylides, complexes with extremely short uranium–carbon bonds (2.29 Å) were formed. The compound $Cp_3U{-}CH{=}PMe_3$ had a $J^{13}C{-}^1H$ coupling constant of 95 Hz and yet the neutron diffraction study showed that there was no evidence of an agostic interaction with the uranium atom. In solution the complex may have an agostic hydrogen interaction, but this could not be determined.[209] Treatment of $Cp_3UCl$ with $Li(CH_2)_2PR_2$ gave a series of complexes shown in Eq. 14.196.[210]

An oxo-centered trimetal cluster of two uranium atoms and one magnesium atom has been characterized. It contained two bridging (**H** type) and two terminal (**A** type) ylide ligands.[211]

Lanthanide and actinide ylides readily interacted with the terminal carbonyl group of metal carbonyl compounds in contrast to most other metal–carbon double bonded compounds. This is illustrated in Eq. 14.197 for $CpFe(CO)(\mu\text{-}CO)_2(CO)FeCp$[212] and Eq. 14.198 for $CpMn(CO)_3$.[213] The addition products were similar to the silyl complexes $(CO)_5Cr{=}C(OSiMe_3)CH{=}PMe_3$ discussed


Cp3UCl + Li(CH2)2PMePh
Cp3U—C(H)=PMe2Ph
green
D18
Cp3UCl + 2 Li(CH2)2PPh2
Cp3UCHPMePh2 + Li(CH2)2PPh2
D19
– CpLi
E25G6
Cp3UCl + 3 Li(CH2)2PPh2
E26

(14.196)

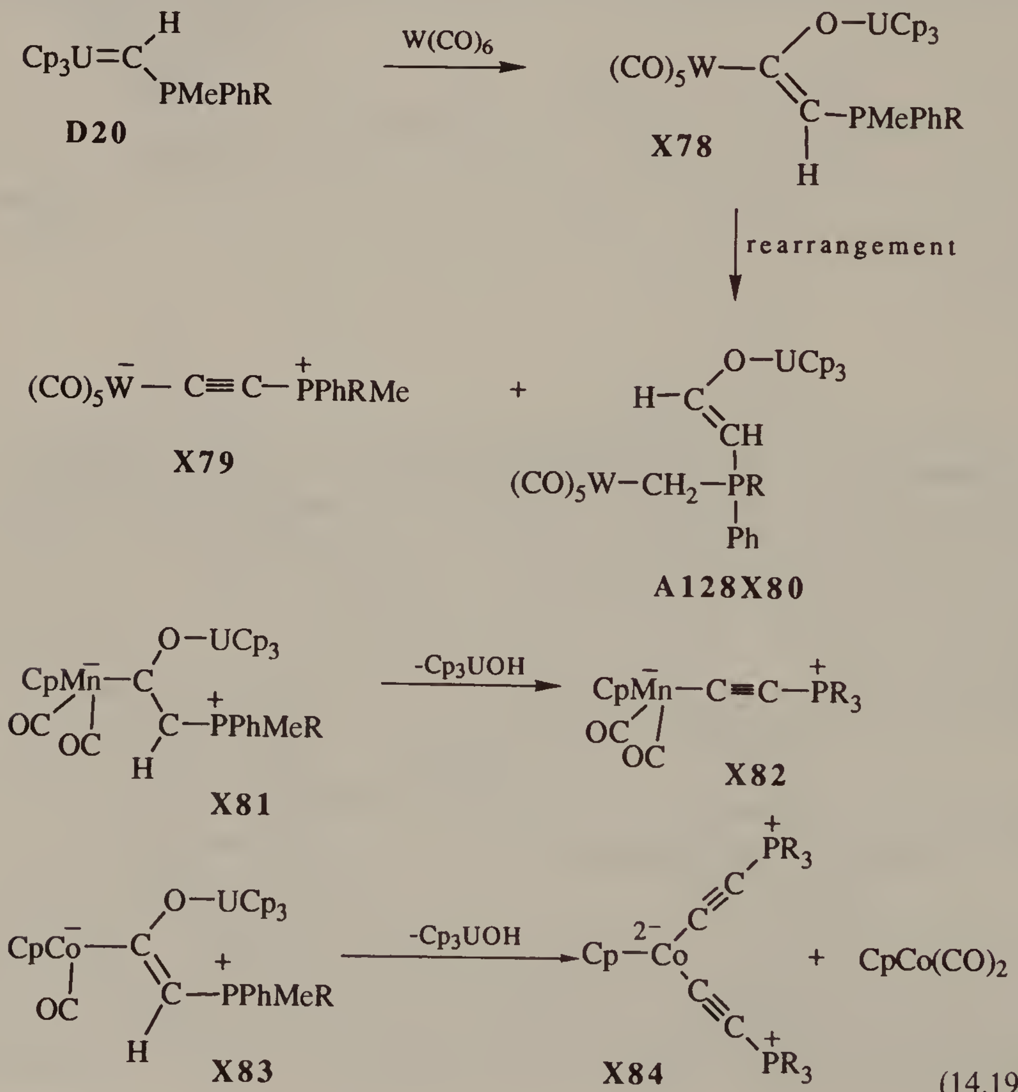

D19
X74
– Cp4U
A127X75
X76

(14.197)

(14.198)

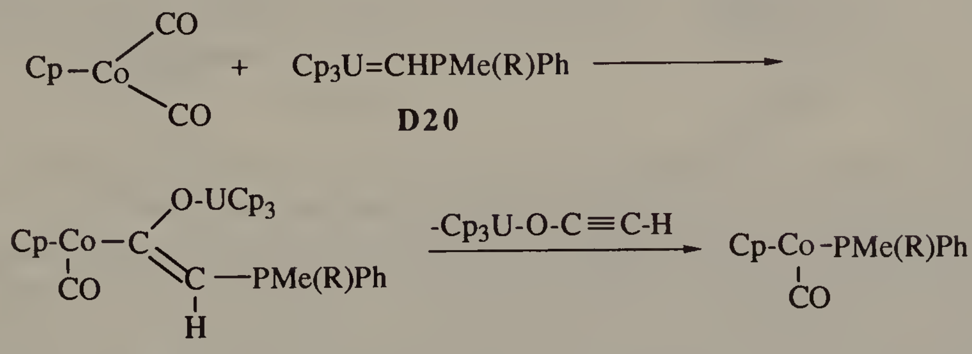
earlier.[214] The reaction described in Eq. 14.197 is complex, but the facile removal of the $Cp_4U$ group and its oxophilic character are clearly evident.

A most interesting series of reactions of the uranium ylide occurred with tungsten hexacarbonyl,[215] which concluded with the formation of a new carbon–carbon bond and a Stevens-type rearrangement. This is similar to previously discussed Wittig reactions of metal carbonyls with ylides and bis-ylides. The manganese-type reaction is remarkable because the oxophilicity of uranium(IV) results in the loss of $Cp_3UOH$ and the formation of new carbon–carbon bonds from metal carbonyl complexes (Eq. 14.199).[216]



(14.199)

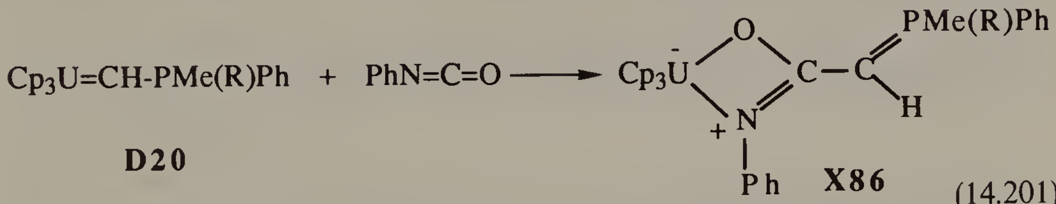
The interaction of $CpCo(CO)_2$, however, was different than the other metal carbonyls in that a uranium oxyacetylide was eliminated and no metal acetylide was formed. The reaction sequence is apparently more complicated and involves a number of steps which have not been delineated (Eq. 14.200).[217]



**X85**

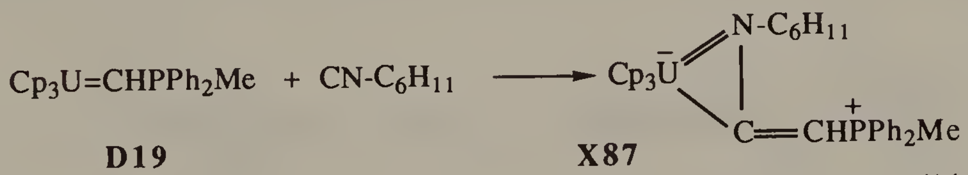
(14.200)

Addition to carbon dioxide-type molecules also occurred, such as the insertion of isocyanate into the uranium–carbon bond (Eq. 14.201).[218]



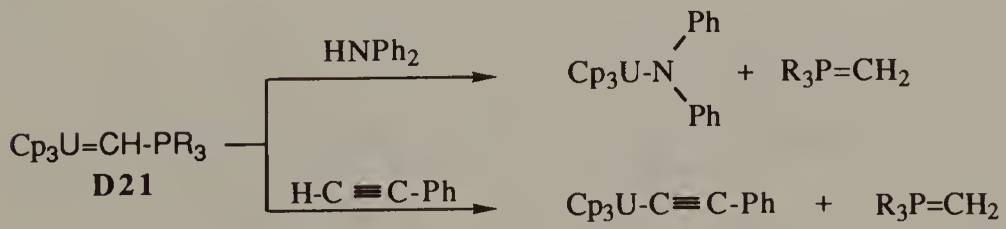
(14.201)

Uranium ylides will readily insert into carbon–nitrogen bonds to give a uranaazacyclopropene (Eq. 14.202).[219]



(14.202)

Metathesis-type reactions can occur with $Cp_3U{=}CHPR_3$ and acidic bonds (Eq. 14.203), although no reactions were observed with alkenes.[220]



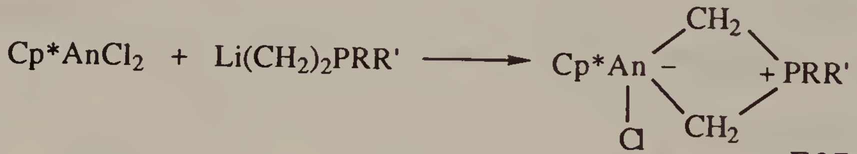
(14.203)

Treatment with carbon monoxide resulted in insertion into the carbon–metal bond (Eq. 14.204).[221]

**D21** **X88** (14.204)

The insertion of acetonitrile into the uranium–carbon bond resulted in an amido uranium ylide complex, $Cp_3UNC(Me)CHP(Ph)_2Me$ (**X89**).[222]

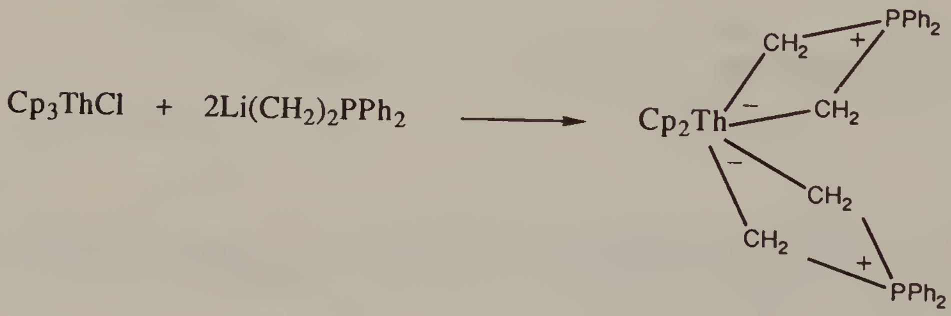
There is an interesting difference between lanthanide and actinide metals carrying the Cp ligand and the Cp* ligand. For instance, Cp* complexes of uranium and thorium reacted with dimethyl or diphenylphosphonium ylides (Eq. 14.205) but the second chlorine atom was not replaced.[223] This contrasts with $CP_3ThCl$ where replacement of one Cp ligand occurred and the ylide formed type **E** complexes (Eq. 14.206).[224] The ylide ligand, $^-CH{=}PR_3$, can be a monodentate ligand with compounds of the type $Cp_2(X)M$, M = Zr (Eq. 14.207), whereas actinide $Cp_2{*}(X)An$ complexes formed heterocyclic com-



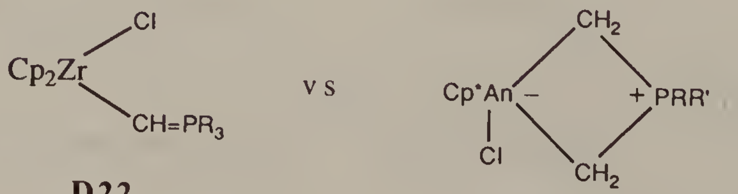
**E27**

R,R' = Me,Ph

An = U,Th (14.205)

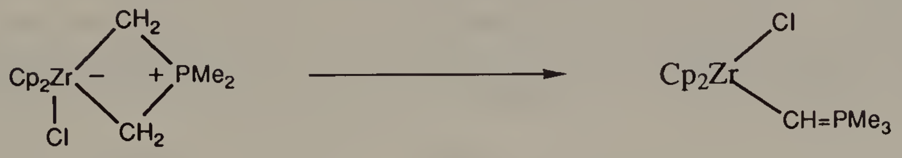


(14.206)



**D22** **E29** (14.207)

pounds of type E. Thus the lanthanide complex survived heating to 100°C, whereas the zirconium complex easily rearranged (Eq. 14.208).[224]

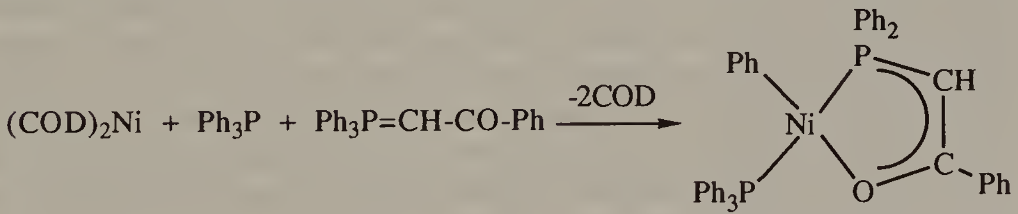


**E6** **D8** (14.208)

## 14.11 THE FUTURE OF YLIDE TRANSITION METAL CHEMISTRY

This chapter has illustrated the breadth and scope that ylide-transition metal chemistry has taken since its discovery 30 years ago. Besides the synthesis of novel structural bonding types and new interpretative modes of reaction, transition metals and ylides have introduced some novel reactions. Nowhere is this more evident than in their use as catalysts. Attempts to use rhodium ylide complexes in hydrogenation and esterification catalysis have been reported.[225] The triphenylphosphoniumcyclopentadienide complex $[Rh(\eta^5\text{-}C_5H_4PPh_3)(CO)_2]PF_6$ (**C13**) catalyzed the cyclotrimerization of 3-hexyne and dimethyl acetylenedicarboxylate, although the reaction rates were somewhat lower than with $[Cp\text{-}Rh(CO)_2]_2$.

The most progress has been in the area of polymerization catalysis. Early reports centered around the treatment of benzoylmethylenetriphenylphosphorane with bis(cyclooctadiene)nickel(0) in the presence of triphenylphosphine to form a square planar nickel phenyl complex which bears a diphenylphosphinoenolate chelate ligand (Eq. 14.209). This complex was highly active

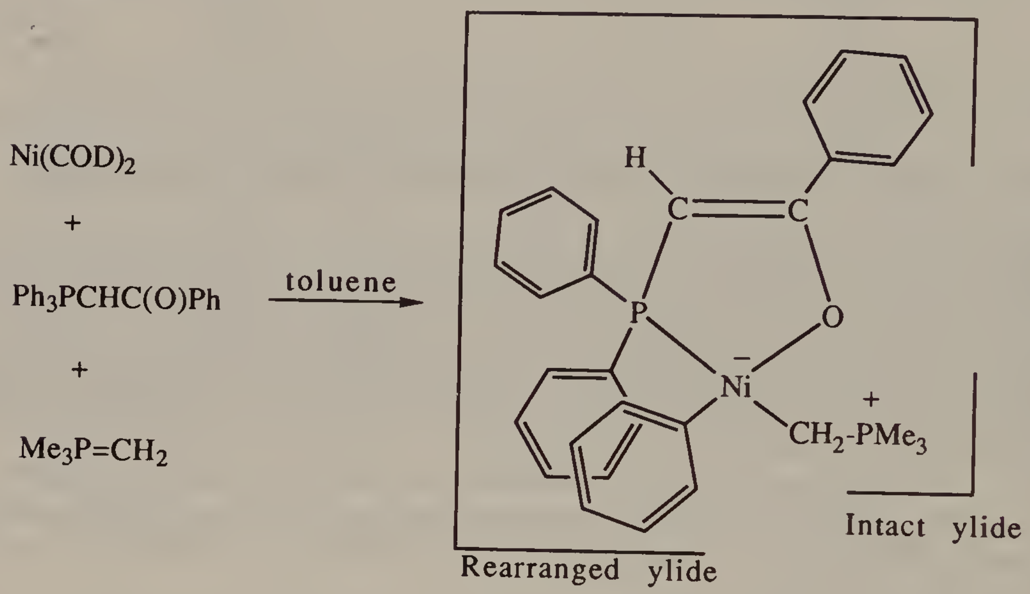


**F6X90** (14.209)

without any cocatalyst for the linear oligomerization of ethylene.[226] At 50 bar and 50°C, for example, a turnover of 6000 mol ethylene/mol Ni has been achieved. The reaction was highly selective and proceeded to form 99% linear $C_4$–$C_{30}$ olefins with up to 98% terminal double bonds. The catalyst is a model system for the "Shell Higher Olefin Process" (SHOP). The analogous arsenic ylide $Ph_3AsCHCOPh$ formed a catalyst (**F7X91**) with lower activity and selectivity.[227] The homogeneous P-ylide catalyst can be supported on inorganic or polymeric supports.[228]

An unusual 2,$\omega$ linkage of $\alpha$-olefins took place using bis(trimethylsilyl) amino-bis(trimethylsilylimino)phosphorane with nickel(0) compounds. The in situ catalyst had an activity of $10^3$ mol $C_2H_4$/mol of Ni.[229]

Catalysts with considerably higher activity were formed when two ylide ligands were employed. These catalysts had both a rearranged ylide and a structurally intact ylide in the coordination sphere (Eq. 14.210).[230] By variation of the intact ylide portion of the catalyst, activities which exceeded $0.5 \times 10^5$ mol $C_2H_4$/mol Ni could be observed. The activities were correlated with $^{31}P$ NMR chemical shifts and photoelectron spectroscopic results. The bis-ylide nickel catalysts not only produced highly linear low molecular weight olefins, but the specific choice of ylide allowed selective control for a variety of molecular weight ranges between $10^3$ and $n \times 10^6$ g/mol. Thus, in a unique chemical way catalytic access has been provided to soft and hard waxes, high density polyethylene (HDPE), and ultrahigh molecular weight polyethylene (UHMW-PE). The average molecular weight increased with the ylide sequence for compounds **1**–**7** shown in Figure 14.3.[231]



**A129F8X92**

(14.210)

To further activate ylide nickel catalysts, aluminum alkoxides/alkyls have been used as cocatalysts, such as in ethylene/$\alpha$-olefin copolymerizations for the synthesis of linear low density polyethylenes with short chain branches (LLDPE).[232] Alkyl aluminum halides have been used effectively to activate the catalyst system for the polymerization of dienes like butadiene.[233]

Branched polyethylenes are accessible with bis(ylide) nickel systems in two other ways, which used only ethylene without the need of adding a comonomer: (a) through ylide ligands, which induced a nonlinear specificity, and (b) through novel bimetallic, bifunctional catalysts. The latter were formed by treating a

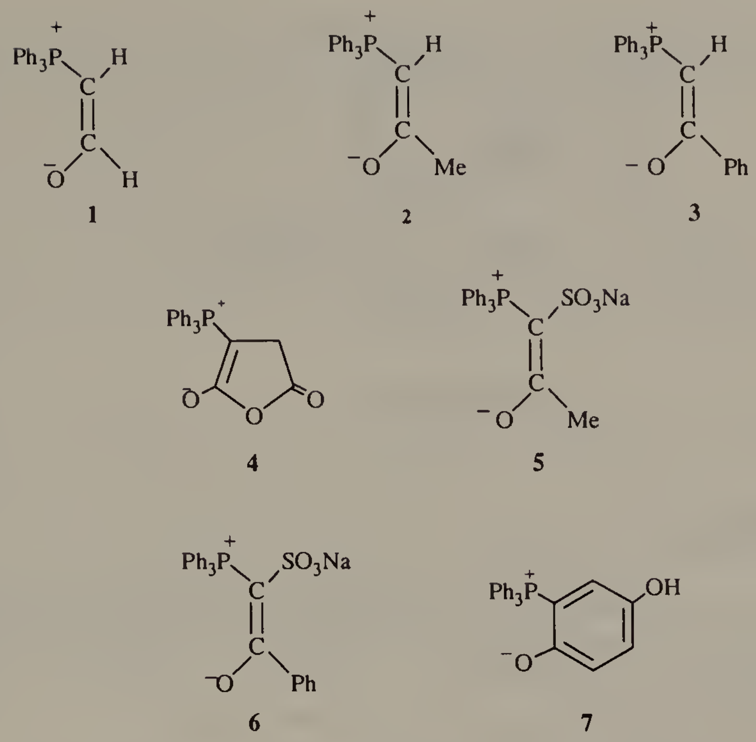
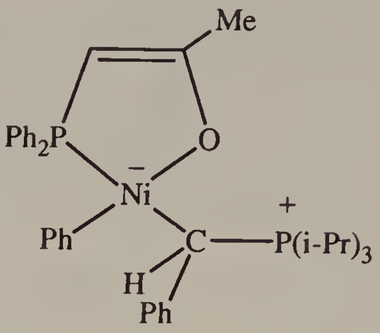


Figure 14.3 Ylides used in nickel complex catalysts for alkene polymerization (ref. 231).

heterogeneous surface chromium (II) catalyst with a homogeneous ylide nickel catalyst. Such ylide Ni/Cr catalysts even produced polyethylene with long-chain branches, which are not accessible through simple ethylene/α-olefin copolymerization.[234]

Other applications, which include nonpolar and polar solvents and substrates, widen the scope of ylide nickel catalysts. Although the coinsertion of ethylene and carbon dioxide using nickel ylide catalysts is still stoichiometric,[235] exposure of the catalyst first to ethylene and then to CO successfully gave copolymers of $C_2H_4$/CO.[236] Furthermore, copolymerization of ethylene with polar functionalized monomers was successful when the vinyl group and the functionalized group were separated by a spacer of two or more methylene units.[236]

Homo-, co-, and terpolymers of acrylics have been efficiently prepared by using nickel ylide catalysts of the type shown in Eq. 14.211.[237] More recently the bis(ylide) nickel catalysts have shown superior performance in acetylene polymerization, especially in polar solvents. The normalized polymerization activity in DMSO reached 500 mol $C_2H_2$/mol Ni/bar./hr., which most likely exceeds all other known nickel catalysts in this polymerization.[238] The remarkable catalytic profile of these ylide nickel catalyst complexes opens for the first time synthetic access to novel polyacetylenes in a highly polar polymer matrix. The soluble graft copolymers indicate that major drawbacks in polyacetylene can be overcome.[239]



(14.211)

**A130F9X93**

## REFERENCES

[1] Kaska, W. C.; Reichelderfer, R. F. *J. Organomet. Chem.* **1974**, *78*, C 47; Kaska, W. C.; Mitchell, D. K.; Reichelderfer, R. F. *J. Organomet. Chem.* **1973**, *47*, 391; Kaska, W. C. *Coord. Chem. Rev.* **1983,** *48*, 1.

[2] Schmidbaur, H. *Nachr. Chem. Tech. Lab.* **1979**, *27*, 620.

[3] Werner, H. *Angew. Chem.* **1983**, *22*, 927.

[4] Ostoja Starzewski, K. A.; tom Dieck, H. *Inorg. Chem.* **1979**, *18*, 3307.

[5] Stein J.; Fackler, J. R.; Papariza, C.; Chen, H. W. *J. Am. Chem. Soc.* **1981**, *103*, 2192.

[6] Ostoja Starzewski, K. A.; tom Dieck, H.; Bock, H. *J. Organomet. Chem.* **1974**, *65*, 311.

[7] Ostoja Starzewski, K. A.; Bock, H. J. *J. Am. Chem. Soc.* **1976**, *98*, 8486.

[8] Ostoja Starzewski, K. A.; Richter, W.; Schmidbaur, H. *Chem. Ber.* **1976**, *109*, 473.

[9] Schwerdtfeger, K., Master's Thesis, University of Frankfurt a. M., 1976.

[10] Ostoja Starzewski, K. A.; Feigel, M.; Rieser, J. *Phosphorus Sulfur* **1983**, *18*, 448.

[11] Ostoja Starzewski, K. A.; Schmidbaur, H. unpublished results.

[12] Cardin, D. J.; Lappert, M. F.; Raston C. L. *The Chemistry of Organozirconium and Hafnium Compounds*; Halsted Press: New York. 1986.

[13] Schwartz, J. *Pure Appl. Chem.* **1980**, *52*, 733.

[14] Schwartz, J.; Gell, K. I. *J. Organomet. Chem.* **1980**, *189*, C1.

[15] Schmidbaur, H.; Scharf, W.; Fuller, H. J. *Z. Naturforsch.* **1977**, *32B*, 858.

[16] Kaska, W. C. unpublished results.

[17] Erker, G.; Czisch, P.; Mynott, R. *Z. Naturforsch.* **1985**, *40b*, 1177.

[18] Erker, G.; Korek, U.; Peterson, J. L. *J. Organomet. Chem.* **1988**, *355*, 121.

[19] Erker, G.; Czisch, P.; Mynott, R.; Tsay, Y. H.; Krüger, C. *Organometallics* **1985**, *4*, 1310.

[20] de Boer, H. J. R.; Akkermann. O. S.; Bickelhaupt, F.; Erker, G.; Czisch, P.; Mynott, R.; Wallis, J. M.; Krüger, C. *Angew. Chem.* **1986**, *25*, 639.

[21] Erker, G.; Czisch, P.; Benn, R.; Rufinska, A.; Mynott, R. *J. Organomet. Chem.* **1987**, *328*, 101.

[22] Erker, G.; Korek, U.; Peterson, J. L. *J. Organomet. Chem.* **1988**, *355*, 121.

[23] Erker, G.; Korek, U.; Schlund, R.; Krüger, C. *J. Organomet. Chem.* **1989**, *364*, 133.

[24] Erker, G.; Czisch, P.; Krüger, C.; Wallis, J. M. *Organometallics* **1985**, *4*, 2059.

[25] Moore, E. J.; Santersiero, B. D. *Acta. Cryst.* **1988**, *C44*, 1913.

[26] Moore, E. J.; Santersiero, B. D. *Acta. Cryst.* **1988**, *C44*, 1911.

[27] Straus, D.; Grubbs, R. H. *J. Am. Chem. Soc.* **1982**, *104*, 5499.

[28] Karsch, H. H.; Müller, G.; Krüger, C. *J. Organomet. Chem.* **1984**, *273*, 195.

[29] Baldwin, J. C.; Keder, N. L.; Strouse, C. E.; Kaska, W. C. *Z. Naturforsch.* **1980**, *35B*, 1289; Sundermeyer, J.; Weber, K., Uürnberg, O. *J. Chem. Soc. Chem. Commun.* **1992**, 1631.

[30] Schmidbaur, H.; Pichl, R. *Z. Naturforsch.* **1985**, *40B*, 352.

[31] Fandos, R.; Meetsma, A.; Teuben, J. H. *Organometallics* **1991**, *10*, 59.

[32] Manzer, L. E. *Inorg. Chem.* **1976**, *15*, 2567.

[33] Schmidbaur, H.; Scharf, W.; Füller, H. J. *Z. Naturforsch.* **1977**, *32b*, 858.

[34] Karsch, H. H.; Deubelly, B.; Grauvogel, G. *Abstracts, IX FECHEM Conference on Organometallic Chemistry*, Heidelberg, Germany, 1991.

[35] Schmidbaur, H. *Angew. Chem.* **1983**, *22*, 907.

[36] Scharf, W.; Neugebauer, D.; Schubert, U.; Schmidbaur, H. *Angew. Chem.* **1978**, *17*, 601.

[37] Schmidbaur, H.; Pichl, R.; Müller, G. *Angew. Chem.* **1986**, *25*, 574.

[38] Rice, G. W.; Ansell, G. B.; Modrick, M. A.; Zentz, S. *Organometallics* **1983**, *2*, 154.

[39] Gell, K. I.; Schwartz, J. *Inorg. Chem.* **1980**, *19*, 3207.

[40] Erker, G.; Sosna, F.; Betz, P.; Werner, S.; Kruger, C. *J. Am. Chem. Soc.* **1991**, *113*, 564.

[41] Tikkanen, W.; Zilles, Y. W. *Organometallics* **1991**, *10*, 2266.

[42] Holy, N. L.; Nalesnik, T. E.; Warfield, L. T. *Inorg. Nucl. Chem. Lett.* **1977**, *13*, 569; Demerseman, B.; Dixneuf, P. H. *J. Organomet. Chem.* **1981**, *210*, C20.

[43] Schrock, R. R.; Sharp, P. R. *J. Am. Chem. Soc.* **1978**, *100*, 2389; Schrock, R. R. *Acc. Chem. Res.* **1979**, *12*, 98.

[44] Sharp. P. R.; Schrock, R. R. *J. Organomet. Chem.* **1979**, *171*, 43; McLain, S. J.; Wood, C. D.; Messerle, L. W.; Schrock, R. R.; Hollander, F. J.; Youngs, W. J.; Churchill, M. R. *J. Am. Chem. Soc.* **1978**, *100*, 5962.

[45] Berry, D. H.; Koloski, T. S.; Carroll, P. J. *Organometallics* **1990**, *9*, 2952.

[46] Hieber, W.; Winter, E.; Schubert, E. *Chem. Ber.* **1962**, *95*, 3070.

[47] Fandos, R.; Gomez, M.; Royo, P. *Organometallics* **1987**, *6*, 1581.

[48] Fandos, R.; Gomez, M.; Royo, P. *Organometallics* **1989**, *8*, 1604.

[49] Gibson, V. C.; Parkin, G.; Bercaw, J. E. *Organometallics* **1991**, *10*, 220.

[50] Churchill, M. R.; Young, W. J. *Inorg. Chem.* **1981**, *20*, 382; Belmonte, P.; Schrock, R. R.; Churchill, M. R.; Youngs, W. J. *J. Am. Chem. Soc.* **1980**, *102*, 2859; Belmonte, P. A.; Cloke, F. G. N.; Schrock, R. R. *J. Am. Chem. Soc.* **1983**, *105*, 2643.

[51] Manser, L. E. *Inorg. Chem.* **1976**, *15*, 2567.

[52] Kaska, W. C.; Mitchell, K. D.; Reichelderfer, R. F.; Korte, W. D. *J. Am. Chem. Soc.* **1974**. *96*, 2847; Creaser, C.; Kaska, W. C. *Transition Met. Chem.* **1978**, *3*, 360; Malisch, W.; Blau H.; Voran, S. *Angew. Chem.* **1978**, *17*, 360.

[53] Angelici, R. J.; Blacik, L. J. *Inorg. Chem.* **1972**, *11*, 1754.

[54] Ahn, S.; Beck, G.; Fehlhammer, W. P. *J. Organomet. Chem.* **1991**, *418*, 365.

[55] Fehlhammer, W. P.; Zinner, G.; Beck, G.; Fuchs, J. *J. Organomet. Chem.* **1989**, *379*, 277.

[56] Knoll, L. *J. Organomet. Chem.* **1978**, *155*, C3.

[57] Kaska, W. C.; Mitchell, D. K.; Reichelderfer, R. F.; Korte, W. D. *J. Am. Chem. Soc.* **1974**, *96*, 2847.

[58] Malisch, W.; Blau, H.; Voran, S. *Angew. Chem.* **1978**, *17*, 780.

[59] Endrich, K.; Alburquerque, P.; Korswagen, R. P.; Ziegler, M. L. *Z. Naturforsch.* **1988**, *43B*, 1293.

[60] Scordia, H.; Kergoat, R.; Kubicki, M. M.; Guerchais, J. E. *Organometallics* **1983**, *2*, 1681.

[61] tom Dieck, H.; Bock, H. *Z. Naturforsch.* **1966**, *21B*, 739.

[62] Knoll, L. *J. Organomet. Chem.* **1979**, *182*, 77. Kaska, W. C. *Coord. Chem. Rev.* **1983**, *48*, 1. Schmidbaur, H. *Angew. Chem.* **1983**, *22*, 907. Weber, L. In *The Chemistry of the Metal–Carbon Bond*; Hartley, F. R.; Patai, S., Eds.; Wiley: New York, 1982. Dirk, S. *Angew. Chem.* **1992**, *31*, 411. Bassi, I. W.; Scordamaglia, R. *J. Organomet. Chem.* **1973**, *51*, 273. Ostoja Starzewski K. A.; tom Dieck, H.; Franz, K. D.; Hohmann, F. *J. Organomet. Chem.* **1972**, *42*, C35.

[63] Ostoja Starzewski, K. A.; tom Dieck, H. *Inorg. Chem.* **1979**, *18*, 3307 and references therein; *Phosphorus* **1976**, *6*, 177.

[64] See Weber, L. *Angew. Chem.* **1983**, *22*, 516 for details of metal complexes with sulfur ylides.

[65] Dimroth, K.; Kaletsch, H. *J. Organomet. Chem.* **1983**, *247*, 271; Cashman, D.; Laylor, F. J. *J. Organomet. Chem.* **1971**, *32*, 351; Kotz, J. C.; Pedrotty, D. G. *J. Organomet. Chem.* **1970**, *22*, 425.

[66] Fischer, H.; Weber, L. *Chem. Ber.* **1984**, *117*, 3340.

[67] Weber, L.; Wewers, D.; Luecke, E. *Z. Naturforsch.* **1985**, *40B*, 968; Weber, L.; Wewers, D.; Boese, R. *Chem. Ber.* **1985**, *118*, 3570.

[68] Hubbard, J. L.; McVicar, W. K. *Organometallics* **1990**, *9*, 2683.

[69] Endrich, K.; Alburquerque, R. P.; Korswagen, P.; Ziegler, M. L. *Z. Naturforsch.* **1988**, *43B*, 1293.

[70] Casey, C. P.; Burkhardt, T. J. *J. Am. Chem. Soc.* **1972**, *94*, 6543.

[71] Schutt, W.; Ulrich, N.; Kreissl, F. R. *J. Organomet. Chem.* **1991**, *408*, C5. Doyle, R. A.; Angelici, R. J. *J. Organomet. Chem.* **1989**, *375*, 73. Adams, H.; Bailey, N. A.; Gauntlett, J. T.; Harkin, I. M.; Winter, M. J.; Woodward. S. *J. Chem. Soc. Dalton* **1991**, 1117.

[72] Kreissl, F. R.; Held, W. *Chem. Ber.* **1977**, *110*, 799; Fischer, H. *J. Organomet. Chem.* **1979**, *170*, 309; Fischer, H.; Fischer, E. O.; Kreiter, C. G.; Werner, H. *Chem. Ber.* **1974**, *107*, 2459; Pickering, R. A.; Angelici, R. J. *J. Organomet. Chem.* **1982**, *225*, 253.

[73] Casey, C. P.; Burkhardt, T. J.; Bunnell. C. A.; Calabrese, J. C. *J. Am. Chem. Soc.* **1977**, *99*, 2127.

[74] Alt, H. G.; Engelhardt, H. E.; Filippou, A. C. *J. Organomet. Chem.* **1988**, *355*, 139.

[75] Agh-Atabay, N. M.; Canoira, L. J.; Carlton, L.; Davidson, J. L. *J. Chem. Soc. Dalton* **1991**, 1175; Carlton, L.; Baker, W. A.; Davidson, J. L. *J. Organomet. Chem.* **1990**, *394*, 177.

[76] Kreissl, F. R.; Kreiter, C. G.; Fischer, E. O. *Angew. Chem.* **1972**. *11*, 643; Kreissl, F. R.; Kreiter, C. G.; Fischer, H. *Chem. Ber.* **1973**, *106*, 1262.

[77] Fischer, H.; Reindl, D. *J. Organomet. Chem.* **1990**, *385*, 351.

[78] Weber, L.; Matzke, T.; Boese, R. *Chem. Ber.* **1990**, *123*, 739.

[79] Foch, P. L.; Mathey F. *Syn. Lett.* **1990**, 171.

[80] Uedelhoven, W.; Neugebauer, D.; Kreissl, F. R. *J. Organomet. Chem.* **1981**, *217*, 183; Kreissl, F. R.; Friedrich, P.; Lindner, T. L.; Huttner, G. *Angew. Chem.* **1977**, *16*, 314; Kreissl, F. R. *J. Organomet. Chem.* **1975**, *99*, 305.

[81] Jamison, G. M.; White, P. S.; Templeton, J. L. *Organometallics* **1991**, *10*, 1954; Jamison, G. M.; Bruce, A. E.; White, P. S.; Templeton, J. L. *J. Am. Chem. Soc.* **1991**, *113*, 5057.

[82] Kurras, E.; Rosenthal, U.; Mennenga, H.; Oehme, G. *Angew. Chem.* **1973**, *12*, 854; Kurras, E.; Mennenga, H.; Oehme, G.; Rosenthal U.; Engelhardt, G. *J. Organomet. Chem.* **1975**, *84*, C13; Kurras, E.; Rosenthal, U. *J. Organomet. Chem.* **1978**, *160*, 35.

[83] Brookhart, M.; Green, M. L. H.; Wong. L-L. *Prog. Inorg. Chem.* **1988**, *36*, 1.

[84] Lindner, E.; Berke, H. *Chem. Ber.* **1974**, *107*,. 1360; Berke, H.; Lindner, E. *Angew. Chem.* **1973**, *12*, 667.

[85] List, A. K.; Hillhouse, G. R. *Organometallics*, **1989**, *8*, 2010.

[86] Cooper, N. J.; Green, M. L. H. *J. Chem. Soc. Dalton* **1979**, 1121.

[87] Arzoumanian, H.; Baldy, A.; Lai, R.; Metzger, J.; Peh, M. L. N.; Pierrot, M. *J. Chem. Soc. Chem. Commun.* **1985**, 1151; Lai, R.; Bot. S. L.; Baldy, A.; Pierott, M.; Arzoumanian, H. *J. Chem. Soc. Chem. Commun.* **1986**, 1208; Lai, R. In *Advances in Metal Carbene Chemistry*; Schubert, U. Ed.; Kluwer Academic Publishers: Norwell, MA 1989; p. 171.

[88] Bleschmitt, K.; Zahn, T.; Ziegler, M. L. *Angew. Chem.* **1985**, *24*, 702.

[89] Mitchell, D. K.; Korte, W. D.; Kaska, W. C. *J. Chem. Soc. Chem. Commun.* **1970**, 1384; Goldberg, S. Z.; Duesler, E. N.; Raymond, K. N. *Inorg. Chem.* **1972**, *11*, 1397; Kaska, W. C.; Mitchell, D. K.; Reichelderfer, R. F. *J. Organomet. Chem.* **1973**, *47*, 391.

[90] Wong, W. K.; Tam, W.; Gladysz, J. A. *J. Am. Chem. Soc.* **1979**, *101*, 5440.

[91] Lappas, D.; Hoffmann, D. M.; Folting, K.; Huffman, J. C. *Angew. Chem.* **1988**, *27*, 587.

[92] Brown, D. A.; Glass, W. K.; Kreddon, K. M. *J. Organomet. Chem.* **1991**, *413*, 233; Chung, Y. K.; Choi, H. S.; Sweigart, D. A.; Connelly, N. G. *J. Am. Chem. Soc.* **1982**, *104*, 4245.

[93] Knoll, L. *J. Organomet. Chem.* **1980**, *193*. 47.

[94] Knoll, L. *Z. Naturforsch.* **1977**, *32B*, 1268.

[95] Lindenberger, H.; Birk, R.; Orama, O.; Huttner, G.; Berke, H. *Z. Naturforsch.* **1988**, *43B*, 749.

[96] Blau, H.; Malisch, W. *Angew. Chem.* **1980**, *19*, 1019; Malisch, W.; Blau, H.; Schubert, U. *Angew. Chem.* **1980**, *19*, 1020; Korswagen, R.; Alt, R.; Speth, D.; Ziegler, M. L. *Angew. Chem.* **1981**, *20*, 1049; Malisch, W.; Blau, H.; Schubert, U. *Chem. Ber.* **1983**, *116*, 690; Blau, H.; Malisch, W.; Weickert, P. *Chem. Ber.* **1982**, *115*, 1488.

[97] Blau, H.; Malisch, W. *Angew. Chem.* **1980**, *19*, 1020; Blau, H.; Griessmann, K. H.; Malisch, W. *J. Organomet. Chem.* **1984**, *263*, C5.

[98] Crocco, G. L.; Gladysz, J. A. *J. Chem. Soc. Chem. Commun.* **1986**, 1154; Crocco, G. L.; Lee, K. E.; Gladyz, J. A. *Organometallics* **1990**, *9*, 2819. For S-ylide analogs see McCormick, F. B.; Gleason, W. B.; Zhao, X.; Heah, P. C.; Gladyz, J. A. *Organometallics* **1986**, *5*, 1778.

[99] Nubel, P. O.; Brown, T. L. *J. Am. Chem. Soc.* **1984**, *106*, 644.

[100] Alt. H. G.; Engelhardt, H. E.; Steinlen, E. *J. Organomet. Chem.* **1988**, *344*, 227; Alt, H. G.; Engelhardt, H. E.; Rogess, R. D. *J. Organomet. Chem.* **1989**, *362*, 117.

[101] Kolobova, N. E.; Zhvanko, O. S.; Ivanov, L. L.; Batsanov, A. S.; Struchkov, Y. T. *J. Organomet. Chem.* **1986**, *302*, 235; *ibid.* **1984**, *265*, 271.

[102] Casey, C. P.; Vosejpka, P. C.; Asljam, F. R. *J. Am. Chem. Soc.* **1990**, 112, 3713.

[103] Mandal, S. K.; Ho, D. M.; Orchin, M. *J. Organomet. Chem.* **1990**, *397*, 313.

[104] Alvarez, B.; Miguel, D.; Riera, V.; Miguel J. A.; Garcia, S. G. *Organometallics* **1991**, *10*, 384; Miguel, D.; Riera, V.; Miguel, J. A.; Gomez, M.; Solans, X. *Organometallics* **1991**, *10*, 1683; Granda, S. G.; Jeannin, Y.; Miguel, D.; Miguel, J. A.; Riera, V. *Organometallics* **1991**, *10*, 3005.

[105] Schmidbaur, H.; Costa, T.; Milewski-Mahrla, B.; Köhler, F. H.; Tsay, Y. H.; Krüger, C.; Abart, J.; Wagner, F. E. *Organometallics* **1982**, *1*, 1266.

[106] Jeffery, J. C.; Navarro, R.; Razay, H.; Stone, F. G. A. *J. Chem. Soc. Dalton* **1981**, 2471.

[107] Müller, G.; Neugebauer, D.; Geike, W.; Köhler, F. H.; Pebler, J.; Schmidbaur, H. *Organometallics* **1983**, *2*, 257.

[108] Zdanovitch, V. I.; Kolobova, N. E.; Vasyukova, N. I.; Nekrasov, Y. S.; Panosyan, G. A.; Petrovskii, P. I.; Zhakaeva, A. Z.; *J. Organomet. Chem.* **1978**, *148*, 63; *ibid.* **1974**, *64*, C25.

[109] Malisch, W.; Blau, H.; Voran, S. *Angew. Chem.* **1978**, *17*, 780; Stasunik, A.; Malisch, W. *J. Organomet. Chem.* **1984**, *270*, C56; Malisch, W.; Blau, H.; Blank, K.; Krüger, C.; Liu, L. K. *J. Organomet. Chem.* **1985**, *296*, C32; Stasunik, A.; Malisch, W. *Z. Naturforsch.* **1984**, *39B*, 56; Stasunik, A.; Malisch, W. *J. Organomet. Chem.* **1983**, *247*, C47.

[110] Cherkas, A. A.; Doherty, S.; Cleroux, M.; Hogarth, G.; Randall, L. H.; Breckenridge, S. M.; Taylor, N. J.; Carty, A. J. *Organometallics* **1992**, *11*, 1701.

[111] Blau, H.; Malisch, W. *J. Organomet. Chem.* **1982**, *235*, C1; Griessmann, K. H.; Stasunik, A.; Angerer, W.; Malisch, W. *J. Organomet. Chem.* **1986**, *303*, C29.

[112] Seyferth, D.; Hoke, J. B.; Wheeler, D. R. *J. Organomet. Chem.* **1988**, *341*, 421; Jensen, M. P.; Sabat, M.; Johnston, D. H.; Jones, L. M.; Shriver, D. F. *J. Organomet. Chem.* **1990**, *383*, 279; Henrick, K.; McPartlin, M. *J. Chem. Soc. Dalton* **1982**, 899.

[113] Korswagen R.; Alt, R.; Speth, D.; Ziegler, M. L. *Angew. Chem.* **1981**, *20*, 1049.

[114] Caballero, C.; Chavez, J. A.; Göknur, O.; Löchel, I.; Nuber, B.; Pfisterer, H.; Ziegler, M. L.; Alburquerque, P.; Eguren, L.; Korswagen, R. P. *J. Organomet. Chem.* **1989**, *371*, 329.

[115] Guerchais, V.; Astruc, D.; Nunn, M.; Cowley, A. W. *Organometallics* **1990**, *9*, 1036; Guerchais, V.; Lapinte, C.; Thepot, J. Y.; Toupet, L. *Organometallics* **1988**, *7*, 604; Pelling, S.; Botha, C.; Moss, J. R. *J. Chem. Soc. Dalton* **1983**, 1495.

[116] King, R. B.; Bhattacharyya, N. K.; Holt, E. M. *Inorg. Chem.* **1991**, *30*, 1174.

[117] Weber, L.; Lucke, E.; Boese, R. *Chem. Ber.* **1989**, *122*, 809.

[118] (a) Kaska, W. C.; Mitchell, D. K.; Reichelderfer, R. F.; Korte, W. D. *J. Am. Chem. Soc.* **1974**, *96*, 2847. (b) Kao, S. C.; Lu, P. P. Y.; Pettit, R. *Organometallics* **1982**, *1*, 911.

[119] Lindenberger, H; Birk, R.; Orama, O; Huttner, G.; Berke, H. *Z. Naturforsch.* **1988**, *43B*, 749; Berke, H.; Groessmann, U.; Huttner, G.; Orama, O. *Z. Naturforsch.* **1984**, *39B*, 1759.

[120] Bohle, D. S.; Heineke, D.; Tirpicchio, A.; Camellini, M. T.; Vahrenkamp, H. *Angew. Chem.* **1990**, *29*, 896.

[121] Hester, D. M.; Yang, G. K. *J. Chem. Soc. Chem. Commun.* **1991**, 1498; Hester, D. M.; Yang, G. K. *Organometallics* **1991**, *10*, 369.

[122] Karsch, H. H. *Angew. Chem.* **1982**, *21*, 311; Karsch, H. H. *Chem. Ber.* **1978**, *111*, 1650.

[123] Schmidbaur, H.; Blaschke, G. *Z. Naturforsch.* **1980**, *35B*, 584.

[124] Churchill, M. R.; DeBoer, B. G. *Inorg. Chem.* **1977**, *16*, 1141.

[125] Deeming, A. J.; Powell, N. I.; Whittaker, C. *J. Chem. Soc. Dalton* **1991**, 1875; Langenbahn, M.; Stoeckli-Evans, H.; Süss-Fink, G. *J. Organomet. Chem.* **1991**, *402*, C12; Deeming, A. J.; Nuel, D.; Powell, N. I.; Whittaker, C. *J. Chem. Soc. Chem. Commun.* **1990**, 68; Deeming, A. J.; Didiev, N.; Powell, N. I.; Whittaker, C. *J. Chem. Soc. Dalton* **1992**, 757. For a sulfur-containing ylide triosmium cluster see Adams, R. D.; Babin, J. E.; Tasi, M. *Organometallics* **1987**, *6*, 1717.

[126] Kirchner, K.; Taube, H. *J. Am. Chem. Soc.* **1991**, *113*, 7039.

[127] Schmidbaur, H.; Jeong, J.; Schier, A.; Graf, W.; Wilkinson, D. L.; Müller, G.; Krüger, C. *New J. Chem.* **1989**, *13*, 341; Green, M. L. H.; Qin, J.; O'Hare, D.; Bunting, H. E.; Thompson, M. E.; Marder, S. R.; Chatakondu, K. *Pure Appl. Chem.* **1989**, *61*, 817; Schmidbaur, H.; Deschler, U.; Seyferth, D. *Z. Naturforsch*, **1982**, *37B*, 950.

[128] Dave, T.; Berger, S.; Bilger, E.; Kaletch, H.; Pebler, J.; Knecht, J.; Dimroth, K. *Organometallics* **1985**, *4*, 1565.

[129] Burell, A. K.; Clark, G. R.; Richard, C. E. F.; Roper, W. R.; Wright, A. H. *J. Chem. Soc. Dalton* **1991**, 609.

[130] Barrau, J.; Ben-Hamida, N.; Agrebi, H.; Satge, J. *Inorg. Chem.* **1990**, *29*, 1674; Nakazawa, H.; Johnson, D. L.; Gladysz, J. A. *Organometallics* **1983**, *2*, 1846; Yu. Y. S.; Angelici, R. J. *Organometallics* **1983**, *2*, 1018.

[131] Des Abbayes, H.; Clement, J. C.; Laurent, P.; Yaouanc, J. J.; Tanguy, G.; Weiberger, B. *J. Organomet. Chem.* **1989**, *359*, 205.

[132] Haffner, A.; Bieri, J. H.; Prewo, R.; von Philipsborn, W.; Salzer, A. *Angew. Chem.* **1983**, *22*, 713; Hackett, P.; Johnson, B. F. G.; Lewis, J.; Jaouen, G. *J. Chem. Soc. Dalton* **1982**, 1247.

[133] Cosslett, L.; Kane-Maguire, L. A. D. *J. Organomet. Chem.* **1979**, *178*, C17.

[134] Karsch, H. H. Klein, H. F.; Kreiter, C. G.; Schmidbaur, H. *Chem Ber.* **1974**, *107*, 3692; Brauer, D. J.; Krüger, C.; Roberts, P. J.; Tsay, Y. H. *Chem Ber.* **1974**, *107*, 3706.

[135] Malisch, W.; Blau, H.; Weickert, P.; Griessmann, K. H. *Z. Naturforsch.* **1983**, *38B*, 711.

[136] Marder, T. B.; Fulz, W. C.; Calabrese, J. C.; Harlow, R. L.; Milstein, D. *J. Chem. Soc. Chem. Commun.* **1987**, 1543. For related cobalt chemistry see Klein, H. F.; Hammer, R. *Angew. Chem.* **1976**, *15*, 42.

[137] Grey, R. A.; Anderson, L. R. *Inorg. Chem.* **1977**, *16*, 3187.

[138] Blaschke, G.; Schmidbaur, H.; Kaska, W. C. *J. Organomet. Chem.* **1979**, *182*, 251; Schmidbaur, H.; Blaschke, G.; Füller, H. J.; Scherm, H. P. *J. Organomet. Chem.* **1978**, *160*, 41; Fraser, T. E.; Füller, H. J.; Schmidbaur, H. *Z. Naturforsch.* **1979**, *34B*, 1218.

[139] Schmidbaur, H.; Costa, T. *Chem. Ber.* **1982**, *115*, 1367.

[140] Holy, N. L.; Baenziger, N. C.; Flynn, R. M. *Angew. Chem.* **1978**, *17*, 686; Tresoldi, G.; Recca, A.; Finocchiaro, P.; Faraone, F. *Inorg. Chem.* **1981**, *20*, 3103; Bombieri, G.; Tresoldi, G.; Faraone, F.; Bruno, G. *Inorg. Chim. Acta* **1982**, *57*, 1; Rerek, M. E.; Basolo, F. *J. Am. Chem. Soc.* **1984**, *106*, 5908.

[141] McKinney, R. J. *Inorg. Chem.* **1982**, *21*, 2051.

[142] Werner, H.; Schippel. O.; Schulz, M. *J. Organomet. Chem.* **1991**, *417*, 149; Werner, H. *Angew. Chem.* **1983**, *22*, 927.

[143] Werner, H.; Feser, R.; Paul, W.; Hoffmann, L. *J. Organomet. Chem.* **1981**, *219*, C29; Werner, H.; Hoffmann, L.; Paul, W. *J. Organomet. Chem.* **1982**, *236*, C65; Werner, H.; Paul, W.; Ferser, R.; Zolk, R.; Thometzek, P. *Chem. Ber.* **1985**, *118*, 261; Werner, H.; Hoffmann, L.; Feser, R.; Paul. W. *J. Organomet. Chem.* **1985**, *281*, 317.

[144] Werner, H.; Paul, W. *Chem. Ber.* **1985**, *118*, 3032.

[145] Braudt, L.; Green, M.; Parkins, A. W. *Angew. Chem.* **1990**, *29*, 1046.

[146] Clark, G. R.; Roper, W. R.; Wright, A. H. *J. Organomet. Chem.* **1984**, *273*, C17.

[147] Angelici, R. J.; Blacik, L. J. *Inorg. Chem.* **1972**, *11*, 1754.

[148] Heydenreich, F.; Mollbach, A.; Wilke, G.; Dreeskamp, H.; Hoffmann, E. G.; Schroth, G.; Seevogel, K.; Stempfle, W. *Isr. J. Chem.* **1972**, *10*, 293; Malisch, W.; Blau, H.; Voran, S. *Angew. Chem.* **1982**, *21*, 919.

[149] Kaska, W. C.; Mitchell, D. K.; Reichelderfer, R. F.; Korte, W. D. *J. Am. Chem. Soc.* **1974**, *96*, 2847.

[150] Birch, R. R.; Calabrese, J. C.; Ittel, S. D. *Organometallics* **1988**, *7*, 1642.

[151] Pörschke, K. R.; Wilke, G.; Mynott, R. *Chem. Ber.* **1985**, *118*, 298; *ibid.* **1984**, *117*, 56.

[152] Booth, B. L.; Smith, K. G. *J. Organomet. Chem.* **1981**, *220*, 229.

[153] Heydenreich, F.; Mollbach, A.; Wilke, G.; Dreeskamp, H.; Hoffmann, E. G.; Schroth, G.; Seevogel, K.; Stempfle, W. *Isr. J. Chem.* **1972**, *10*, 293; Jolly, P. W.; Wilke, G. *The Organic Chemistry of Nickel*, Academic: NY, 1974; Vol. 1, p. 38.

[154] Mayer, J. M. *Comments Inorg. Chem.* **1988**, *8*, 125.

[155] Booth, B. L.; Smith, K. G. *J. Organomet. Chem.* **1981**, *220*, 219.

[156] Ostoja Starzewski, K. A.; Born, L. *Organometallics* **1992**, *11*, 2701, and literature cited; Klabunde, U.; Ittel. S. D. *J. Mol. Catal.* **1987**, *41*, 123.

[157] Keim, W.; Kowaldt, F. H.; Goddard, R.; Krüger, C. *Angew. Chem.* **1978**, *17*, 466.

[158] Brauer, D. I.; Krüger, C.; Roberts, P. J.; Tsay, Y. H. *Chem. Ber.* **1974**, *107*, 3706.

[159] Moore, D. S.; Robinson, S. D. In *Advances in Inorganic and Radiochemistry*; Emeleus, H. J.; Sharpe, A. G., Eds.; Academic: New York, 1986; Vol. 30, p. 1.

[160] Schmidbaur, H.; Scherm, H. P. *Chem Ber.* **1978**, *111*, 797.

[161] Schmidbaur, H. *Pure Appl. Chem.* **1980**, *52*, 1057.

[162] Blaschke, G.; Schmidbaur, H.; Kaska, W. C. *J. Organomet. Chem.* **1979**, *182*, 251.

[163] Karsch, H. H.; Klein, H. F.; Schmid, G. *Chem. Ber.* **1974**, *107*, 93.

[164] Schmidbaur, H.; Deschler, U.; Milewski-Mahrla, B. *Angew. Chem.* **1981**, *20*, 586.

[165] Gong, J. K.; Peters, T. B.; Fanwick, P. E.; Kubiak, C. P. *Organometallics* **1992**, *11*, 1392.

[166] Baldwin, J. C.; Kaska, W. C. *Inorg. Chem* **1979**, *18*, 686.

[167] Krüger, C.; Sekutowski, J. C.; Goddard, R.; Füller, H. J.; Gasser, O.; Schmidbaur, H. *Isr. J. Chem.* **1976/77**, *15*, 149; Schmidbaur, H.; Gasser, O.; Krüger, C.; Sekutowski, J. C. *Chem. Ber.* **1977**, *10*, 3517.

[168] Hooker, J. F.; Stryker, J. M. *J. Am. Chem. Soc.* **1990**, *112*, 464.

[169] Kermode, N. J.; Lappert, M. F.; Skelton, B. W.; White, A. H.; Holton, J. *J. Organomet. Chem.* **1982**, *228*, C71; Englter, C.; Moss, J. R.; Niven, M. L.; Nassimbeni, L. R.; Reid, G. *J. Organomet. Chem.* **1982**, *232*, C78; *ibid.* **1986**, *315*, 255.

[170] Hooker, J. F.; Stryker, J. M. *Organometallics* **1988**, *7*, 2082.

[171] Azam, K. A.; Frew, A. A.; Lloyd, B. R.; Manojlovic-Muir, L.; Kenneth, M.; Puddephatt, R. J. *J. Chem. Soc. Chem. Commun.* **1982**, 614.

[172] Scherer, O. J.; Jungmann, H. *J. Organomet. Chem.* **1982**, *228*, C61.

[173] Michelin, R. A.; Mozzon, M.; Facchin, G.; Braga, D.; Sabatino, P. *J. Chem. Soc. Dalton.* **1988**, 1803.

[174] Lin, I. J. B.; Shy, H. C.; Liu, C. W.; Liu, L. K.; Yeh, S. K. *J. Chem. Soc. Dalton* **1990**, 2509.

[175] McCrindle, R.; Arsenaujlt. G. J.; Guptga, A.; Hampden-Smith, M. J.; Rice, R. E.; McAlees, A. J. *J. Chem. Soc. Dalton* **1991**, 949.

[176] Metternich, H. J.; Niecke, E.; Nixon, J. F.; Bartsch, R.; Hitchcock, P. B.; Meidine, M. F. *Chem. Ber.* **1991**, *124*, 1973.

[177] Vicente, J.; Chicote, M. T.; Baeza, J. F.; Lahoz, F. J.; Lopez, J. A. *Inorg. Chem.* **1991**, *30*, 3617.

[178] Fontaine, X. L. R.; Herring, A. M.; Markham, D. P.; Shaw, B. L. *J. Organomet. Chem.* **1990**, *394*, 699; Herring, A. M.; Markham, D. P.; Shaw, B. L.; Thornton-Pett, M. *J. Chem. Soc. Chem. Commun.* **1987**, 643.

[179] Alcock, N. W.; Pringle, P. G.; Bergamini, P.; Sostero, S.; Traverso, O. *J. Chem. Soc. Dalton* **1990**, 1553.

[180] Albanese, Y. A.; Staley, D. L.; Rheingold, A. L.; Burmeister, J. L. *J. Organomet. Chem.* **1989**, *375*, 265.

[181] Vincente, J.; Chicote, M. T.; Fernandez-Baeza, J. *J. Organomet. Chem.* **1989**, *364*, 407. See also Facchin, G.; Bertani, R.; Zanotto, L.; Calligaris, M.; Nardin, G. *J. Organomet. Chem.* **1989**, *366*, 409; *J. Chem. Soc. Dalton* **1987**, 1381. Albanese, J. A.; Rheingold, A. L.; Burmeister, J. L. *Inorg. Chim. Acta* **1988**, *150*, 213. Uson, R.; Fornies, Y.; Navarro, R.; Ortega, A. M. *J. Organomet. Chem.* **1987**, *334*, 389. Teagle, J. A.; Burmeister, J. L. *Inorg. Chim. Acta* **1986**, *118*, 65. Sanehi, R.; Bansal, R. K.; Mehrotra, R. C. *Ind. J. Chem. Sect. A.* **1985**, *24A*, 1031; *Ind. J. Chem. Sect. A.* **1985**, *24A*, 398. Illingworth, M. L.; Teagle, J. A.; Burmeister, J. L.; Fultz, W. C.; Rheingold, A. L. *Organometallics*, **1983**, *2*, 1364. Onishi, M.; Ohama, Y.; Hiraki, H.; Shintani, H. *Polyhedron*, **1982**, *1*, 539.

[182] Uson, R.; Fornies, J.; Navarto, R.; Espinet, P.; Mendivil, C. *J. Organomet. Chem.* **1985**, *290*, 125.

[183] Carmona, E.; Guttierez-Puebla, E.; Monge, A.; Marin, J. M.; Paneque, M.; Poveda, M. L. *Organometallics* **1989**, *8*, 967; *ibid.* **1984**, *3*, 1438. For related palladium chemistry see Rybin, L. V.; Petrovskaya, E. A.; Rubinskaya, M. I.; Kuzmina, L. G.; Structzkov, Y. T.; Kaverin, V. V.; Koneva, N. Y. *J. Organomet. Chem.* **1985**, *288*, 119.

[184] Tresoldi, G.; Faraone, F.; Piraino, P.; Bottino, F. A. *J. Organomet. Chem* **1982**, *231*, 265.

[185] König, H.; Menu, M. J.; Dartiguenave, M.; Dartiguenave, Y.; Klein, H. F. *J. Am. Chem. Soc.* **1990**, *112*, 5351.

[186] Klein, H. F.; Haller, S.; König, H.; Dartiguenave, M.; Dartiguenave, Y.; Menu, M. J. *J. Am. Chem. Soc.* **1991**, *113*, 4673.

[187] Schmidbaur, H.; Adlkofer, J.; Heinmann, M. *Chem. Ber.* **1974**, *107*, 3697; Schmidbaur, H.; Franke, R. *Angew. Chem.* **1973**, *12*, 416; *Chem. Ber.* **1975**, *108*, 1321; Yamamoto, Y.; Schmidbaur, H. *J. Organomet. Chem.* **1975**, *96*, 133; *ibid.* **1975**, *97*, 479; Schmidbaur, H. *Angew. Chem.* **1983**, *22*, 907.

[188] Yamamoto, Y.; Konno, H. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 1327.

[189] Schmidbaur, H.; Franke, R. *Inorg. Chim. Acta.* **1975**, *13*, 85; Schmidbaur, H.; Mandl, J. R.; Frank, A.; Hüttner, C. H. *Naturwissenschaften* **1976**, *63*, 585; Schmidbaur, H.; Mandl. J. R. *Chem. Ber.* **1976**, *109*, 466.

[190] Schmidbaur, H. Scherm, H. P. *Z. Naturforsch.* **1979**, *34B*, 1347.

[191] Zeller, E.; Beruda, H; Kolb, A.; Bissinger, P.; Riede, J.; Schmidbaur, H.; *Nature* **1991**, *352*, 141 and references therein. Schmidbaur, H; Gasser, O. *Angew. Chem.* **1976**, *15*, 502.

[192] Grohmann, A.; Riede, J.; Schmidbaur, H. *Nature* **1990**, *345*, 140.

[193] Schmidbaur, H.; Franke, R. *Inorg. Chim. Acta* **1975**, *13*, 84. Schmidbaur, H.; Mandl, J. R.; Frank A.; Huttner, G. *Chem. Ber.* **1976**, *109*, 466. Fackler, J. P.; Basil, J. D. *Organometallics* **1982**, *1*, 871. Schmidbaur, H.; Mandl, J. R. *Naturwissenschaften* **1976**, *63*, 585. Schmidbaur, H.; Mandl, J. R.; Wagner, F. E.; van de Vondel, D. F.; van der Kelen, G. P. *J. Chem. Soc. Chem. Commun.* **1976**, 170.

[194] Raptis, R. G.; Fackler, J. P.; Basil, J. D.; Dudis, D. S. *Inorg. Chem.* **1991**, *30*, 3072 and references therein. See also Raptis, R. G.; Porter, L. C.; Emrich, R. J.; Murray, H. H.; Fackler, J. P. *Inorg. Chem.* **1990**, *29*, 4408. Heinrich, D. D.; Fackler, J. P. *Inorg, Chem.* **1990**, *29*, 4402. Raptis, R. G.; Fackler, J. P.; Murray, H. H.; Porter, L. C. *Inorg. Chem.* **1989**, *28*, 4057. Knachel, H. C;. Dudis, D. S.: Fackler, J. P. *Organometallics* **1984**, *3*, 1312. Trzcinska-Bancroft, B.; Khan, M. N. I.; Fackler, J. P. *Organometallics* **1988**, *7*, 993. See also Davies, J. A.; Dutremez, S.; Pinkerton, A. A.; Vilmer, M. *Organometallics* **1991**, *10*, 2956 for similar reactions with $[Pd_2Cl_2(\mu\text{-dppm})_2]$ (dppm=$Ph_2PCH_2PPh_2$).

[195] Schmidbaur, H.; Hartmann, C.; Reber, G.; Muller, G. *Angew. Chem.* **1987**, *26*, 1146.

[196] Uson, R.; Laguna, A.; Laguna, M.; Jimenez, J.; Jones, P. G. *J. Chem. Soc. Dalton* **1991**, 1361; Uson, R.; Laguna, A.; Laguna, M.; Gimenu, M. C. *J. Chem. Soc. Dalton* **1989**, 1883.

[197] Uson, R.; Laguna, A.; Laguna, M.; Jimenez, J.; Jones P. G. *Angew. Chem.* **1991**, *30*, 198. See also Uson, R.; Laguna, A.; Laguna, M.; Tarton, M. T.; Jones, P. G. *J. Chem. Soc. Chem. Commun.* **1988**, 740.

198 Schmidbaur, H.; Hartmann, C. *Angew. Chem.* **1986**, *25*, 575.

199 Lin, I. J. B.; Liu, C. W.; Liu, L. K.; Yuh-Sheng, W. *Organometallics* **1992**, *11*, 1447.

200 Schmidbaur, H.; Scherbaum, F.; Huber, B.; Müller, G. *Angew. Chem.* **1988**, *27*, 419.

201 Zybill, C.; Müller, G. *Organometallics* **1987**, *6*, 2489.

202 Vicente, J.; Chicote, M. T.; Saura-Llamas, I.; Jones, P. G.; Base, K. M.; Erdbrugger, C. F. *Organometallics* **1988**, *7*, 997. Vicente, J.; Chicote, M. T.; Laguna, M. C.; Jones, P. G. *J. Chem. Soc. Dalton* **1991**, 2579. For additional work on Ag and Au A-type ylide complexes see Vicente, J.; Chicote, M. T.; Saura-Llamas, I.; Turpin, J.; Fernandez-Baeza, J. *J. Organomet. Chem.* **1987**, *333*, 129; *J. Organomet. Chem.* **1987**, *331*, 409; Jones, P. G. *J. Organomet. Chem.* **1988**, *345*, 405; Uson, R.; Laguna, A.; Uson, A.; Jones, P. G.; Meyer-Baese, K. *J. Chem. Soc. Dalton* **1988**, 341; Vicente, J.; Chicote, M. T.; Saura-Llamas, I.; Jones, P. G. *Organometallics* **1989**, *8*, 767; Uson, R.; Laguna, A.; Laguna, M.; Uson, A.; Gimeno, M. C. *J. Chem. Soc. Dalton* **1988**, 701; *Synth. React. Inorg. Met-Org. Chem.* **1988**, *18*, 69; Vicente, J.; Chicote, M. T.; Saura-Llamas, I. *J. Chem. Soc. Dalton* **1990**, 1941.

203 Schumann, H.; *Chem. Ztg. Chem. App.* **1976**, *100*, 336; Schumann, H.; Reier, F. W. *J. Organomet. Chem.* **1982**, *235*, 287; Schumann, H.; Reier, F. W. *J. Organomet. Chem.* **1982**, *235*, 287.

204 Schumann, H.; Reier, F. W.; Dettlaff, M. *J. Organomet. Chem.* **1983**, *255*, 305.

205 Schumann, H.; Albrecht, I.; Reier, F. W.; Hahn, E. *Angew. Chem.* **1984**, *23*, 522.

206 Wong, W. K.; Chen, H.; Chow, F. L. *Polyhedron* **1990**, *9*, 875. For comparison with the dynamic behavior of similar actinide complexes see Cramer R. E.; Roth, S.; Edelmann, F.; Bruck, M. A.; Cohn, K. C.; Gilje, J. W. *Organometallics* **1989**, *8*, 1192.

207 Schumann, H.; Reier, F. W.; Palanidis, E. *J. Organomet. Chem.* **1985**. *297*, C30; Schumann, H.; Reier, F. W. *J. Organomet. Chem.* **1984**, *269*, 21.

208 Watson, P. L. *J. Chem. Soc. Chem. Commun.* **1983**, 276.

209 Stevens, R. C.; Bau, R.; Cramer, R. E.; Afzal, D.; Gilje, J. W.; Koetzle, T. F. *Organometallics* **1990**, *9*, 694; Cramer, R. E.; Bruck, M. A.; Edelmann, F.; Afzal, D.; Gilje, J. W.; Schmidbaur, H. *Chem. Ber.* **1988**, *121*, 417.

210 Cramer, R. E.; Maynard, R. B.; Gilje, J. W. *J. Am. Chem. Soc.* **1978**, *100*, 5562; Cramer, R. E.; Maynard, R. B.; Gilje, J. W. *Inorg. Chem.* **1981**, *20*, 2467; Cramer, R. E.; Maynard, R. B.; Paw, J. C.; Gilje, J. W. *J. Am. Chem. Soc.* **1981**, *103*, 3589; Cramer, R. E.; Mori, A. L.; Maynard, R. B.; Gilje, J. W.; Tatsumi, K.; Nakamura, A. *J. Am. Chem. Soc.* **1984**, *106*, 5920.

211 Cramer, R. E; Bruck, M. A.; Gilje, J. W. *Organometallics* **1988**, *7*, 1465.

212 Cramer, R. E.; Higa, K. T.; Pruskin, S. L.; Gilje, J. W. *J. Am. Chem. Soc.* **1983**, *105*, 6749.

213 Cramer, R. E.; Higa, K. T.; Gilje, J. W. *J. Am. Chem. Soc.* **1984**, *106*, 7245.

214 Malisch, W.; Blau, H.; Schubert, U. *J. Organomet. Chem.* **1982**, *232*, C33; *Chem. Ber.* **1983**, *116*, 690.

215 Cramer, R. E.; Jeong, J. H.; Gilje, J. W. *Organometallics* **1986**, *5*, 2555.

216 Gilje, J. W.; Cramer, R. E. *Inorg. Chim. Acta* **1987**, *139*, 177.

217 Cramer, R. E.; Jeong, J. H.; Richmann, P. N.; Gilje, J. W. *Organometallics* **1990**, *9*, 1141.

218 Cramer, R. E.; Jeong, J. H.; Gilje, J. W. *Organometallics* **1987**, *6*, 2010.

219 Cramer, R. E.; Panchanatheswaran, K.; Gilje, J. W. *Angew Chem.* **1984**, *23*, 912.

220 Gilje, J. W.; Cramer, R. E.; Bruck, M. A.; Higa, K. T.; Panchanatheswaran, K. *Inorg. Chim. Acta.* **1985**, *110*, 139; Cramer, R. E.; Engelhardt, U.; Higa, K. T.; Gilje, J. W. *Organometallics* **1987**, *6*, 41.

221 Cramer, R. E.; Maynard, R. B.; Paw, J. C.; Gilje, J. W. *Organometallics* **1982**, *1*, 869.

222 Cramer, R. E.; Panchanatheswaran, K.; Gilje, J. W. *J. Am. Chem. Soc.* **1984**, *106*, 1853.

223 Cramer, R. E.; Roth, S.; Edelmann, F.; Bruce, M. A.; Cohn, K. C.; Gilje, J. W. *Organometallics* **1989**, *8*, 1192.

224 Cramer, R. E.; Roth, S.; Edelmann, F.; Bruce, M. A.; Cohn, K. C.; Gilje, J. W. *Organometallics* **1989**, *8*, 1192.

225 Grey, R. A.; Anderson, L. R. *Inorg. Chem.* **1977**, *16*, 3187.

226 Keim, W.; Kowaldt, F. H.; Goddard, R.; Krüger, C. *Angew. Chem.* **1978**, *17*, 466.

227 Keim, W.; Behr, A.; Limbacker, B.; Krüger, C. *Angew. Chem.* **1983**, *22*, 503.

228 Peukert, M.; Keim, W. *J. Mol. Catal.* **1984**, *22*, 289.

229 Keim, W.; Appel, R.; Storeck, A.; Krüger, C.; Goddard, R. *Angew. Chem.* **1981**, *20*, 116; Fink, G.; Mohring, V. *Angew. Chem.* **1985**, *24*, 1001.

230 Ostoja Starzewski, K. A.; Witte, J. *Angew. Chem.* **1985**, *24*, 599.

231 Ostoja Starzewski, K. A.; Witte, J. *Angew. Chem.* **1987**, *26*, 63; Ostoja Starzewski, K. A.; Witte, J. In *Transition Metal Catalyzed Polymerization*; Quirk, R. P. Ed.; Cambridge University Press: Cambridge, 1988; p. 472.

232 Ostoja Starzewski, K. A.; Witte, J.; Bartl, H. (to Bayer AG) DE-OS 3445090, 1986; *Chem. Abstr.* **1987**, *105*, 153694; Kissin, Y. V.; Beach, D. L. Y. *Polymer Chem. Ed.* **1989**, *27*, 147.

233 Ostoja, Starzewski, K. A. (to Bayer AG) DE-OS 3916211, 1990; *Chem. Abstr.* **1991**, *114*, 144226.

234 Ostoja Starzewski, K. A.; Witte, J.; Reichert, K. H.; Vasiliou, G. In *Transition Metals and Organometallics as Catalysts for Olefin Polymerization*; Kaminsky, W.; Sinn, H., Eds; Springer Verlag: Berlin, 1988; p. 349.

235 Behr, A.; Keim, W.; Thelen, G. *J. Organomet. Chem.* **1983**, *249*, C38.

236 Klabunde, U.; Ittel, S. D. *J. Mol. Catal.* **1987**, *41*, 123; Klabunde, U.; Tulip, T. H.; Roe, D. C.; Ittel. S. D. *J. Organomet. Chem.* **1987**, *334*, 141.

237 Ostoja Starzewski, K. A.; Witte, J. (to Bayer AG) DE-OS 3700196, 1988; *Chem. Abstr.* **1989**, *110*, 76280.

238 Ostoja Starzewski, K. A.; Witte, J. *Angew. Chem.* **1988**, *27*, 839.

239 Ostoja Starzewski, K. A.; Bayer, G. M. *Angew. Chem.* **1991**, *30*, 961.

# INDEX

In this index the appearance of the word **ylide** by itself means a phosphonium ylide unless otherwise indicated. Also, the listing of a class of compounds (e.g., amines) without a modifier refers to syntheses of that class of compounds.

ISBN 0-471-52217-1