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THE HETERCYCLIC CHEMISTRY OF PHOSPHORUS

The Heterocyclic Chemistry of Phosphorus:

SYSTEMS BASED ON THE PHOSPHORUS-CARBON BOND

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10 9 8 7 6 5 4 3 2 1

To Gordon, Howard, and Carol

Preface

The phenomenal growth rate and prospect for exciting research activity in that aspect of heterocyclic chemistry concerned with the element phosphorus prompted the writing of this book. While the entire field of organophosphorus chemistry has been characterized by great vitality over the last three decades, the acceleration has been greatest with the cyclic derivatives. There is abundant documentation of this statement. In his classical comprehensive monograph of 1950 on organophosphorus chemistry,[1] Kosolapoff included only about 20 structures that are heterocyclic. F. G. Mann, one of the pioneers of heterocyclic phosphorus chemistry, wrote the first review[2a] on the subject in 1950; it required only 15 pages to cover the 15 references on the 11 ring systems. By 1970, when Mann published a second edition of the monograph,[2b] 351 pages, 503 references, and 90 selected ring systems (of about 150 known) were involved. The explosive rate of growth has continued, and now lengthy review articles are appearing on specialized aspects of the field (e.g., multicyclic systems containing only carbon and phosphorus[3] and stereochemistry of phosphorus ring systems[4]). In spite of this current interest, which is worldwide in scope, many fascinating areas remain open for exploration. For those interested in feats of synthesis or the devising of new synthetic methods, from the smallest monocyclics to complex multicyclics there are many ring systems that require attention. Problems for the stereochemically inclined are in abundance; unusual conformational features are present that challenge preconceived ideas from carbocyclic chemistry. Fundamental properties of bonding, the consequences of electron delocalization, and tests of the troublesome concept of "aromaticity" are all open for study with phosphorus heterocycles. New observations of structure-spectra relations are made with regularity, and important contributions to the development of ^{1}H, ^{13}C, and ^{31}P nmr spectroscopy in particular have come from studies based on phosphorus heterocycles. Practical applications for the heterocycles are also benefits from their study; especially promising is their potential use as medicinals, an aspect of phosphorus chemistry receiving renewed attention as a result of recent discoveries of antibiotic[5] and antiviral[6] activity in relatively simple structures.

This book is designed to provide an introduction for nonspecialists to this fascinating field, while still being of value to experienced workers by virtue of the depth of the coverage. It makes no effort to treat every aspect of heterocyclic phosphorus chemistry; instead emphasis is given to synthetic methods, selected properties, and practical nmr spectroscopy as the primary tool for structure assignment. The level of presentation assumes no special knowledge of phosphorus chemistry, and the style attempts to teach and correlate information rather than just cite research results in review fashion.

Certain limitations had to be placed on the breadth of the coverage to keep the book of reasonable size. By no means could an all-inclusive treatment of the known heterocycles be given, nor could all references be cited for those topics that were selected for discussion. The literature has been consulted for pertinent references that were available as late as mid-1979. Many different atoms have been placed in rings with phosphorus, and a number of the heterocycles do not even have carbon-phosphorus bonds present. Indeed, extremely important areas of research are represented by such structures as the cyclic phosphates, of profound significance in biological chemistry, and by the phosphazenes, which have only P—N bonds. Yet to include such structures in a book of the proposed type would so expand its size and so dilute its relation to conventional heterocyclic organic chemistry that the decision was made early to *limit the coverage to only those ring systems where phosphorus is bonded to carbon*. Even this restriction requires a further refinement to obtain a subject of manageable scope: only systems where phosphorus is bonded to *two carbons* are treated in the chapters on synthetic methods. Their synthesis is more challenging, their resistance to hydrolysis is greater, interconversions among the various types of phosphorus functional groups are possible, and resemblance to the better-known areas of heterocyclic nitrogen and sulfur compounds can be found with this type of system rather than those based on the presence of P-to-heteroatom linkages. However, chapters on spectroscopy and other properties make extensive use of examples with additional heteroatoms in the ring. Even here, a decision to limit the discussion to systems where only oxygen, nitrogen, or sulfur is present was required. Some fascinating new works on systems where silicon, boron, arsenic, germanium, and so on, are present will not be mentioned.

The author has worked some twenty years in this field. The research of many students at Duke University during this period has provided the background and the incentive for the preparation of this book, and to each of them I express my deep appreciation for many, many hours of experimental work, and subsequent stimulating discussions. Such heavy involvement in a research area can lead to a personal bias in the selection of topics and the depth of the discussion, and the author admits to the presence of this bias in the way this book was composed and references chosen.

I am extremely grateful to Peg Steele Musser for the superb way in which she typed the manuscript and prepared structural formulas. The construction of the manuscript also benefited from the truly professional advice and assistance of Sharlene Y. Griffin, a valued associate of many years' standing. Appreciation is also expressed to Eric Smith, Librarian of the Chemistry Department, for assistance in locating literature items.

With a book that in a way evolved over many years, the lives of numerous people have had indirect but positive influence on its development. Two are thanked here for playing special and significant roles that greatly contributed to the outcome: Rev. Harriott Johnson Quin during the formative stages, and Alice W. Watkins in bringing it to a conclusion.

LOUIS D. QUIN

Durham, North Carolina
July, 1980

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1 G. M. Kosolapoff, *Organophosphorus Compounds* (John Wiley, New York, 1950).

2 a. F. G. Mann, *The Heterocyclic Derivatives of Phosphorus, Arsenic, Antimony, and Bismuth* (Wiley-Interscience, New York, 1950); b. 2nd ed., 1970.

3 S. D. Venkataramu, G. D. Macdonell, W. R. Purdum, M. El-Deek, and K. D. Berlin, *Chem. Rev.* **77**, 121 (1977).

4 M. J. Gallagher, in *Stereochemistry of Heterocyclic Compounds*, edited by W. L. F. Armarego (Wiley-Interscience, New York, 1977), Chap. 5.

5 D. Hendlin et al., *Science* **166**, 122 (1969); E. Bayer et al., *Helv. Chim. Acta* **55**, 224 (1972).

6 T. H. Maugh II, *Science* **192**, 128 (1976).

Contents

chapter one

Introduction to Phosphorus-Containing Ring Systems and Some General Characteristics

Phosphorus heterocycles are found in the usual broad variety of ring size and ring multiplicity so familiar to the entire field of heterocyclic chemistry. It is convenient for present purposes to subdivide the family into six classes, bearing in mind the restriction explained in the Preface that one bond to carbon must be present. The six classes are the following:

1. The parent monocyclics containing only carbon and phosphorus.
2. Bicyclic derivatives of the parents, where benzene, cycloalkane, or heterosubstituted rings are fused to one face.
3. Tricyclic, tetracyclic, that is, higher derivatives of the parents.
4. Rings with two or more phosphorus atoms present, and their bicyclic, multicyclic, and bridged derivatives.
5. Systems where one O, N, or S atom accompanies P in the same ring, and bicyclic and higher derivatives (thus omitting multiheteroatom systems).
6. Multicyclic or caged systems where a ring is bridged by a fragment of one or more atoms, and where phosphorus is found at any ring position.

For each class, a table is provided in Section 1.1 of the known ring systems as recorded in *Chemical Abstracts,* whose indices have been surveyed through December 31, 1978 (Vol. 89). No claim is made that *every* ring system has been included, although there was an effort made to accomplish this.

The majority of these ring systems will not be specially mentioned again in this book, as many are the result of highly specific syntheses that give only a small number of derivatives of limited interest or incomplete characterization. However, to aid the reader who might be interested in learning about a particular system, the *Chemical Abstracts* (*C.A.*) Registry Numbers are provided for the systems. (Some systems reported in the literature but not yet recorded in the *C.A.* Parent Compound Handbook as of the May 1979 Cumulative Supplement are not included.) This number will lead the reader to the correct *C.A.* name for the parent ring, and indices can then be searched under this name for the various known derivatives. Another use of these numbers is to find the proper entry in the Parent Compound Handbook of *C.A.* The Registry Numbers listed are generally those for the maximally unsaturated parents, with phosphorus in the tricovalent state. Most of these parents have never been synthesized, however. Some systems also have Registry Numbers for the fully saturated parent systems but, in order to keep their size under control, these are not included in the tables. Some comments to be made with regard to the nomenclature of the parent carbon phosphorus cycles will prove helpful in locating these separately indexed compounds.

Mann's monograph[1] of 1970 provides valuable discussion and referencing of the ring systems known up to that time. So that the reader will know that this discussion exists about certain systems and can benefit from this valuable work, the tables include the proper page reference to Mann's monograph, indicated by the prefix M. This device also reveals immediately just how many new systems have been created in a period shorter than a decade. What is *not* revealed is the intensive effort that also has gone into the study of the older but fundamental systems. Accomplishments here, however, form the major part of several chapters of this book.

As further introduction to the nature and scope of cyclic phosphorus chemistry, each of the six classes of systems is separately discussed.

1.1 SURVEY OF KNOWN RING SYSTEMS

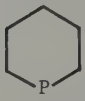
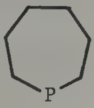
1.1.1 The Monocyclic Parents (Table 1.1)

By far the largest amount of research effort has been expended on this class, and the compounds are studied in depth in later chapters of this monograph. They are of vital importance in current research as model systems for developing our understanding of structure-spectra relationships, stereochemistry, and electron delocalization phenomena. Knowledge of their nomenclature is essential to any study of cyclic phosphorus chemistry, as the multicyclic and heterosubstituted systems derive their names from these parents. The names are formed from the prefix "phosph," modified to "phosphor" when the next syllable starts with "in" or "ine." The standard suffixes of heterocyclic nomenclature then indicate the size of the ring and also if the ring is fully unsaturated or fully saturated. In the table below, the proper suffixes (underlined) have been applied to show the full name for the first ten members of the series. Thereafter, a different system develops that is based on substitution of a carbon in the alicyclic name by "phospha" (e.g., phosphacycloundecane, phosphacyclododecane, etc.).

Ring Size	Unsaturated	Saturated
3	phosphirene	phosphirane
4	phosphete	phosphetane
5	phosphole	pholspholane
6	phosphorin	phosphorinane
7	phosphepin	phosphepane
8	phosphocin	phosphocane
9	phosphonin	phosphonane
10	phosphecin	phosphecane

Compounds with intermediate levels of saturation are indexed in *C.A.* as hydro derivatives of the unsaturated parent. Prior to the 1972-1976 Cumulative Index, the important dihydro derivatives of the 5-membered ring were indexed as phospholenes (2- or 3-); this name is acceptable by the IUPAC system, and is in common usage. Indeed, the most easily synthesized ring system of all appears to be the phospholene system, and it has attracted the bulk of recent research attention. The 6- and 4-membered rings are next in importance, whereas very little is known yet about the 3-membered ring or any of those with more than 6 members. They repre-

TABLE 1.1 Monocyclic Systems[a]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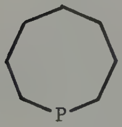
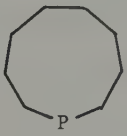
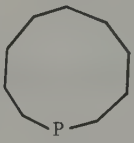
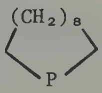
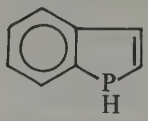
				
292-67-1	65355-82-0	40827-21-2	40997-17-9	

[a] In this and Tables 1.2-1.6, the formulas do not indicate the degree of saturation but merely the arrangement of the atoms in the ring. The Registry Numbers, however, are usually for the fully unsaturated forms even when not presently known. The Mann references similarly lead to the unsaturated forms.

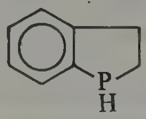
sent a wide-open area for research. The fully unsaturated 5- and 6-membered rings have received much attention because of their possession of the Hückel number of electrons required for "aromaticity." An extensive chemistry is developing around the phosphole and phosphorin systems as this matter is studied. Special attention is given this subject in Chapter 8. It should be immediately recognized, however, that by no means do these unsaturated systems occupy the same role in cyclic phosphorus chemistry as they do in nitrogen (pyrrole and pyridine) or sulfur (thiophene) chemistry; they are much more difficult to prepare and, for comparable structures, lack the high stability of their N or S counterparts. The phosphonin ring also corresponds to a Hückel system ($4n + 2$, $n = 2$) but has not yet been studied from this standpoint.

1.1.2 Bicyclic Systems (Table 1.2)

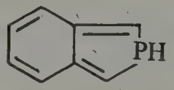
The benzo derivatives of the saturated 5- and 6-membered rings are among the better known phosphorus heterocycles, and their common names, as well as those of their unsaturated forms, are used for indexing in *C.A.*:



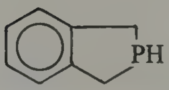
Phosphindole



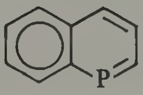
Phosphindoline



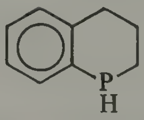
Isophosphindole



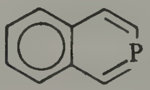
Isophosphindoline



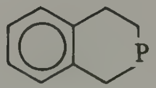
Phosphinoline



Tetrahydrophosphinoline

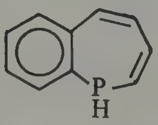


Isophosphinoline



Tetrahydroisophosphinoline

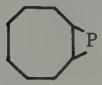
Benzo derivatives of other rings are named in the usual way from the monocyclic parent:



1H-Benzo[b]phosphepin

Derivatives where the benzene ring is partially or fully reduced remain rare, although, as is shown in Chapter 2, ready access to reduced phosphindoles is now possible. Such compounds may be found in *C.A.* as hydro derivatives. Fusion of

TABLE 1.2 Bicyclic Systems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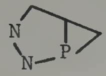

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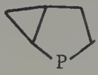
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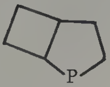
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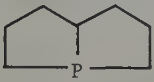
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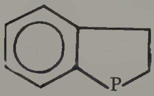
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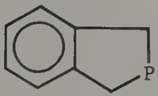
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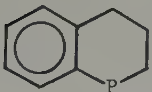
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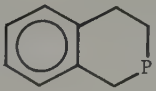
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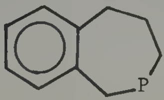
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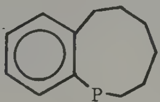
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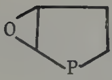

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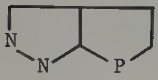

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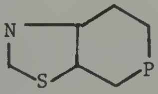

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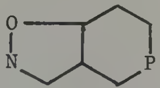

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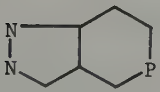

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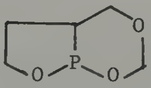

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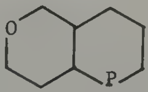
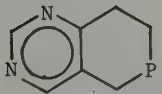
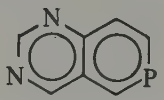


57305-53-0



39525-09-2

the parent monocycle to a heterocyclic ring has not yet produced many systems, and boundless opportunities for research can be found in such compounds. The rules of heterocyclic nomenclature give priority as parents to rings containing O, N, or S over P, as in the examples below:

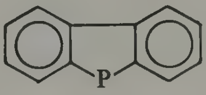


Phosphorino[4,3-d]pyrimidine

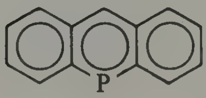
1H-Phospholo[3,4-d]isoxazole

1.1.3 Systems with Three or More Rings (Table 1.3)

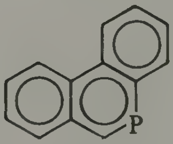
Multicyclic structures provide an active area of current research and much still remains to be done in this field. Prior to 1970, the bulk of the work had been performed on the dibenzophosphole system and indeed Mann[1] only lists nine systems



in this class, including structures with heteroatoms in fused rings. *C.A.* uses the common names for the tricyclic derivatives of the 6-membered ring:



phosphanthrene



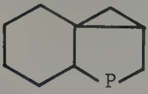
phosphanthridine

These substances are of current interest in the study of aromaticity in phosphorus cycles. Also of recent interest are tetracyclic structures having the ring arrangement of the steroids.

1.1.4 Multiphosphorus Rings (Table 1.4)

Another fast-growing area is based on the incorporation of two or more phosphorus atoms in the various cyclic systems containing carbon. The field is small, however, when compared to the vastness of the multinitrogen family, and there is only one

TABLE 1.3 Systems with Three or More Rings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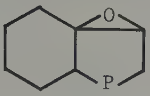
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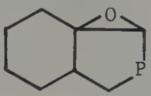
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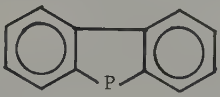
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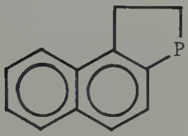
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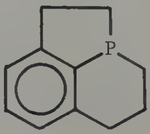
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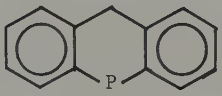
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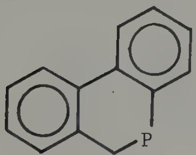
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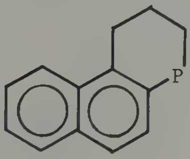
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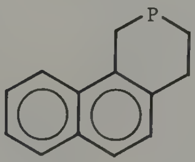
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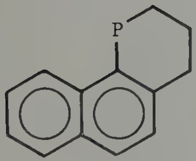
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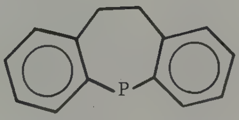
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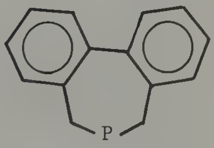
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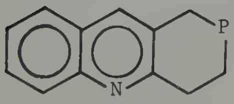
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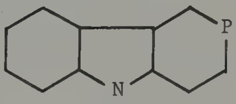
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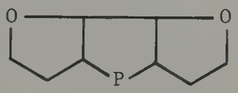
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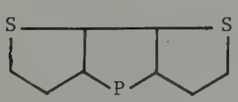
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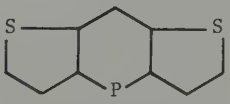
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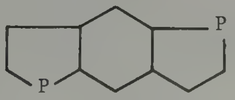
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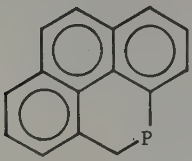

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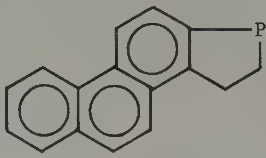

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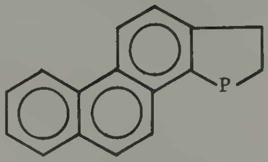

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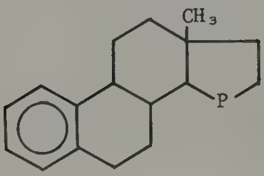

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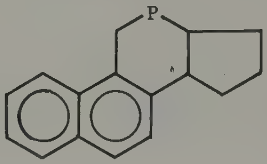

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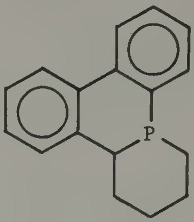

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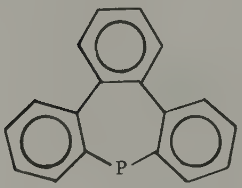

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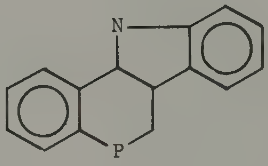

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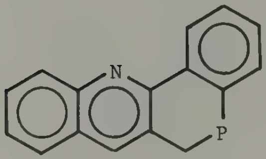

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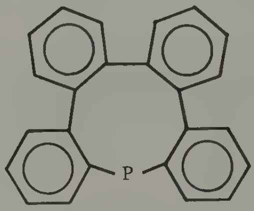

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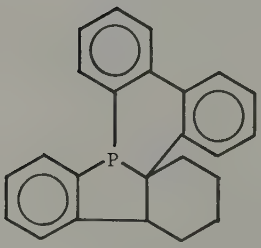

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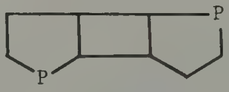

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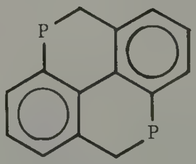

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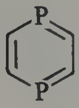
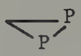
ring at present that has the complete unsaturation of an aromatic system, namely, the formal counterpart of the pyrazine system:



1,4-Diphosphorin

This aspect of multiphosphorus cyclic chemistry would seem to offer excellent opportunities for research.

TABLE 1.4 Systems with More Than One P in One Ring



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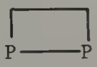

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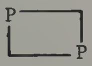

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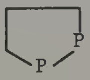
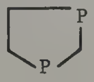


288-25-5



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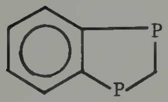

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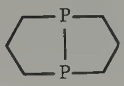

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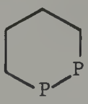

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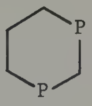

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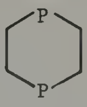

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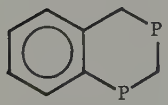

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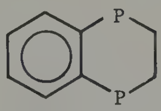

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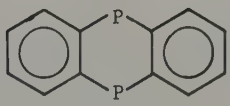

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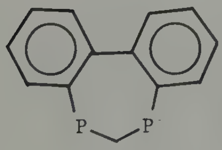

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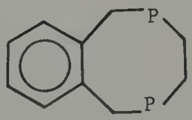

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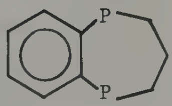

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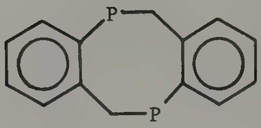

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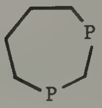

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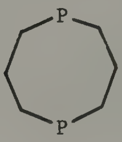

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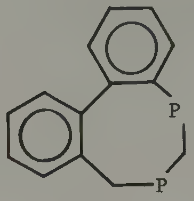

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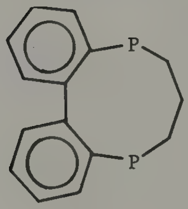

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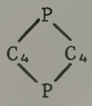

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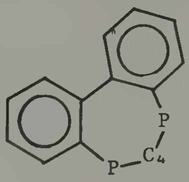

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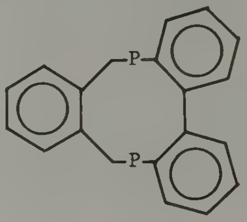

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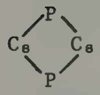

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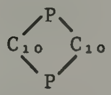

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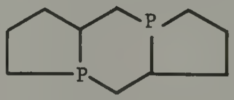

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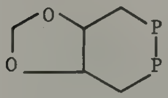

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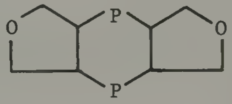

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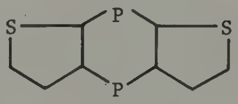

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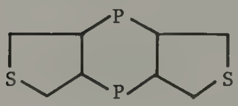

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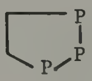

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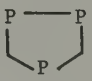

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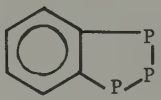

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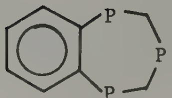

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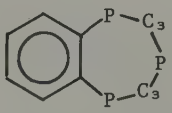

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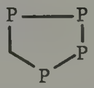

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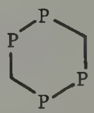

51392-73-5

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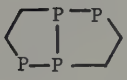

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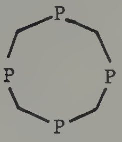

M,207

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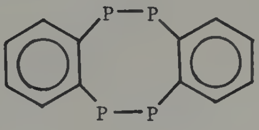

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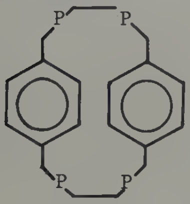

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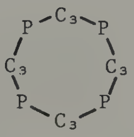

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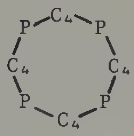

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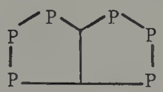
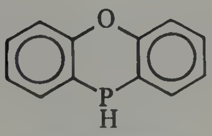


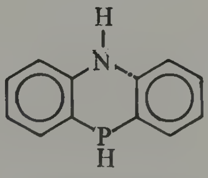
68109-27-3

1.1.5 Rings with One O, N, or S Accompanying P (Table 1.5)

Innumerable structural possibilities can result from the replacement of one or more ring carbons by O, N, or S. No effort has been made to compile a table of all such known systems; Table 1.5 includes only systems where one O, N, or S replaces a carbon of a phosphorus heterocycle. The diversity of the field is clearly delineated even by this abridged treatment, however. Bridged-ring and cage systems bearing one O, N, or S have been included in Table 1.6. Two notes on nomenclature in this class are necessary. (1) Two common names for well-known systems are in use by *C.A.* for indexing purposes:

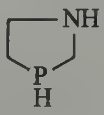


Phenoxaphosphine



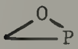
Phenophosphazine

(2) Fully saturated derivatives of 5-membered rings containing both P and N bear the suffix "idine" and are indexed accordingly.

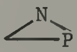


1,3-Azaphospholidine

TABLE 1.5 Systems with One P and O, N, or S

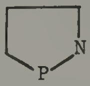


157-27-7



50510-29-7

63919-57-3



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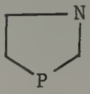
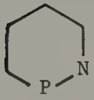
288-15-3



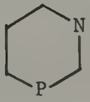
M,211

16412-97-8

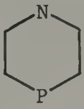


M,222

289-84-9



23135-60-6



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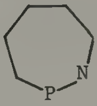
290-55-1



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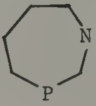

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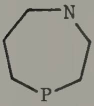
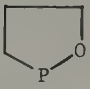


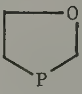
42853-92-9

287-36-5

25885-35-2



288-20-0



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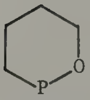

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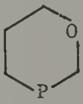
289-88-3



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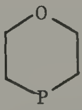

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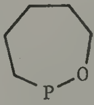
290-71-1



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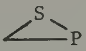

157-28-8

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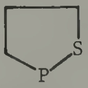

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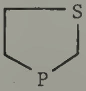

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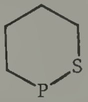

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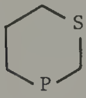

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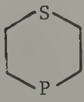

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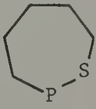

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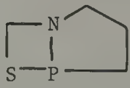

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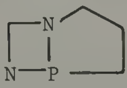

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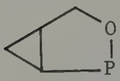

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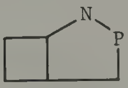

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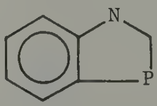
63992-71-2



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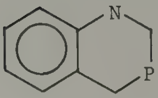

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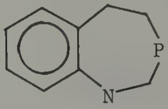

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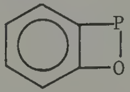

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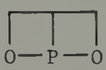

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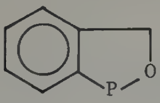

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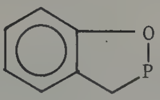

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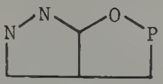

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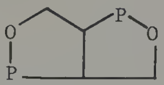

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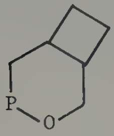

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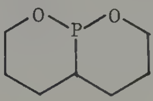

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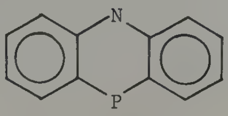

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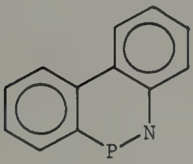
261-84-7



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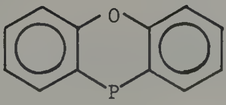
230-22-8



M,289

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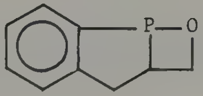

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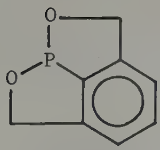
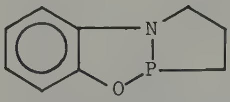
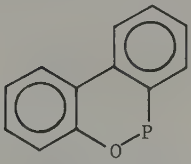


52951-59-4



63413-20-7



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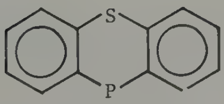

M,328

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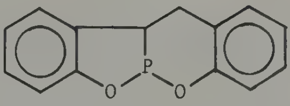

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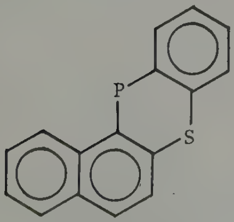
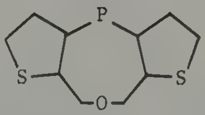


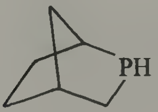
56087-62-8



53974-41-7

1.1.6 Bridged-Ring and Cage Systems (Table 1.6)

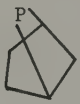
The bridging of a phosphorus-containing cycle with a fragment of one or more atoms can lead to many new structures, but only in recent years has much progress been made in this area. Mann[1] lists only seven systems; Table 1.6, which excludes several systems with more than one O, N, and S present, reveals that 63 are now known! Some of the rapid progress in this intriguing area has been the result of the application of photochemical techniques to phosphorus chemistry. The compounds are named by the carbon-replacement technique, using the prefix "phospha," as in the example below:



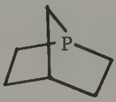
2-Phosphabicyclo[2.2.1]heptane

TABLE 1.6 Bridged-Ring or Cage Systems

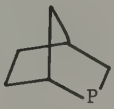
58118-12-0



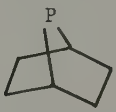
7127-55-1



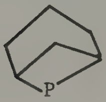
29310-25-6



61770-48-7



7616-77-5



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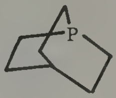

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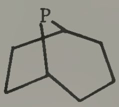

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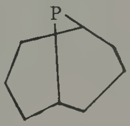

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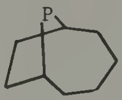

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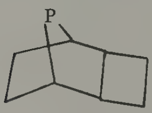

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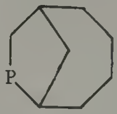

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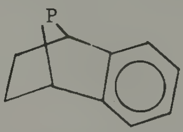

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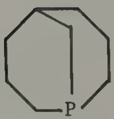

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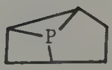

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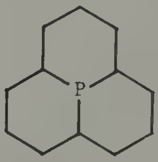

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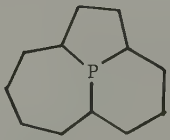

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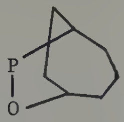

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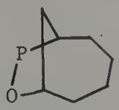

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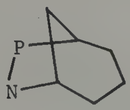

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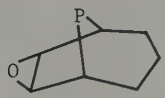

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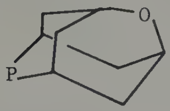

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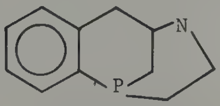

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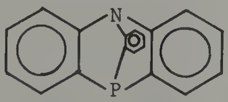

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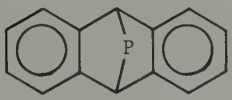

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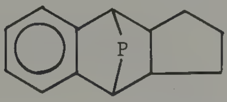

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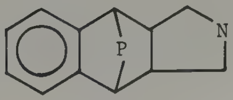

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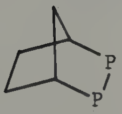

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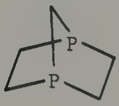

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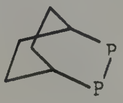

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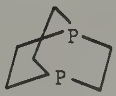

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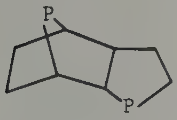

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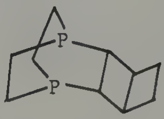

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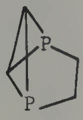

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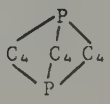

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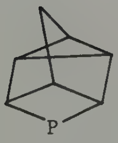

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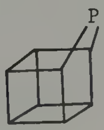

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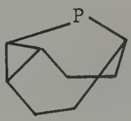

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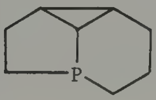

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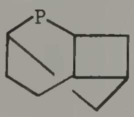

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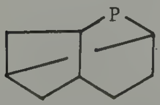

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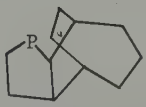

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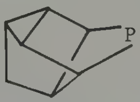

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TABLE 1.6 continued


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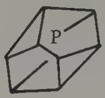
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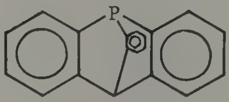
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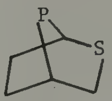
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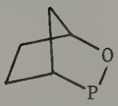
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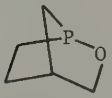
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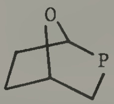
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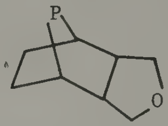
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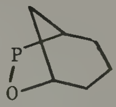
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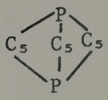
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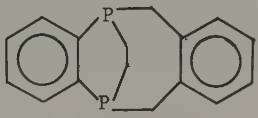
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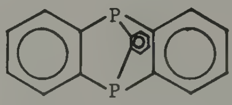
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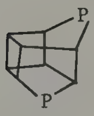
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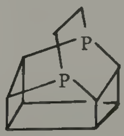
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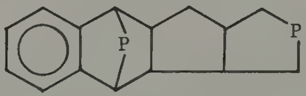
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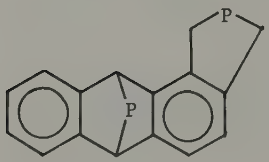
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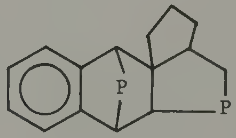
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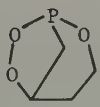
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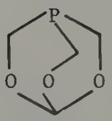
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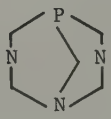
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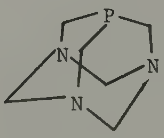
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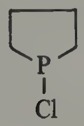
1.2. THE STRUCTURE ABOUT PHOSPHORUS IN CYCLIC SYSTEMS

Having surveyed the many ways in which the phosphorus atom can appear in rings, attention is now turned to consideration of the functionality that resides with this atom. Many possibilities exist, and a broad range of chemical reactivity, volatility, and solubility properties can be generated by modification of the phosphorus function in a given ring system. This plethora of functional groups and the complexity of the nomenclature system tends to scare off the uninitiated from entering the world of organophosphorus chemistry, but the special requirement in a ring—of having one or two bonds to carbon—has the ameliorating effect of reducing the number of functional group possibilities. Furthermore, the naming system for cyclic phosphorus compounds is much simpler than for noncyclics; any substituent on phosphorus is simply designated with a number and prefix or suffix (for multiply bonded O or S) and attached to the name of the parent heterocycle. The complexity resulting in a name by designation of the oxidation state of phosphorus, so common in noncyclic structures, does not exist here.



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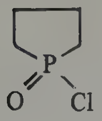
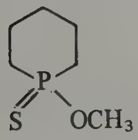
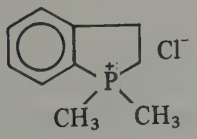


1-Chlorophospholane 1-oxide

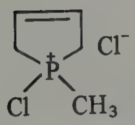


1-Methoxyphosphorinane 1-sulfide

The only other nomenclature feature to note results from the appearance of phosphorus in positively charged condition, when the heterocycle name is modified with the suffix "ium." Such compounds are indexed by *C.A.* under this heading:



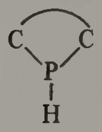
1,1-Dimethylphosphindolinium chloride

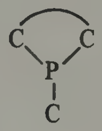


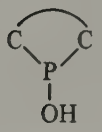
1-Chloro-1-methyl-3-phospholenium chloride

To understand the properties of the various functions, and to appreciate their similarity to the noncyclic family of organophosphorus compounds, it is helpful to recognize the class names of each of the functions, and to associate properties with them. One group of functions is easily cataloged as trivalent or P(III), where phosphorus retains a lone pair of electrons. Bonding to the lone pair can then result in a second class [tetravalent or P(IV)]. In this state, a form of multiple (π-) bonding can develop from back-donation of a lone pair on a bonding atom (usually O or S), but this is not a necessary feature of the P(IV) condition because the common atoms C and Cl lack the back-donation possibility. A third class has phosphorus in pentavalent [P(V)] condition, a situation of less common occurence in cyclic phosphorus chemistry. The nature of each of these three classes of functions is described below for the case where phosphorus is bonded to two ring carbons. Even less common but of great interest is the P(II) state, found primarily in the phosphorins; discussion of this unique form of double bond is deferred to Chapter 8.

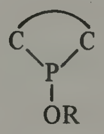
1.2.1 Trivalent Functions

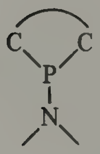

Secondary phosphine

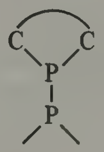

Tertiary phosphine


Phosphinous acid[a]


Phosphinous halide


Alkyl phosphinite


Phosphinous amide
or
aminophosphine


Diphosphine

---

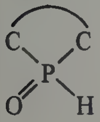
[a] Except in rare circumstances, phosphinous acids undergo a form of tautomerism [($R_2P{-}OH \rightleftharpoons R_2P(0)H$)] heavily favoring the phosphoryl form. They are, however, known in the form of esters or amides.

1.2.2 Tetravalent Functions with π-Bonding

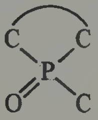
The phosphoryl group, with its π-bonding, may be expressed by various symbols, as seen below:

$$\gtrdot P{=}O \qquad \gtrdot \overset{+}{P}{-}\overset{-}{O} \qquad \gtrdot P{\rightarrow}O$$

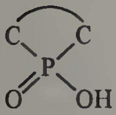
No one formula adequately expresses the structure and properties of this group; the first will be used consistently through this monograph, however. For a detailed discussion of the π-bonding in phosphorus chemistry, the recent text by Emsley and Hall[2] should be consulted.



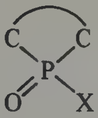
Secondary phosphine oxide



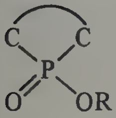
Tertiary phosphine oxide



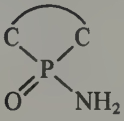
Phosphinic acid



Phosphinic halide



Alkyl phosphinate

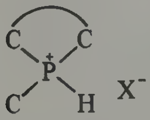


Phosphinamide

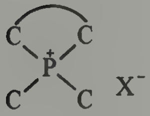
Similar structures exist where sulfur replaces oxygen, but are less common in cyclic phosphorus chemistry, at its present stage of development. With the exception of the tertiary phosphine sulfides ($R_3P{=}S$) they are not encountered in this monograph.

1.2.3 Tetravalent Functions with Positive Phosphorus

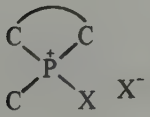
P(IV) compounds with positive phosphorus include:



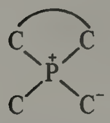
Phosphine salts



Quaternary phosphonium salts



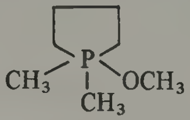
Halophosphonium halides



Phosphonium ylides or alkylene phosphoranes

1.2.4 Pentacovalent Functions

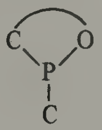
Functions of this type are routinely named as phosphoranes. The best known and most stable structures in cyclic phosphorus chemistry have more than one alkoxy group present; examples with five bonds to carbon are rare.



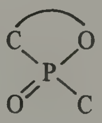
λ^5-Methoxydimethylphospholane

The "λ^5" designation is used to indicate that the phosphorus in a parent heterocycle is in pentacovalent condition.

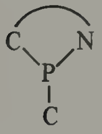
The phosphinous acid and phosphinic acid structures in the form of esters and amides are present also in cycles where phosphorus is bonded to carbon and oxygen:



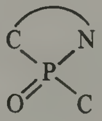
Phosphinite



Phosphinate

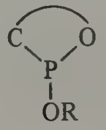


Phosphinous acid amide

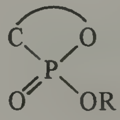


Phosphinamide

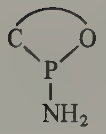
Where the external substituent is not carbon but is an alkoxy or amino group, the structure is that of the phosphonous or phosphonic acids:



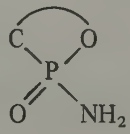
Phosphonite



Phosphonate



Phosphonamidite

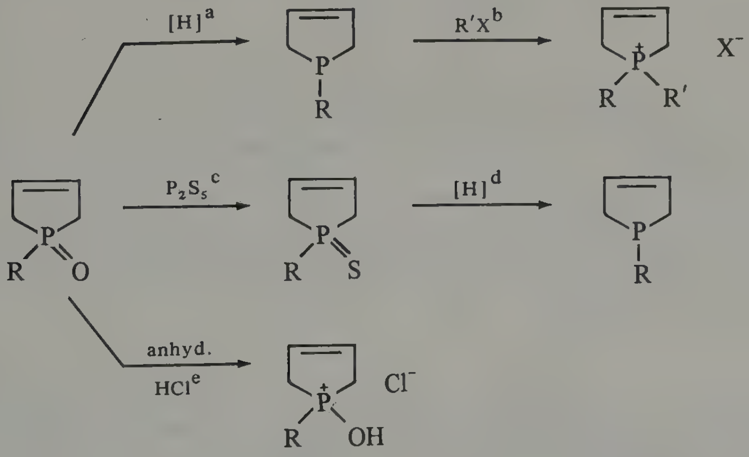


Phosphonamide

1.3 INTERCONVERSIONS AMONG THE COMMON FUNCTIONS OF CYCLIC PHOSPHORUS COMPOUNDS

Because many of the synthetic methods of cyclic phosphorus chemistry are capable of producing systems with only a single type of functionality at the heteroatom, an essential part of the field is the ability to bring about interconversions among the various functional groups wherever possible. The reactions and their conditions are frequently those that have been developed in the older and larger area of noncyclic phosphorus chemistry and have been reviewed in detail in other treatises. The comprehensive work by Kosolapoff and Maier[3] is especially valuable, and in the discussion to follow references are made to the proper volume (Roman numeral) and page of this series (designated K-M for convenience). In this section, it is shown how a few functional groups, specifically selected as those commonly formed in typical heterocyclic syntheses, can be transformed to other useful functions.

The first example is the *phosphine oxide* group, a widely encountered, highly stable function. It is especially readily formed as the end-product of the McCormack diene-RPX$_2$ cycloaddition synthesis of the phospholene system that is discussed in detail in Chapter 2. Typical transformations that have been successfully performed are summarized below:



[a] Preferred reagents are Cl_3SiH, $C_6H_5SiH_3$, Si_2Cl_6 (general reference: K-M I, 45).

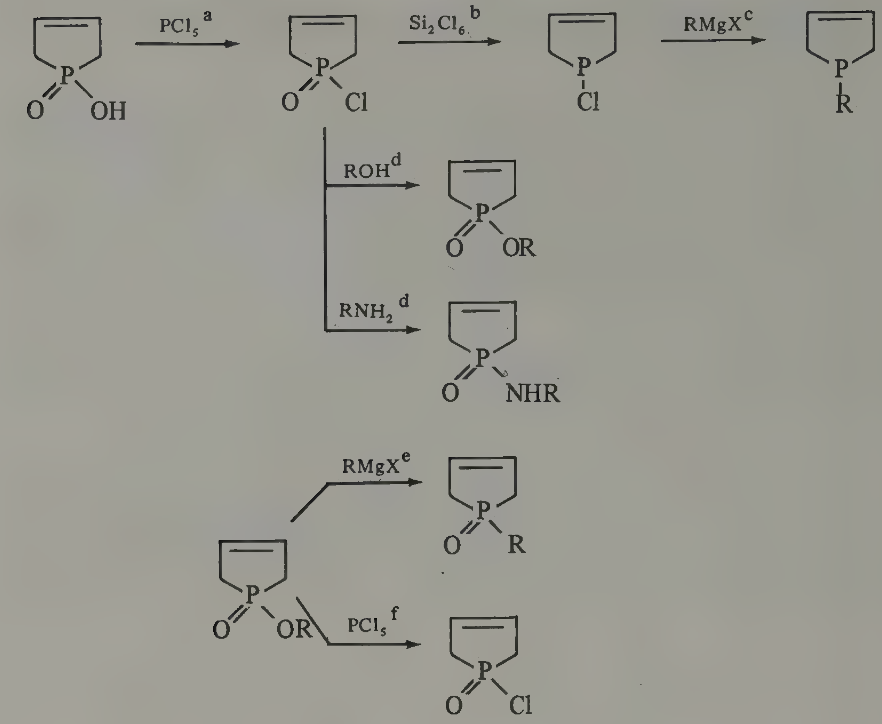
[b] A variety of 1° and 2° halides have been used in quaternizations; 3° halides generally undergo elimination (general reference: K-M IV, 190).

[c] Useful because removal of S from P is easier than O (Ref. 4).

[d] Useful reagents are $LiAlH_4$, Si_2Cl_6, etc. (K-M I, 47).

[e] The function produced is of no special value but the reaction illustrates the potential in the phosphoryl group for activity as a weak base.

The McCormack method can also produce *phosphinic acids* or *phosphinates*, which then can undergo many transformations:



[a] Other halogenating agents also are useful (general reference: K-M IV, 156).

[b] This sequence is especially useful in providing a bridge between the P(IV) and P(III) series of compounds (Ref. 5).

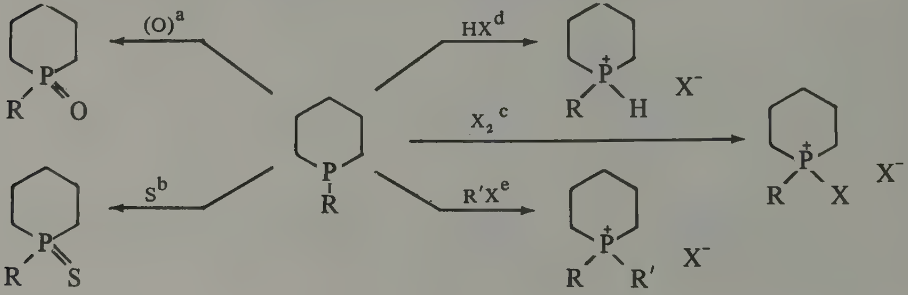
[c] Great versatility exists in the organometallic compounds that can replace halogen on P(III) (general reference: K-M I, 32).

[d] Nucleophilic displacements of halogen from phosphorus are among the best-known of organophosphorus reactions, and many possibilities exist (general reference: K-M IV, 179).

[e] General reference: K-M III, 357.

[f] General reference: K-M IV, 158.

A well-known phosphorinane synthesis (Chapter 3) produces *tertiary phosphines* directly; products derivable from them are illustrated below:



[a] Easily accomplished, even by accidental exposure to air! Commonly used reagents are 5-15% H_2O_2, m-$ClC_6H_4CO_3H$, $KMnO_4$, and so on (general reference: K-M III, 343).

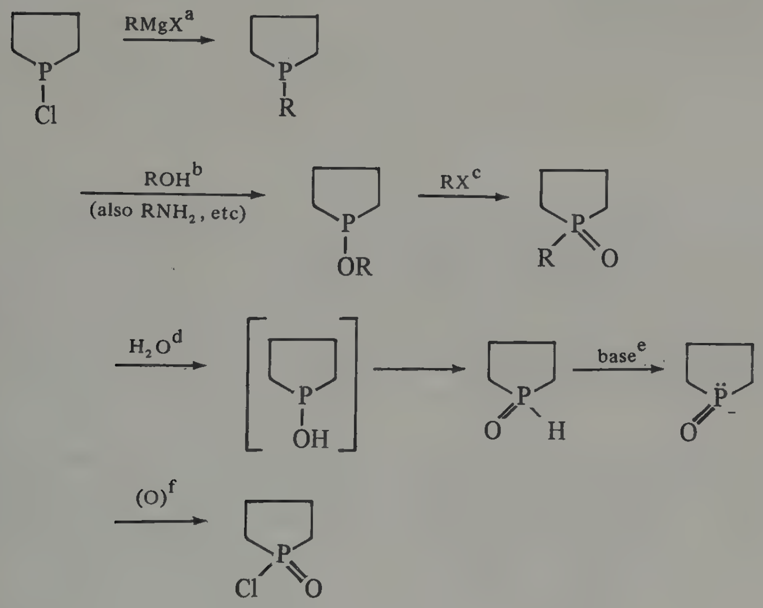
[b] A general reaction of phosphines (K-M IV, 3).

[c] A general reaction of phosphines with Cl_2 or Br_2; the products are rapidly hydrolyzed to phosphine oxides with water.

[d] Phosphines have basicity similar to tertiary amines, and are readily converted (reversibly) to solid salts; a very useful property for product isolation, as in N chemistry (K-M I, 77).

[e] General reference: K-M II, 190.

Phosphinous halides are directly produced by reaction of a di-Grignard reagent with PCl_3 or PBr_3, and are extremely reactive and useful reagents:



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[a] General reference: K-M I, 32.

[b] P(III) halides are subject to attack by a variety of nucleophiles (general references: K-M IV, 100, 473).

[c] This is the well-known Arbusov rearrangement, here serving as a synthesis of phosphine oxides (general reference: K-M III, 360).

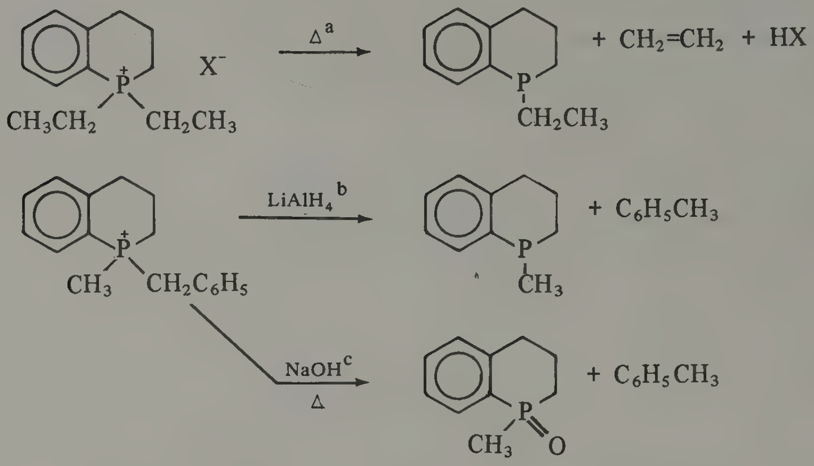
[d] P(III) halides are easily hydrolyzed; the proton of the resulting –OH group invariably migrates to P, giving a phosphoryl derivative (general reference: K-M IV, 469).

[e] Anions of secondary phosphine oxides are easily generated, and undergo alkylation, Michael reactions, and so on (general reference: K-M IV, 487).

[f] General reference: K-M IV, 165.

A useful cyclization procedure in the benzo series involves internal quaternization of an *ortho*-(haloalkyl)arylphosphine, to form *quaternary phosphonium salts.*

Though less useful than other functions for transformations, techniques have been devised for specific cleavage of one P-C bond.

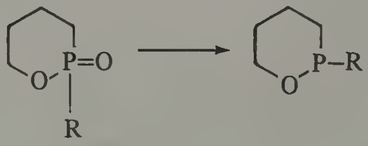


[a] Temperatures in excess of 300°C are required for such cleavages, with ethylene as the preferred leaving olefin (general reference: K-M I, 47).

[b] Benzyl groups are very readily cleaved by metallic hydrides (general reference: K-M I, 54).

[c] Generally accomplished with concentrated (20-40%) aqueous base at reflux; allyl, benzyl, and phenyl groups are the most readily cleaved (K-M III, 349).

Cyclic *phosphonates* and *phosphonamides* are more difficult to transform; for the former, cleavage of the internal P-O bond can be a special problem. Little use has been made in heterocyclic chemistry of the potential for reduction of these functions with hydrides to P(III) forms.



1.4 LABORATORY WORK WITH CYCLIC PHOSPHORUS COMPOUNDS

1.4.1 Safety

It is a matter of profound regret that the entire field of organophosphorus chemistry bears a stigma from the widely publicized toxic properties of a few highly specific structural types. The anticholinesterase activity of certain derivatives of phosphoric acid and some phosphonic acids can be extraordinarily high, and, although they are valuable insecticides, the potential for willful destruction of human beings is an ever-present threat. This biological activity, however, depends upon the alkylating ability of the phosphorus compound, and the great majority of cyclic phosphorus compounds lack this ability. Nevertheless, ester derivatives that contain very easily replaced groups should be treated as potentially toxic substances. Another well-known toxic compound is phosphine (PH_3), and again this has generated the feeling that all organic phosphines are highly toxic substances. There appear to be no firm data to support this feeling,[6] but phosphines should always be treated with special caution. Some phosphonium salts have ganglionic blocking activity[7] and can cause neuromuscular paralysis,[8] and likewise should be handled with special care. Although there can be no laboratory complacency in dealing with *any* new organic chemicals, it is likely that the problem of toxicity in cyclic phosphorus chemistry is no greater than it is in nitrogen or sulfur chemistry, and routine safety precautions and handling procedures are generally sufficient.

1.4.2 Stability and Handling

Two classes of compounds present the greatest problems in handling— the phosphines and the halophosphorus derivatives. The former are generally subject to rapid oxidation by air, and should routinely be prepared in a nitrogen or argon atmosphere. Transfers are conveniently made in glove bags, or the more elaborate dry boxes for specially sensitive materials. Phosphines that are volatile generally are malodorous, and it is common practice to submerge contaminated apparatus in an oxidizing bath (e.g., Clorox) immediately upon disassembly. Halophosphorus compounds can also be air oxidized if trivalent, but these as well as P(IV) halides have the additional problem of being water sensitive. The use of freshly dried reagents and solvents is essential in handling these materials, and again blankets of nitrogen or argon must be used in reaction vessels and for transfers.

Phosphine oxides and to a lesser extent phosphonium salts can be quite hygroscopic, and their proper handling has to take this into account. Very few of these compounds resist the usual procedures of drying, however; the use of vacuum ovens or Abderhalden pistols, or desiccation under high vacuum are all useful techniques for preparing anhydrous samples. The high polarity and hydrogen-bonding tendency of the phosphoryl group does cause some remarkable water-solubility effects, and frequently a compound with more than ten carbons will be quite soluble in water. Chloroform extraction is usually an effective way to recover such compounds, but the water solubility can be so high that continuous extraction is necessary.

Trivalent compounds are much more volatile than their tetravalent counterparts, and generally can be distilled *in vacuo*. Even some phosphine oxides, which are almost always solids when pure and dry, can be distilled *in vacuo*; the Kugelrohr technique is especially valuable for such compounds.

Phosphorus compounds can be analyzed or purified by gas or liquid chromatography in conventional ways with common materials, provided the special problems of air oxidation and hydrolysis are considered. The high polarity of phosphine oxides does make it difficult to elute them from columns with any but the more polar solvents, and frequently poor separation of similar structures results. Excellent descriptions of the chromatographic behavior of phosphorus compounds have been published by Halmann,[9a] and cyclic structures do not require any special techniques unless they involve the more unstable species, such as those of high unsaturation or ring strain.

1.5 SPECTROSCOPY WITH CYCLIC PHOSPHORUS COMPOUNDS

1.5.1 NMR Techniques

By far the most useful spectroscopic technique in cyclic phosphorus chemistry is nuclear magnetic resonance. So important are the spectra resulting from the ^{1}H, ^{13}C, and ^{31}P nuclei that the decision has been made to devote separate chapters (5-7) in this monograph to each technique. Interpretations require extensive knowledge of effects with model compounds, and these chapters are designed to provide this background. No practical work in modern phosphorus chemistry can progress far without intimate utilization of one or more of these techniques, and most current structural proof work is based directly on them. In addition, details of stereochemistry and conformation, effects of electron delocalization, and so on unfold in such studies.

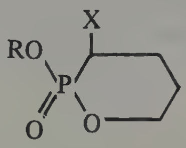
1.5.2 Infrared Spectroscopy

Infrared spectroscopy is extensively used in phosphorus chemistry to determine the nature of the phosphorus functional group, as quite characteristic signals are associated with them. In cyclic compounds, other absorption peaks arising from the carbon skeleton and other functional groups will appear in their usual ranges and generally require no comment.

Recent reviews[9b,10] of IR spectroscopy of phosphorus compounds are extremely helpful in defining the frequency ranges of the phosphorus functional groups of common heterocycles. The most important vibrations in such compounds are P=O and P=S stretching, P-O-H stretching and bending, P-O-C stretching (in exocyclic as well as endocyclic bonding), P-H stretching and bending, P-NH stretching and bending and so on. Especially useful in heterocyclic chemistry (and elsewhere) is the stretching of P=O, for the signal from this polar group is intense and normally readily visible. Thomas[10] provides tables of frequencies for several types of heterocyclic compounds, and the list is extended in a research publication.[11] In general, cyclic structure increases the P=O stretching frequency ($\nu_{P=O}$) about 30 cm^{-1} relative to noncyclic counterparts, and most heterocyclic phosphine oxides fall in the range 1170-1220 cm^{-1}. There is some correlation with ring strain because (using the more recent table[11] of data) phosphetanes and 1-phosphabicyclo[2.2.1]-

heptane fall at the high-frequency end and phosphorinanes at the low-frequency end. However, phospholane oxides have frequencies closer to the low than the high end of the range.

Phosphoryl stretching is sensitive to the electronic characteristic of the P-substituents, and the value for a given compound may be calculated remarkably well from an expression that employs additive constants for the various substituents. Of interest in heterocyclic chemistry is the replacement of C by an alkoxy group to create phosphinates, either exocyclic or endocyclic. Such a substitution invariably produces a shift of $\nu_{P=O}$ to high frequency by about 30 cm^{-1}. Two other common effects in heterocyclic chemistry are the introduction of an α,β double bond, which generally produces little change in $\nu_{P=O}$ (but definitely influences $\nu_{C=C}$ with a low-frequency shift), and cis,trans isomerism, which can be accompanied by quite pronounced effects. Thus the trans isomers of the 1,2-oxaphosphorinanes below have $\nu_{P=O}$ at about 30 cm^{-1} to higher frequency than the cis isomers[9].



1.5.3 Ultraviolet Spectroscopy

UV spectroscopy has found considerable utility in the study of multiply unsaturated cyclic phosphorus compounds. While none of the common P functions are usefully chromophoric by themselves in the near ultraviolet, interactions with π-systems do occur to shift their maxima to longer wavelength, and strong, distinct spectra appear for such systems as the phosphorins and the phospholes. These and other spectra are discussed in Chapter 8 and serve to illustrate the nature of the influence of P(III) and P(IV) groups on conjugated double bonds.

1.5.4 Mass Spectrometry

This technique is becoming increasingly important in heterocyclic phosphorus chemistry, and fragmentation patterns of a number of systems have been established. A review of the literature through about 1973[12] was recently published and, along with a slightly earlier one,[9a] provides an excellent background of the field as well as detailed treatment of the heterocyclic systems studied. Included[12] are derivatives of the phosphiranes, phospholes and fused phospholes, phosphorinanes, phenoxaphosphines, phenothiaphosphines, and benzotriphospholes. With this background, readers can develop an appreciation for the application of this powerful technique in special cases of heterocyclic structure elucidation. As a further aid to locating specific cases where mass spectrometry has been used, the supplementary tables to the *Chemical Reviews*[13] article on multicyclic phosphorus compounds are available. These tables provide references to compounds studied by this (and other) techniques. No further discussion of Mass Spectrometry is provided in this monograph; this is not an attack on its value, but an insurance that adequate room is left to cover NMR techniques, which are far more commonly used and subject to many useful generalizations.

1.5.5 Electron Spin Resonance Spectroscopy

A review of ESR spectroscopy of phosphorus compounds was published in 1977.[14] To the present, the technique has not been widely used to study heterocyclic compounds, although there are certain systems that have benefited greatly from probes of radical species by ESR. This is especially true of such delocalized π-systems as the phosphorins that can form radical cations or anions, and phospholes (radical anions). The P(V) phosphoranes based on 2,2′-phenylene or bisphenylene fusion to phosphorus have also been converted to radicals of form $R_4P\cdot$ with electron delocalization. Phosphoranyl radicals with the electron localized on P in a heterocyclic system are known in the 1,3,2-dioxaphospholane and -phosphorinane systems.

1.5.6 X-Ray Diffraction

Discussion of the application of this highly specialized but extremely useful technique in cyclic phosphorus chemistry is deferred to Chapter 8, where the results obtained for many ring systems are summarized. Suffice it to say that the detailed, fundamental knowledge of molecular architecture that can be gained from this technique has had profound impact on the development of the field in recent years, and many other problems can be solved with its application.

1.6 THE REVIEW LITERATURE OF HETEROCYCLIC CHEMISTRY

Two major sources of information have already been cited, namely, the survey of the entire field as of 1970 by Mann[1] and a 1977 review of multicyclic structures containing only carbon and phosphorus.[13] The compound tables of Kosolapoff and Maier[3] contain many references to known heterocycles along with their methods of preparation. Other reviews include the following:

K. D. Berlin and D. M. Hellwege, "Carbon-Phosphorus Heterocycles," *Topics Phos. Chem.* 6, 1 (1969); supplement, *Phosphorus* 1, 81 (1971).

M. Davies and A. N. Hughes, "Cyclic Phosphonium Ylides," *J. Heterocyclic Chem.* 9, 1 (1972).

K. Dimroth, "Delocalized Phosphorus-Carbon Double Bonds. Phosphamethincyanines, γ^3-Phosphorins and λ^5-Phosphorins," *Fortschritte Chem. Forsch.* 38, 1 (1973).

M. J. Gallagher, in *Stereochemistry of Heterocyclic Compounds*, edited by W. L. F. Armarego Wiley-Interscience, New York, 1977, Chap. 5.

R. F. Hudson and C. Brown, "Reactivity of Heterocyclic Phosphorus Compounds," *Accts. Chem. Res.* **5**, 204 (1972).

A. N. Hughes and D. Kleemola, "Phospholes, the Aromaticity Problem," *J. Heterocyclic Chem.* **13**, 1 (1976).

L. S. Khaikin and L. V. Vilkov, "Molecular Structures of Cyclic Organo-phosphorus Compounds," *Russian Chemical Reviews* **41**, 1060 (1972).

F. Mathey, "Phosphole Chemistry," *Topics in Phosphorus Chemistry* Vol. 10, edited by M. Grayson and E. J. Griffith Wiley-Interscience, New York, 1980.

L. D. Quin, "Trivalent Phosphorus Compounds as Dienophiles," in "*1,4-Cycloaddition Reactions*," edited by J. Hamer Academic Press, New York, 1967, Chap. 3.

F. Ramirez, "Oxyphosphoranes," *Accts. Chem. Res.* **1**, 168 (1968).

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1 F. G. Mann, *The Heterocyclic Derivatives of Phosphorus, Arsenic, Antimony, and Bismuth* 2nd ed. Wiley-Interscience, New York, 1970.

2 J. Emsley and D. Hall, *The Chemistry of Phosphorus* Harper and Row, London, 1976, Chap. 2.

3 G. M. Kosolapoff and L. Maier, *Organic Phosphorus Compounds,* John Wiley, New York, 1972), Vols. 1-6.

4 K. Moedritzer, *Synth. React. Inorg. Metal-Org. Chem.* **4**, 119 (1974).

5 K. Naumann, G. Zon, and K. Mislow, *J. Am. Chem. Soc.* **91**, 7012 (1969).

6 Ref. 3, Vol. 1, p. 89.

7 (a) K. H. Ginzel, H. Klupp, O. Kraupp, and G. Werner, *Arch. Exper. Pathol. Pharmacol.* **217**, 173 (1953); (b) L. Schmidt, *ibid.*, **241**, 538 (1961).

8 K. H. Ginzel, H. Klupp, O. Kraupp, and G. Werner, *Arch. Exper. Pathol. Pharmacol.* **221**, 336 (1954).

9 M. Halmann, *Analytical Chemistry of Phosphorus Compounds*, Wiley-Interscience, New York, 1972; (a) Chap. 2,3; (b) Chap. 5; (c) Chap. 6.

10 L. C. Thomas, *Interpretation of the Infrared Spectra of Organophosphorus Compounds* Heyden, London, 1974.

11 R. B. Wetzel and G. L. Kenyon, *J. Am. Chem. Soc.* **96**, 5189 (1974).

12 I. Granoth, *Topics Phos. Chem.* **8**, 41 (1976).

13 S. D. Venkataramu, G. D. Macdonell, W. R. Purdum, M. El-Deek, and K. D. Berlin, *Chem. Rev.* **77**, 121 (1977).

14 P. Schipper, E. H. J. M. Jansen, and H. M. Buck, *Topics Phos. Chem.* **9**, 407 (1977).

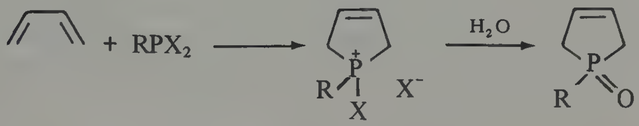
chapter two

Principles of Forming 5-Membered Ring Compounds in Phosphorus Chemistry

The 5-membered ring is by far the most commonly encountered phosphorus cyclic system, and it is fitting that a discussion of the important synthetic methods of this branch of heterocyclic chemistry begin here. That this ring is so common is the consequence of the discovery of a very simple, remarkably versatile 1,4-cycloaddition reaction that occurs between conjugated dienes and P(III) halides. The first report of this reaction appeared in the patent literature of 1953, by W. B. McCormack of the E. I. du Pont de Nemours Company; seldom have patents proved to have the impact on synthetic organic chemistry that has resulted from this work! Furthermore, the products have proved to have substantial commercial value. Especially valuable is the interaction with isocyanates; phospholene oxides are potent catalysts for the condensation to form carbodi-imides, a reaction of importance in the polymer field. Other useful methods also exist for construction of the 5-membered ring, and are included in this chapter. Techniques for forming fused-ring systems are now resulting in many novel substances, and are the subject of later sections. Many of the compounds have played important roles in studies of stereochemical and spectroscopic properties of cyclic phosphorus compounds. These studies are outside the scope of the present chapter, which is strictly devoted to reactions of synthetic value, but they are encountered frequently in Chapters 5-7 of this book. Similarly, the important subject of the delocalization of electrons in the phosphole system is deferred to Chapter 8.

2.1 SYNTHESIS OF PHOSPHOLENE OXIDES BY THE McCORMACK CYCLOADDITION REACTION

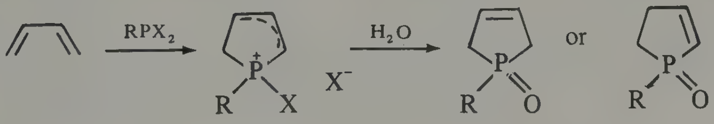
In his 1953 patents,[1] McCormack reported the synthesis and characterization of seventeen products resulting from the reaction outlined below:



Included were thirteen different dienes and eight different phosphonous dihalides. The initial cycloadducts are members of the highly reactive halophosphonium halide family; these were not isolated but were hydrolyzed to phosphine oxides. The products, properly referred to as phospholene oxides, represented a new class of heterocyclic system that was quite stable, easily handled, and purified.

This early work has been reviewed in detail,[2] as have extensions through about 1969.[3] With the advent of structural analysis by NMR spectroscopy, it became necessary to modify some of the originally assigned structures in order to allow for the double-bond migration that occurs in the initial cycloadduct[4] and hence appears in the phospholene oxides.[4,5]

The cycloaddition, however, can proceed with high product specificity, and by proper choice of the P(III) reactant and conditions it is frequently possible to obtain a quite pure sample of either the 3-phospholene (1) or 2-phospholene (2) system.

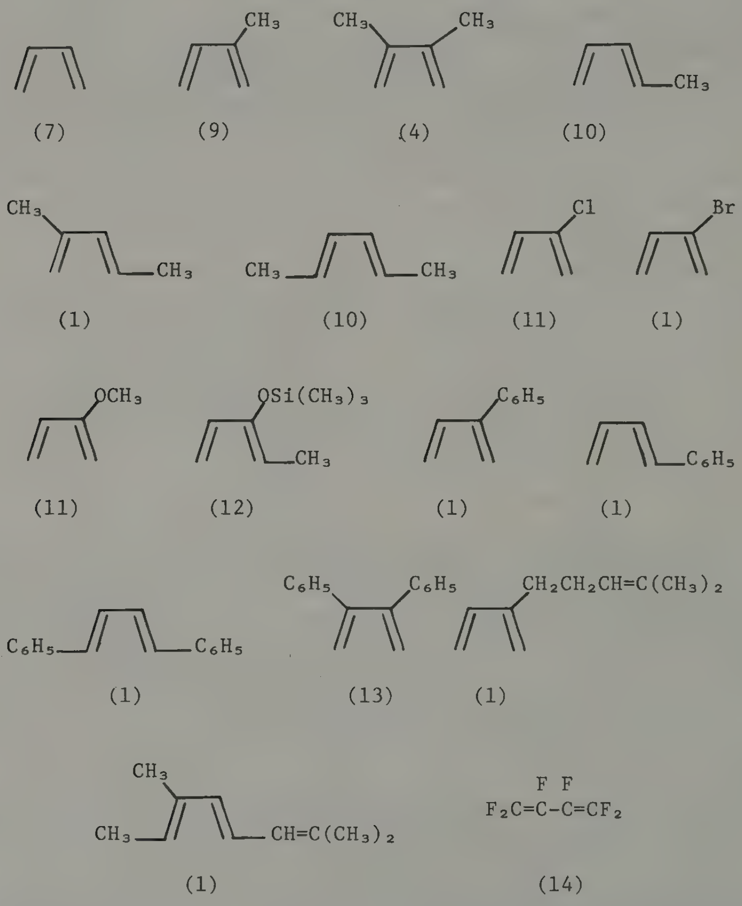


1 2

Where mixtures are obtained, separation by physical means (distillation, chromatography, or fractional crystallization) is frequently possible. The 3-phospholene oxide, unless stabilized by alkyl substituents on both sp^2 carbons, can also be rearranged with base[4] to the 2-isomer, presumably because of stabilization resulting from a form of conjugation of the double bond with the phosphoryl group. This property will be encountered again, especially in regard to its effect on NMR spectra. In some cases rearrangement can be effected by aqueous acid, or even by heat alone.[4]

The usual procedure for conducting the cycloaddition involves leaving the diene and phosphonous dihalide at room temperature for prolonged periods (days or weeks) and in the presence of a polymerization inhibitor (copper stearate or alkylated phenols are the most popular). Although some reactions have been run neat, it is more common to use a diluent such as a C_5-C_6 alkane or benzene, from which the adduct generally precipitates as a white crystalline solid, but occasionally as a dark gum. Solvents such as methylene chloride or chloroform can also be used, and will keep the adduct in solution. Other solvents (e.g., $POCl_3$[6]) have a definite rate-increasing effect. Some cycloadditions can also be run in refluxing solvent; the reaction period can be greatly reduced, but side reactions, especially polymerization, can become a serious problem with certain reactant combinations. Products of hot cycloadditions also seem invariably to have undergone the double-bond rearrangement, consistent with the proposal[4] that the rearrangement occurs at the cycloadduct stage. A very thorough study of the conditions for performing some especially useful cycloadditions has recently been published,[7-9] and should be consulted for practical advice on reaction variables.

TABLE 2.1 Noncyclic Dienes Used in McCormack Reactions[a]



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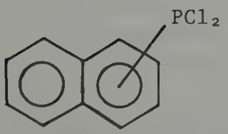
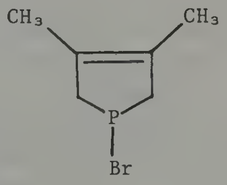
[a] Numbers in parentheses are selected literature references.

The second stage of the procedure, hydrolysis of the cycloadducts, can also be conducted in various ways, with definite influence on the ratio of the double bond isomers. If the adduct is simply added to water with no control of the high acidity or heat that develops, the product is largely or exclusively the 2-isomer. The other extreme is to hydrolyze by addition to cold, concentrated $NaHCO_3$ or dilute NaOH solution, which is preferable when the 3-isomer is the desired product. Although some (especially P-aryl) phospholene oxides precipitate from aqueous solutions on formation, others have high water solubility and require solvent extraction for their recovery. Chloroform is commonly used for this purpose. Yields in McCormack reactions are so variable as to make generalizations difficult; frequently an adduct is harvested and the mother liquor allowed to continue the reaction.

TABLE 2.2 Phosphonous Dihalides and Phosphinous Halides Used in the McCormack Reaction[a]

CH_3PCl_2	$CH_3CH_2PCl_2$	$n\text{-}C_4H_9PBr_2$	$C_6H_5CH_2PBr_2$
(15)	(16)	(17)	(18)
$CH_3(C_6H_5)C{=}CHPCl_2$	$CH_3(i\text{-}C_5H_{11}O)C{=}CHPCl_2$	$C_6H_5PCl_2$	
(19)	(19)	(8)	
$C_6H_5PBr_2$	$p\text{-}CH_3C_6H_4PCl_2$	$p\text{-}CH_3CH_2C_6H_4PCl_2$	
(4)	(1)	(20)	
$p\text{-}(i\text{-}C_3H_7)C_6H_4PCl_2$	$3,4\text{-}(CH_3)_2C_6H_3PCl_2$	$p\text{-}ClC_6H_4PCl_2$	
(20)	(20)	(21)	
$p\text{-}BrC_6H_4PCl_2$	$p\text{-}(CH_3)_2NC_6H_4PCl_2$	$p\text{-}CH_3OC_6H_4PCl_2$	
(21)	(20)	(1)	
 	$(CH_3)_2PCl$	 	
(1)	(22)	(23)	

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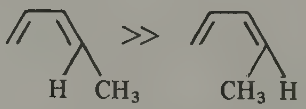
[a] Numbers in parentheses are selected literature references.

In Table 2.1 are shown the noncyclic dienes that have been used in McCormack cycloaddition and in Table 2.2 the phosphonous dihalides are found. One phosphinous chloride (R_2PCl) has also been used and forms a quaternary phosphonium salt directly; a cyclic phosphinous bromide is reported by one group[22b] to add normally to form a spiro phosphonium salt, but a different product has also been reported from such a combination (Table 2.4, reaction 5). In these tables, only selected references are provided regarding the use of a particular reactant. It should in principle be possible to obtain cycloadducts from any combination of these (and related) reactants. The position of the double bond in the products is under primary control by the phosphorus compound, and a useful correlation is that alkyl-PCl_2 reactants give high yields of 3-isomers, whereas aryl-PCl_2 gives almost exclusively 2-isomer. Aryl-PBr_2 compounds give the 3-isomer. Reaction conditions do influence the outcome, however, and the above generalities are true only for room-temperature cycloadditions.[7]

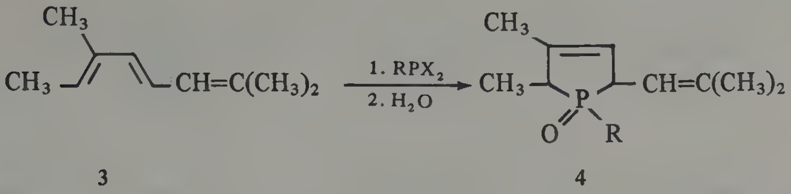
The rate of a particular cycloaddition is controlled by structural features in both reactants. Phosphonous dibromides react faster than dichlorides, with alkyl derivatives faster than aryl. In the diene, a general order of reactivity is

1,3-Dienes with a cis substituent on C-1 have not been useful in this cycloaddition; as is true for other Diels-Alder type reactions, this is probably due to a steric effect that interferes with the diene's assuming the cisoid conformation requisite for the cycloaddition to occur.



The effect is so pronounced that a cis, trans mixture of 2,4-pentadiene can be used as the reactant at room temperature and only the trans isomer will react.[10,24] Another structural limitation in the diene is that unsaturated electron withdrawing groups (-COOR, -CN, etc.) seem to prevent the reaction. This was first pointed out by McCormack, but appears not to have been tested in subsequent work. Some very valuable products would result from such dienes if the proper combinations or conditions were found.

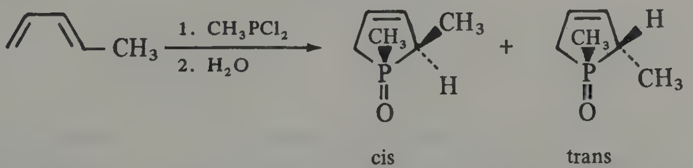
One conjugated triene (3) has been used in a McCormack reaction,[1] but at one terminus the forbidden *gem*-dimethyl group was present. This probably allowed the other two double bonds to behave in normal 1,4-cycloaddition fashion (to form 4), although the product has not been spectrally characterized.



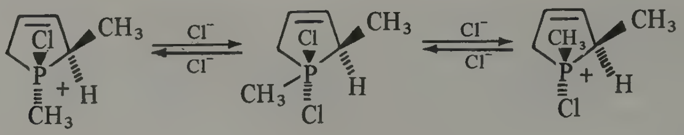
Conjugated trienes do give 1,6-cycloadducts with SO_2 in a closely related cheletropic process, [25] and it is entirely possible that such cycloaddition will occur with P(III) halides as well. There could result a valuable new approach to 7-membered rings from this extension of the McCormack reaction.

The structure of the P-substituent also influences the reaction rate. Although primary alkyl groups allow fast reactions, branching on the α-carbon seems to bring in a steric effect that retards the formation of the cyclic adduct. Thus, CH_3PCl_2 is faster in its reactions than $CH_3CH_2PCl_2$. The literature has little to say on this point but there are some unpublished observations[26] that *t*-butyl–PCl_2 will not participate in a room-temperature cycloaddition, whereas isopropyl-PCl_2 is very slow. Cyclohexyl–PCl_2 and 2-norbornyl–PCl_2 are also impractically slow. It must be pointed out, however, that no detailed study of reaction kinetics as a function of structure has yet been performed for the McCormack reaction and all observations are only qualitative.

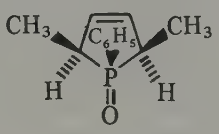
Two points of stereochemistry have importance in the McCormack reaction. First, because the phosphorus function can be a chiral center, the presence of another chiral center at C-2 of the products will result in the formation of a pair of diastereoisomers (each racemic). The first example[10,24] of this phenomenon was provided by the use of *trans*-piperylene as the diene in reaction with CH_3PCl_2.



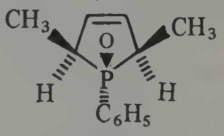
Such isomer mixtures are separable by fractional distillation or gas chromatography. The isomer ratio can be quite variable, and depends in part on the conditions used in the hydrolysis. A 1:1 ratio was obtained in the above example; from the $C_6H_5PBr_2$ adduct, cis predominated over trans by a ratio of 2:1.[10] Because of rapid (on the NMR time scale) equilibration through the pentacovalent bipyramidal form of the adduct, in which the most electronegative chlorine atoms occupy the two apical positions, the halophosphonium halides do not themselves give spectroscopic evidence of the isomerism at room temperature.[10] The separate forms can be detected, however, if the halide ion is bound in an anion such as $AlCl_4^-$ which is non-nucleophilic and unable to generate the pentacovalent form.[27]



The second point of stereochemistry appears when the product has chirality at both C-2 and C-5, for four diastereoisomers (each a racemic mixture) can theoretically result. However, only two diastereomers are in fact formed from an appropriate diene such as *trans*, *trans*-2,4-hexadiene,[10,28] and NMR studies easily reveal that both products have the cis orientation of the methyls at C-2 and C-5. The isomerism, then, occurs at phosphorus.

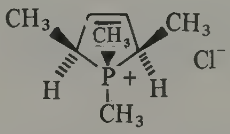


cis,cis (73%)



trans,trans (27%)

A clue to the mechanism of the McCormack reaction is provided by this observation, as well as an earlier one by Bond, Green, and Pearson,[22] who also showed the 2,5-methyls to be cis in the cycloadduct (5) of $(CH_3)_2PCl$ and the same hexadiene.



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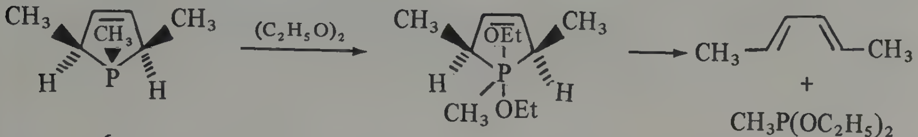
The stereospecificity of the cycloaddition suggests it to be a concerted reaction, and the formation of a *cis*-2,5-dimethyl derivative from a trans, trans-substituted diene implies that the process occurs in a disrotatory fashion. This is the expected result of a [4+2] thermal electrocyclic process, cheletropic in this case. It is the mechanism by which SO_2 adds to dienes, and by which the reverse reaction (elimination of SO_2 from the 3-sulfolene) takes place. Reversibility of the McCormack process is not to be expected, as the ionic product actually obtained is not the same as the initial cycloadduct. However, the element of reversibility for this process was established in an indirect way, by formation of a nonionizable pentacovalent 3-phospholene derivative by another approach, and then observing the stereochemistry of its decomposition.[29] This was accomplished by preparing *cis*, *cis*-2,5-dimethyl-3-phospholene (6) and adding two ethoxy groups with diethyl peroxide. The product (7) then decomposed spontaneously to form *trans*, *trans*-2,4-hexadiene, in the expected disrotatory manner. (A footnote in the same paper[29] points out that the CH_3PCl_2 adduct with this diene in very dilute acetonitrile solution does release some of the diene, suggesting that reversibility of the McCormack reaction *can* be a possibility.)



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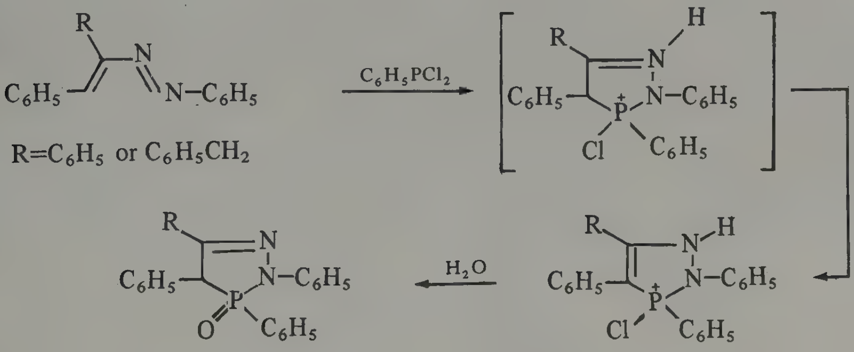
A similar fragmentation occurs when 1-phenyl-3,4-dimethyl-3-phospholene is treated with dialkyl peroxides.[30] In this study, a cyclic peroxide (1,2-dioxane) was used and also led to the reverse McCormack; in the P(V) form, the two oxygens must be apical–equatorial or equatorial–equatorial, eliminating the possibility that a diapical situation is required in the transition state.

An unusual and potentially very valuable modification of the McCormack procedure results when the diene is replaced by an azo-olefin.[31,32] Cycloaddition occurs in the usual manner with phosphonous dichlorides, and adduct hydrolysis then gives the novel 1,2,3-diazaphospholene ring system. Only a few such derivatives have been reported as yet, but much new chemistry could result from extension of this reaction.



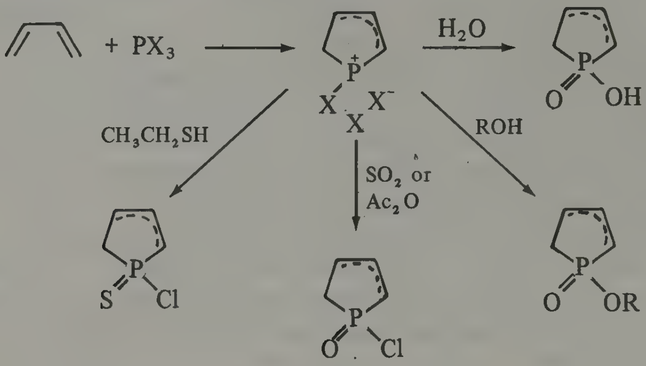
cis, trans

The initial adduct was shown to rearrange readily, as NMR revealed the ring proton to be bound to N. Hydrolysis was also accompanied by rearrangement, giving a cis, trans mixture, just as in conventional McCormack reactions.

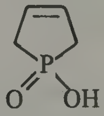
2.2 SYNTHESIS OF PHOSPHINIC DERIVATIVES OF PHOSPHOLENES BY CYCLOADDITION REACTIONS

Some ten years after the issuing of the McCormack patents, a group in Germany[33] and one in Russia[34] announced that the common inorganic halides PCl_3 and PBr_3

also underwent cycloaddition with dienes, under conditions similar to those used for RPX_2 compounds. This was a discovery of considerable practical importance; cheap, readily available substances could in one step produce a very valuable heterocyclic system, without, as before, needing to synthesize an expensive phosphonous dihalide starting material. The cycloadducts were then hydrolyzed to phosphinic acids or reacted to give other derivatives:



Hasserodt, Hunger, and Korte[33] noticed that isomeric products could be obtained from the reaction of a given diene with PCl_3 or PBr_3, and they deduced by spectrosopic techniques, as well as by ring-opening ozonolysis, that the isomer from the PBr_3 synthesis has the 3-phospholene structure whereas the 2-phospholene is formed from PCl_3. Cycloadducts from 1,3-dienes with 2,3-disubstitution are less likely to rearrange, and their isomer mixtures are dominated by the 3-form. It thus became possible to synthesize pure specimens of simple cyclic phosphinic acids such as 8 or 9 and to subject them to the conventional conversions of such acids.



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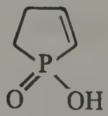

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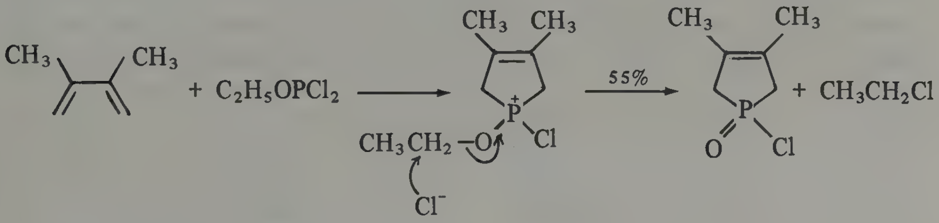
These results led this research group to reexamine McCormack products from $C_6H_5PCl_2$, whereupon it was recognized for the first time that a double-bond rearrangement could also occur in this cycloaddition.

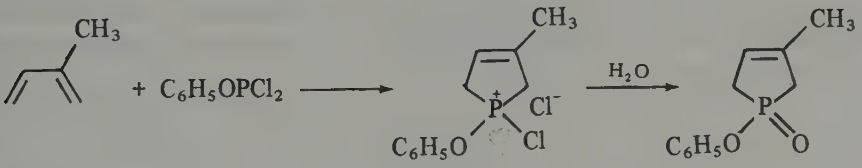
To emphasize the synthetic value of this process, the case of the PBr_3 reaction with 2,3-dimethylbutadiene may be cited. The reactants are mixed in an alkane solvent at −10°C; an 85.3% yield of the solid cycloadduct is obtained after 1 hr! However, butadiene and isoprene are less reactive as dienes, and PCl_3 is less reactive than PBr_3, so that some combinations require the several-week period typical of McCormack-type reaction. A detailed study of the PCl_3–butadiene reaction conditions has been reported by Moedritzer,[35] who achieved a yield of 86% by conducting the reaction in an autoclave at 100° for 15 hr, and then 110° for

3 hr, using $P(OCH_2CH_2Cl)_3$ as solvent. Another recent advance[36,37] is to conduct the reaction in acetone, as this gives the phosphinic chloride in one step.

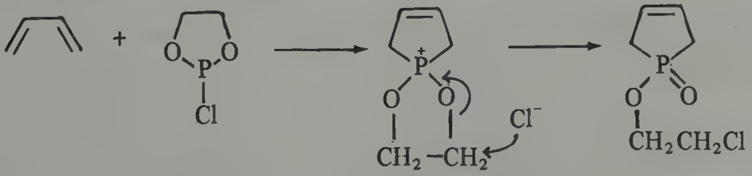
A different approach to phosphinic structures was developed independently by Russian chemists, who found that chlorophosphites also undergo cycloaddition with conjugated dienes.[21,38] The conditions required were quite different, however; reactions for several hours in sealed tubes at 100°-120°C are typical. Inhibitors again are required to prevent polymerization. It is remarkable that rearrangement of the double bond does not seem to occur in these reactions; they therefore constitute clean approaches to 3-phospholene derivatives. Alkyl dihalophosphites[21] give phosphinic chlorides directly as final products, a result of dealkylation of the alkoxy group in the initial adduct by halide ion.



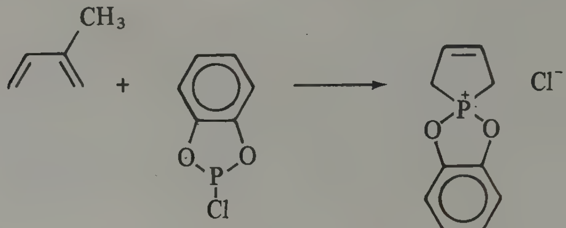
Such halides are valuable intermediates, for organometallics can displace halide and provide P-substituents that are not obtainable from the use of phosphonous dihalides. Aryl dihalophosphites form adducts whose aryl–oxygen bonds are resistant to the second stage of halide ion attack and that give phosphinates after hydrolysis.



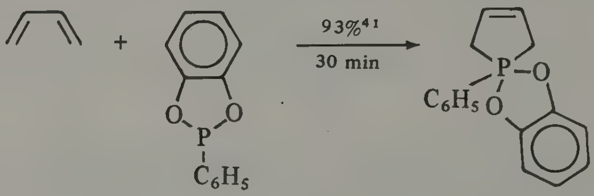
Cyclic halophosphites derived from glycols and PCl_3 have been studied extensively; as a result of the alkyl–oxygen cleavage,[38,39] they lead to haloalkyl esters of the cyclic phosphinic acids. Cyclic bromophosphites behave similarly.[40]



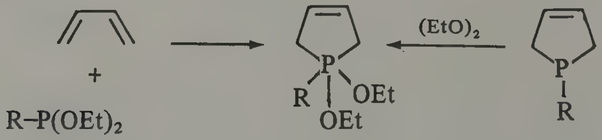
The resistance of aryl–oxygen bonds to the second-stage cleavage leads to yet another type of product when *o*-phenylene halophosphites are used; stable spirocyclic oxyphosphonium salts are formed, in yields as high as 80–85%.[39]



Although all of the cycloadditions discussed to this point have in common the fact that the initial pentacovalent cycloadduct is stabilized by loss of halide ion that drives the reaction forward, it is also possible to use glycol or catechol esters of phosphonous acids that give the initial pentacovalent adduct as a stable, isolable product. This remarkable result was announced in 1969 by two research groups.[41,42] In some cases the reaction is exothermic and complete in less than 1 hr.



The reaction has been used with both aryl-[43,44] and alkyl-[45] phosphonites; the cyclic structure in the ester seems to be essential in increasing the electrophilicity of phosphorus. Simple trialkylphosphites fail to react with dienes,[46] a result hardly unexpected, as the structure formed (e.g., **10**) would resemble that approached by dialkylperoxide addition to P(III) phospholenes, which are known to undergo retro-McCormack reaction.[29,47]



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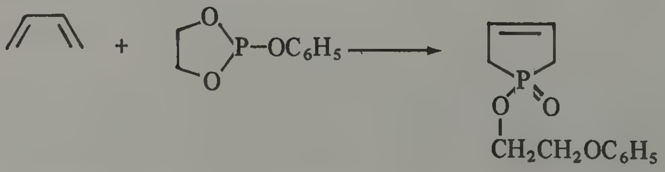
On the other, a cyclic phosphite (e.g., phenylethylene phosphite[48]) does condense to provide a P(IV) derivative:



No consideration seems to have been given yet to the stereochemistry of those cycloadditions that give stable pentacovalent forms. For example, in recent papers, piperylene was condensed with *o*-phenylene methyl-[49] or ethyl[50]-phosphonites to form the expected pentacovalent adducts; no mention was made of the possibility that cis, trans forms could result, and indeed spectral analysis of the products seemed to indicate that a single species was present. There was, for example, only one ^{31}P NMR signal reported for the P-methyl product. Acid hydrolysis is said to form 3-phospholene oxides from these pentacovalent forms, and it would be interesting to determine if *cis*- or *trans*-1,2-dimethyl-3-phospholene 1-oxide (or both) were formed. The useful test of stereochemistry with *trans*, *trans*-2,4-hexadiene has not yet been made. If stereospecific in condensations with piperylene, the method could become a valuable source of one isomer in pure form. In forming P(IV) derivatives with halophosphites, however, cis, trans isomers do develop from the use of piperylene,[51] as in the RPX_2 condensations.

The Russian chemists have given a considerable amount of effort to studying relative reactivities of dienes with various P(III) esters, and many papers have appeared on this subject. Although more is known here about such matters than about reactions involving PX_3 or RPX_2 as the dienophile, it is evident that an interplay of steric and electronic factors in both reactants is involved, making it difficult to interpret some of the trends observed.

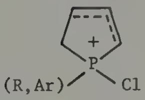
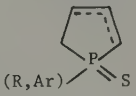
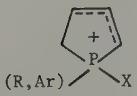
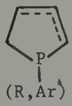
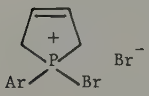
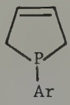
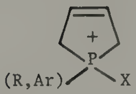
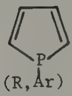
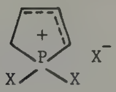
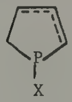
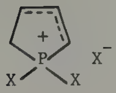
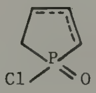
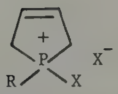
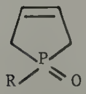
2.3 SOME TRANSFORMATIONS OF THE PHOSPHOLENE RING SYSTEM

The phospholene system is an intriguing partner in chemical reactions because of its multiplicity of sites for reaction. Many new derivatives can be formed by proper use of this reactivity, and much work has been conducted in recent years toward this end. Frequently the products are derivatives of the saturated (phospholane) system, and indeed the best approach to functionalized phospholanes is through the phospholenes. With few exceptions, the 5-membered ring is retained in these reactions; one instance of ring cleavage in phosphonium salts (1-phenyl-1-alkyl derivatives of 2- and 3-phospholenes) upon treatment with 1.7 N alcoholic KOH has been reported.[52]

An excellent general lesson in the useful reactions and properties of phosphorus heterocyclic chemistry is a benefit of a consideration of this aspect of phospholene chemistry. However, to tabulate all known reactions of phospholenes would be beyond the purpose of this chapter, whose primary concern is with synthetic methods. Reactions with synthetic value are numerous enough and it is with their description that this section is primarily concerned.

Reactions with the cycloadducts themselves are not as well known and are dominated by the high reactivity of the phosphorus function. A variety of useful substances can be prepared from them, however, and these reactions are summarized in Table 2.3. Not shown are hydrolysis and alcoholysis, types that have already received attention. The products from reactions 2-6 have a rich chemistry

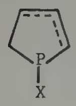
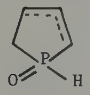
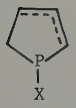
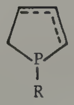
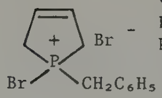
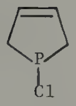
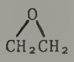
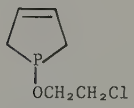
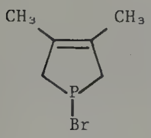
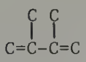
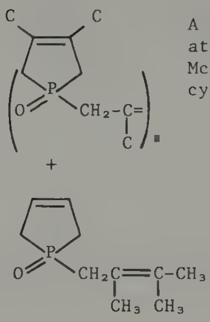
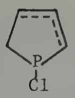
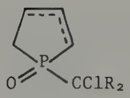
TABLE 2.3 Direct Reactions on McCormack Cycloadducts

No.	Adduct Type	Reagent	Product	Notes	Selected References
1		H_2S		Excellent route to phospholene sulfides.	1, 53, 54
2		Mg, THF		Useful P(III) synthesis (LiAlH$_4$ used also^{55}); if 2-substituent present, product is mostly *trans*.	15, 28
3		n-BuLi		Also a useful phosphine synthesis.	56
4		Diazabicycloundecene		Versatile route to phospholes.	17, 56, 57
5		$(C_6H_5)_3P$		Highly reactive to nucleophiles; useful intermediates.	58, 23
6		SO_2 or $(CH_3CO)_2O$		Also highly reactive to nucleophiles.	33
7		RCOOH + RNH_2		Other product is an amide; proposed as a new peptide synthesis.	59

of their own, in accord with their functional group types. The phospholes from reaction 4 are considered more fully in Section 2.7. The phosphinous chlorides from reaction 5 are highly useful reactants, and a summary of their known reactions is provided separately as Table 2.4.

Other P(IV) derivatives can be considered collectively, and together they present an intriguing array of reactions, mostly occurring on ring carbons rather than on phosphorus. In fact, it is convenient to categorize the reaction by the site of attack,

TABLE 2.4 Reactions of 1-Halo Phospholenes

No.	Phospholene Reactant	Reagent	Product	Notes	Selected References
1		H_2O		Provided first examples of sec. phosphine oxides of phospholenes.	58
2		RMgX		Useful alternative phosphine synthesis when RPX_2 fails in diene reaction.	18
3		$C_6H_5CH_2Br$		Unusual nucleophilic power for a phosphinous halide; product is same as from a McCormack reaction.	18,60
4					61, 62
5		 $\begin{array}{c}\mathrm{C}\quad\mathrm{C}\\ \mathrm{C{=}C{-}C{=}C}\end{array}$		A failure in an attempted McCormack cycloaddition.	63
6		$R_2C{=}O$			61

either an activated $-CH_2-$ or the phosphorus functionality, or the double bond by additions. For 2-phospholenes displacements of substituents on an sp^2 carbon are also possible.

Additions to the double are summarized in Table 2.5. It will be seen that both 2- and 3-phospholenes undergo some conventional electrophilic additions (reactions 3

TABLE 2.5 Additions to the Double Bond of P(IV) Phospholene Derivatives

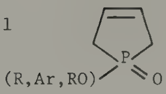
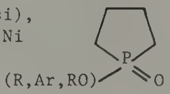
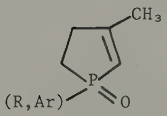
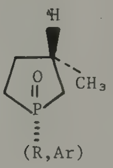
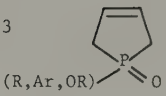
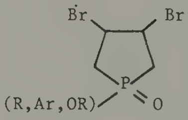
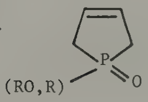
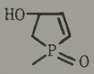
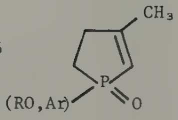
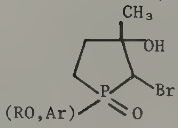
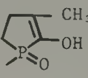
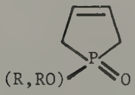
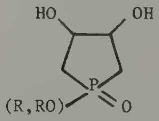
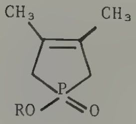
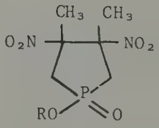
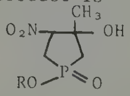
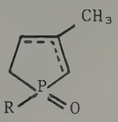
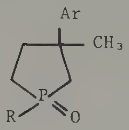
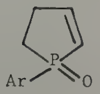
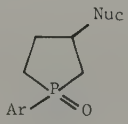
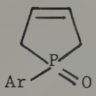
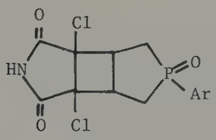
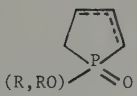
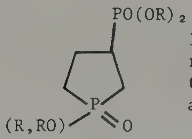
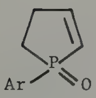
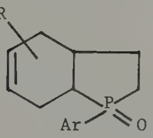
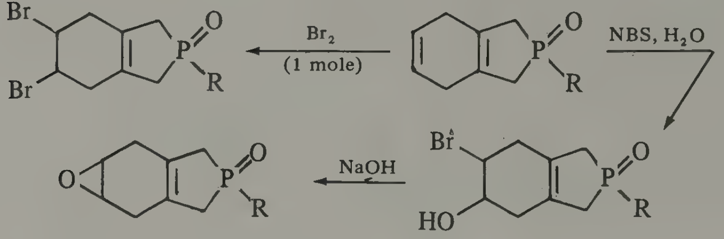
No.	Phospholene Reactant	Reagent	Product	Notes	Selected References
1		H_2 (<50 psi), Pt, Pd or Ni		H_2 approach is not regiospecific.	1,66
2		H_2 (<50 psi), Pt, Pd or Ni		H_2 approach is exclusively from P=O face.	67
3		Br_2		Useful with 2-phospholenes as well.	68,69
4		$ArCO_3H$ or CH_3CO_3H		Stereospecific; fails with monocyclic 2-phospholenes; epoxides rearranged by base to 	70,71,72
5		N-Bromoacetamide, H_2O		Forms epoxide with aq. NaOH that can be rearranged with BF_3 to 	73
6		potassium osmate, H_2O_2			74
7		N_2O_4		with 3-CH_3, product is 	75

TABLE 2.5 continued

No.	Phospholene Reactant	Reagent	Product	Notes	Selected References
8		ArH (C_6H_6, C_6H_5Cl)		Useful synthesis of 3,3-disubstituted phospholanes.	76
9		Nucleophiles: $\bar{O}H$, $\bar{C}N$, $\bar{O}R$, R_2NH		Provides useful functionality on ring.	77,78
10		dichloromaleimide, hν		Intermediate for phosphepin synthesis (Chapter 4).	79
11		$(RO)_2P(O)H$ >100°		3-Isomers presumably rearrange first, then nucleophile adds.	80,81,82
12				Useful as a phosphindole synthesis (Section 2.8).	83,84

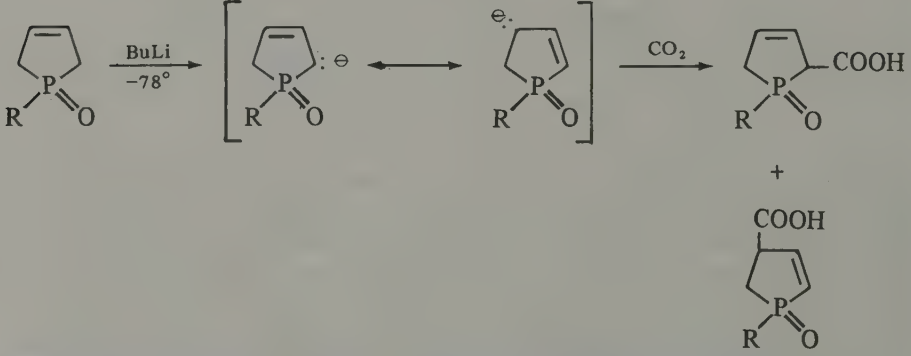
and 4), but that 2-phospholenes can also undergo additions of nucleophiles as a form of the Michael condensation (reactions 9 and 10). This reactivity is a clear consequence of the interaction of the P(IV) function with the adjacent π-system, or with a developing anion on the α-carbon that would form on addition of a nucleophile to the β-carbon. It is common to think of this interaction as involving the d-orbitals on phosphorus, but this useful concept continues to be debated (a valuable treatment of this subject has recently appeared[64]). There is strong reason to believe that the phosphoryl group contributes to deactivation of the double bond in the 3-position to electrophiles; the double bond here resists addition of

some conventional agents such as the hydrogen halides or concentrated H_2SO_4. Possibly this is due to an initial protonation on P=O to form a species ($\overset{+}{P}$—OH) that resists a second attack by H^+ on the double bond. Other electrophilic additions are much slower than would be expected for a normal double bond, a property that has been used to advantage in the selective attack on a cyclohexene moiety when fused to a 3-phospholene oxide[65]:



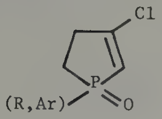
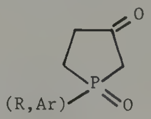
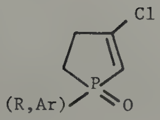
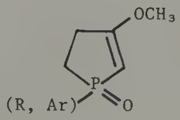
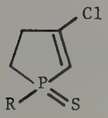
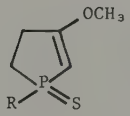
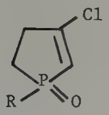
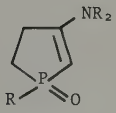
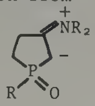
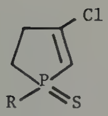
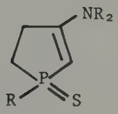
Another consequence of the interaction of P(IV) groups with adjacent π-systems or developing carbanions is seen in the facile displacement of halogen when present on the β-carbon of 2-phospholene derivatives. This activity is absent in 3-phospholenes, although frequently they can be rearranged in the course of such a reaction and then give the product of the 2-isomer. Many useful materials can be made by such displacements; those that are known are summarized in Table 2.6.

A particularly valuable property of 3-phospholenes is their ability to form carbanions at the doubly activated α-position by action of a strong base, usually butyllithium. The carbanions then react in a conventional manner to form a host of derivatives. That the double bond plays a role in delocalizing the negative charge is evident from several instances where attack occurs on a γ-carbon along with the expected α-attack, as in the example below.[88]



The basic medium then causes double-bond rearrangement into conjugation with the carbonyl group. Product separation is feasible if such mixtures are obtained. Some of the many examples are summarized in Table 2.7.

TABLE 2.6 Displacements of 3-Substituents in P(IV) 2-Phospholenes

No.	Phospholene Reactant	Reagent	Product	Notes	Selected References
1		$H_2O(H^+)$		First synthesis of a phospholanone; has high enol content.	11,85,86
2		$NaOCH_3$		Hydrolysis gives 3-phospholanones.	11,85,86
3		$NaOCH_3$		Hydrolyzed to 3-phospholanone sulfide; non-enolic.	54
4		R_2NH		Spectra show strong contribution from 	87
5		R_2NH (RNH_2)		Similar resonance to above.	87

The final group of reactions accomplishes a modification of the phosphorus functionality, again a synthetically valuable capability. Table 2.8 catalogs these useful processes.

2.4 THE McCORMACK REACTION IN THE FORMATION OF MULTICYCLIC AND BRIDGED-RING SYSTEMS

The great versatility of the McCormack reaction becomes quite obvious by its extension to dienes that are constructed around cyclic systems. Although a diene

TABLE 2.7 Reactions of Carbanions Formed from P(IV) Phospholene Derivatives with *n*-Butyllithium[a]

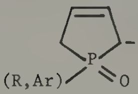
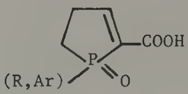
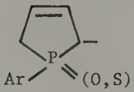
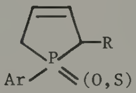
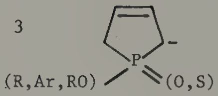
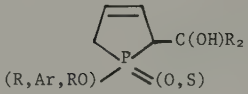
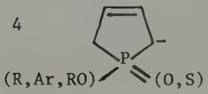
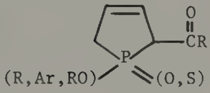
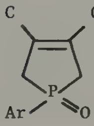
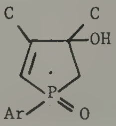
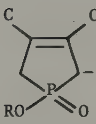
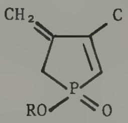
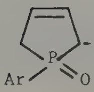
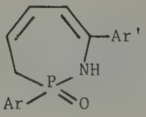
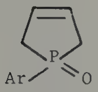
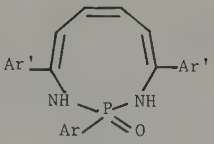
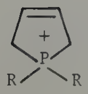
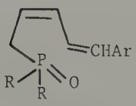
No.	Phospholene Reactant	Reagent	Product	Notes	Selected References
1		CO_2		4-COOH also forms; double bond rearranges.	88,89
2		RX		No double bond rearrangement.	89,90,91
3		$R_2C{=}O$		4-Product also forms.	89,90,91
4		RCOOR			89,91
5		O_2			92
6		O_2 then dehydration		Exocyclic double bond favored; rare isomer of a phosphole oxide.	92
7		Ar'CN		One of the few cleavages of a ring P-C; useful azaphosphepin synthesis.	93

TABLE 2.7 continued

No.	Phospholene Reactant	Reagent	Product	Notes	Selected References
8		excess BuLi, Ar'CN		Variant of No. 7.	94
9		t-C_4H_9OK, then ArCHO		Wittig reaction with a cyclic ylide. Continuation gives a triene.	95

[a]Except No. 9.

TABLE 2.8 Modification of a P(IV) Function in Phospholenes

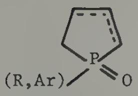
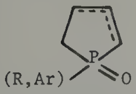
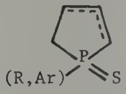
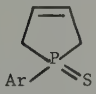
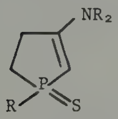
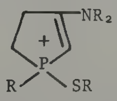
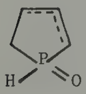
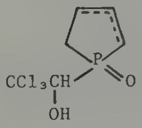
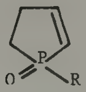
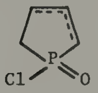
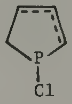
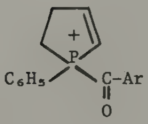
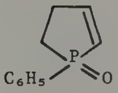
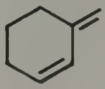
No.	Phospholene Reactant	Reagent	Product	Notes	Selected References
1		$HSiCl_3$, $H_3SiC_6H_5$, Si_2Cl_6		Highly useful route to phosphines.	96,97,98
2		P_2S_5			99
3		Nickel-locene, RX		Initial product is Ni complex, broken with NaCN.	100,101
4		RX		Unusual nucleophilicity in P=S, derived from electron release from enamine.	87
5		Cl_3CHO			58

TABLE 2.8 continued

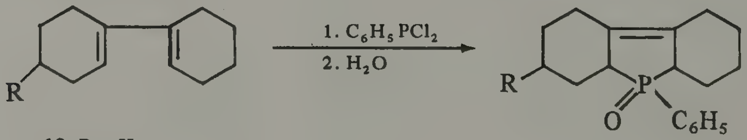
No.	Phosphole Reactant	Reagent	Product	Notes	Selected References
6		5N NaOH (1:4 H_2O-DMSO)		Most stable anion (phenyl, benzyl) is lost.	52
7		Si_2Cl_6			58
8		H_2O		Useful more for its non-P product, an aromatic aldehyde; starting salts obtained from ArCOCl + P(III) phospholene.	102

such as **11** is forbidden for obvious geometric reasons, dienes such as 1-vinylcycloalkenes, 1,2-dimethylenecycloalkanes, and even endocyclic dienes are conceivable reactants. In addition, benzo groups may be found on the cycloalkane ring, and heteroatoms may replace ring carbons. Examples of all of these possibilities are now known, and some very valuable structures of far greater complexity than those resulting from noncyclic dienes are becoming available. The field is still in its infancy, however.



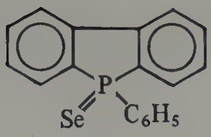
11

McCormack included[1] among his characterized phospholene oxides those derived from dienes **12** and **13**.

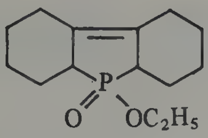


12, R = H
13, R = CH_3

The former was later used by Campbell and co-workers,[103] who subjected the phospholene oxide to dehydrogenation with selenium at 270°–380° to form dibenzophosphole 1-selenide (**14**) in 25% yield.

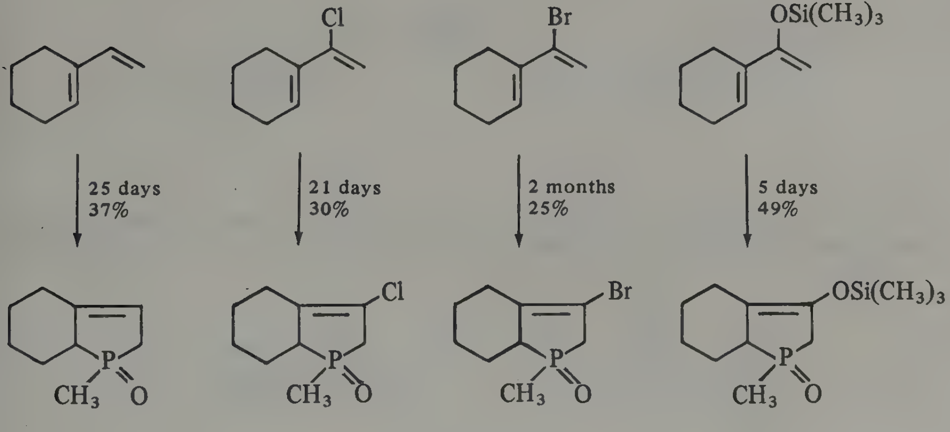


14



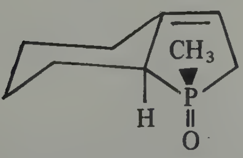
15

The cycloadduct from **12** and $C_6H_5PBr_2$ was recently prepared by Mathey and Thavard[104] for use as a precursor of the phosphole (see Section 2.7). Diene **12** was also shown to react smoothly with PCl_3, with product isolation as the ethyl phosphinate (**15**) in 75.7% yield.[33] No other type of cyclic diene was used until 1976, when the group of vinylcyclohexenes below was shown to react readily with CH_3PCl_2 at room temperature.[105]

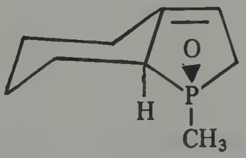


16 **17**

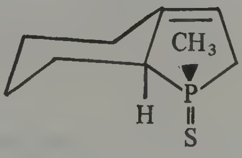
Because a chiral center is generated at an α-carbon, the product is a mixture of diastereoisomers. ^{13}C NMR techniques (see Chapter 6) allow the assignment of structure; the P-CH_3 signal is sensitive to its steric environment and is easily observed in a relatively upfield position in the more crowded cis isomers. Treatment of the cycloadducts with H_2S gave the sulfides,[54] but with remarkable stereospecificity that provided only the cis isomer (**18**).



cis

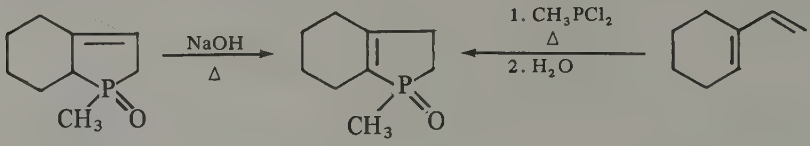


trans



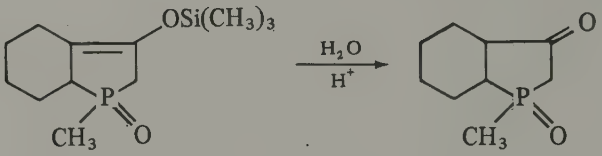
18

Compound **16** is easily rearranged with base (65%) to **19**, a compound also obtainable by conducting the cycloaddition in refluxing hexane, followed by hydrolysis (42 hr, 64% yield).



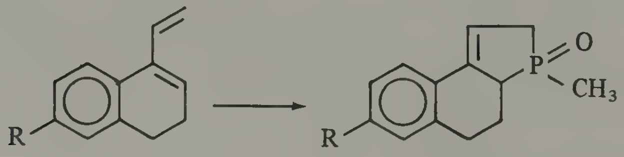
19

Compound **17** is of special interest in that acid hydrolysis smoothly converts it to the 3-keto derivative **20**. Many derivatives are potentially available from such a ketone.

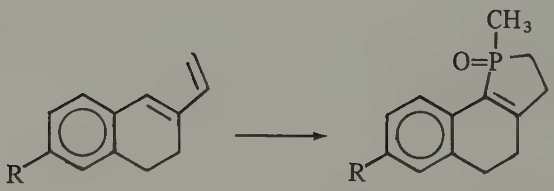


20

The same research group then applied the cycloaddition to benzo derivatives, with equal success.[105–109] Some examples are shown below:



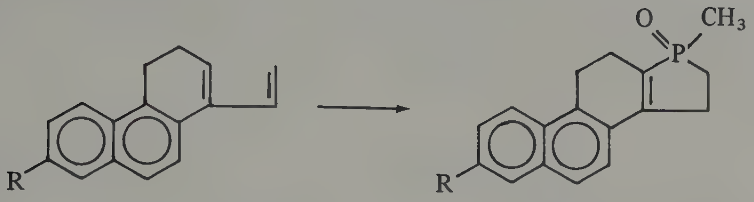
21 R = H, 56%[105]
22 R = OCH_3, 53%[108]



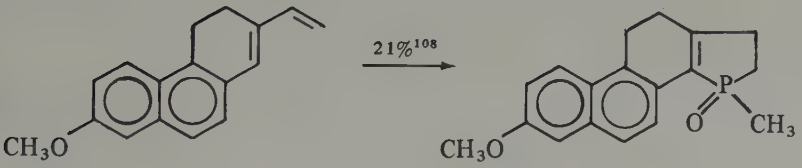
23, R = OCH_3, 37%[109]

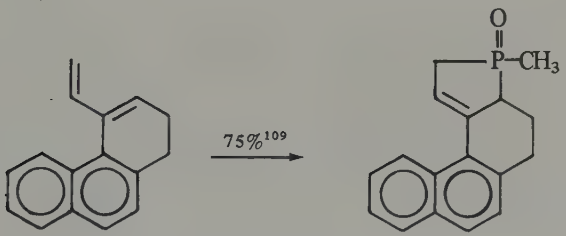
Again the double bond was easily rearrangeable to give the 2-phospholene isomer.

A further extension then led to the creation of tetracyclic systems, and here the power of the McCormack reaction for the production of the phosphasteroid system was first demonstrated.[106,108]

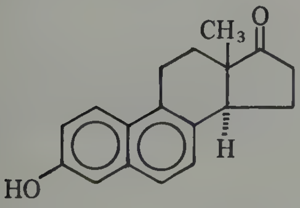


24, R = H, 72.5%[107]
25, R = OCH_3, 66%[108]

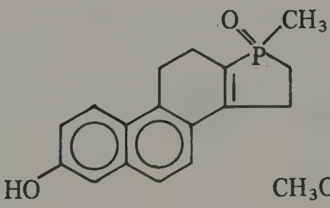




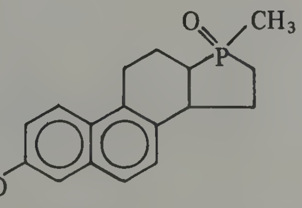
The skeleton of **25** resembles that of the hormone equilenin (**26**), a resemblance that was increased[108] by cleavage of the CH_3O group (**27**) or hydrogenation of the double bond (**28**).



26



27



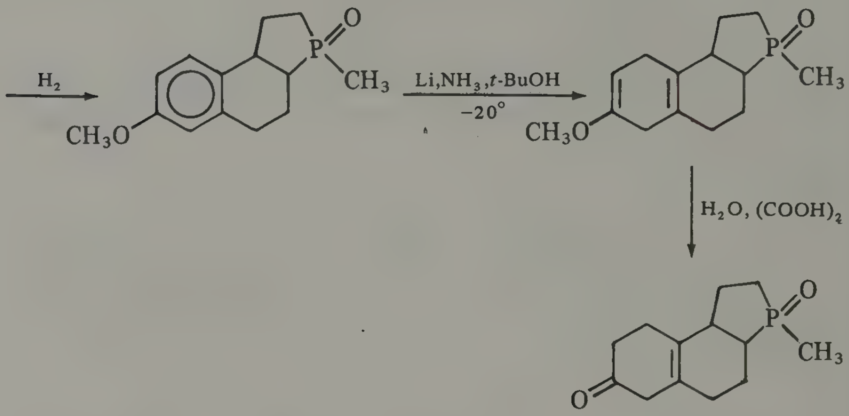
28

It is obvious that many steroids with P in the D-ring can be produced from the

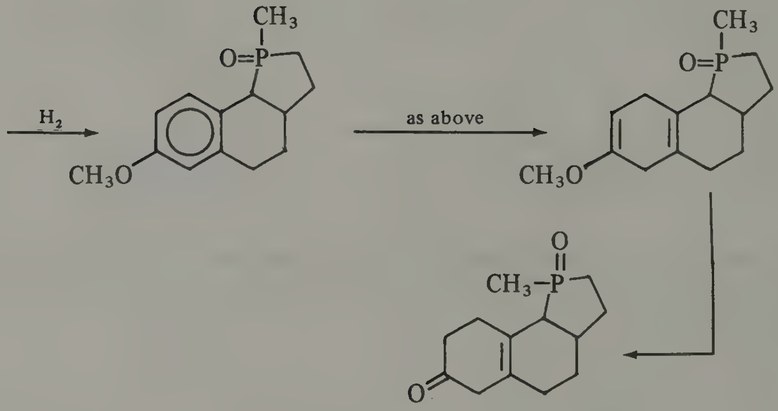
McCormack route, a task that will be made especially interesting if biological properties are found in such substances. Modifications to increase the resemblance to natural substances (e.g., installation of the angular 18-CH_3) would be of special value.

By using the Birch reduction technique (Li metal in liquid NH_3) on the hydrogenated methoxyphenyl derivatives from tricyclic compounds 22 and 23, still other novel structures can be produced.

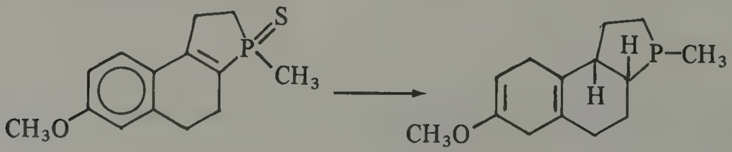
22



23



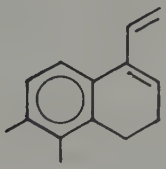
Birch conditions applied to a 2-phospholene sulfide additionally caused reduction of the styrenoid double bond and removal of sulfur, giving the phosphine 29 with presumably trans ring fusion.



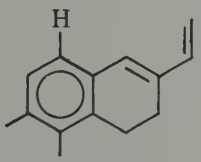
29

This represents a new reduction technique for phosphine sulfides, which may prove useful in other syntheses.

It was noticed in these studies[108] that bi- or tri-cyclic dienes of structural fragment **30** were much faster than those of structure **31** in their reaction with CH_3PCl_2.

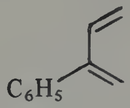


30

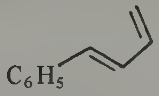


31

This may parallel an observation made by McCormack for noncyclic phenylbutadienes; diene **32** is slower in its reaction than is **33**.



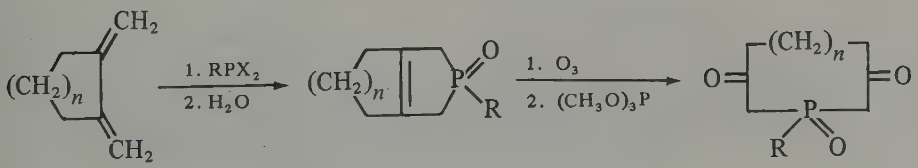
32



33

Although the presence of linear conjugation in **31** and **33** and cross conjugation in **30** and **32** may be associated with this effect through providing different orders of stability to the dienes, it is also possible that in the cyclic systems there are special steric effects that cause the difference. Thus, the presence of *peri*-like interaction between the ortho proton on the aromatic ring in **31** and the approaching phosphorus atom may retard the cycloaddition. Alternatively, steric effects may cause energy differences to appear in the bond rotation that must occur in the concerted, disrotatory cycloaddition. Regardless of origin, it is clearly an effect that interferes with McCormack cycloaddition as a means of obtaining certain types of multicyclic structures.

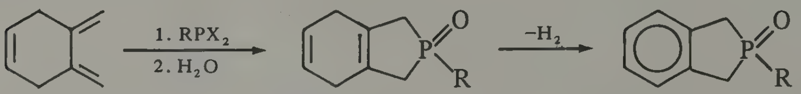
McCormack mentioned in his original patent that 1,2-dimethylenecyclohexane would participate in the cycloaddition, but no definite product was described. Recent work[110] has shown that such dienes cycloadd exceptionally rapidly, and an important use has developed for bicyclic phospholene oxides so obtained. These substances are smoothly cleaved by ozone to form ring-expanded phosphine oxides, making possible the construction of many new phosphorus heterocycles.



n = 0, 1, or 2

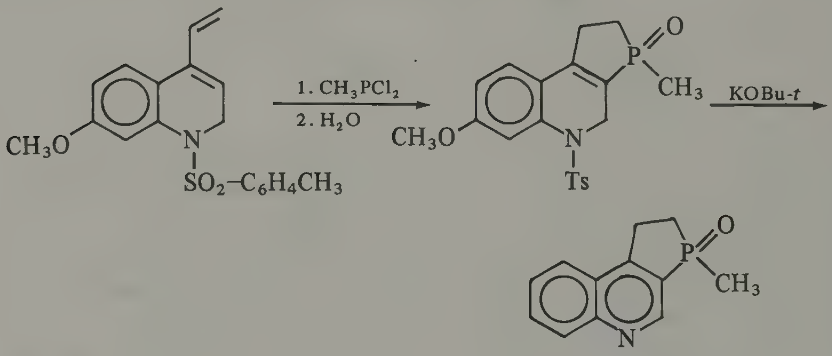
These new large-ring systems are discussed further in Chapter 4, but it is obvious that a powerful new use of the McCormack reaction is contained in this sequence.

Yet another application of bicyclic McCormack products was developed from the observation that 4,5-dimethylene cyclohexene also condensed smoothly with P(III) halides.[65]



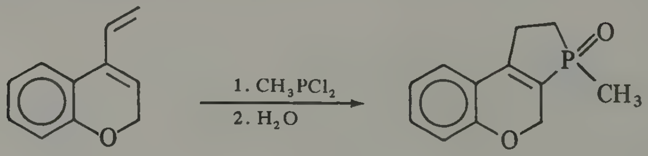
These phospholene derivatives could be dehydrogenated to form isophosphindolines in good yield; this new isophosphindoline synthesis is discussed further in Section 2.8.

The concept of including a heteroatom in a ring that is part of the diene has only recently been tested, but can open up pathways to entirely new types of heterocyclic systems. The feasibility of this approach was amply demonstrated by the cycloaddition of a vinyl dihydroquinoline derivative[111]:



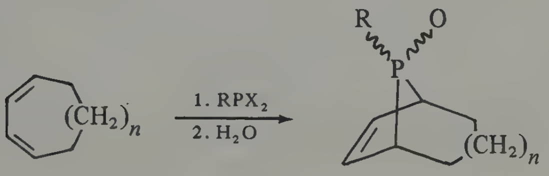
34

The cycloaddition proceeded with excellent yield (75%). Aromatization of the dihydropyridine ring was then effected by elimination (82%) of the N-protecting group as $CH_3C_6H_4SO_2H$, forming a new heterocyclic system (34) comprised of a phospholene group fused to quinoline. The cycloaddition method is applicable to the corresponding oxygen heterocycle, but in modest yield (11–15%). The diene in this case is very easily dimerized, which reduces the yield. This is a problem that will likely be encountered again with the introduction of these unique dienes to the McCormack reaction.

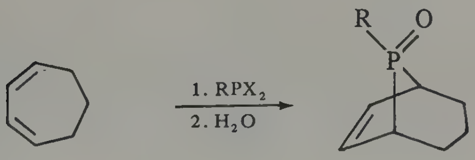


Many new mixed heteroatom systems can be conceived as arising from this approach, and if combined with the ring-opening ozonolysis it would not be limited to the construction of only 5-membered phosphorus rings but 9-membered rings as well.

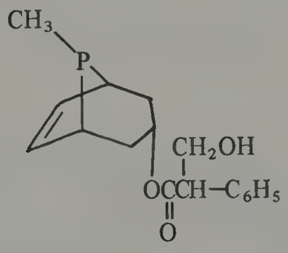
Another novel use of the McCormack reaction has resulted in bridged bicyclic systems. This rests upon the use of an endocyclic diene, which when of the proper ring size can add a P(III) reactant in the usual way.



The only success achieved so far with this approach has been with the C_7 diene (n=1); Awerbouch and Kashman[112] showed that cycloaddition occurred with RPX_2 as readily as with many noncyclic dienes, although PBr_3 failed to react. With $C_6H_5PCl_2$, a single isomer was obtained, with the stereochemistry shown below. With CH_3PCl_2, this isomer predominated in a 2:1 mixture with the other isomer.

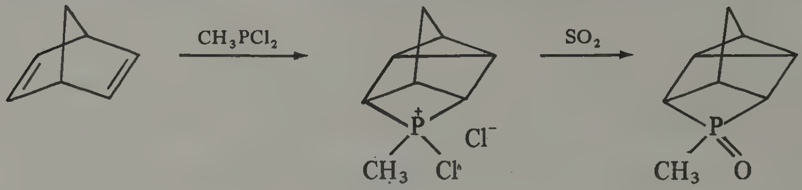


A number of the usual reactions of phospholene chemistry were applied successfully to these new compounds. An intriguing derivative included in this study is the phosphorus analog of tropine:



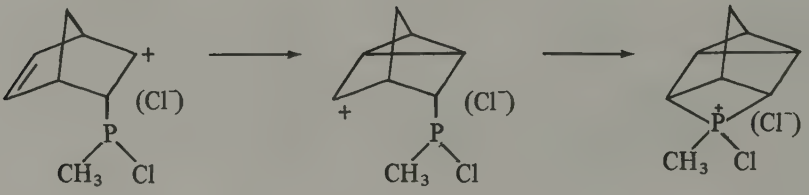
Earlier attempts to employ cyclopentadiene[1] and 1,3-cyclooctadiene[15] in condensation with CH_3PCl_2 failed. The latter diene is also known[113] to act poorly in conventional Diels–Alder reactions because of conformational effects that interfere with the attainment of the proper geometry. However, endocyclic dienes of other ring sizes remain to be explored and could become sources of other bridged-ring phosphorus compounds.

Although not a true conjugated diene, norbornadiene has been found[114] to give a product with CH_3PCl_2 that is of interest because of its unusual cage structure.



35

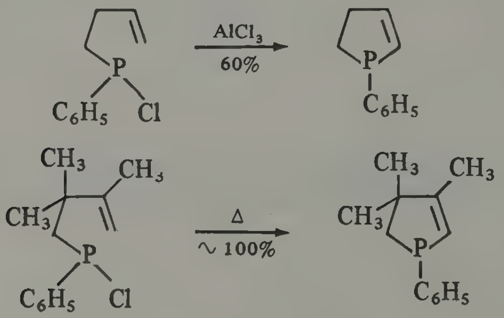
This synthesis has been repeated recently[115]; yields of 35 have been improved, and various derivatives, including stereoisomers at P, have been prepared. The reaction would appear to depend on electrophilic character in CH_3PCl_2 creating a carbonium ion intermediate that allows the familiar bridging characteristic of the norbornadiene system to set in:

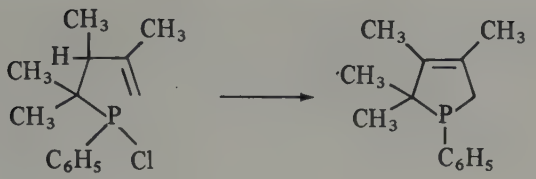


2.5 OTHER SYNTHESES OF PHOSPHOLENES

Although phospholene chemistry is dominated by the cycloaddition reaction in its various forms, other methods do exist for the synthesis of the ring systems, and they need brief mention to close out the discussion of this fascinating ring.

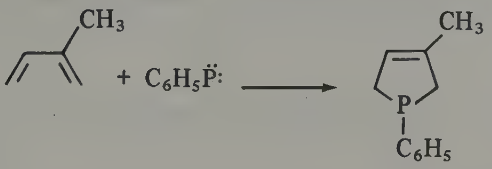
Heating at 150°, or treatment with chlorine or $AlCl_3$, causes cyclization of alkenyl phenylphosphinous chlorides.[116]



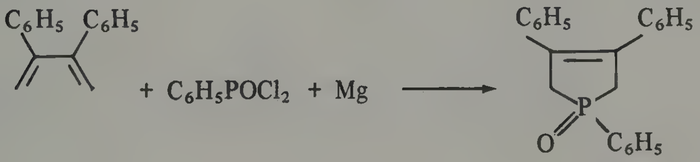


The 2,2-dimethyl feature in the last structure is of special significance, for it cannot result directly from any McCormack-type cycloadditions due to the steric congestion problem. The starting methylated phosphinous chlorides are readily obtained from phosphetanes (see Chapter 4) and the overall method has practical value.

Another phospholene synthesis depends on a cycloaddition with dienes of a rare P(I) reactant, phenyl phosphinidene.[117] The phosphinidene is produced in the presence of the diene by heating pentaphenylpentaphosphine at 150°–180° for 20 hr. The reaction does not broaden the scope of phospholene synthesis but is of interest in the unusual nature of the dienophile. Yields are in the 10–25% range.



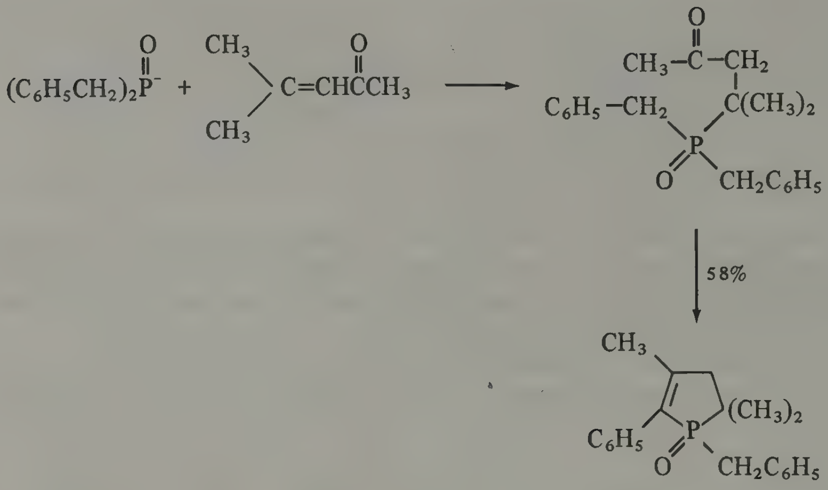
The oxy or thio forms of phenylphosphinidene have also been generated[118] in the presence of simple dienes, but they tend to give 6-membered rings from Diels–Alder cycloadditions. In one case, however, a low yield (10%; 37% after allowance for recovered diene) of a 3-phospholene was obtained.



36

This reaction is easily carried out (in THF, 1 hr with cooling), and the phosphorus reagent is readily available, but this method is not competitive with the McCormack route to obtain the 3-phospholene oxide from the same diene; a yield of 80% of **36** was obtained from the diene and $C_6H_5PBr_2$ on heating at 50° for two days.[118]

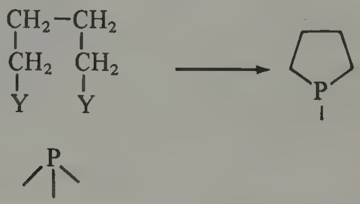
A more versatile new method[119] depends on an intramolecular aldol condensation of a CH_2 group doubly activated by phosphoryl and phenyl to close the 5-membered ring. The requisite starting compounds are derived from Michael condensation of the anion of secondary phosphine oxides with α,β-unsaturated ketones.



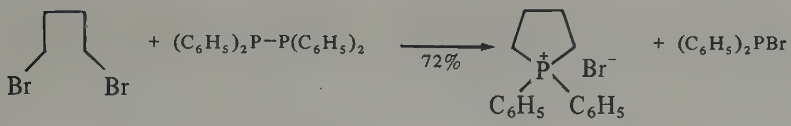
Several examples of this cyclization were given. Especially valuable is the ability to generate the α,α-disubstituted derivatives forbidden in the McCormack route.

2.6 PHOSPHOLANES AND PHOSPHOLANOLS FROM DIRECT CYCLIZATION PROCEDURES

The phospholane ring had been known for nearly 40 years[120] before the discovery of the McCormack reaction and the utility of its products for transformation to phospholanes. The first pre-McCormack approach, one that has been modified in various ways over the years, starts with a difunctional 4-carbon fragment and requires twofold attack by some phosphorus species.



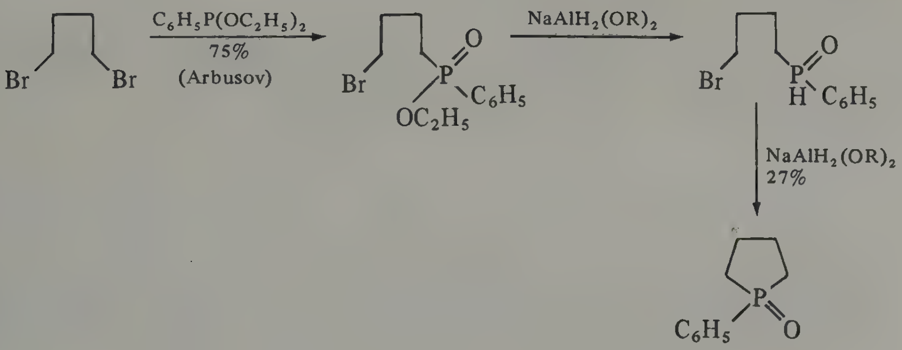
Where Y is BrMg-, a phosphonous dihalide is then used,[120] but as can be expected of a di-Grignard the yield is low. More recently, CH_3PSCl_2 has been used,[121] providing a synthesis of phospholane 1-sulfides directly. If Y is halogen, the P species can be a metallic phosphide of a primary phosphine ($C_6H_5PLi_2$,[122] 30%), or a primary phosphine in the presence of base ($C_6H_5PH_2$,[123] 32%). Yet another approach employs a disubstituted P fragment,[124] resulting in phosphonium salt formation. The fragment $[(C_6H_5)_2P]$ is derived from heating the diphosphine in the presence of a dihalide.



Such quaternary salts are subject to phenyl cleavage by NaOH and are useful precursors of phospholane oxides.

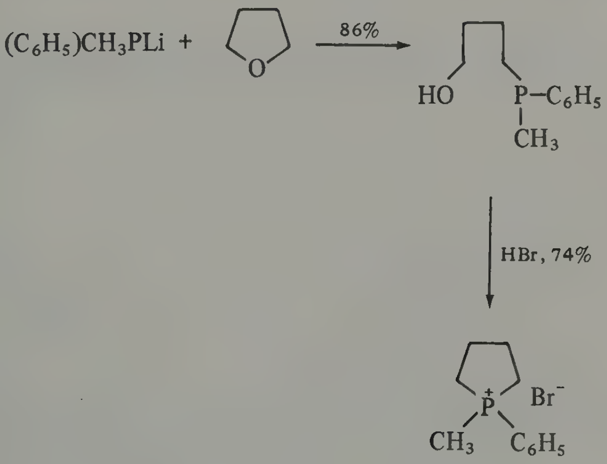
More recent syntheses of phospholanes are based on a two-step approach, first generating a 4-substituted butyl group on a suitable phosphorus function for a distinct second-stage cyclization.

1 (Ref. 125)



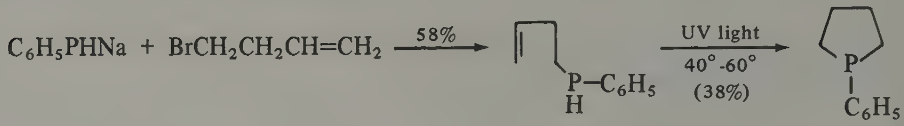
The aluminum hydride has R=$OCH_2CH_2OCH_3$; it is a commercially available mild reducing agent that functions here first to displace $-OC_2H_5$ by $-H$ from phosphorus and then to generate an anion from the secondary phosphine oxide.

2 (Ref. 126)

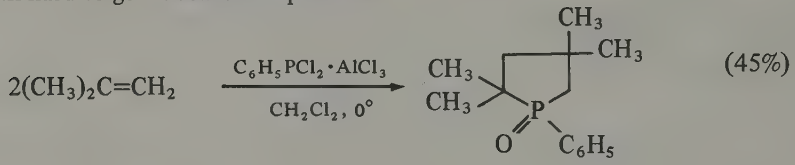


The intermediate alcohols of this route are isolated and then cyclized in a second step. Four other phospholanium salts were prepared by this method.

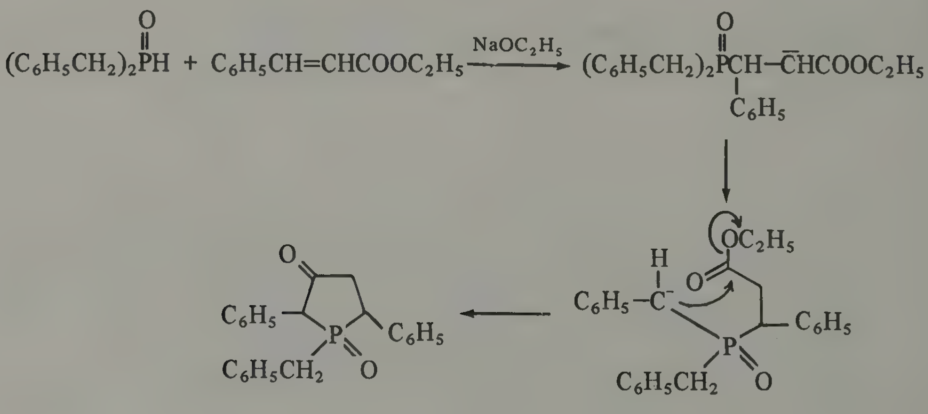
3 (Ref. 127)



A method depending on the dimerization of an olefin to produce the 4-carbon fragment of a phospholane has just been announced.[128] The scope of the reaction has not yet been explored, but it could become a valuable source of phospholanes with hard-to-get substitution patterns.

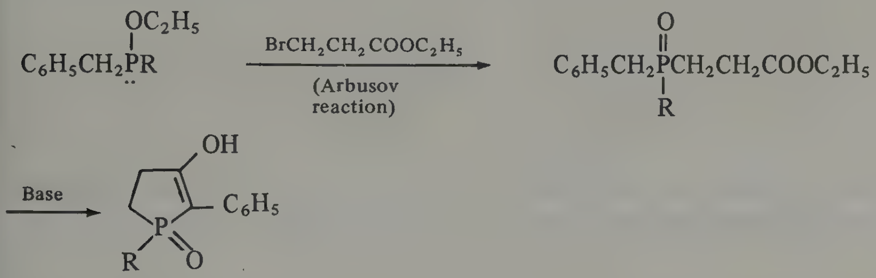


Many of the above methods are also capable of producing 6-membered rings by using the proper fragment. The methods are not readily extended to preparing C-substituted rings, and are surpassed in versatility by approaches via phospholenes. Cyclizations have recently been announced, however, that do overcome this limitation by producing 3-keto derivatives of phospholanes (3-phospholanones). Indeed, such compounds first became accessible from McCormack products (hydrolysis of 3-methoxy-2-phospholene oxides[11]), but the new approach[129] has considerable versatility and the distinct advantage of being able to form valuable multicyclic structures. Eight new phospholanones were initially reported in 40–70% yield. (The method resembles one already described[119] that uses keto rather than ester derivatives and results in 2-phospholene formation.)

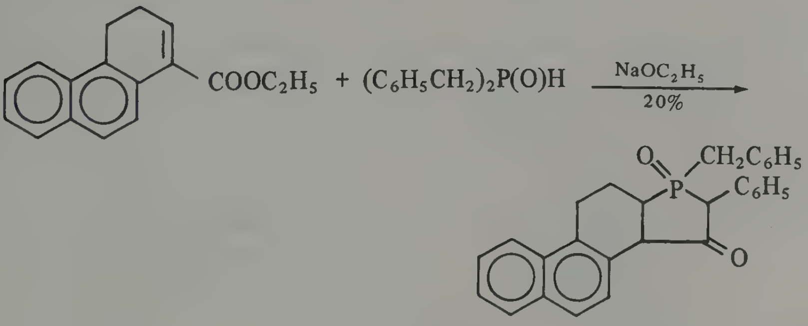


37

The same synthesis was developed separately by another group[130] and provided valuable spectroscopic data. The starting secondary phosphine oxide must have at least one benzyl group; by rearrangement, this leads to an anion (such as **37**) that attacks the ester group to close the ring. The high enolic character first seen in 1-methyl-3-phospholanone[11] appeared in many of the compounds. It is in part a result of conjugative phosphoryl stabilization of the double bond, but also a consequence of the strong hydrogen-bonding ability of this group, acting to stabilize the enol. Indeed, the enol character is so strong that another new synthesis[131] of 3-phospholanones reports them as 3-hydroxy-2-phospholene oxides. This synthesis involves a similar cyclization to that just presented but derives its starting materials from a different source.



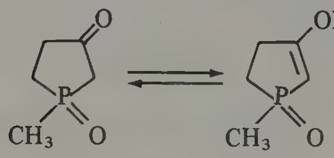
Both syntheses require a benzylic group on phosphorus, which provides a phenyl ring to aid in stabilizing the anion formed, and consequently all products so far reported have a 2-phenyl substituent. It is quite likely that other activating groups can be found that will avoid this problem, and that such cyclization procedures will become quite useful in phospholanone synthesis in the future. Their versatility has already been demonstrated by the construction of multicyclic structures, an especially intriguing one being that with the steroid skeleton (**38**).



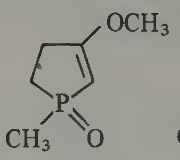
38

Synthetic innovation of this type has been lacking for many families of phosphorus heterocycles, and many opportunities exist for applying newer techniques of organic synthesis to their preparation.

The 3-phospholanones are highly useful materials as synthetic intermediates, and also can be approached from phospholene derivatives with ease (Table 2.6, reactions 1, 2, 3; see also Ref. 70 for routes via oxidation of a 4-hydroxy-2-phospholene oxide and Ref. 73 for BF_3 rearrangement of 3,4-epoxy phospholenes). A number of transformations are possible with them, although many remain to be explored. The enolic hydroxyl of **40**, the enol form of ketone **39**, may be methyiated[85] with CH_2N_2 or carboethoxylated with $ClCOOC_2H_5$ and Na OC_2H_5, forming **41** and **42**.



39 40



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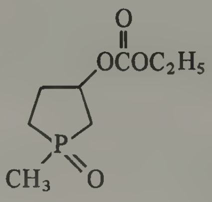
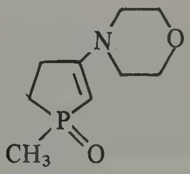


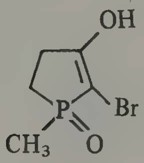
42

The carbonyl group may be employed[85] to form an enamine (**43**), although the product is not homogeneous and contains some of the 3-isomer.



43

(A better approach[87] to enamines is by amine attack on the 3-chloro-2-phospholene oxide or sulfide—reaction 4, Table 2.6.) The α-position of the phospholanones is activated, and a bromo compound (**44**) that is entirely enolic was formed with *N*-bromosuccinimide. Dialkylation at the α-position occurred on Michael reaction with methyl vinyl ketone, forming **45**.



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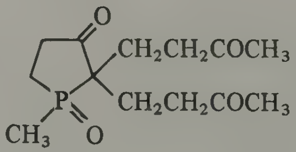
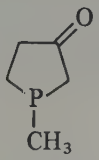


45

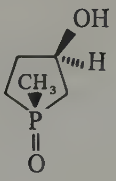
A similar Michael product was obtained from the P-C_6H_5 compound.[12] The phosphoryl group of phospholanone 1-oxides can be deoxygenated in the presence of the carbonyl,[85] and although the yield was modest (21%) this reaction with

$HSiCl_3$ provided the first sample of a ketophospholane[85,132] (46), a stable distillable liquid.

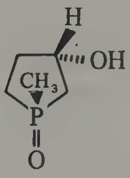


46

The enolic character of the 3-phospholanone oxides interferes with its reaction with organometallic reagents or hydride reducing agents,[85] but catalytic hydrogenation proceeds smoothly to give the hydroxy derivatives as a cis (40%), trans (60%) mixture.[132]

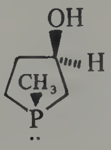


cis

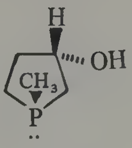


trans

Various reducing systems worked well on the nonenolic ketophosphine[132] 46, however, and gave alcohol mixtures generally dominated (60–80%) by the cis form.

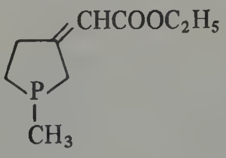


cis

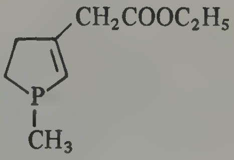


trans

Silane deoxygenation of the 3-phospholanol oxide mixture is also a source of these alcohols.[132] The carbonyl in phosphine **46** is quite normal and adds Grignard reagents to form tertiary alcohols, or Wittig reagents to form a mixture of exocyclic (47, 35%) and endocyclic (48, 65%) olefinic products.[132] It is unusual to obtain such an olefin mixture in Wittig reactions, but it is seen in Chapter 3 that a similar result is obtained with 4-phosphorinanones.

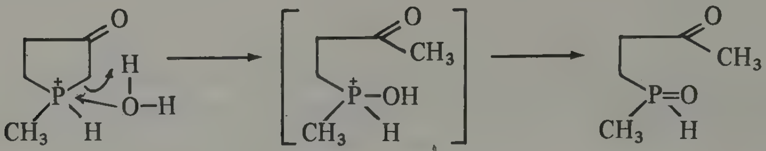


47



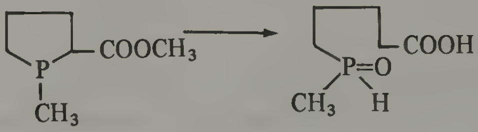
48

Another unusual property discovered[133] in the 3-phospholanone was its sensitivity to ring cleavage by acid. This unexpected behavior occurred on refluxing a solution of the phosphine in 91% formic acid saturated with HCl; ketophosphine oxide **49** was obtained in 51% yield, presumably as a result of nucleophilic attack on positive phosphorus made possible by the expulsion of a resonance-stabilized carbon fragment:



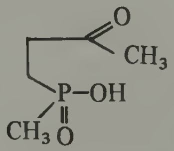
49

There is some generality to this type of cleavage, for in the same study it was found that the β-carbonyl of phosphine ester **50** provided the same influence and allowed cleavage in the formic acid-HCl medium to provide acid **51**.



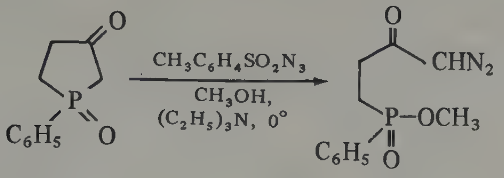
50 **51**

Two instances of facile ring cleavage of 3-phospholanone oxides have been reported. Refluxing **39** in 2 $\underline{\mathrm{N}}$ NaOH gave an 84% yield of phosphinic acid (**52**) as a result of the attack of $\mathrm{O}\bar{\mathrm{H}}$ on phosphorus, with displacement of a carbanionic group that is then protonated.



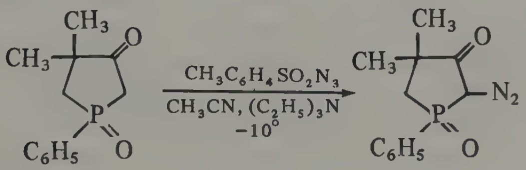
52

Reaction of 1-phenyl-3-phospholanone 1-oxide with tosyl azide in methanol containing triethylamine gave the noncyclic product **53** in 81% yield,[86] resulting from cleavage of an intermediate diazo compound.

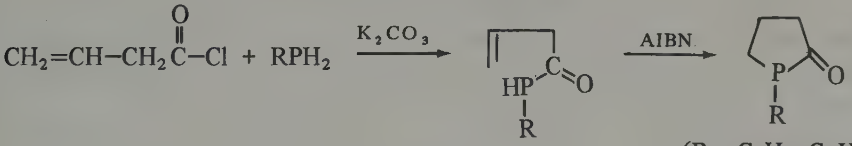


53

However, later workers[134] found that conducting a similar reaction at −10° in the absence of methanol led to a stable cyclic diazo derivative of the phospholanone.

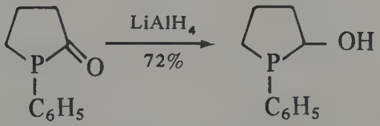


Although considerable attention is presently being given to the useful 3-phospholanone system, 2-phospholanones have been more difficult to obtain, and there has been only one report of their synthesis. Issleib and co-workers[135] showed that unsaturated acyl phosphines could be intramolecularly cyclized under free radical conditions created by the use of azobisisobutyronitrile (AIBN) and, depending on chain length, there could result 5- or 6-membered rings.



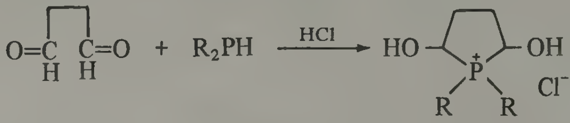
(R = C_6H_5, C_6H_{11})

The products were distillable liquids. The phosphorus was found to be alkylated to form rather unstable phosphonium salts, but no definite P-oxide or P-sulfide could be formed by conventional reactions. On the other hand, the carbonyl was readily reduced to give the first example of a 2-phospholanol, also a distillable liquid.



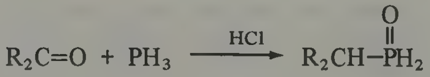
This new cyclization procedure, and the valuable 2-phospholane derivatives it makes available, are welcome additions to the field.

P(IV) derivatives of phospholanols have been prepared by direct cyclization reactions. 2,5-Phospholandiols (**54**) are formed[136] by reaction of succinaldehyde with secondary phosphines in a strongly acid medium.



54

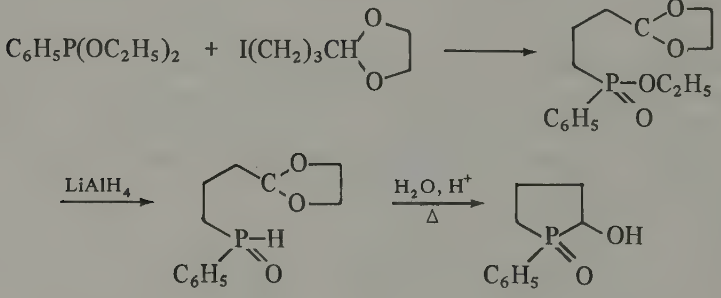
It is noteworthy that the acidic medium failed to cause dehydration to the phosphole system; more strenuous conditions might accomplish this, providing a new, simple route to these valuable compounds (see Section 2.7). There is a similarity between this reaction and the well-known Paal-Knorr route to pyrroles, which normally employs ammonia in the reaction with a γ-dicarbonyl compound. However, phosphine itself, as well as primary phosphines, behave quite differently with carbonyl compounds, and are not known to form phospholes. Thus, primary phosphine oxides can result from phosphine interaction with carbonyls.[136]



$$R_2C{=}O + PH_3 \xrightarrow{HCl} R_2CH{-}\overset{\overset{O}{\|}}{P}H_2$$

It is because of such special behavior that some other well-known cyclization techniques can be expected to fail with phosphines.

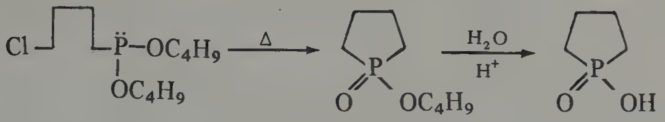
A quite different approach has been used to form 2-phospholanol oxides.[137] These result from intramolecular addition of the P-H of a secondary phosphine oxide to a δ-carbonyl group. The latter is masked as a ketal while the phosphorus function is being generated and is then released with acid.



The yield in the last step was 45%, providing the product with cis OH and P = O. The 2-methyl and 5-hydroxymethyl derivatives were prepared in similar fashion.

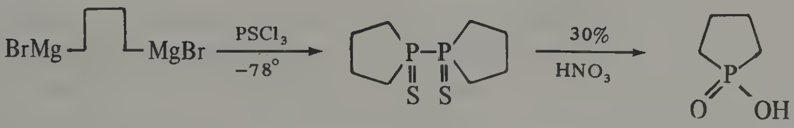
Ring closures that produce P-functional phospholanes also are known. They are summarized below.

1 (Ref. 138)



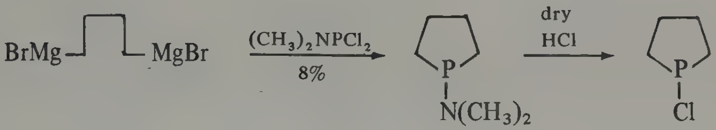
This internal Arbusov reaction provided the first sample of the phosphinic acid, now readily obtainable by hydrogenation of the corresponding 3-phospholene derivative of McCormack origin.

2 (Ref. 139)



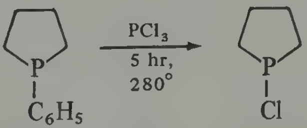
Several derivatives retaining the P-P bond can also be made from the intermediate.

3 (Ref. 140)

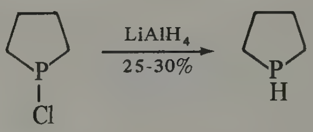


55 56

Better yields were later reported[141] for $(C_2H_5)_2NPCl_2$. Although the yield is poor in this process, the first product (**55**) is of value as a precursor of 1-chlorophospholane (**56**); it is well known that the P-N bond is cleaved by anhydrous HCl to form NH and PCl groups. This cyclic phosphinous chloride is a highly reactive substance, of potential value in synthesis for the introduction of a phospholanyl group in many structures. Fortunately, a much better synthesis has been reported;[142] it involves the cleavage of a P-C_6H_5 bond in a preformed 1-phenylphospholane.



Several of the transformations expected for this compound were reported. Especially valuable is a synthesis based on $LiAlH_4$ reduction that provides the parent phospholane.

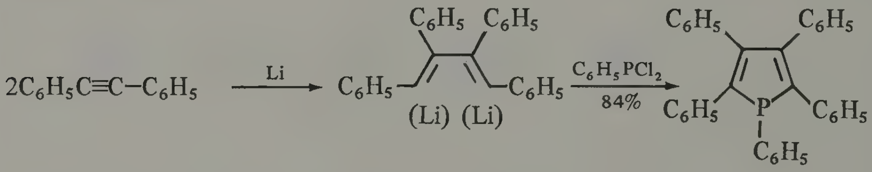


Phospholane had previously been prepared by pyrolysis of the BH_3 adduct of the dimethylamino derivative.[140]

2.7 SYNTHESIS OF PHOSPHOLES

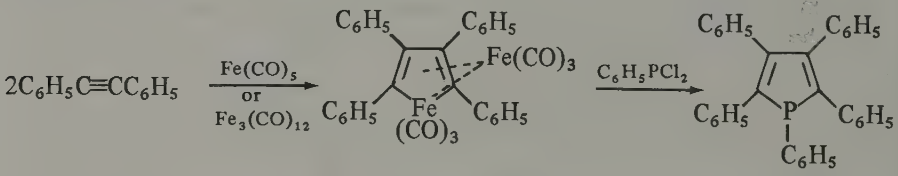
The heteroaromatic compounds pyrrole, thiophene, and furan have long played central roles in heterocyclic chemistry; they have been the source of endless discussion on the nature of the electron delocalization present, and their derivatives constitute some of the most important of heterocyclic compounds. The first phosphorus-containing analog to this group of compounds, on the other hand, was not synthesized until 1959, and then in the form of the pentaphenyl derivative and by methods that did not lend themselves to adaptation for the production of simpler compounds. These methods are illustrated below:

1 (Refs. 143, 144)



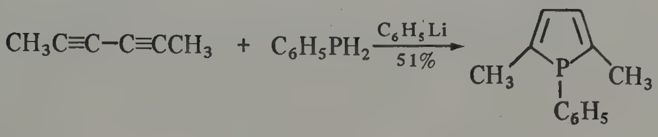
The product was a yellow, high-melting point (256°–257°) stable solid; its discovery proved that the phosphole ring system could be constructed and was of great importance in activating an entire field of research. The lithio derivative also can be converted with I_2 to the 1,4-di-iodo compound, which condenses with the species $C_6H_5PNa_2$ to form the same phosphole.

2 (Refs. 145, 146)



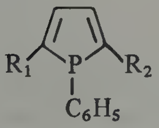
Discovered almost simultaneously, this reaction gave the same phosphole as the preceding reaction.

Given the large number of methods for constructing pyrroles from ammonia or amines, it is surprising that *only one* of these has been reported as being applicable to phosphole synthesis. Significant differences in chemical reactivity do exist between N and P derivatives–P-H structures have reduced basicity but greater oxidizability–and these differences will have to be taken into account in any comparative synthetic approach. Thus, an attempt to perform the classical Paal–Knorr reaction of a 1,4-dicarbonyl compound with $C_6H_5PH_2$ failed.[147] The one reaction that is common to both phosphole and pyrrole synthesis was announced by Märkl and Potthast[148] in 1967 and gave the first phosphole (57) without C-phenyl substituents. Four other phospholes were also prepared.



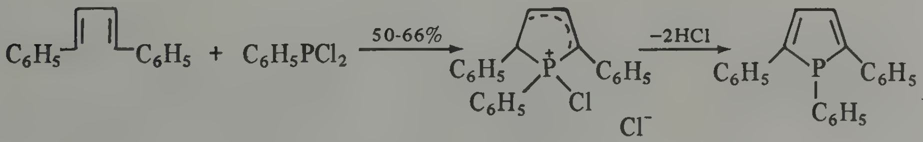
57

Bis(hydroxymethyl)phenylphosphine was also used at elevated temperatures in the presence of pyridine as a source of phenylphosphine but gave lower yields (nil for the reaction above). Märkl's phosphole was the first to give spectral indications of "aromaticity," a property obscured by the C-phenyl groups of the other known phospholes. This property of phospholes is described in detail in Chapter 8 and no further comment will be made in the present discussion. Märkl's method remains attractive and has been used by others,[149] but it has the limitation of providing rings with 2,5-substitution. Only P-phenyl derivatives have so far been shown to be practical products. Those phospholes prepared include:



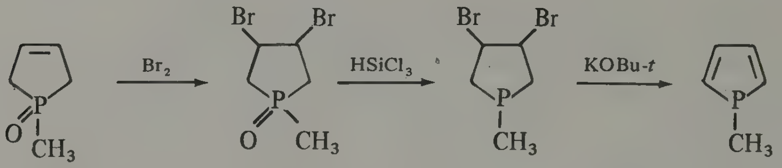
$R_1 = R_2$ = phenyl[149]
$R_1 = R_2$ = 2-naphthyl[149]
$R_1 = R_2$ = *p*–tolyl[149]
$R_1 = R_2$ = *p*-Br-phenyl[149]
$R_1 = R_2 = CH_3$[148]
$R_1 = CH_3, R_2 = C_6H_5$[149]
$R_1 = CH_3, R_2 = C_6H_5CH_2CH_2$[149]
R_1 = *i*-Pr, $R_2 = C_6H_5$[149]

It remained for the McCormack reaction to break the barrier to the synthesis of even simpler phospholes, and to phospholes with functional groups on the ring. As early as 1962, it was reported[103] that heating 1,4-diphenylbutadiene with $C_6H_5PCl_2$ at 226°-230° gave the yellow 1,2,5-triphenylphosphole, at that time the simplest phosphole known. Similarly, 1,2,3,4-tetraphenylbutadiene gave the known pentaphenylphosphole.[147] To rationalize these reactions it has been assumed that McCormack cycloaddition occurs first and that the product loses HCl at the high temperatures employed.

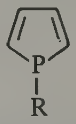


However, it has been reported that no cycloadduct forms at 100° between the two reactants, and the mechanism remains uncertain. In any case, the reaction is highly useful and still is the method of choice for preparing 1,2,5-triphenylphosphole. Attempts to prepare other phospholes than the tri- and penta-phenyl derivatives have not been successful.[147]

A more clear-cut use of the McCormack reaction was also announced in 1967, and this gave the simplest of all phospholes known to this day, 1-methylphosphole.[150] This method starts with either P-alkyl or P-phenyl 3-phospholene oxides from the McCormack reaction:



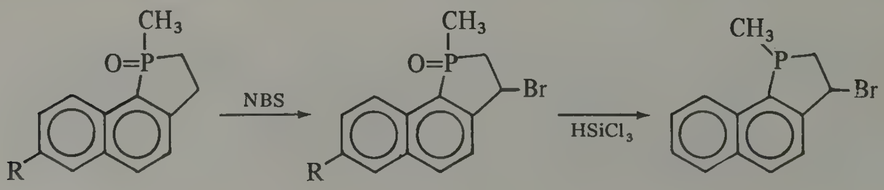
Although P-methylphosphole was only obtained in a 9% yield as an 85% pure specimen by this route, it did play an important role in demonstrating that unusual chemical and physical properties resided in the phosphole system, consistent with the presence of delocalization.[68] This method was later applied to several other phospholes with greater success[18]; product stability and yield increased with ring substitution, and it was possible to prepare and distill the following phospholes in the indicated yields for the last step:

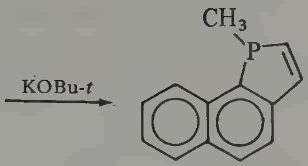


$R = C_6H_5CH_2-$, 26%
$R = C_6H_5CH_2CH_2-$, 10.1%
$R = p\text{-}ClC_6H_4-$, 17.3%

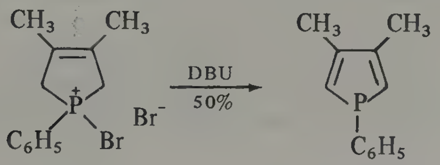
The synthesis of 1-phenylphosphole by virtually the same route, independently developed, was reported in 1968 by Märkl and Potthast.[151] Phenylsilane was used for the deoxygenation, and diazabicycloundecene (DBU) was used for the dehydrohalogenation. It was noted in these syntheses that some of the corresponding P(III) 3-phospholene was also formed; it was easily removed by an HCl wash, because its basicity is that of a tertiary phosphine (pK_a 7-8) whereas the basicity of the phosphole, like that of a pyrrole, is greatly reduced (pK_a 0.5).[68]

A variant[152] of the above procedure that has proved useful for multicyclic phosphole synthesis employs a 2-phospholene oxide as starting material and depends upon *N*-bromosuccinimide to install a bromine atom that can later be eliminated as HBr:

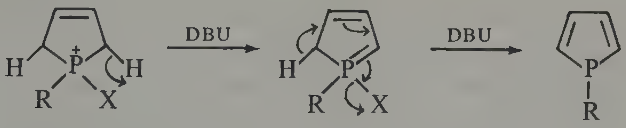




The most recently introduced (1969) phosphole synthesis, with the greatest demonstrated versatility and simplicity, is that of Mathey,[17,56,57] which uses the McCormack cycloadducts directly in a one-step dehydrohalogenation reaction. The reagent for this step is DBU, which generally performs its task at room temperature. Yields can be quite acceptable, as in the example below:

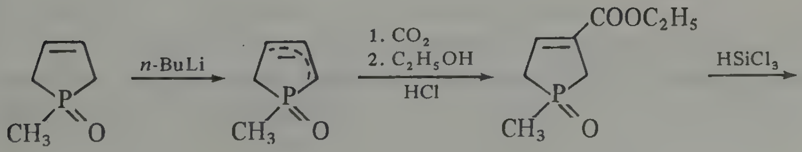


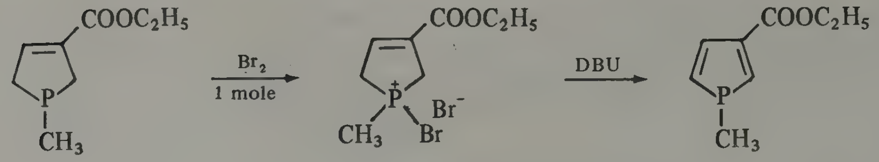
Both P-aryl and P-alkyl derivatives have been prepared by this method; results are generally better with the former, and the method fails with the CH_3PCl_2-butadiene adduct. A possible cause of the poor yields in the P-CH_3 series is a competing dehydrohalogenation at the CH_3 group. Phosphole formation is probably initiated by α-proton abstraction:



Only 3-phospholenium derivatives can be used in this process, which in the aryl series necessitates the use of aryl-PBr_2 rather than aryl-PCl_2 in the cycloaddition in order to avoid double-bond rearrangement.

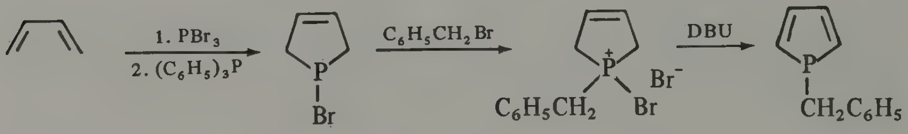
A useful modification of the Mathey approach to phospholes involves the conversion of P(III) phospholenes to halophospholenium halides by addition of one mole of halogen; the structures, of course, are the same as formed in the McCormack cycloaddition and therefore can be dehydrohalogenated. This technique was first used to prepare C-functional phospholes[153]; the $-COOC_2H_5$ group was installed on a 3-phospholene, as discussed in Section 2.3, and the halogenation-dehydrohalogenation procedure then applied:





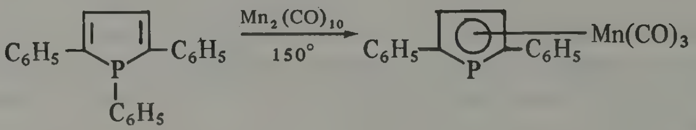
By this device, phospholes can be prepared from halophospholenium ions that are inconvenient, or impossible, to form by direct McCormack cycloaddition.[18]

Another variation also takes advantage of the fact that 1-bromo-3-phospholenes can be alkylated on P, an unusual reaction for a phosphinous halide, again giving the halophospholenium halide structure. Because the 1-bromophospholenes are formed readily by dehalogenation of PBr_3-diene cycloadducts, the method offers another useful way of getting around difficulties in a RPX_2-diene cycloaddition. Thus, $C_6H_5CH_2PBr_2$ is very slow in forming the cycloadduct needed for synthesis of 1-benzylphosphole; the approach taken below[18] avoids this problem:



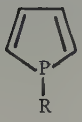
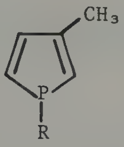
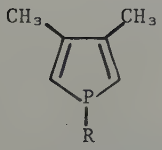
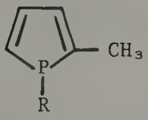
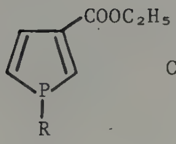
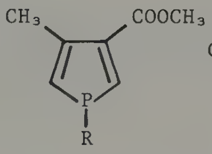
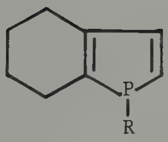
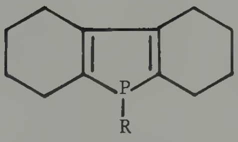
The scope of Mathey's method is obvious from the range of phospholes that have been prepared by it (see Table 2.9). A recent innovation has been the formation of multicyclic phospholes, as shown in Table 2.9.

The rich chemistry found in pyrroles, thiophenes, and furans that results from their high susceptibility to electrophilic substitution reactions is (to the present) totally lacking in phospholes. The only successful electrophilic attack (e.g., acylation) on the phosphole nucleus has been achieved when this moiety is present as the phosphole anion complexed with manganese in a structure called a "phosphacymantrene."[154] The preparation of such a system, which has unique properties possibly describable as "aromatic," is shown below (see also Chapter 8).

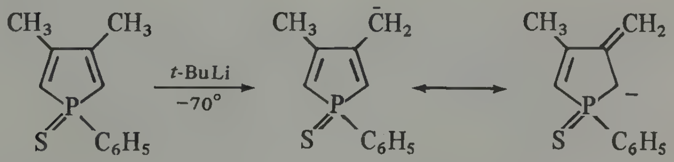


With this exception, the preparation of functionalized phospholes requires indirect techniques, such as that already mentioned for the synthesis of phosphole-3-carboxylates. Another method for preparing functionalized phospholes has been described by Mathey.[155-157] This involves the generation of an anion by proton abstraction from a 3-methyl group of a phosphole sulfide; charge is distributed onto

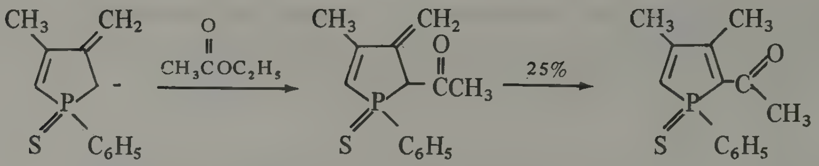
TABLE 2.9 Phospholes Synthesized by the Mathey Dehydrohalogenation of Halophospholenium Halides

	R		R
	n-C_4H_9[17] C_6H_5[17]		CH_3[18] n-C_4H_9[17] C_6H_5[49] $C_6H_5CH_2$[18]
	CH_3[17,18] n-C_4H_9[17] C_6H_5[57] $C_6H_5CH_2$[18] CH_3OCH_2[60] CH_3SCH_2[60] $NCCH_2CH_2$[60]		CH_3[18]
	CH_3[18]		CH_3[18]
	CH_3[152]		C_6H_5

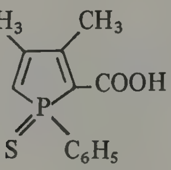
the 2-position of the ring, and both sites are then sensitive to electrophiles such as acyl derivatives.

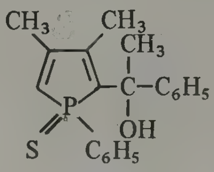


Although attack can occur at either anionic center, attack at the 2-position can be favored so that the resulting carbonyl product rearranges to reform the phosphole system.

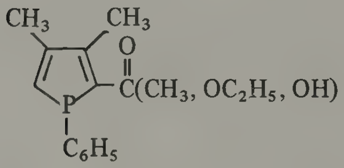


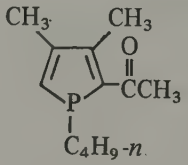
Similarly, carbon dioxide, diethyl carbonate, and acetophenone led to phospholes:

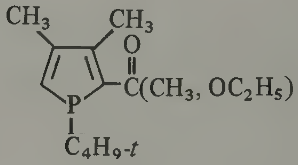




Such products can then be desulfurized with tertiary phosphines [n-Bu_3P or $(NCCH_2CH_2)_3P$].[158] Examples of phospholes made by this route are

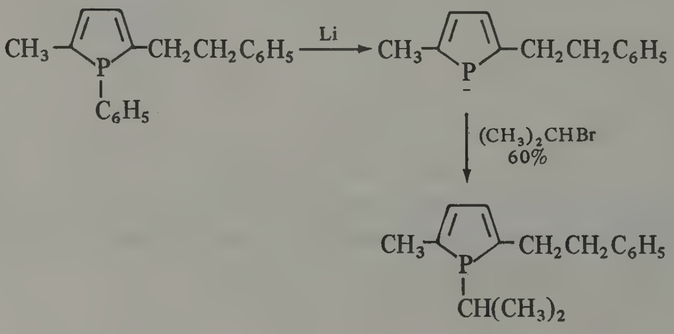






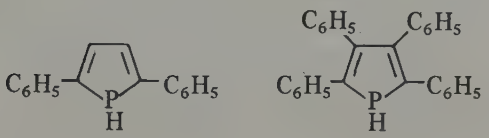
The method in its present stage of development is limited to the formation of 3,4-dimethylphosphole derivatives.

Another modification of phospholes that is synthetically useful involves the cleavage of a P-phenyl group by metals to form a phospholide ion.[159] This process occurs in excellent yield with metals such as potassium or lithium, usually on refluxing in a THF medium. The dark red-brown anion can then be used to create new structures about the phosphorus atom. For the most part, it has been alkylation that has been practiced so far, and many new phospholes have been prepared. The starting P-phenylphospholes used have had 2,5-, 3,4- or 2,3,4,5-substitution, but there seems to be no reason why simpler structures should not react as well. C-Alkyl substituents do not interfere, as in the illustrative reaction below.[149]



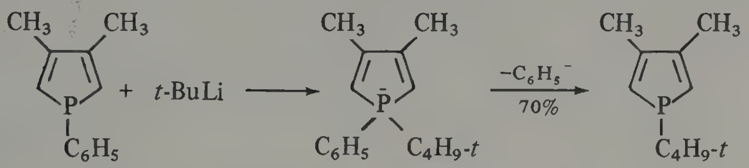
This phosphole would have been most difficult to prepare by any of the methods based on McCormack-derived starting materials. The power of the combination of the Märkl diyne synthesis, used to form the starting P-phenylphosphole, and the phospholide ion alkylation is clearly displayed here.

Phospholide ions are useful in other ways; they can be quenched with water to form 1H-phospholes and these products can be oxidized to form phosphinic acids. The method has provided the only examples of 1H-phospholes known to date:

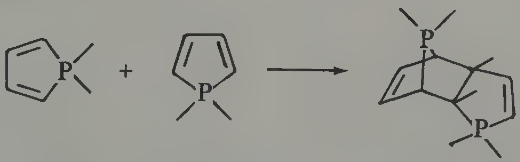


The C-phenyl substituents, as in other phospholes, tend to obscure the nature of the parent ring, and it cannot yet be stated that the 1H-phospholes in general are a stable class of compounds. Experimental work in this area is clearly called for, especially in connection with probes of structural effects on the degree of delocalization in the system.

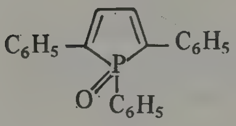
Another route that accomplishes replacement of P-phenyl by an alkyl group depends on attack on P by a carbanion, presumably to form an unusual phosphoranyl anion which decomposes by ejection of phenyl anion.[156] The first synthesis of a *t*-butylphosphole was accomplished this way.



P(IV) derivatives of phospholes are know but many are extremely easily dimerized by a Diels-Alder reaction. In the P(IV) condition, the phosphole system lacks the pair of electrons on phosphorus that can participate in cyclic delocalization, and it behaves simply as an activated diene. The situation is the same as found in thiophene chemistry.



Phosphole 1-oxides generally give such dimers spontaneously; only multiphenyl derivatives (**58, 59**) are stable as monomers. Dimerization is also a property of phosphinates in this system; 1-ethoxyphosphole 1-oxide for example, dimerizes very rapidly,[69] although the 3,4-diphenyl derivatives[13] with either phosphinate (**60**) or phosphinic acid (**61**) structure are stable. The 2,5-diphenyl (**62**) and tetraphenyl (**63**) derivatives of the phosphinic acid also resist dimerization.[160]



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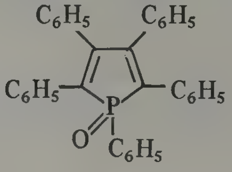

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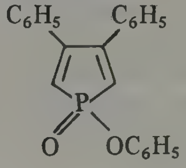

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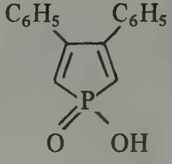

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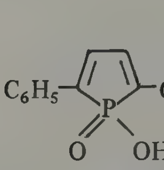

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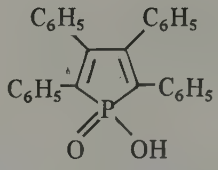
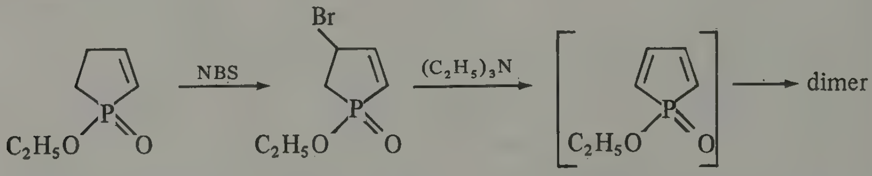
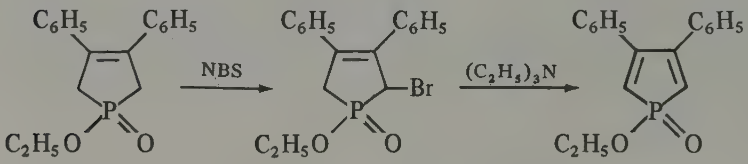


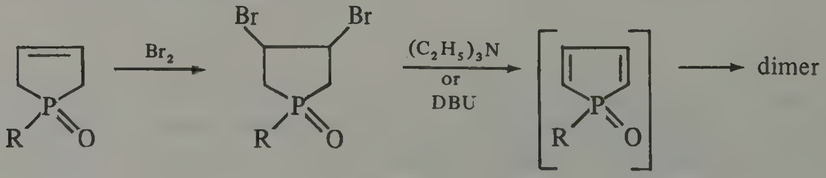
63

Many phosphole sulfides with C-substituents,[56] and some phospholium salts,[161] remain monomeric; they are better known than the phosphoryl species and, as already noted, the sulfides can be used for synthetic purposes. Although the P(IV) phosphole derivatives are generally synthesized by additions to the phosphorus atom of the P(III) phosphole, another approach has been developed that avoids the need for creating these intermediates. The methods used by Westheimer for preparing 1-ethoxyphosphole oxides are illustrative.[13,69]



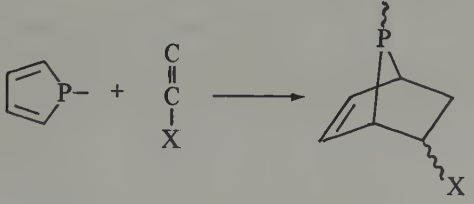


Phosphole oxide dimers can be obtained directly by dehydrobromination of 3,4-dibromophospholane oxides.[157]



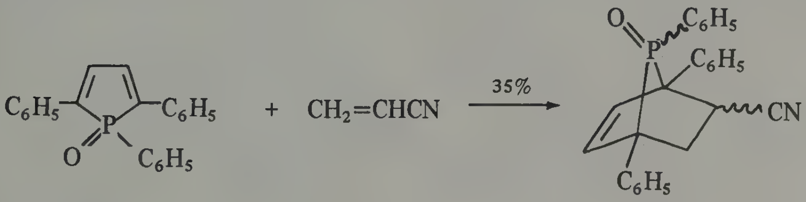
The dimers are formed with complete stereospecificity and, even when several chiral centers are generated simultaneously, only one structure is formed. An X-ray analysis[162] of one dimer (from 1-ethoxyphosphole 1-oxide) proved that the rings were joined with endo fusion, and that at each phosphorus the configuration adopted was that where P=O projected to the center of the system (as shown in **65**). It has yet to be established if the same configuration occurs at P in the dimers of phosphine oxides or sulfides, however, although this is the structure commonly written for the dimers.

The rapid Diels-Alder dimerizations of phosphole derivatives raises the question of the practicality of using other dienophiles in condensation with phosphole so as to produce the 7-phosphabicyclo[2.2.1]heptane system:

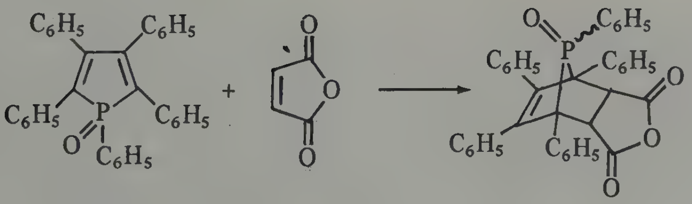


No P(III) phosphole, however, has yet been shown to take this reaction path with dienophiles. The lone pair on phosphorus retains its nucleophilic character and reacts with the α,β-unsaturated system. A recent paper[163] has shown that in the reaction of 1,2,5-triphenylphosphole with acetylene dicarboxylate products are formed from a 1:2 ratio of the reactants. With P(IV) compounds, better results have been obtained and the following syntheses have been documented:

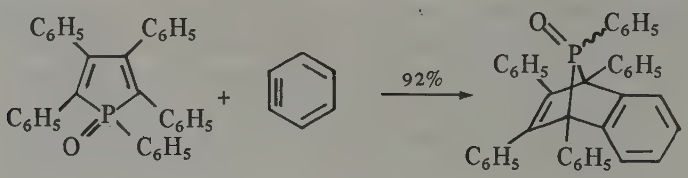
1 (Ref. 164)



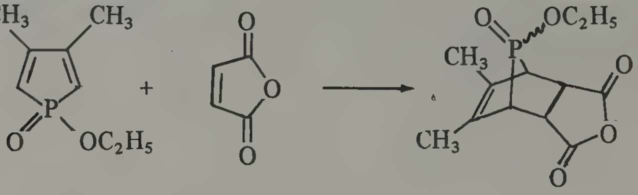
2 (Ref. 145)



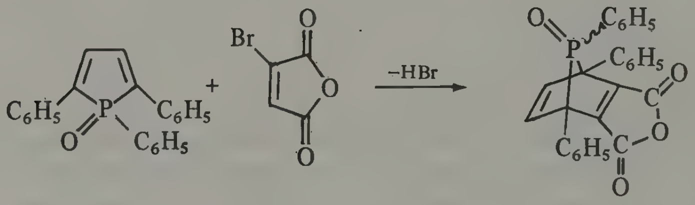
3 (Ref. 165)



4 (Ref. 166)

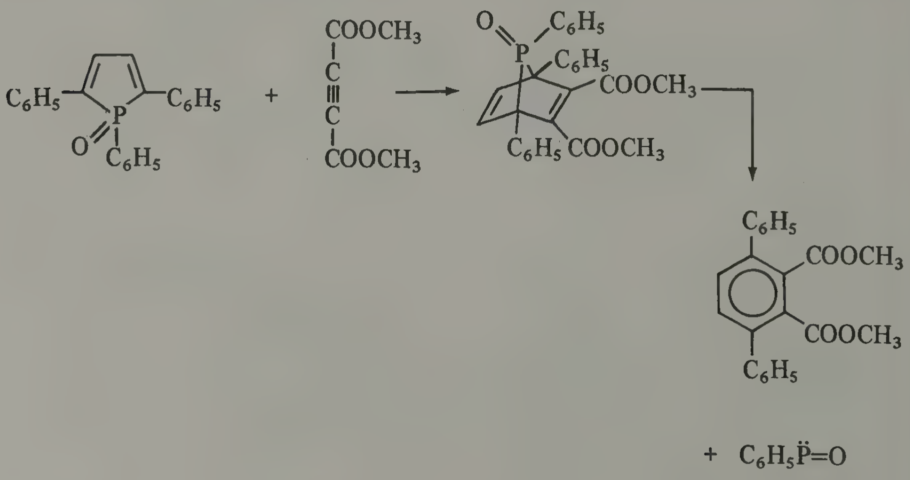


5 (Ref. 117b)



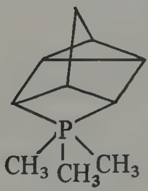
64

A frequently encountered problem is the spontaneous loss of the P-bridge under the sometimes strenuous reaction conditions used. This appears to occur routinely when dimethyl acetylenedicarboxylate, a favorite dienophile because of its high reactivity, is used, for example[147]:

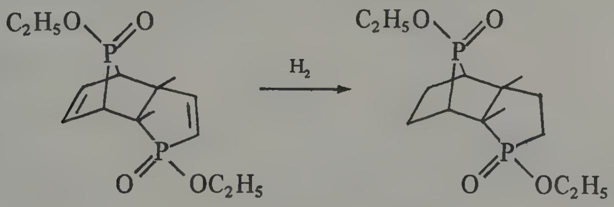


Proof that this bridge is lost in such reactions as the unusual phenylphosphinidene oxide was obtained by trapping it with, for example, methyl alcohol to form methyl phenylphosphinate, $C_6H_5PH(O)OCH_3$.[165] This reaction may be a form of a reverse-McCormack, but an attempt to trap the phosphinidene oxide with isoprene was not successful.

Another difficulty with the Diels-Alder adducts is that attempts to deoxygenate phosphorus with the usual silane reagents also causes loss of the bridge (as for **64**). The mechanism of this process has received no formal consideration, but a possible explanation is that a P(V) intermediate develops from the attack at P=O of the silane, and a reverse-McCormack reaction occurs. Precedent for reverse-McCormacks has already been noted, and their occurrence with a P(V) structure lacking the capability for stabilization by ionization is not surprising. The proof of this proposal would be found in the identification of the expelled P fragment, which has not yet been accomplished. Of relevance to this proposal is the observation[115] that when the P(V) caged structure below is prepared there is some decomposition to norbornadiene and $(CH_3)_3P$. This is, of course, the reverse of the process followed in the addition of CH_3PCl_2 to the diene,[114] and it illustrates the capability for reversal when stabilization by loss of halide ion cannot occur.

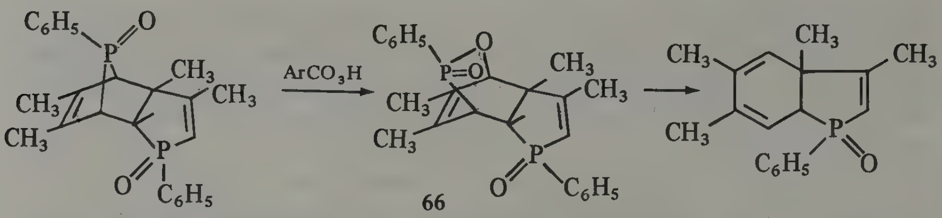


The dimers of phospholes represent a largely untapped source of valuable phosphorus heterocycles containing the 7-phosphabicyclo[2.2.1]heptane moiety. Hydrogenation of one dimer has proved successful,[166] but attempts to P-deoxygenate the dimer oxides causes loss of the bridge, as in the Diels-Alder adducts, and again a reverse-McCormack reaction can be proposed.

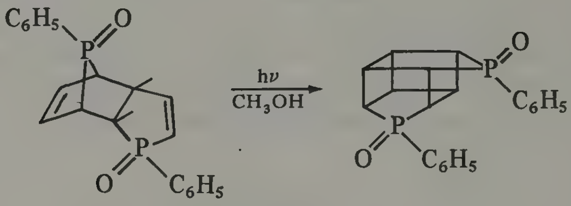


65

A similar problem was encountered on attempted epoxidation with *m*-chloroperbenzoic acid; a Baeyer-Villiger type of reaction is believed to occur,[167] giving a species (**66**) stable enough for characterization but losing its bridge on standing or warming. The decomposition of **66** resembles a reverse [4+2] cycloaddition, a process known for the parent monocyclic unsaturated 1,2-oxaphosphorinane and of use as a source of the [RPO_2] species.[168]

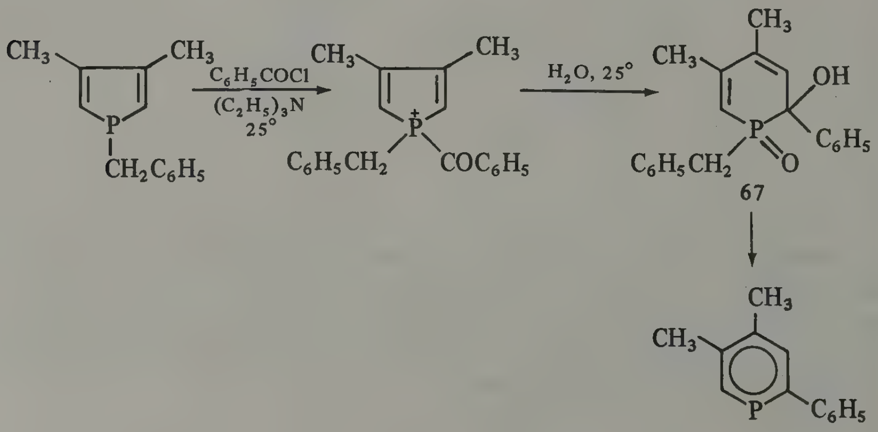


Were the [4+2] mechanism not available for the decomposition (i.e., were the double bond absent) the bridged product would probably be quite stable, as there is no unusual ring strain in a bicyclo[2.2.2]octane system. A more promising use of the dimer oxides is in an intramolecular cyclization reaction occurring between the two double bonds.[169] This [2+2] cycloaddition is brought about photochemically, and produces a novel cage structure.



For this reaction to occur would require that the 2-phospholene oxide moiety be fused in the endo orientation that is predicted from the X-ray analysis performed[162] on the dimer of 1-ethoxyphosphole oxide (65). Other uses of phosphole dimers include the formation of phosphindole derivatives, as is discussed in Section 2.8. Many other possibilities exist, and research in this area can be expected to produce other unusual structures and results.

A synthetic use for phospholes that provides phosphorins of unusual substitution pattern is discussed in Chapter 3. Basically, the method involves acylation of phosphorus and rearrangement of the salt to a dihydrophosphorin 1-oxide[156] (e.g., 67), which is then dehydrated and reduced to the fully unsaturated phosphorin.[170]

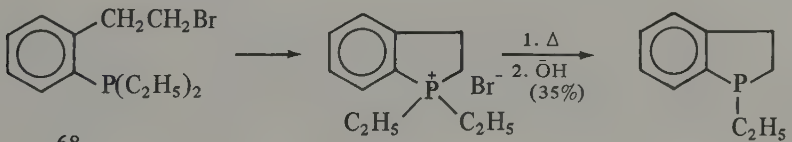


Although only certain phospholes seem likely to undergo the acylation to form a salt that resists the usual dimerization, the bridging of the gap between 5- and 6-membered rings is of real synthetic importance and may well stimulate even more work in phosphole chemistry.

2.8 PHOSPHINDOLES AND THEIR PARTIALLY SATURATED DERIVATIVES

Although the phosphindoline system was constructed comparatively early (1951, Mann and Millar[171]) in the heterocyclic era of organophosphorus chemistry, the parent phosphindole system remained unknown until 1967, when Rausch and Klemann described the synthesis of 3-*n*-butyl-1,2-diphenylphosphindole.[172] The system is of great importance in the development of heterocyclic phosphorus chemistry; the structural similarity to indoles makes phosphindole derivatives obvious targets of synthetic work designed to uncover new substances with biological activity. The potential for aromaticity in the phosphindole system has also been a force behind the upsurge in recent research activity. The upsurge is indeed pronounced; several new synthetic methods have been developed for the phosphindoline system, and there now exist practical ways of converting these to phosphindoles. Direct phosphindole synthesis is still limited in scope, although two reactions that give specific compounds have been recently announced. Again, as in the synthesis of phospholes, application of the many indole-forming reactions to phosphorus chemistry has not yet been a factor in the development of this field. It will also be noticed that only one example is known where the benzo group bears a substituent (CH_3); for biological purposes, it would be extremely desirable to obtain phenolic derivatives, as well as other types that are included in indoles of biological importance.

Most of the methods for phosphindoline synthesis involve intramolecular cyclizations of aryl derivatives that contain a reactive phosphorus function. The earliest method, that of Mann and Millar,[171] subjected the specially synthesized phosphine 68 to intramolecular quaternization (X^-=picrate, 29%); the product on pyrolysis at 350° lost ethylene and gave (after neutralization) the phosphine 69 in 35% yield.



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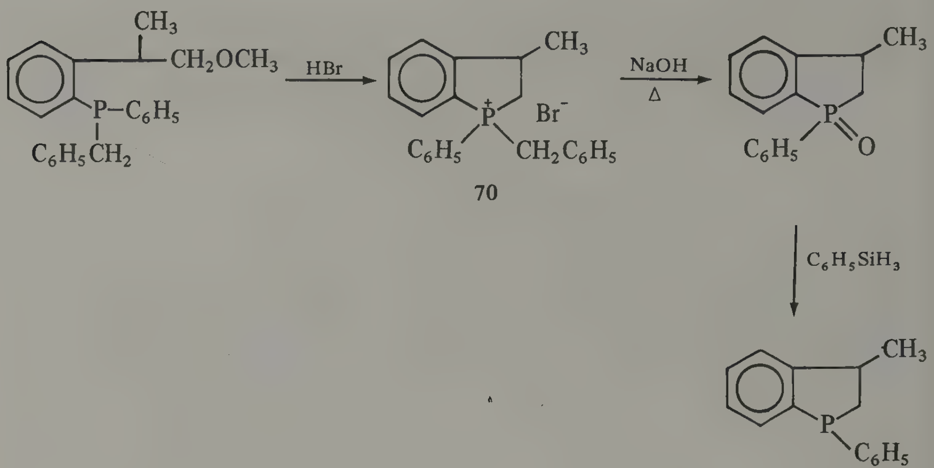
69

Mislow and co-workers[149] later used the same general approach to synthesize quaternary salt 70 but introduced a different technique to obtain the final phosphine 71. This involved base-cleavage of a P-benzyl group (an excellent leaving group from phosphonium salts) to form a phosphine oxide from 70 and then the now-familiar silane reduction procedure to form the phosphine.



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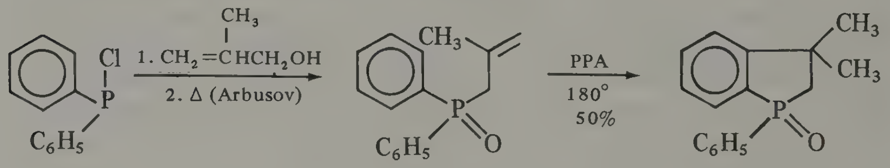
Intramolecular cyclization of species capable of generating carbonium ions in the proper position of a side chain on phosphorus relative to a phenyl-P grouping forms the basis of another approach. The method of Berlin and co-workers depends on allyl groups attached to phosphine oxides (e.g., 72)[173] to generate the carbonium ion, which then attacks the ortho position:



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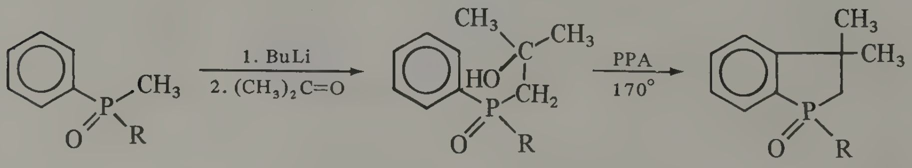
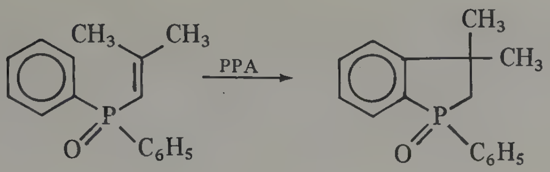
Phosphinolines can also result from such cyclizations if the carbonium ion is more stabilized in the γ-position to phosphorus. Warren and co-workers[174] prefer to use alcohols in a PPA-promoted cyclization, pointing out the ease of obtaining them from simple P-methyl phosphine oxides via carbanion formation:



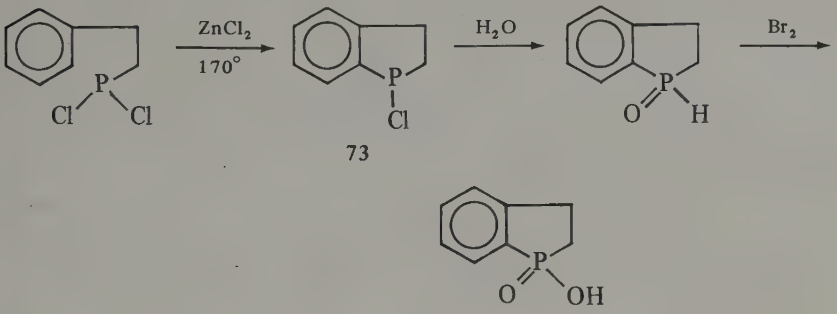
R = CH_3 or C_6H_5

Warren also used P-vinyl (and allyl, like Berlin) groups to generate the carbonium ion.



These cyclizations are remarkable in that they involve electrophilic attack at the strongly deactivated ortho position of P(IV)-phenyl derivatives. Both phosphoryl and phosphonium groups are meta directors, but intramolecular cyclizations are of course always achieved with a lower energy barrier, and in these cases high-temperature conditions with relatively long-lived (3°) carbonium ions are involved.

Another type of intramolecular cyclization is based on the concept of a P(III) halide on a side-chain serving as an electrophilic agent towards a benzene ring.[175]



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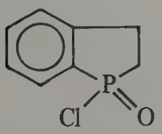
The starting phosphonous dichloride is derived from bis (β-phenethyl) cadmium and PCl_3. The phosphinous chloride 73 is not isolated but hydrolyzed and oxidized with bromine to the phosphinic acid 74. From the acid, Swan and co-workers prepared the acid chloride 75, a ready source of both ester 76, and via Grignard reagents, the phosphine oxides 77.



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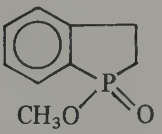

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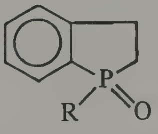

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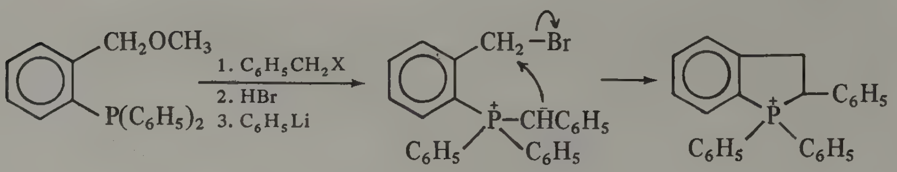
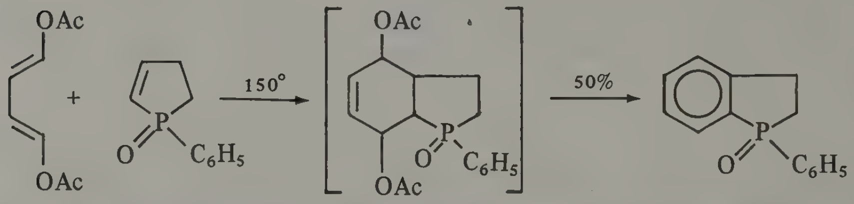
$R = C_2H_5$,
C_6H_5,
$CH_2{=}CH$

It will be seen subsequently how these materials can be converted to the aromatized phosphindole form.

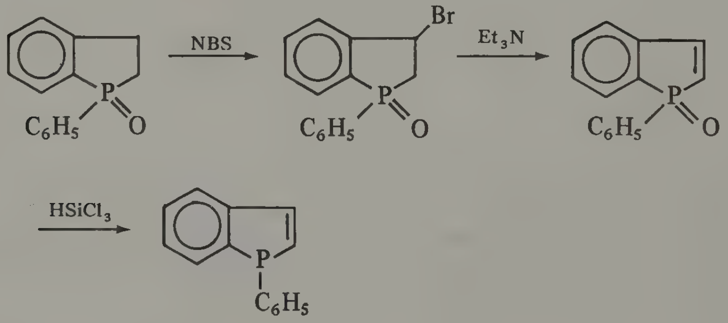
A final type of intramolecular cyclization to consider is that of Märkl,[176] in which the negative carbon of an ylide undergoes alkylation.



A totally different approach[83] to phosphindolines is based on the dienophilic character of a 2-phospholene oxide to develop the fused 6-membered ring. By using a diene with groups capable of olefin-forming elimination, the benzene ring was then generated. The entire synthesis is achieved in a single operation.

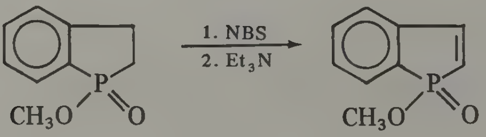


This compound is important in the development of phosphindole chemistry, for it was the first phosphindoline to be transformed, by a series of conventional reactions, into the unsaturated system.

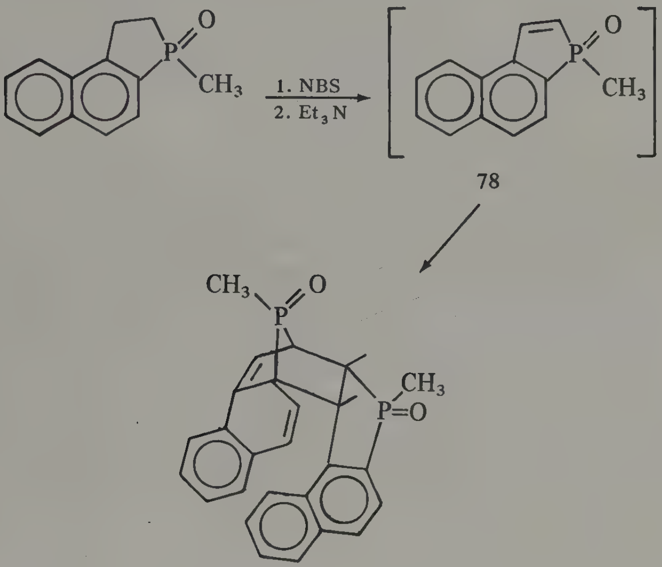


Although not the first phosphindole to be synthesized, it was the simplest, and its spectral properties (^1H NMR chemical shifts) were interpreted in a manner similar to those of 1-substituted phospholes to indicate a measure of "aromaticity."

Swan and co-workers[175] later used the bromination-dehydrobromination sequence to convert a phosphindoline to a phosphindole, which carried the phosphinate structure.



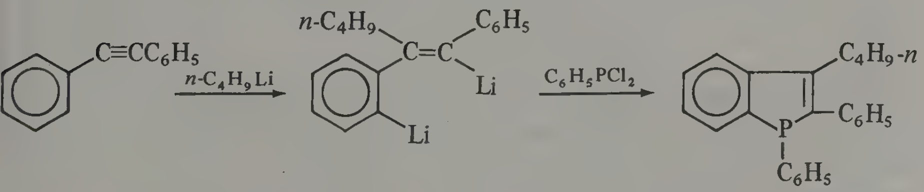
Notable in both syntheses is the stability of the P(IV) form to dimerization; benzene aromaticity would have to be destroyed in this process. Phosphine oxides or phosphinates of monocyclic phospholes, it will be recalled, dimerize on formation. However, a case is known where dimerization with loss of aromaticity does take place; benzophosphindole 1-oxide (78) gives a dimer (as a single isomer) on its formation by the same sequence of reactions[152]:



78

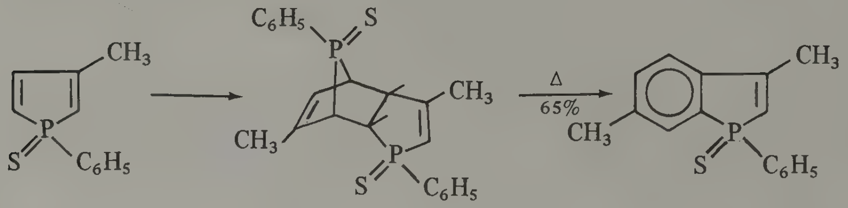
The dimer could have one of several isomeric structures; that shown above is a tentative assignment.

The accomplishment of the very first phosphindole synthesis belongs to Rausch and Klemann.[172] Although their synthesis has quite limited scope, it did show that the system was capable of existence, and the method found use in later studies by Mislow and co-workers[149] and by Hughes et al.[177] The Rausch-Klemann synthesis made use of the dilithio derivative prepared by reacting diphenylacetylene with *n*-butyllithium; with $C_6H_5PCl_2$ cyclization occurred to form the phosphindole system directly.

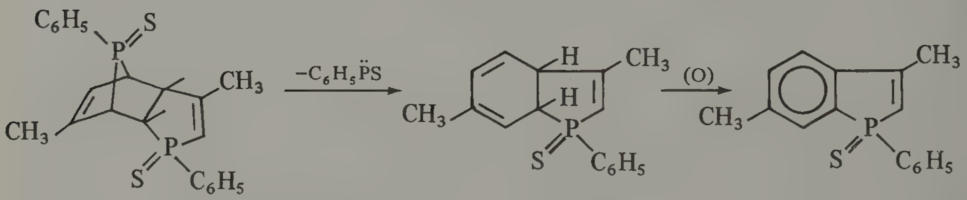


Mislow's group employed ethyllithium, and thus formed the 3-ethyl phosphindole.

The most recent phosphindole systhesis[178] uses yet another approach: bridge-eliminating pyrolysis of a phosphole sulfide dimer, in a process that further indicates the synthetic utility of such dimers.



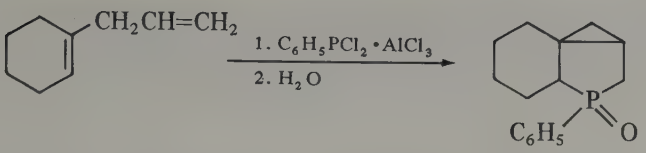
This method could prove to be of considerable value, although it has not yet been extended to the formation of any other phosphindoles. The position of the methyl on the benzo group does not seem to have been proved conclusively, as it depends on a tenuous assignment (from ^1H NMR evidence[57]) of the same methyl in the starting dimer. An intriguing point about the synthesis is the manner in which the loss of the bridge produces the aromatic ring. As already noted, $C_6H_5\ddot{P}O$ can be eliminated when an aromatic system can be produced, but here this reverse-McCormack process would give a dihydroaromatic. One would then have to assume that an oxidation by some species in the medium, or thermal dehydrogenation, had occurred to generate the phosphindole:



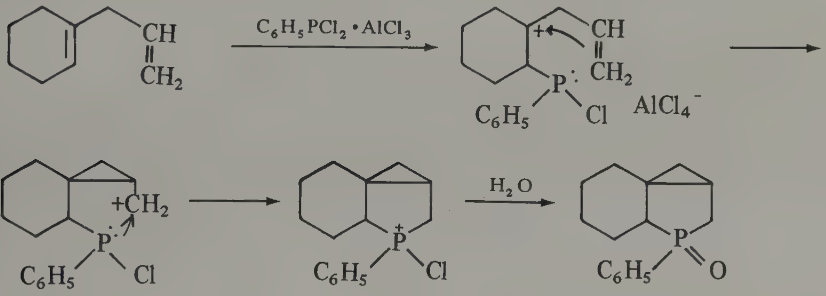
An alternative that needs consideration is that the species lost is actually $C_6H_5P(S)H_2$, a primary phosphine sulfide, or its equivalent, which would give the phosphindole directly. No experimental evidence bears on the mechanism of this process as yet.

Just as has been observed for the monocyclic phospholes, a P-phenyl group can be cleaved from the phosphindole system with metals. The resulting anion is available for alkylation to produce useful new derivatives.[149,179]

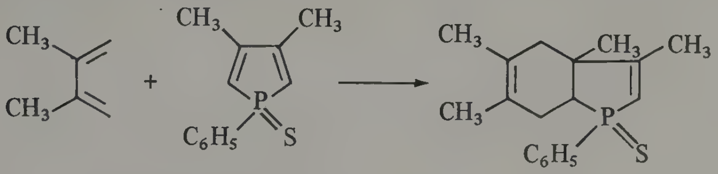
Phosphindoles with full or partial reduction of the benzo group are only now beginning to appear in the literature. Several compounds of this type have been prepared by McCormack reactions and were discussed in Section 2.4. Other approaches to them are known, however. From the work of Kashman et al.,[180] the novel reaction below resulted:



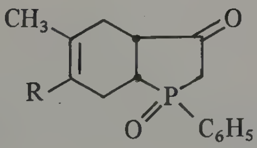
The use of $RPX_2 \cdot AlCl_3$ complexes in reaction with olefins is seen in Chapter Four to constitute the major route to the 4-membered ring system. The second double bond of the nonconjugated diene used here is responsible for the different result. A possible mechanism proposed by Kashman et al. is the following:



In another study, Kashman et al.[181] used a phosphole sulfide as a dienophile towards 2,3-dimethylbutadiene:

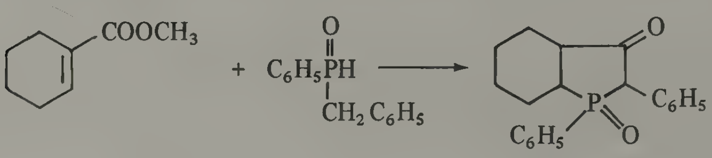


As is noted in Section 2.10, Kashman also used the method to make tetracyclic compounds of steroidal skeleton. 2-Phospholene oxides also undergo Diels-Alder cycloadditions with simple dienes,[182] and it is obvious that a number of new reduced phosphindoles could result from this approach. Also effective as a dienophile[183] is the 2-phospholen-4-one that results from oxidation of the corresponding alcohol (Table 2.5, reaction 4). Cycloaddition with dienes has provided the ketones below but it is obvious that many other systems can be developed by this Diels-Alder approach and, as is seen in Section 2.10, the method has already been used to produce the 17-phosphasteroid system.



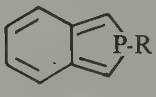
R= H or CH_3

The Bodalski-Pietrusiewicz[129] method of preparing 3-phospholanones can also be applied to the synthesis of multicyclic systems; pertinent to the present discussion, a reduced phosphindole has been obtained by their method.



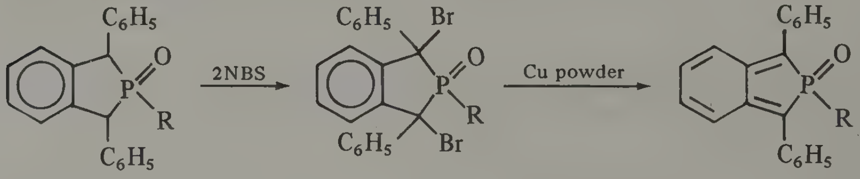
2.9 ISOPHOSPHINDOLES AND ISOPHOSPHINDOLINES

Although several syntheses now exist for the isophosphindoline system, the fully aromatic structure (79) has not yet been achieved. The recent accomplishment[184]



79

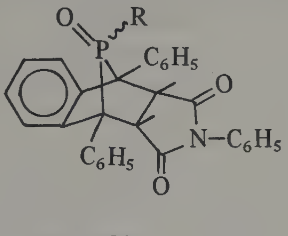
of the synthesis of isoindole and the demonstration of its high reactivity might suggest that developing techniques for the synthesis of the isophosphindoles will be a formidable (but worthwhile) challenge. P-Oxides of isophosphindoles have, however, been prepared and, although the system is so reactive that no isolation of a pure substance has yet been accomplished, there have been obtained crystalline dimers and Diels-Alder adducts that leave no doubt as to the existence, however fleeting, of the monomeric form. This great reactivity is, of course, due to the absence of any aromatic stabilization in this 8π-electron system, although some form of conjugation is indicated to be present by the UV absorption maximum.[185] The isophosphindole P-oxides have been approached from the isophosphindolines, whose syntheses are outlined later in this section. The first synthesis (of 80) was accomplished in 1970 by Holland and Jones,[186] as follows:



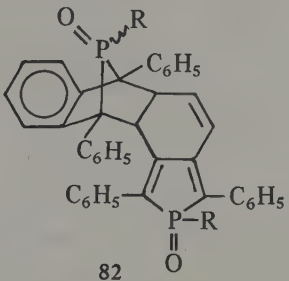
80

R = CH_3 or C_6H_5

It was found that the dimer (yellow) of 80 formed instantly but that the monomer (violet) could be regenerated in refluxing xylene. In this medium, as during initial formation, the monomer could be trapped as Diels-Alder adducts with cyclopentadiene or *N*-phenylmaleimide. A typical structure (from the latter dienophile) is shown as 81, whereas the dimer is proposed to have structure 82.

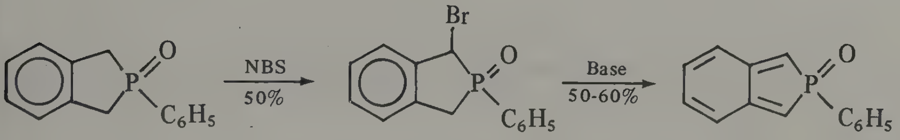


81



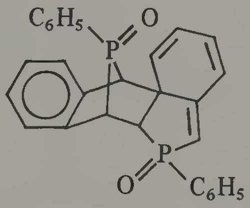
82

This structure is consistent with its yellow color (1,2,5-triphenylphosphole oxide, whose structure is incorporated in the dimer, is yellow) and its ^1H NMR spectrum; a crystalline diol also is formed with OsO_4. In another synthesis (Chan and Nwe[187,188]) the simpler isophosphindole oxide 83 was obtained, again with isolation as a dimer or a Diels-Alder adduct.



83

Whereas Holland and Jones utilized a double bond of the benzo group in forming the proposed dimeric structure 82, Chan and Nwe make use of a double bond in the phosphole ring, and propose structure 84 for their product.

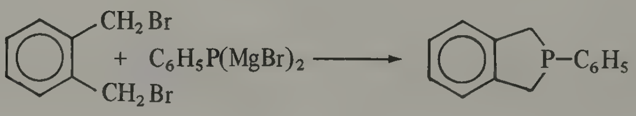


84

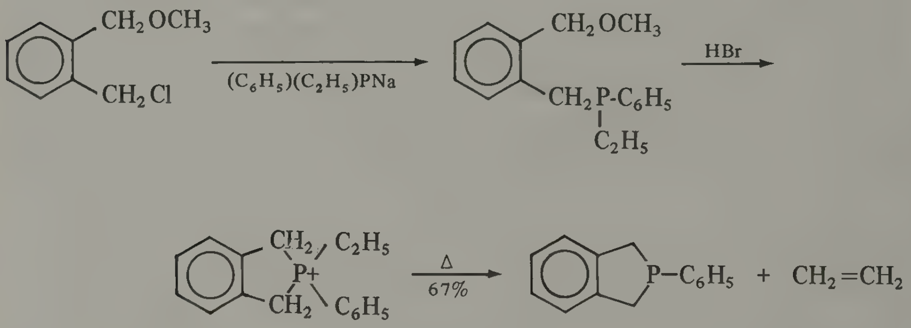
Their dimer is colorless, in striking contrast to Holland and Jones', and they make no mention of color in the formation of the monomer. Their proposed structure is consistent with the ^1H NMR spectral data, which show that only one proton is on an sp^2 carbon adjacent to P, whereas two would be present if the Holland-Jones structure had been formed. In each instance of dimerization, a single pathway is followed, even though many isomers are conceivable. The discrepancy in dimer structures calls for further investigation. A direct experiment that could show that the P atoms are differently connected would be based on ^{31}P NMR spectroscopy, because the three bonds separating these nonequivalent atoms in structure **84** would lead to pronounced coupling between them, as is observed for phosphole dimers[189] (Chapter 5), whereas little or no coupling would be observed in the 5-bond separation of **82**. If the assigned structures are confirmed, the different mode of dimerization would probably have to be attributed to a steric effect of the C-phenyl groups, which would end up in a more crowded environment in the Chan-Nwe dimer structure.

In each of the isophosphindole syntheses, it is conceivable that a silane reduction could be performed on the bromo intermediate before the dehalogenation or dehydrohalogenation, thus arriving at the highly desired phosphine, but this possibility has not yet been described in the literature.

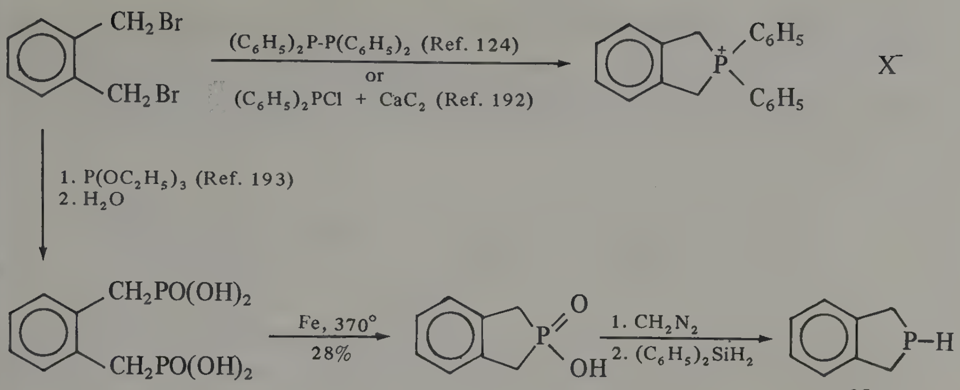
Isophosphindoline chemistry is in a far more advanced stage, and several methods have been used to produce this quite stable system. For the most part, the methods start with a benzene derivative containing ortho substituents that can undergo ring closure. The first synthesis, that of Mann, Millar, and Stewart,[190] employed *o*-xylylene dibromide in a reaction with $C_6H_5P(MgBr)_2$, ultimately obtaining a 4% yield of the isophosphindoline.



A better approach[191] employed the sequence below.



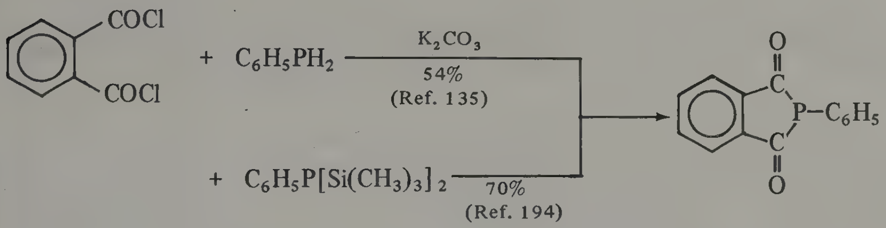
The thermal elimination of ethylene from an appropriate phosphonium salt is frequently a useful device for recovering a phosphine from the salt formed in a cyclization reaction. More recent syntheses based on *o*-xylylene dibromide are shown below.



85

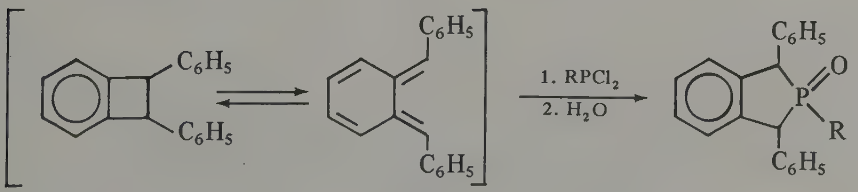
The latter sequence is of special interest in providing a reactive phosphinic acid intermediate; this led, via the ester from diazomethane, to the parent 1H-isophosphindoline (85) for the first time.

Phthalyl derivatives are also useful precursors of the isophosphindoline ring, providing 1,3-diketo derivatives.



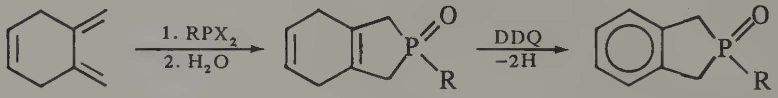
Conceivably, this diketone could be the source of many other derivatives, but marked sensitivity to P-C cleavage has been noted.

A most unusual form of a McCormack reaction has provided yet another isophosphindoline synthesis, albeit one of limited scope. In this process,[185] cycloaddition occurs with the exocyclic diene unit of the *o*-quinonoid tautomer of a benzo-cyclobutene derivative; ring closure with $C_6H_5PCl_2$ or CH_3PCl_2 at 20° for 14 days then reforms the benzene ring while generating a phospholene ring. Yields are 74 and 44%, respectively.



This is the source of the starting material for the isophosphindole 2-oxide synthesis discussed earlier.

The most recent synthesis of isophosphindoles takes yet another approach—first the formation of the phospholene ring by the McCormack reaction, and then the generation of the benzene ring[195]:

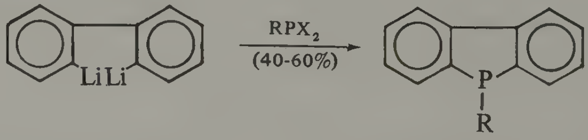


The starting diene can be prepared in reasonable yield and works quite well in the cycloaddition. The best reagent for effecting the dehydrogenation of the product was found to be dicyanodichlorobenzoquinone (DDQ). Overall yields from the diene were 61% for R = CH_3 and 40% for R = C_6H_5. When PBr_3 was used in the process, the phosphinic acid (R = OH) was prepared in 71% yield. This new method competes favorably with other isophosphindoline syntheses and has the advantage of leading to a variety of P-substituents by variations in the RPX_2 reactant. Improved access to the phosphinic acid, with its numerous reaction pathways, is also an advantage of this new method.

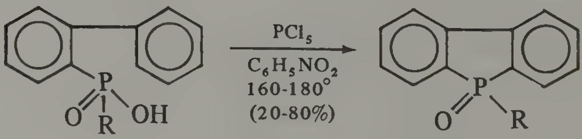
2.10 MULTICYCLIC SYSTEMS CONTAINING A 5-MEMBERED PHOSPHORUS RING

Although dibenzo derivatives of phospholes have been known for some time, other multicyclic structures based on a phosphole ring are relative newcomers to phosphorus heterocyclic chemistry. Nonetheless, they offer many possibilities for research on new compositions of matter, and the area is open for investigation. Dibenzophospholes are somewhat less exciting from this standpoint, as the parent heterocycle is totally imbedded in benzene rings. Several syntheses have been developed for this system; they are extensively discussed in Mann's monograph[3] and, as relatively little new work has been published since his review, only two of the more important methods are mentioned here for illustrative purposes. These are outlined by equation, below.

1 (Ref. 196)

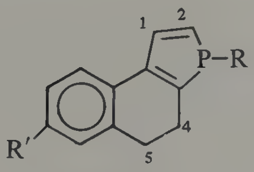


2 (Ref. 197)

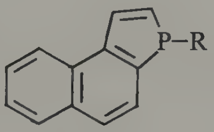


The methods have some tolerance for substituents on the benzene rings and considerable versatility in the nature of the P-substituent.

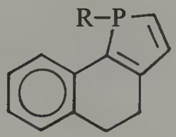
Of more novelty are the tricyclic systems where the phosphole ring is exposed and can contribute to the chemistry.



86



87



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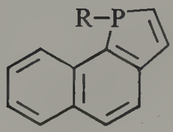
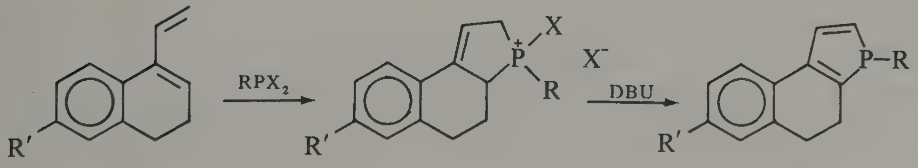


89

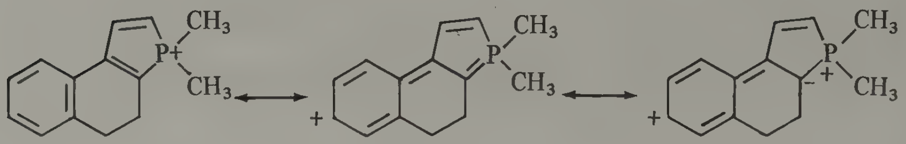
Synthesis of only two of these systems has been accomplished. The 4,5-dihydrobenzo[e]phosphindole system (86) was formed[152] under the conventional conditions of the Mathey DBU-dehydrohalogenation of the McCormack cycloadduct, with the overall yields indicated.



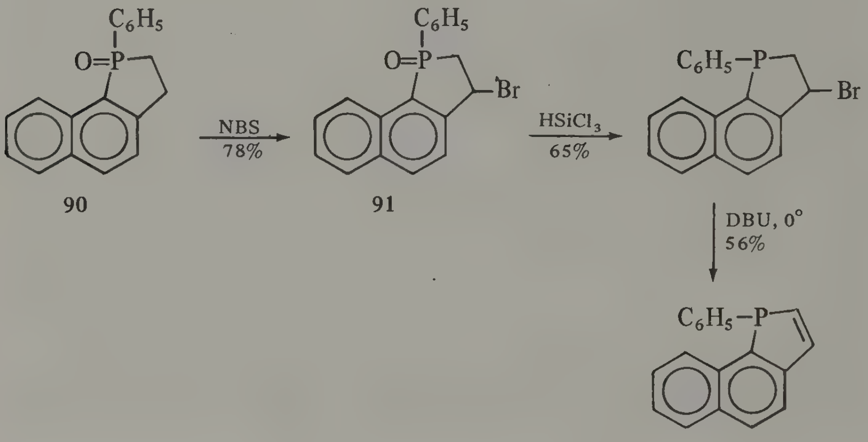
86

$R = CH_3, R' = H$, 20%
$R = CH_3, R' = OCH_3$, 47%
$R = C_6H_5, R' = H$, 40%

The phospholes are stable solids, and although requiring protection from atmospheric oxidation can nevertheless be purified by column chromatographic techniques. The tricyclic framework made no difference in the tendency of the P(III) derivatives to dimerize; the oxides of structure 86 instantly formed a dimer in the usual stereo- and regio-specific way. The methiodides were more stable as monomers, but dimerized on attempted recrystallization. The monomeric methiodides are of interest because of their yellow color, which suggests extensive electron delocalization possibly involving the forms below:



The fully unsaturated benzo[g]phosphindole system (**92**) has been prepared in a manner familiar from earlier discussions of phosphindoles.

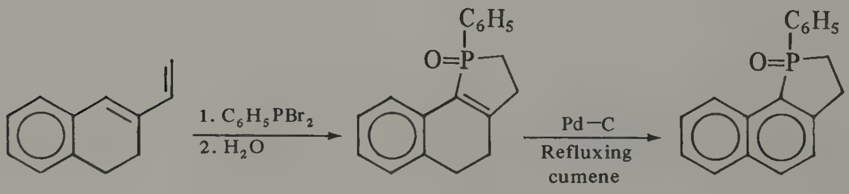


90

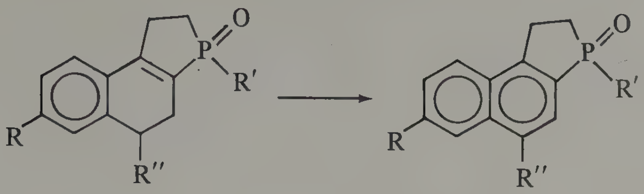
91

92

Again a substance of good stability was formed. The P-oxide of this phosphole (**78**) formed by the dehydrohalogenation of the bromophospholene oxide (**91**), was noted earlier to dimerize rapidly, even though disruption of the aromaticity of a benzene ring is involved. The naphthalene starting compound (**90**) was prepared for this synthesis by dehydrogenation with Pd-C of the corresponding 4,5-dihydro derivative, this having been formed by the McCormack process applied to a 2-vinyldihydronaphthalene:

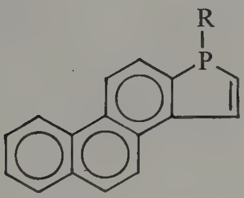


The dehydrogenation appears to provide a fairly general approach to naphthalenophospholanes[107]; in addition to that above, the following examples are now known:

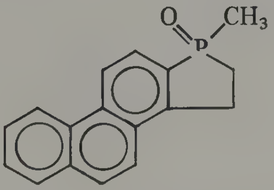


R = H, R′ = CH_3, R″ = H	70%
R = H, R′ = C_6H_5, R″ = H	83%
R = H, R′ = OH, R″ = H	65%
R = CH_3O, R′ = CH_3, R″ = H	65%
R = H, R′ = CH_3, R″ = CH_3	80%

Tetracyclic phosphole derivatives have a special fascination if they are composed in the manner of a steroid. To date, no fully unsaturated member of this series (e.g., **93**) has been synthesized, the closest approach being the dihydro structure **94**.

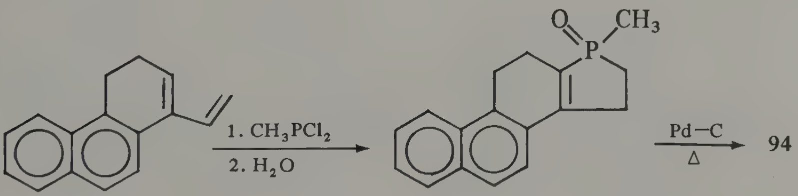


93

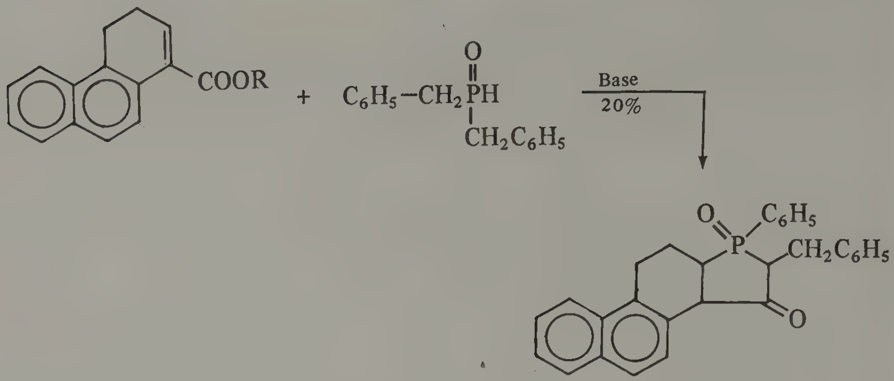


94

This was prepared[107] by a combination of the McCormack procedure with the Pd-C dehydrogenation:

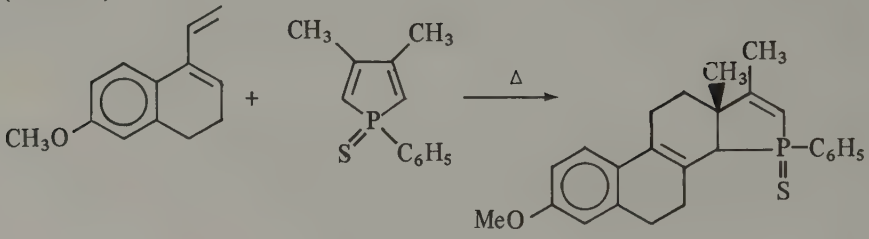


Other steroid-like structures were discussed in Section 2.5 as examples of the application of McCormack reactions to multicyclic synthesis. The steroid system with phosphorus in the D-ring can, however, be approached in several other ways, such as the Bodalski-Pietrusiewicz method [129] (Section 2.6)



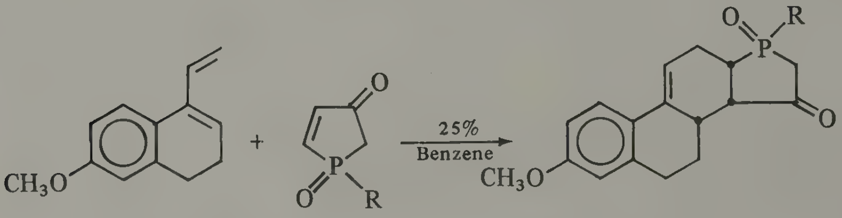
Other methods are outlined below.

1 (Ref. 181)

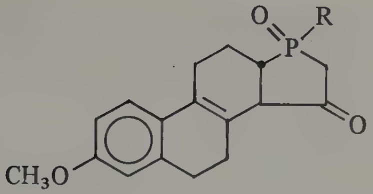


This provides an interesting example of the dienophilic character in a P(IV) phosphole derivative stabilized as the monomer by the proper choice of functionality (thiophosphoryl).

2 (Ref. 183)



This cycloaddition, which was completed in 24 hr, gave the product regiospecifically. Treatment with base caused epimerization, thus giving C/D trans, whereas acid caused rearrangement of the double bond, forming **95** as the final product.



95 (R = C_6H_5 or CH_3)

Steroids with phosphorus replacing carbon in 6-membered ring C are described in Chapter Three.

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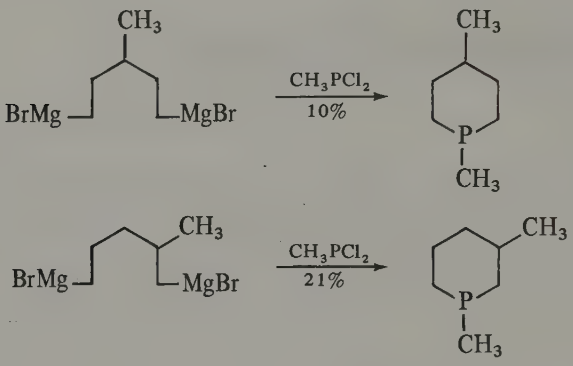
chapter three

Synthetic Methods for 6-Membered Rings

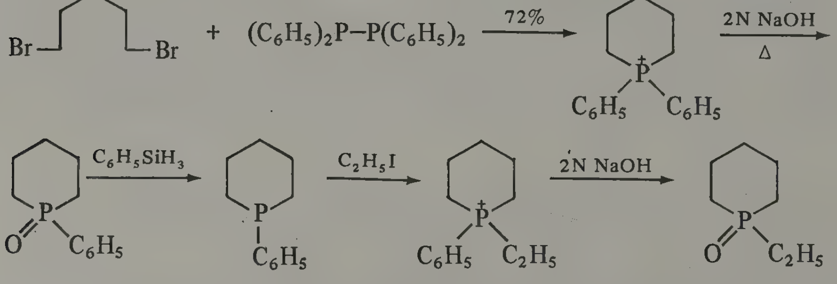
Similar to the case of the 5-membered ring, for many years little work was done on 6-membered phosphorus heterocycles until the 1960s. Prior to that time, a few techniques were available for preparing the parent saturated ring, but no functionalized derivatives were known, stereochemical and conformational aspects had been totally ignored, and few dared to think that fully unsaturated (i.e., aromatic) systems could be constructed. In tracing the explosive growth of knowledge of the 6-membered ring over the last two decades, it is easily concluded that the introduction of reasonably simple synthetic methods made the difference and provided substances from which serious stereochemical studies could begin. As will be seen, a bit later came methods for creating in one cyclizing operation the fully unsaturated (phosphorin) system; from that point detailed treatment of the fascinating properties of this aromatic system began. In this chapter the survey of the major synthetic methods of heterocyclic phosphorus chemistry is continued, with emphasis on those that have contributed to the rapid growth of the field. The important stereochemical aspects of the phosphorinanes are given attention in later chapters on NMR (Chapters 5-7) and conformation (Chapter 8); the aromatic characteristics, both chemical and physical, of the phosphorins are also discussed in Chapter 8. As in the treatment of the 5-membered ring syntheses, there is no intention to provide a complete coverage of the published literature; the selections of research results that have been made help to accomplish the goal of this book, to teach and not to exhaust.

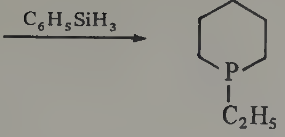
3.1 FORMING THE PARENT PHOSPHORINANE RING SYSTEM

By simply lengthening the carbon chain to five in the reactants used to make the parent phospholane system, it is possible to generate phosphorinanes in useful manner. Methods familiar from Chapter 2—the Grüttner-Wiernik diGrignard-RPX_2 reaction,[1] the Issleib methods using $RPLi_2$[2] or RPH_2[3] with dihalides, the Märkl $(C_6H_5)_2PP(C_6H_5)_2$ reaction with dihalides,[4] the Davies, Downer, and Kirby irradiation of alkenylphenylphosphines,[5] the Maier diGrignard-$RPSCl_2$ reaction[6]—all have been applied to the synthesis of 1-substituted phosphorinanes. One or the other remains the method of choice even today, a situation quite unlike that of phospholanes, where the newer route via the phospholene system is clearly preferable. In fact, the Grüttner-Wiernik method, which appears to have produced 1-phenylphosphorinane as the very first phosphorus heterocycle in 1915, still may be the preferred method for preparing this compound (32-37%[7,8]) as well as the newer 1-methylphosphorinane, and has been extended with modest success to produce C-alkyl derivatives.[9]



Further extensions to other C-substituted phosphorinanes are possible by this method, depending mostly on the availability of the appropriate dihalides. Simple phosphorinanes such as these, and their easily prepared oxides, sulfides, and quaternary salts, continue to play significant roles in studies on stereochemistry. To avoid the necessity of preparing a phosphonous dihalide starting material, an alternative route is available,[10] as illustrated below for the synthesis of 1-ethylphosphorinane. It is based on conventional transformations, following[11] use of the Märkl synthesis of the diphenyl salt.

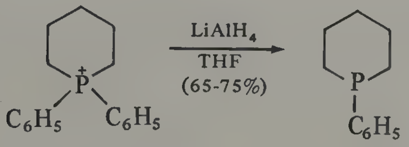




Such a sequence also has been used for preparing 4-methyl-1-phenylphosphorinane,[12] and 4-*tert*-butyl-1-phenylphosphorinane.[13]

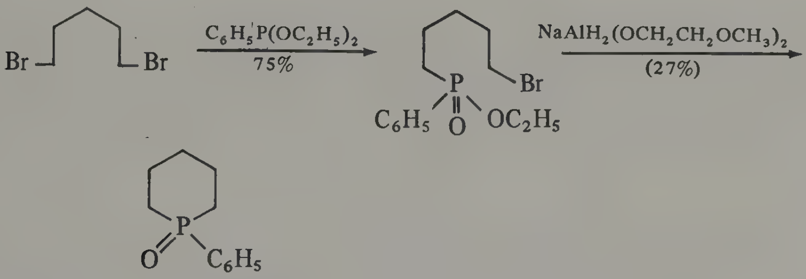
Two other recently introduced methods for 1-phenylphosphorinane synthesis are illustrated below:

1 (Ref. 14)



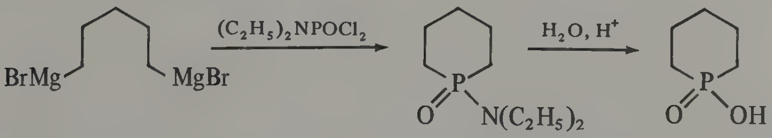
The yield is competitive with the two-step Marsi approach[10] from the same salt.

2 (Ref. 15)



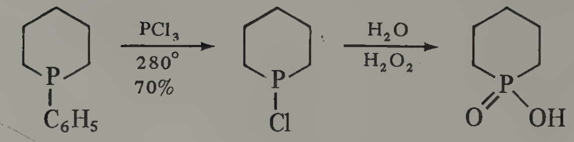
This route has also been discussed as a phospholane synthesis.

The phosphinic acid (2) of the series was first prepared in 1955 by Kosolapoff,[16] employing the diGrignard method to form phosphinic amide (1), which was then hydrolyzed.



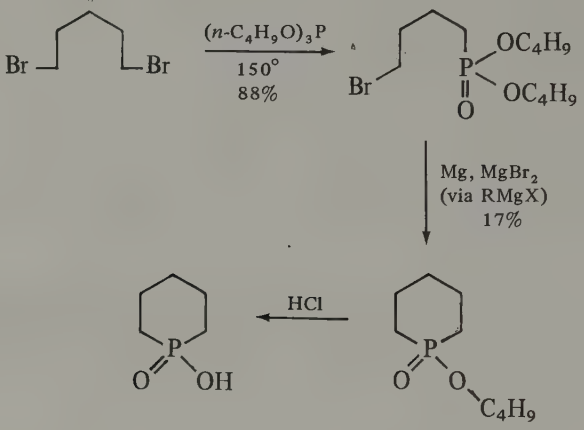
1 2

The most recent synthesis[14] is based on the formation of the phosphinous chloride (3) by the cleavage with PCl_3 of the phenyl group of 1-phenylphosphorinane. The method was discussed earlier as being useful in the phospholane system.



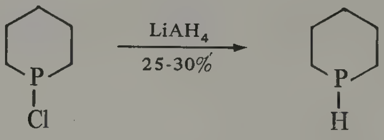
3

For those not anxious to perform a sealed tube reaction with PCl_3, the following route, first presented in an unpublished dissertation (M. Braid, Temple University, 1962) but then confirmed and improved by other workers,[17] is available.



The intermediate step, involving displacement of alkoxide from P by a Grignard reagent, is not always a useful process, however.

The phosphinous chloride of Sommer[14] is also useful as a precursor of 1H-phosphorinane (4).



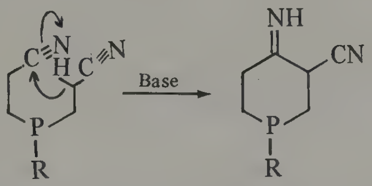
4

This compound, also of interest in conformational studies, was prepared[17] by diphenylsilane reduction at 200° of phosphinic acid (2). These methods should be useful for generating C-substituted 1H-phosphorinanes, which remain unknown at this time.

3.2 C-FUNCTIONAL PHOSPHORINANES

A major event in the development of phosphorinane chemistry was the discovery by a group at The American Cyanamid Co. (Welcher, Johnson, and Wystrach[18]) of a straightforward route to 4-keto derivatives (4-phosphorinanones). This synthesis attracted much attention and stimulated studies that resulted in the first examination of the conformation and stereochemical properties of the ring system. In its own way, the synthesis was a catalyst for the field in the same sense that the McCormack cycloaddition opened up the 5-membered system. In these syntheses, much resemblance will be seen to nitrogen chemistry, unlike the situation with the 5-membered ring.

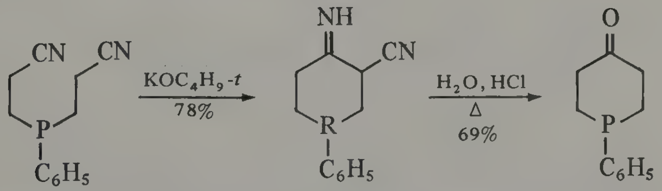
The 4-phosphorinanone synthesis makes use of the familiar Thorpe reaction of dinitriles to form the 6-membered ring.



The key to its success is the ready availability of the requisite dinitriles. The Cyanamid group developed a simple route to such compounds from primary aromatic phosphines,[19] employing a base-catalyzed Michael condensation with acrylonitrile.

$$CH_2{=}CHCN \;+\; C_6H_5PH_2 \xrightarrow[\substack{CH_3CN\\ 82\%}]{\text{Conc. KOH}} C_6H_5P(CH_2CH_2CN)_2$$

The synthesis is completed as shown below.



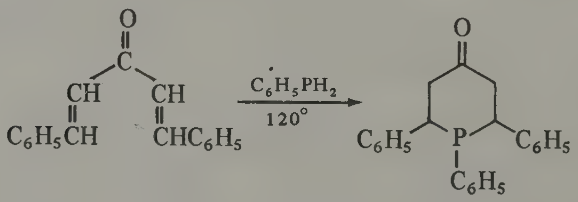
The yields quoted are those for an improved procedure, recently published in *Organic Syntheses,*[20] although the method has been used by a number of other workers. The ketone is a stable, distillable liquid, and has normal properties for a cyclic ketone as well as for a tertiary phosphine. There appears to be no interaction between the two functions. Some years later,[21] it was observed that the hydrolysis could be controlled to produce the ketonitrile or the ketoacid as isolatable intermediates, if desired.

P-Alkyl derivatives of 4-phosphorinanones are synthesized similarly. The requisite alkyl bis(cyanoethyl)phosphines are commonly prepared by an indirect procedure,[22] as primary alkylphosphines do not appear to be acidic enough to form anions under the favored conditions for the cyanoethylation. Tris(cyanoethyl) phosphine, formed in 70-80% as a stable solid from the cyanoethylation of PH_3, is quaternized with an alkyl halide to attach the desired P-alkyl group of the final product. One cyanoethyl group can then be eliminated by action of methoxide ion.

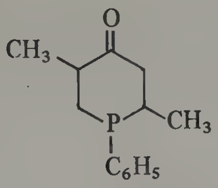
$$P(CH_2CH_2CN)_3 \xrightarrow[\Delta]{RX} \underset{\mathbf{5}}{R\overset{+}{P}(CH_2CH_2CN)_3} \xrightarrow{NaOCH_3} RP(CH_2CH_2CN)_2 + CH_3OCH_2CH_2CN$$

By this procedure, for example, the P-methyl derivative of 5 was prepared in 51% yield from tris(cyanoethyl)phosphine and converted to 1-methyl-4-phosphorinanone in 57% yield.

Further increasing the availability of 4-phosphorinanones, the Cyanamid group of Welcher and Day[23] described another useful synthesis of these compounds. Because primary phosphines had acted in normal fashion in the Michael condensation with acrylonitrile, their reaction with α,β-unsaturated ketones was explored, and good yields of 4-phosphorinanones resulted. From combination of five different phosphines, both aryl and alkyl, with two different ketones (dibenzalacetone and phorone), ten new 4-phosphorinanones were prepared with yields in the 50-70% range.

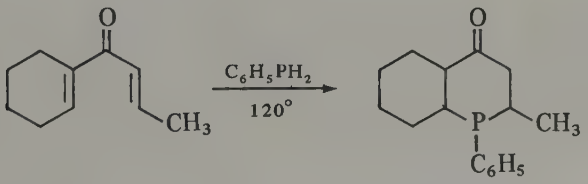


Improved conditions ($NaOCH_3$ as catalyst, 74% yield) for the condensation of phenylphosphine with phorone were published some years later.[24] The conveniently handled bis(hydroxymethyl) derivatives of phosphines, which release the equivalent of phosphine by the action of pyridine, can also be used in the process.[25] Unsymmetrical divinyl ketones are valuable as starting materials that give a different substitution pattern; compound 6, for example, has been obtained[26] from the corresponding divinyl ketone.

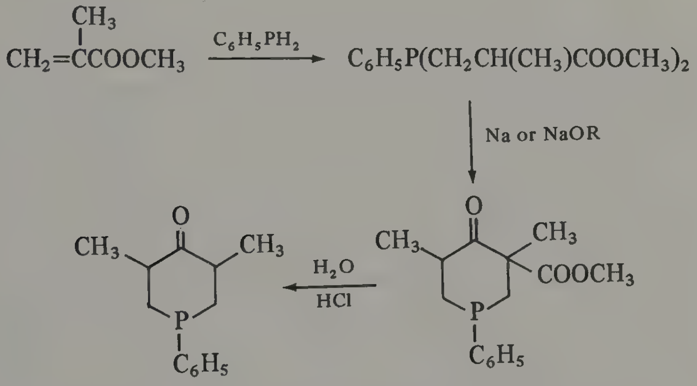


6

One vinyl group has been incorporated in a 6-membered ring, providing the only known route to the phosphadecalone system.[26]

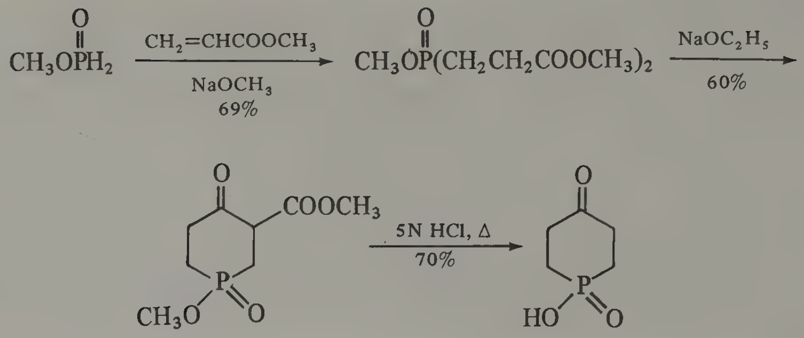


Greater flexibility in the substitution pattern around the ring was provided by the introduction[27-29] of the two-step sequence of Michael condensation of primary phosphines with α,β-unsaturated esters, followed by the Dieckmann condensation of the bis-esters. Methyl methacrylate, for example, gives 3,5-dimethyl-4-phosphorinanones by this route.



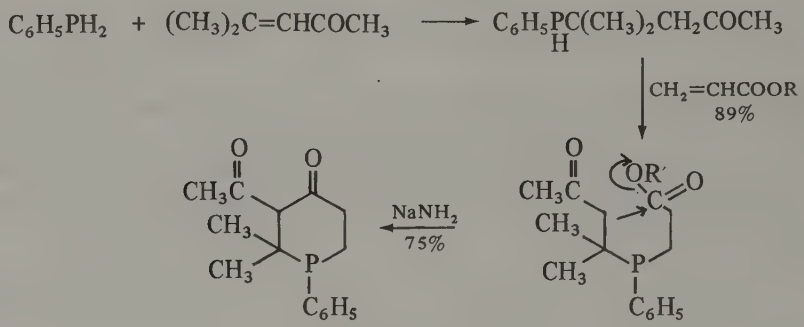
One reference[28] reports yields of 51% and 72% in the last two steps.

A valuable version of the Dieckmann route that provides access to phosphinic derivatives is based on the use of Michael adducts from methyl hypophosphite,[30] which has P(IV) structure.



$$CH_3O\overset{O}{\overset{\|}{P}}H_2 \xrightarrow[NaOCH_3,\ 69\%]{CH_2=CHCOOCH_3} CH_3O\overset{O}{\overset{\|}{P}}(CH_2CH_2COOCH_3)_2 \xrightarrow[60\%]{NaOC_2H_5}$$

In yet another form of intramolecular condensation (Claisen) with carbonyl compounds, Issleib[31] has prepared 3-acyl-4-phosphorinanones. This synthesis employs tertiary phosphines with chains having a γ-keto and a γ-carboalkoxy group. A typical combination is shown below.



$$C_6H_5PH_2 + (CH_3)_2C=CHCOCH_3 \longrightarrow C_6H_5\underset{H}{P}C(CH_3)_2CH_2COCH_3$$

Once the 4-phosphorinanones became available, access to many other derivatives of this ring system was possible, and in condensed form these are listed in Table 3.1. Most of the reactions are typical of cyclic ketones and probably do not differ greatly from what one might expect for the corresponding and more familiar 4-piperidones. What *is* peculiar to the series is the creation of cis, trans isomers when chirality is created at C-4. This isomerism, of course, is a consequence of the chirality already present at phosphorus, as a result of its stability to pyramidal inversion. The recognition in 1965 of this property of phosphorinanes,[32] with the demonstration of the separability of the isomers and techniques for their spectral characterization, opened a new field of exploration. A number of compounds, both P(III) and P(IV), have been synthesized in recent years as models for continuing stereochemical and NMR study. In Table 3.1, it is to be assumed that isomer mixtures are formed whenever a second chiral center is created in a transformation.

In marked contrast to the practice of phospholene chemistry, the P(IV) derivatives of the 4-phosphorinanones have received much less attention than the P(III) counterparts. Perhaps this is due to the fact that the major synthetic methods provide the P(III) form as the first product, whereas the opposite is true for

TABLE 3.1 General Reactions of Trivalent 4-Phosphorinanones

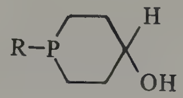
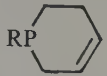
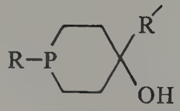
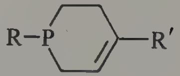
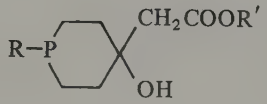
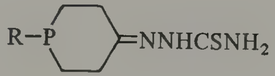
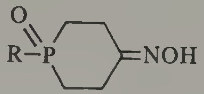
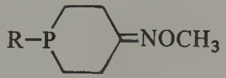
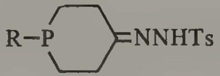
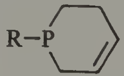
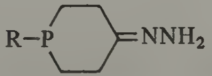
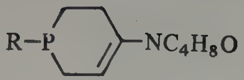
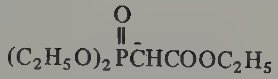
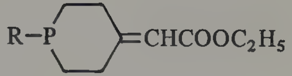
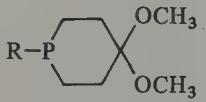
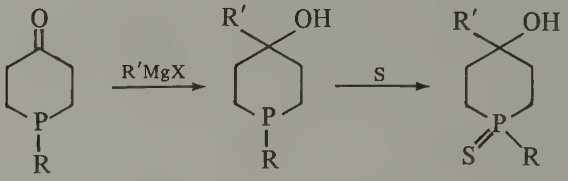
Reagent	Product	Notes	References
$LiAlH_4$		The first of many[34] reducing agents used to create 4-phosphorinanols in high yield; dehydration (Δ, Al_2O_3) gives[35] 	23, 33
$R'MgX$ or $R'Li$		Excellent route to 3° phosphorinanols; may be dehydrated[33] to 	33, 34, 36, 37
$BrZnCH_2COOR'$		Ester reducible by $LiAlH_4$ to $-CH_2OH$ (62.9%)	33
$H_2NNHCSNH_2$		Crystalline derivatives; semicarbazones[23] can also be formed	38
H_2NOH		Unusual act of oxidation by hydroxylamine accompanies oximination	38

TABLE 3.1 continued

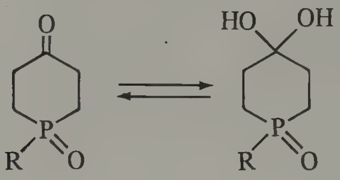
Reagent	Product	Notes	References
H_2NOCH_3		P-oxidation avoided by O-methyl derivative of hydroxylamine; Useful for synthesis with $LiAlH_4$ of  (80%)	39
p–$CH_3C_6H_4SO_2NHNH_2$		Product undergoes Bamford-Stevens reaction with $NaNH_2$ to form  (30%)	39
NH_2NH_2		Product with NaOH, ethylene glycol, 168° (Wolff-Kishner) reduced to phosphorinane (80% for 1,2,6-triphenyl)	14, 23

		Enamine formed with pyrrolidine also; precursors of several bicyclic compounds	40
$(C_6H_5)_3\overset{+}{P}CHR'$		Excellent route to 4-alkylene phosphorinanes ($R' = H$ or C_6H_5)	41, 42
 $(C_2H_5O)_2\overset{O}{\overset{\Vert}{P}}\overset{-}{C}HCOOC_2H_5$		Yield 55% but easily rearranged to endocyclic double bond; use of $(C_6H_5)_3\overset{+}{P}\overset{-}{C}HCOOC_2H_5$ can give mixture of isomers	41
$HC(OCH_3)_3$, HCl		$R{=}C_6H_5$ is solid; first phosphorinane to be analyzed by X-ray diffraction[43]	34

phospholenes. In fact, it is more common to perform chemistry at C-4 at the P(III) stage and then convert to the P(IV) form, a technique used successfully for the formation of 4-phosphorinanol sulfides.[44]

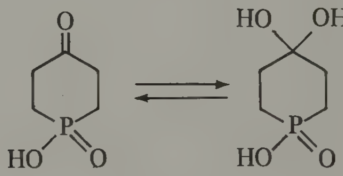


Some of the P(IV) forms possess properties that require a consideration of a transannular influence on the reactivity of the carbonyl group. Thus, it was detected in a ^{13}C NMR study[45] that freshly prepared water solutions of 1-methyl or 1-ethyl 4-phosphorinanone 1-oxide, 1-sulfide, or methiodide all rapidly developed signals for a *gem*-diol from covalent hydration of the carbonyl group.



7 8

The position of equilibrium was markedly dependent on temperature; diol 8, R=CH_3, was the only form detectable at 10° in the equilibrium with ketone 7, whereas at 70° 7 constituted 80-90% of the mixture. For most P(IV) forms, the diol predominated at room temperature. This behavior is totally lacking in the corresponding P(III) compound. An NMR study[30] on the 4-ketophosphinic acid in this series (9) showed the same tendencies.

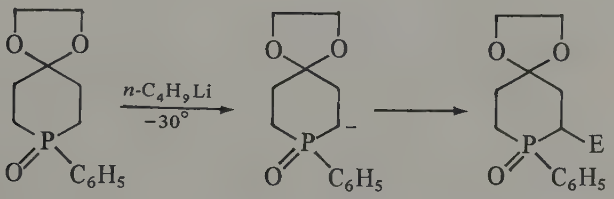


9

The presence of greater reactivity to nucleophiles is not totally unique to phosphorus compounds, however, for the methiodide of N-methyl-4-piperidone also is extensively hydrated covalently, and even the free amine shows about 16%

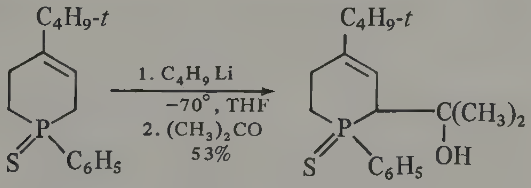
hydration.[46] The nature of the transannular effect remains unknown, although a suggestion has been made that an electric field effect may be involved because the ^{13}C NMR signals for C=O in the P(IV) 4-phosphorinanones show substantial upfield shifts relative to the P(III) forms.

In one synthetic operation in the P(IV) series, Mathey[21] was able to prepare carbanions at the position α- to phosphoryl, provided the carbonyl was first blocked as a ketal, and then subject them to various reactions with electrophiles. Acid hydrolysis regenerated in satisfactory yield the 4-phosphorinanone structure, now bearing 2-substituents. Some selected examples are shown below.

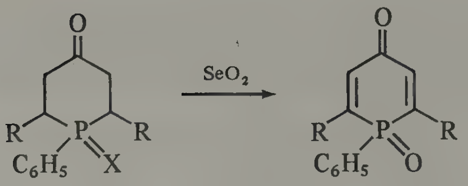


E=Br (from Br_2, 18%)
$C(OH)(CH_3)_2$ (from acetone, 40%)
COC_6H_5 (from $C_6H_5CO_2C_2H_5$, 22%)
COOH (from CO_2, 33%)

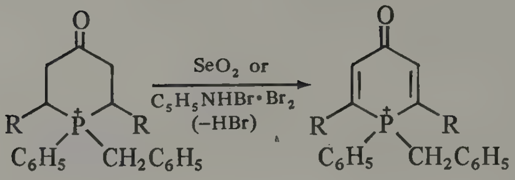
The keto group in the 2-substituted products, as well as in the starting compound, was shown in a later study[42] to participate in the Wittig reaction with $\phi_3\overset{+}{P}\overset{-}{C}H_2$. α-Carbanions can also be easily generated[37] from a $\Delta^{3,4}$-tetrahydrophosphorin sulfide (prepared by dehydration of the 4-phosphorinanol).



4-Phosphorinanones with P(IV) character can also be obtained in doubly unsaturated form, and some fascinating chemistry results from this structural modification. Märkl[47] first observed that 4-phosphorinanones can be dehydrogenated with SeO_2 in boiling ethanol; oxides, sulfides, and even the phosphines and their salts can be so treated, with the first three ending up as the P-oxide (**10**) and the latter retaining its salt structure (**11**). **11** also could be formed by bromination, followed by (sometimes) spontaneous dehydrohalogenation.

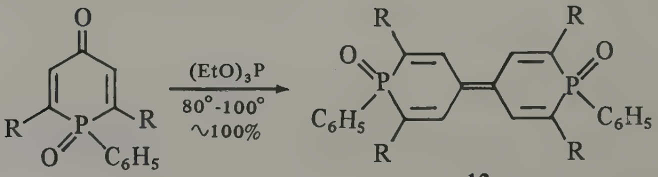


10



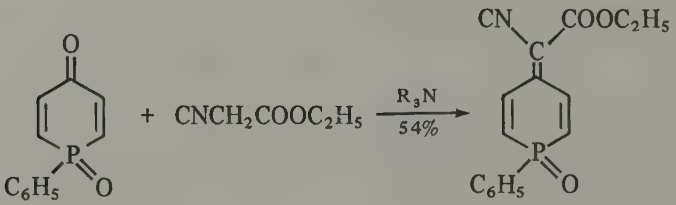
11

The unsaturation strongly influences the phosphoryl group of **10**, for it cannot be reduced to the phosphine with silanes in the usual way. With triethyl phosphite as a reducing agent, attack occurs on carbonyl, causing bimolecular coupling to form the highly unusual species **12**.



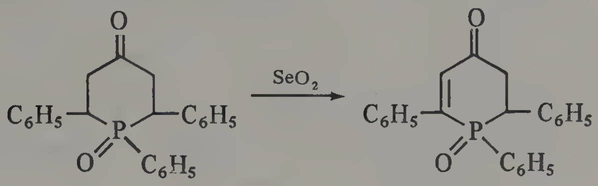
12

The carbonyl of **10** behaves normally in Knoevenagel condensations, and some 4-methylene derivatives have been prepared.[48]



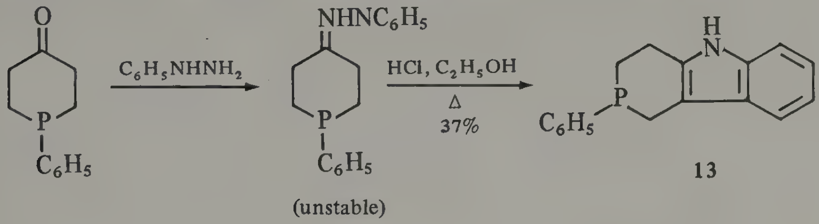
The diphenylmethylene derivatives were formed from **10** on reaction with the quinoline adduct of diphenylketene; fulvenoid derivatives resulted from first converting C=O to CCl_2 with PCl_5 and then reaction with cyclopentadienylidenes. These novel structures are of more interest in connection with phosphorins than with phosphorinanes, however.

In a much later paper, Märkl and co-workers reported[49] that SeO_2 could also effect introduction of a single double bond:



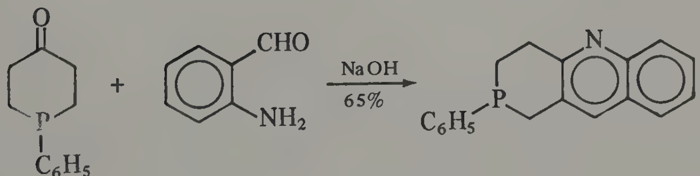
3.3 UTILIZATION OF 4-PHOSPHORINANONES FOR SYNTHESIS OF MULTICYCLIC SYSTEMS

Cyclic ketones have been involved in many syntheses of more complex heterocyclic systems, and it was not long after the discovery of the 4-phosphorinanones that they became candidates for such participation. Gallagher and Mann[50] were the first to achieve such syntheses when they subjected 1-phenyl-4-phosphorinanone to the Fischer indole synthesis and the Friedlander and Pfitzinger quinoline syntheses. With care having been exerted to prevent oxidation at phosphorus, the ketone behaved quite normally and did indeed provide the first examples of fused phosphorinane and pyrrole rings (**13**) and phosphorinane and pyridine rings (**14**, **15**).

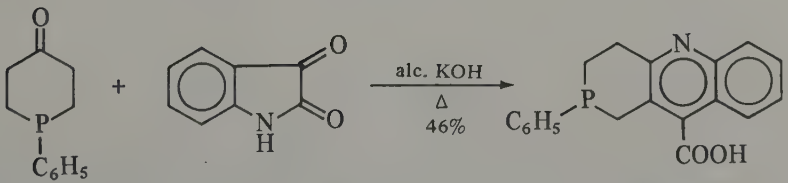


(unstable)

13



14

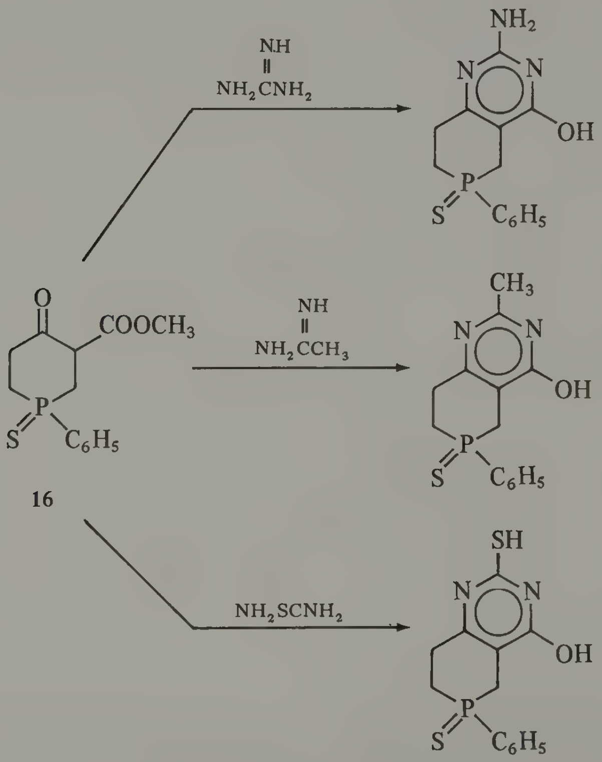


15

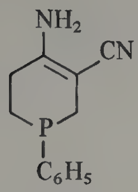
All of the new heterocyclic compounds were stable solids, and **15** was even sublimable. No evidence for zwitterion character in **15** was detected, but this is a property that the more basic P-alkyl, rather than P-phenyl, derivatives would probably exhibit.

With considerable success, later workers[51] used nine P-unsubstituted phenylhydrazones of 1-phenyl-4-phosphorinanone in the Fischer indole synthesis and it is obvious that the phosphorino[4,3-b]indoles are now readily accessible substances. Some of the compounds are highly susceptible to oxidation and can only be isolated as the P-oxides. Typical electronic effects as found in other indole syntheses from the various P-substituents were noted.

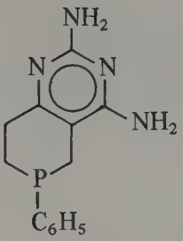
Pyrimidine-fused phosphorinanes have also become available recently. They have been obtained from the 3-carboalkoxy-4-phosphorinanones[27] that result from Dieckmann condensation of bis-esters, or from the enaminonitriles from the Thorpe condensation of bis-nitriles.[52] With the former as the P-sulfide (**16**), yields of 50-80% of pyrimidine derivatives were obtained from the conventional condensations of pyrimidine chemistry.



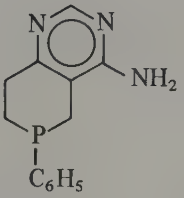
From the enaminonitrile **17**, whose tautomeric structure has been firmly established by spectroscopic means,[50] two other pyrimidines were obtained[52]—**18** (34%) from the use of guanidine, **19** (7%) from formamidine.



17

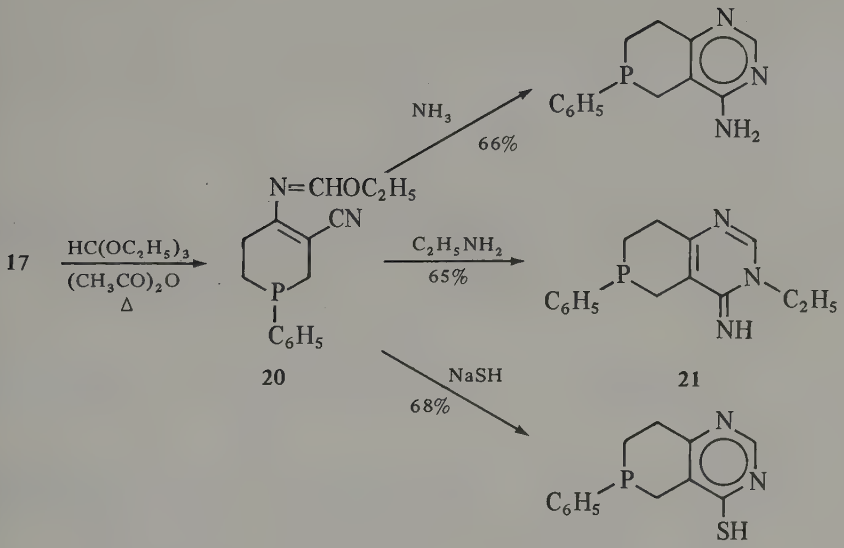


18



19

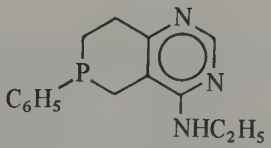
The same workers later[53] introduced another approach that provided the phosphorino[4,3-d]pyrimidine system with additional variability in the substitution pattern about the pyrimidine ring.



20

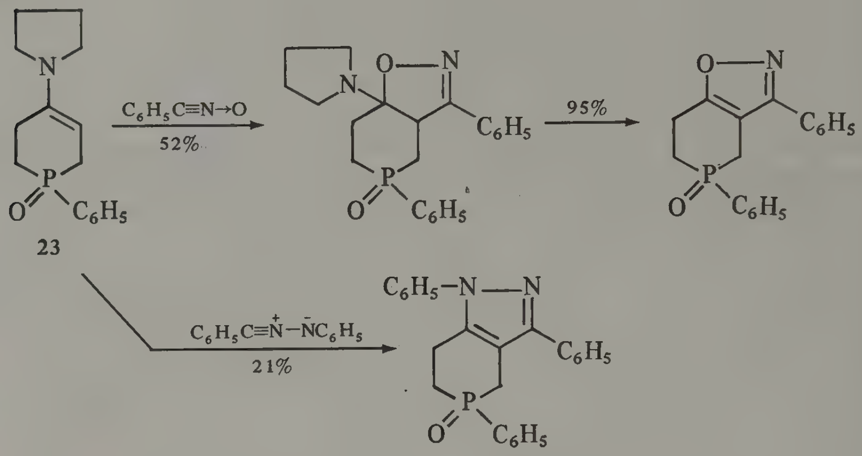
21

The intermediate **20** is isolated only as a crude oil; ethanolic solutions are used directly in the various condensations. Compound **21** then provided the N-ethyl derivative (**22**) by the Dimroth rearrangement.

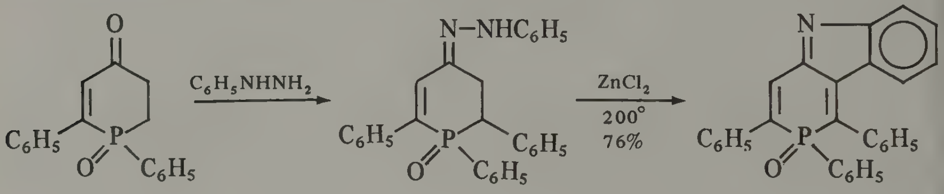


22

A totally different approach to fused heterocycles from 1-phenyl-4-phosphorinanones was developed by Märkl,[40] employing 1,3-dipolar cycloadditions of the enamine derivative (23) of the ketone. Such enamines were formed readily from either the phosphine or its P-oxide in an acid medium with pyrrolidine or morpholine.



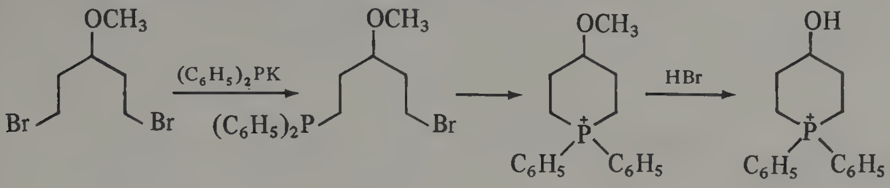
An unsaturated 4-phosphorinanone (Section 3.2) has recently been found[49] to form a phenylhydrazone that undergoes Fischer indolization. The product is a pseudo-indole of a new structural type.



The above examples suggest that only a beginning has been made into the realm of multicyclic structures approachable from 4-phosphorinanones or the Thorpe intermediates. The products that can be obtained are stable, generally crystalline substances, and should attract special attention from the standpoint of potential biological activity.

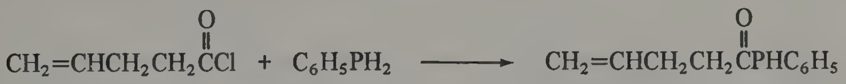
3.4 OTHER TYPES OF FUNCTIONAL PHOSPHORINANES

Hydroxy derivatives of phosphorinanes can be approached by methods other than the additions to the carbonyl of 4-phosphorinanones that are shown in Table 3.1. In an early synthesis, Märkl[54] formed the phosphorinane ring in 46% yield by reacting a methoxy-substituted dihalide with the anion of diphenylphosphine and then cleaving the methoxy from the resulting salt.



This route appears never to have been explored again for functional phosphorinane synthesis, although some obvious extensions are possible.

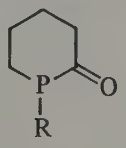
Phosphorinanes with a carbonyl group at the 2- or 3-position have only been prepared in the very recent past, and much remains to be done both in developing synthetic methods and in utilizing them as starting materials. The 2-phosphorinanone structure has been prepared by a process resembling one of the phosphorinane syntheses; a secondary phosphine with an α-keto group in an alkenyl chain is caused to cyclize under free-radical conditions. The key to this process is obtaining the starting keto compound, but it proved to be easily synthesized by the obvious method of acylating a primary phosphine.[55] Little is known about the chemistry of this type of product (24), which formally resembles the amide structure, although it is attracting the attention of those interested in resonance interactions of P(III) with π-systems and in the substantial rotational barriers[56] that develop from such interaction.



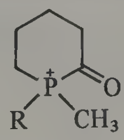
$$CH_2{=}CHCH_2CH_2\overset{O}{\overset{\|}{C}}Cl + C_6H_5PH_2 \longrightarrow CH_2{=}CHCH_2CH_2\overset{O}{\overset{\|}{C}}PHC_6H_5$$

24

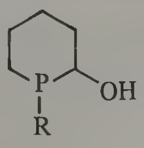
Cyclization occurs on heating in the presence of AIBN, giving a 40% yield (overall) of the 2-phosphorinanone (25) from 24 and 51% for the P-cyclohexyl counterpart. It appears from the limited information so far available that each function possesses its normal chemistry, unperturbed by any resonance interaction. Thus, quaternization with methyl iodide produces the expected salt 26 (yellow) and, more importantly, reduction with $LiAlH_4$ provides the 2-phosphorinanol (27).



25



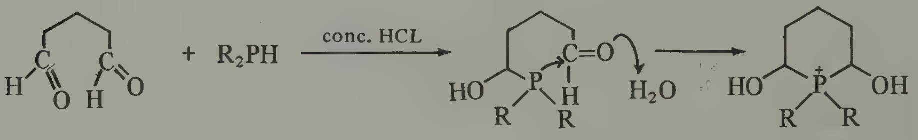
26



27

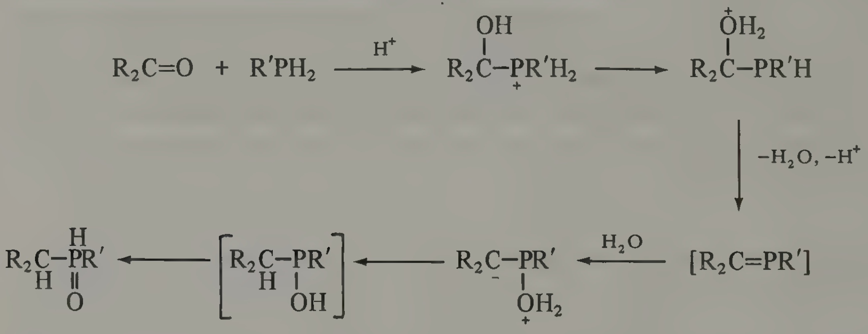
Fascinating possibilities exist here for synthetic and stereochemical work; it is not known, for example, if the 2-phosphorinanol is produced in cis, trans form, or what the intimate association of the two functions does to the conformation of the ring.

2,6-Phosphorinanediols (28) with quaternary phosphorus can be formed in one step in the cyclization of glutaraldehyde with secondary phosphines,[57] just as succinaldehyde under the same conditions has been noted to produce 2,5-phospholanediols.



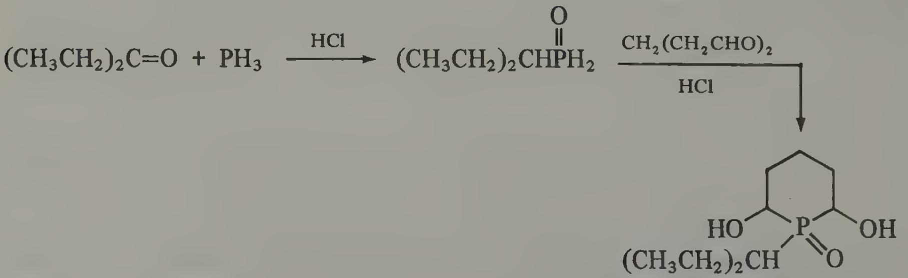
28

Several dialkylphosphines were used successfully in this process, and indeed it is an attractive route to the difunctional phosphorinane system. Again it has not been studied stereochemically, and the possibility of geometrical isomerism has not been considered. Primary phosphines behave differently in their reaction with carbonyls and are involved in an oxidation-reduction process that may be visualized as proceeding through an intermediate with a P-C double bond.

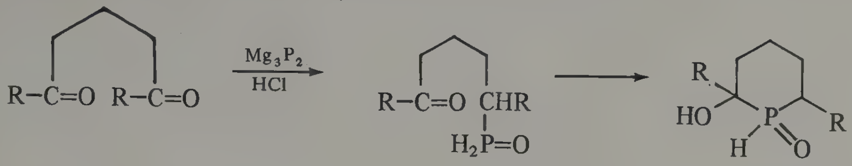


$$R_2C{=}O + R'PH_2 \xrightarrow{H^+} R_2\overset{OH}{\overset{|}{C}}-\underset{+}{P}R'H_2 \longrightarrow R_2\overset{\overset{+}{O}H_2}{\overset{|}{C}}-PR'H \xrightarrow{-H_2O,\,-H^+} [R_2C{=}PR'] \xrightarrow{H_2O} R_2\overset{-}{C}-\underset{\underset{+}{OH_2}}{\underset{|}{P}}R' \longrightarrow \left[R_2\underset{H}{C}-\underset{OH}{\underset{|}{P}}R'\right] \longrightarrow R_2\underset{H}{C}-\underset{O}{\underset{\|}{\overset{H}{P}}}R'$$

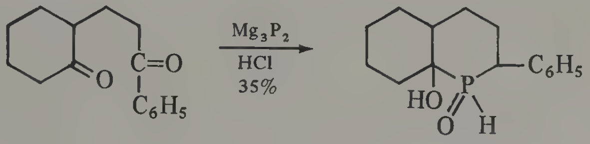
Phosphine itself behaves similarly and produces the rare primary phosphine oxide structure. These substances prove to be useful precursors of heterocycles, for their reaction pathways are limited as a consequence of their P(IV) state. Thus, a one-step synthesis of 2,6-phosphorinanediol 1-oxide is available from phosphine-ketone combinations[58]:



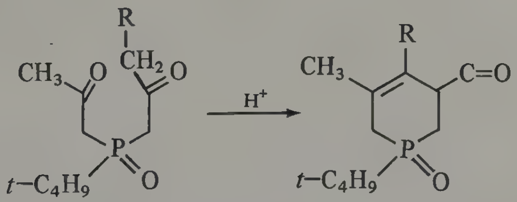
When applied to dialdehydes,[59] this chemistry produced the 2-phosphorinanol structure directly from PH_3 (here generated *in situ*, an advantage over handling the gas), in 25-35% yields.



The secondary phosphine oxide is readily oxidized (H_2O_2) to the phosphinic acid. A valuable extension to the synthesis of bicyclic phosphorinanes has been demonstrated:

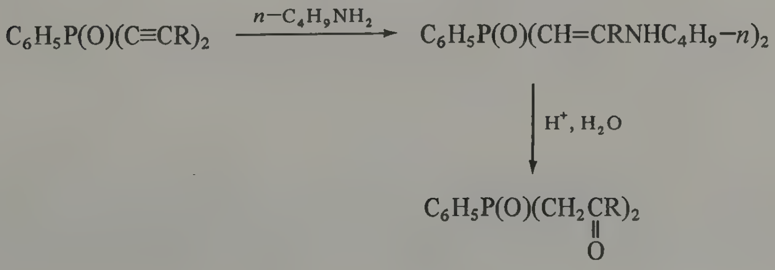


3-Phosphorinanones are another rare class where many research possibilities exist. The first examples contained the group in α,β-unsaturated form (**30**), a result of Märkl's discovery[60,61] that diketones of structure 29 (R = CH_3, C_6H_5, etc.) can undergo intramolecular aldol condensation.



29 **30**

The reaction, already providing an intermediate used in an important phosphorin synthesis (Section 3.8), remains open for exploitation, as the requisite diketones are rather readily prepared species. For example, in an earlier report[62] they were obtained by converting bis-acetylenic phosphine oxides to enamines, followed by hydrolysis.

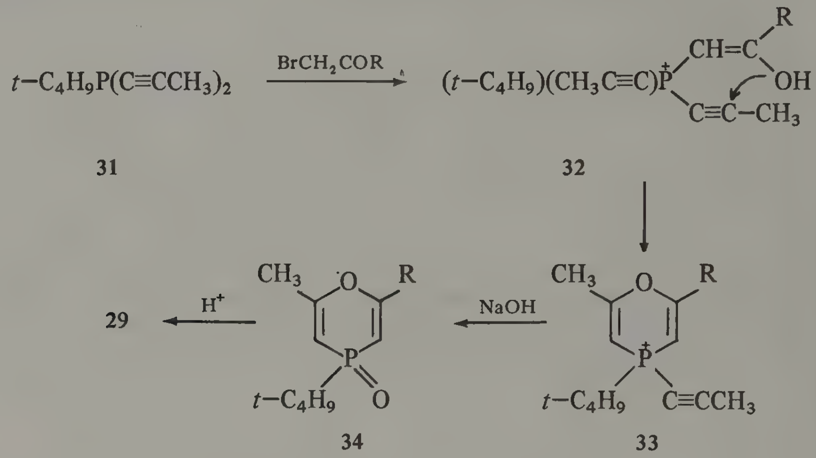


$$C_6H_5P(O)(C{\equiv}CR)_2 \xrightarrow{n-C_4H_9NH_2} C_6H_5P(O)(CH{=}CRNHC_4H_9-n)_2$$

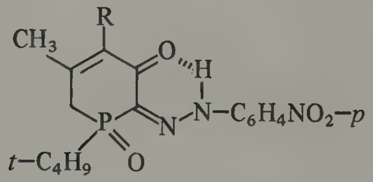
$$\Big\downarrow {\scriptstyle H^+,\, H_2O}$$

$$C_6H_5P(O)(CH_2\underset{\underset{O}{\|}}{C}R)_2$$

Märkl also employed bis-acetylenic derivatives (**31**) to generate diketones but placed them into rather different chemistry. Quaternization of the phosphine group of **31** with a bromomethyl ketone attached a function that through its enol form (**32**) can add to one of the triple bonds, forming the isolatable phosphapyran system (**33**; 95% from **31** for R = CH_3). Displacement of the acetylenic function, a good leaving group, with NaOH provided the phosphine oxide **34** (65%), and in this form the bis-enol ether structure can be hydrolyzed with aqueous acid. The diketones were not isolated but cyclized directly to the 3-phosphorinanones (75% for R = CH_3).



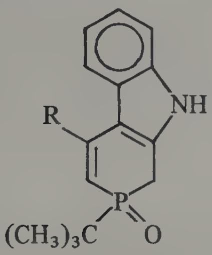
Märkl used only P-*t*-butyl derivatives in this process and it is not yet known if this feature is essential to the success of this route. The ketones of structure **30** are promising intermediates for other materials, with their several sites for reactivity. Märkl has already found that the CH_2 group at the 2-position is activated, and is readily coupled with diazonium salts. With *p*-nitrobenzenediazonium fluoborate, for example, a 1:1 product (**35**) is formed, but in some other cases a bis-coupling product results, presenting some complex tautomeric behavior.



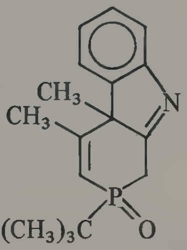
35

Other reactions depending on the active CH_2 group can certainly be anticipated. The keto group forms a phenylhydrazone readily, and Märkl proceeded[49] to subject several examples to Fischer indolization conditions. From the 5-methyl or

5-phenyl derivatives, the new 2-phospha-9-azafluorene system (**36**) was obtained in 65 and 90% yield, while the 4,5-dimethyl derivative provided the system in an isomeric form (**37**). The system **31** will be seen to be convertible to phosphorin derivatives (Section 3.8).

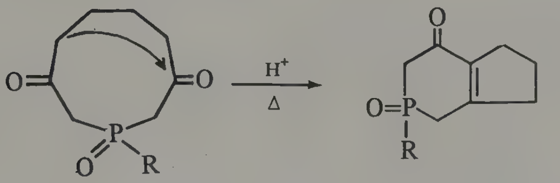


36



37

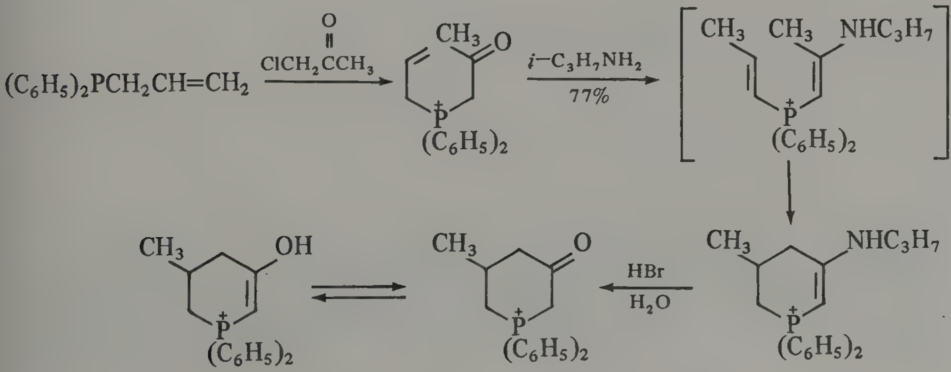
The same α,β-unsaturated ketone structure has been incorporated in bicyclic phosphorinanes.[63] This results from intramolecular aldol condensation of 3,8-diketophosphonane derivatives, recently made available (Section 2.4) by ozonolysis of bicyclic phospholene oxides.



R = CH$_3$, 87%
R = OH, 93%

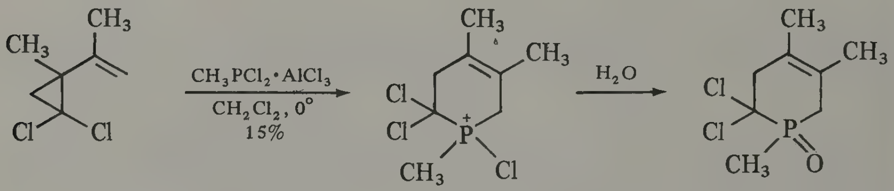
Such compounds could become valuable precursors to novel bicyclic structures, especially if the phosphorin system can be developed in the 6-membered ring.

A route to the saturated 3-phosphorinanone system has recently been described[64]:



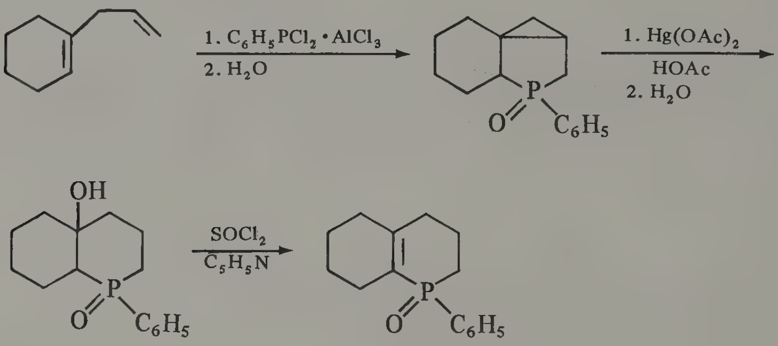
The cyclization is presumed to depend on rearrangement of the allyl to the reactive propenyl phosphonium salt, allowing Michael condensation with the activated methyl to occur. (With some other amines, a different path is followed, forming 1,4-azaphosphorinane derivatives.) The product was found to be intimately involved in tautomeric equilibrium, with the enol form favored through the stabilization of the double bond by conjugation with the positive phosphorus.

Unsaturated phosphorinanes have been noted in Table 3.1 to result from dehydration of 4-phosphorinanols. A new synthesis,[65] however, can provide such substances in the single step shown below, although the yield is low.



The reaction is proposed to involve carbonium ion intermediates, but it bears a remarkable formal similarity to a McCormack cycloaddition where a cyclopropyl group functions as a double bond! The method needs to be perfected, but it could become a useful source of tetrahydrophosphorins.

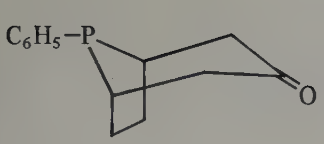
Combination of olefins with P(III) halide-AlCl$_3$ complexes is seen in Chapter 4 to be the major source of phosphetanes, but in the special case of the use of an allylcyclohexene,[66] a tricyclic product is obtained whose cyclopropane ring has been opened to generate the first 1-phosphadecalol. This in turn can be dehydrated to 38, also a new type of compound.



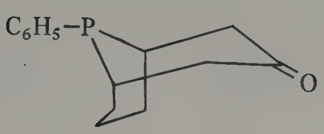
38

3.5 BRIDGED PHOSPHORINANES

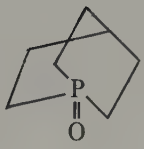
There are various ways in which a phosphorinane ring may be bridged with a small fragment, and work of recent years has led to synthetic methods for the following structures:



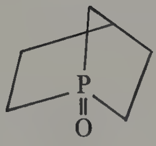
39



40

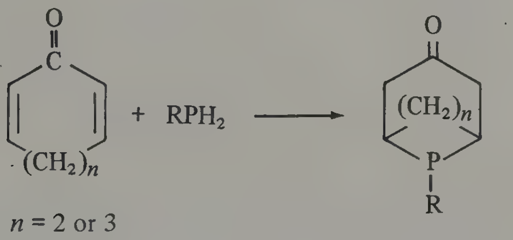


41

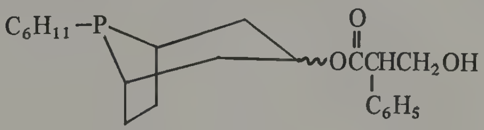


42

Application of the condensation of phosphines with dienones provided systems **39**[67] and **40**[68,69] for the first time; one merely uses a cyclic dienone, which behaves quite normally and provides 4-phosphorinanones with a bridge.



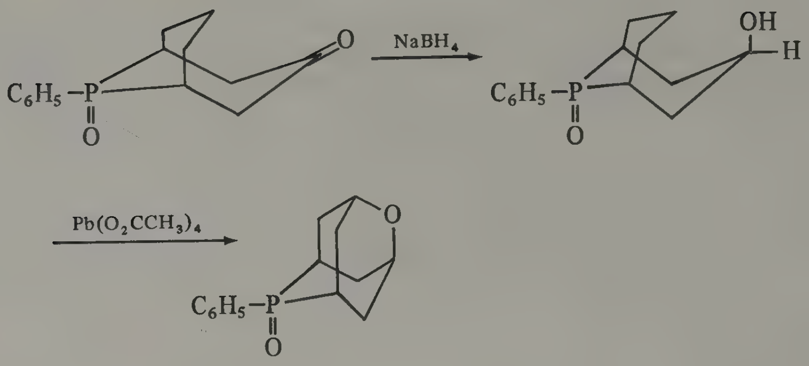
Two novel structures derived from these bridged systems deserve comment. System **39** is the phosphorus counterpart of tropinone; it was converted[70] to the alcohol, esterified, and the P-phenyl group reduced to cyclohexyl in order to mimic the corresponding amine, the highly potent atropine.



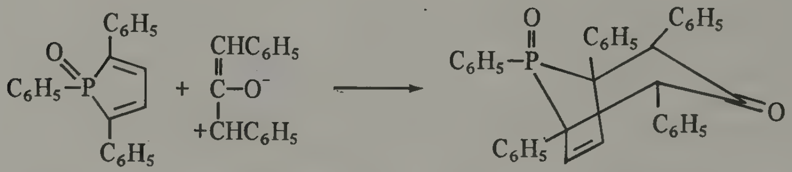
(cis or trans)

43

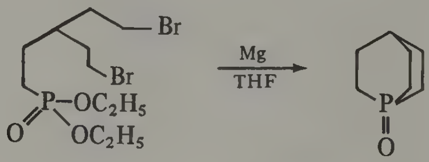
Although there has been no report as yet on biological activity, the idea of modeling phosphorus compounds after potent alkaloids could bring useful results, and many systems exist where this approach could be followed. System **40** has been converted by the steps shown below to a compound with an adamantane-like framework.



A totally different route, also described by Kashman,[71] can lead to system **39** from a phosphole oxide. The oxide, of course, has limited structural variability, for dimerization occurs with all but the polyphenyl derivatives. The bridge is installed with the oxyallylic cation, adding at the 2 and 5 position.

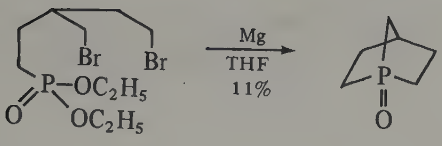


System **41** with its bridgehead phosphorus is of considerable interest for stereochemical and mechanistic reasons, and had been the target of several unsuccessful attempts until it was finally synthesized in 1974. The synthesis is remarkable in its simplicity and in the odds against its success. It involves a procedure already described for phosphorinane synthesis, the intramolecular attack of a Grignard reagent on a phosphonate group. For bicyclic synthesis, one must depend on a di-Grignard reagent displacing both alkoxy groups of a phosphonate, and Wetzel and Kenyon[72] were able to accomplish this in 6% yield from a phosphonate in a dilute THF medium.



41

The same one-step technique was successful in establishing the norbornane skeleton of **42** from a dibromide.

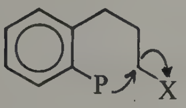


42

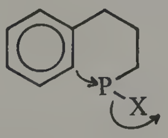
These structures will continue to arouse interest as their properties and those of derivatives such as the phosphines and their salts are studied.

3.6 BENZO DERIVATIVES OF PHOSPHORINANES

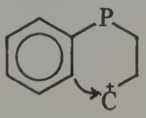
As would be expected, there is strong resemblance between techniques for forming benzophosphorinanes (tetrahydrophosphinolines) and phosphindoles. Three general approaches can be identified from the several syntheses reported since the first was accomplished in 1955, and they can be summarized schematically as follows:



Type 1

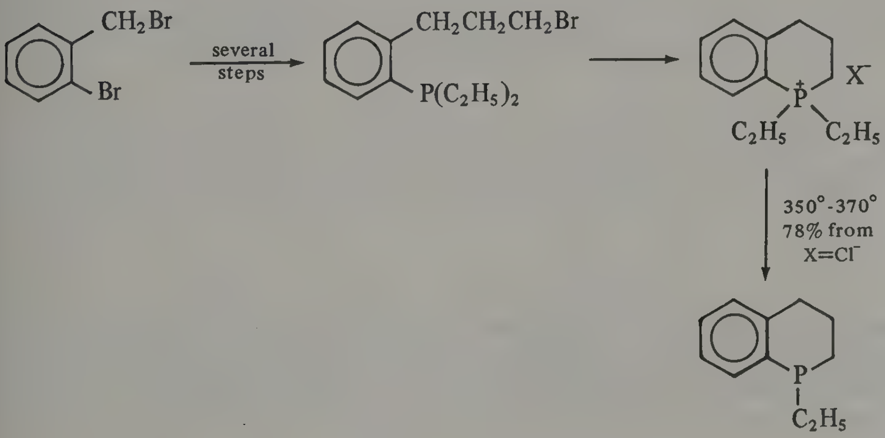


Type 2

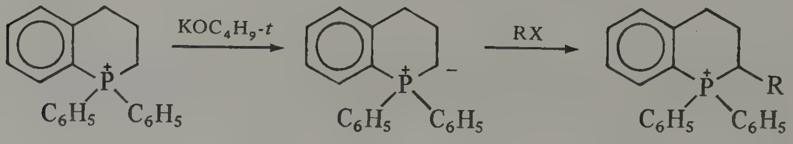


Type 3

Type 1 This approach so far is limited to intramolecular quaternization of 3-halopropyl phosphines. Beeby and Mann[73] employed this method in creating the first known member of the series and completed the synthesis of the phosphine by the thermal cleavage of ethylene as practiced in a phosphindoline synthesis.



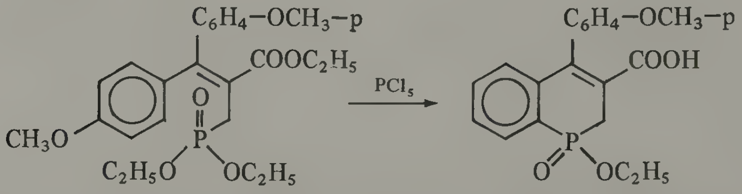
Märkl[74] also prepared quaternary salt **44** by this route. A valuable feature of this salt is that it readily forms a cyclic ylide with strong base that allows alkylation at the 2-position



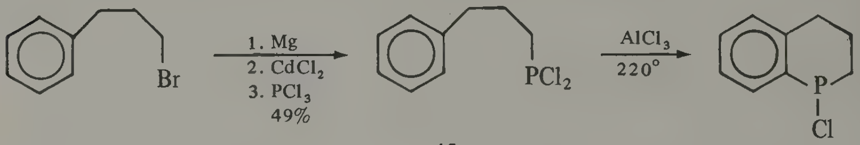
44

Dephenylation to the phosphine oxide was accomplished by aqueous base treatment, as in the phosphindoline series.

Type 2 Closing the cycle by allowing a phosphonic acid function to attack the benzene ring has been accomplished in one case.[75] The yield is poor here, as it is in many other cases where such acid derivatives are used, and it is doubtful that the method has much utility.

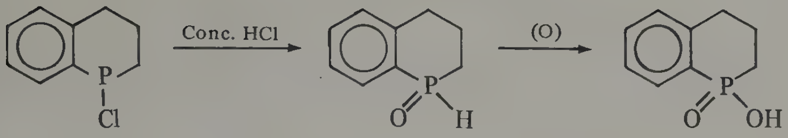


Much better results have recently been reported[76] when a phosphonous dichloride is the attacking group, and indeed the method is probably the best of all in terms of number of steps required and versatility in the phosphorus functionality achievable. The latter point follows from the fact that the initial cyclized product is a phosphinous chloride, which can be put through its paces in the usual way.

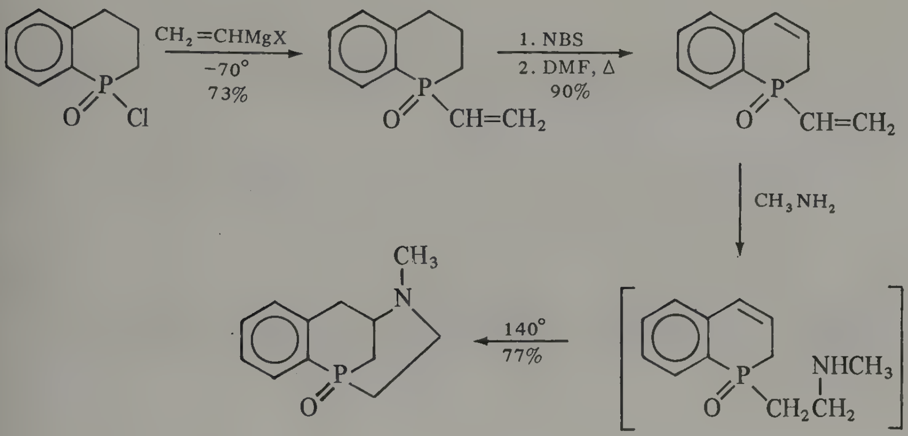


45

Rowley and Swan found it more convenient to perform direct acid hydrolysis on the cyclization mixture from **45**, followed by oxidation with H_2O_2 or Br_2 to isolate the product as the phosphinic acid. A remarkable 91% yield was reported from **45** in this sequence.



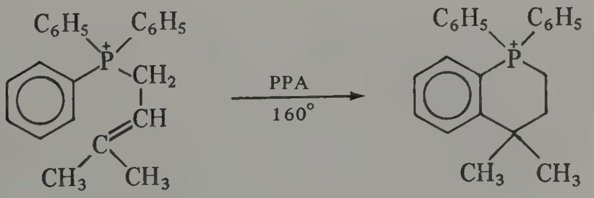
The acid, of course, can be converted to the phosphinic chloride and this in turn to phosphine oxides. A notable achievement[77] came from the preparation of a P-vinyl derivative; Michael addition occurred smoothly with primary amines and a technique was developed for then allowing nitrogen to be attached to the 3-position. The result is the creation of a benzomorphan-like structure (**46**) as found in the morphine alkaloids! The entire sequence is shown below.



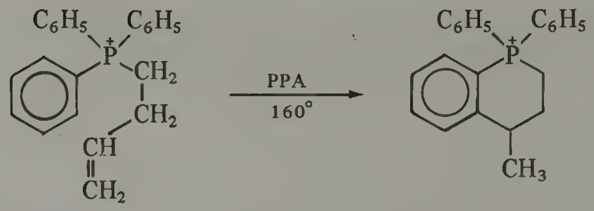
46

Other N-alkyl derivatives were made, as were phosphines in the new system. No derivatives have yet shown any notable analgesic activity.

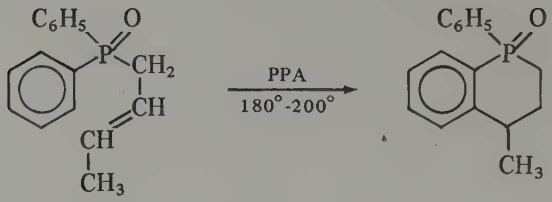
Type 3 Berlin's method of ring closure for phosphindolines, which involves formation of a carbonium ion from PPA and an alkenyl-P(IV) derivative, can be applied to phosphinoline synthesis if the positive charge can be stabilized on the γ-carbon. Illustrative cases where this has been accomplished are shown below.



89%, Ref. 78



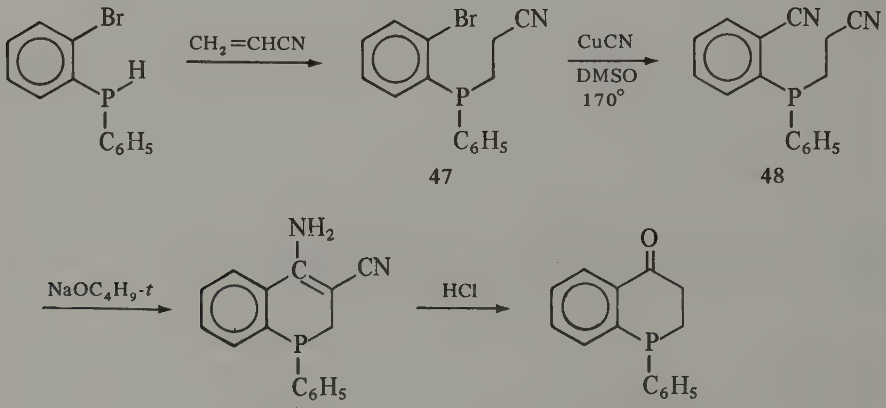
95%, Ref. 78



70%, Ref. 79

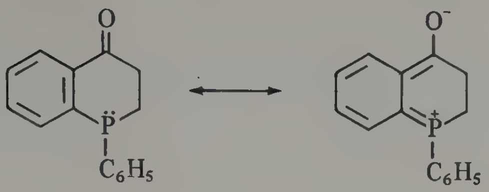
Earlier efforts to close the ring with a carboxyl group as the species generating a carbonium ion had been largely unsuccessful.[80]

4-Phosphinolones are also known, having been generated[80] by an extension of the Thorpe bis-nitrile cyclization. This step worked quite well for the bis-nitrile **48**.



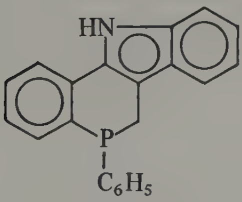
49 50

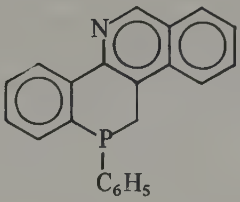
The conversion of **47** to **49**, without isolation of intermediate **48**, occurred in 26% yield; the hydrolysis to form **50** was performed in 55% yield. The phosphinolone is of interest both theoretically and practically. Unlike the corresponding quinolone, there is no significant contribution of a dipolar resonance form (**50a**) where electron release from the heteroatom is involved. This is in general keeping with the character of phenyl-P(III) functions, where such p_π-p_π bonding is not considered important.



50a

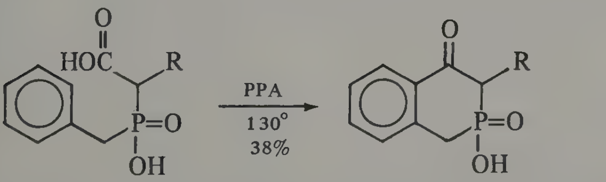
Perhaps because of the unimportance of this resonance, the carbonyl group undergoes conventional condensation reactions and in one report responded[80] to the conditions of the Fischer indole synthesis and Friedlander quinoline synthesis by forming novel tetracyclic products.





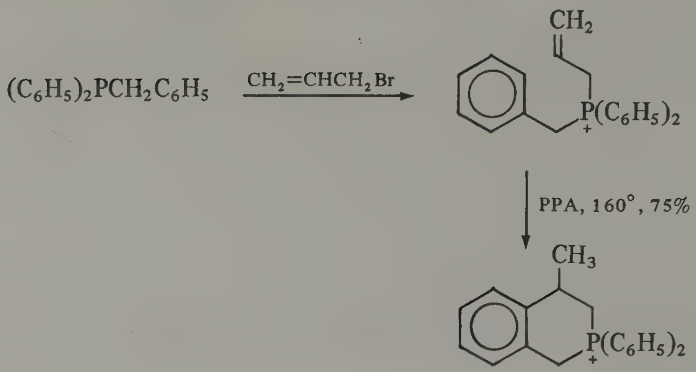
The first tetrahydroisophosphinoline synthesis, achieved as early as 1947,[81] resembles type (1) for tetrahydrophosphinoline synthesis, employing intramolecular quaternization for the ring closure.

A type (3) approach can be recognized in a later method[82] that leads to isophosphinolones:

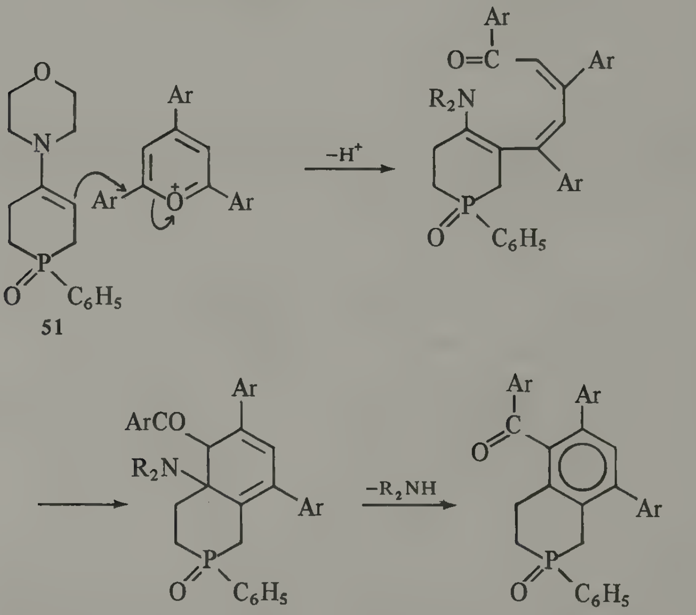


(R = H or CH_3)

The Berlin type (3) approach involving cyclization of alkenyl-P(IV) derivatives has also been adapted to tetrahydroisophosphinoline synthesis[83].



An entirely different approach to tetrahydroisophosphinolines resulted from Märkl and Baier's study[40] of the chemistry of enamines derived from 4-phosphorinanones. The electron-rich β-carbon of the enamine (**51**) was alkylated by the pyrylium ring, forming a species capable of electrocyclic closure to **52**.



51

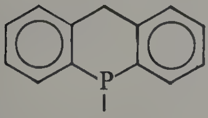
52

53

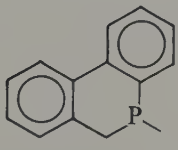
Intermediate **52** aromatized by elimination of the amine, thus generating the tetrahydroisophosphinoline system (**53**). The overall yield for Ar = C_6H_5 was 64.5%.

3.7 TRI- AND TETRA-CYCLIC PHOSPHORINANE DERIVATIVES

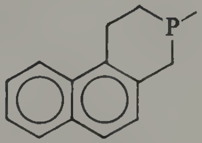
Of the numerous possibilities for tricyclic phosphorinane systems, only a few are known, the most important of which are **54-56**. The first two are also important in dibenzophosphorin chemistry, and these systems are encountered again in Section 3.8.



54



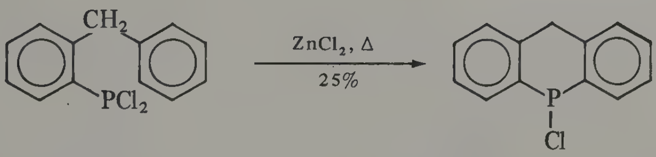
55



56

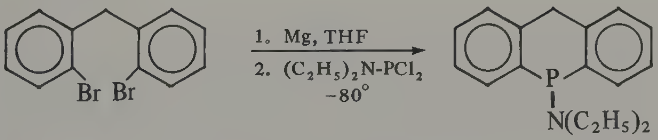
System **54** has been approached by a variety of procedures that close the central ring, as summarized below.

1 (Ref. 84)



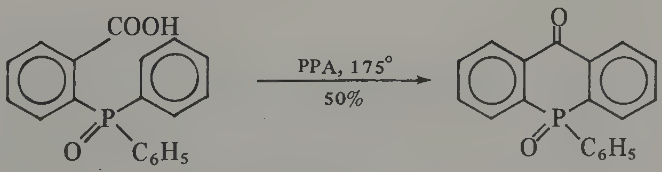
This intramolecular Friedel-Crafts reaction works quite well when P(III) halides are involved; P(IV) derivatives behave poorly in such cyclizations. An improved yield (40%) was later achieved with the use of $AlCl_3$ in CS_2.[85,86] The phosphinous chloride formed, of course, can be converted to many derivatives. The benzylic carbon may also bear a methyl[86] or phenyl[87] substituent, and presumably others as well.

2 (Ref. 85)

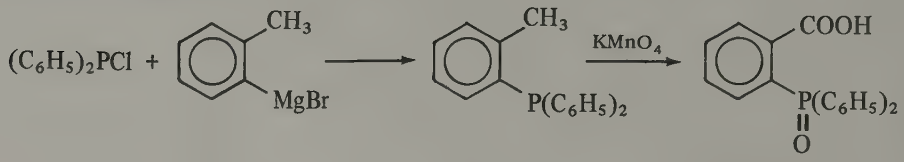


Once formed, the P-N bond can be cleaved with dry HCl to form the phosphinous chloride. The yield of this compound from the starting dibromide was 47%.

3 (Ref. 88)

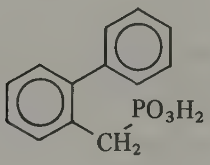


The difficulty of cyclization of P(IV) acids is overcome by this approach, which works well in spite of the deactivation of the ortho position to the phosphoryl group. Since the starting material is rather readily prepared, this may become the method of choice.



The presence of the carbonyl group provides access to other derivatives, some of which are of considerable interest in stereochemical studies on this ring system (Chapters 7 and 8). Two other research groups[89,90] have also reported on this cyclization procedure, one of these[90] extending it to the P-CH_3 derivative (47%), and it is obvious that an active area of research is developing around the new tricyclic ketones.

System **55** can be generated by familiar processes that create the central ring (pyrolysis at 350° of phosphonic acid **57**,[91,92] a low yield process; internal quaternization of phosphine **58**[93]).



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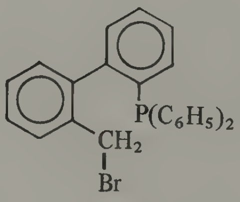
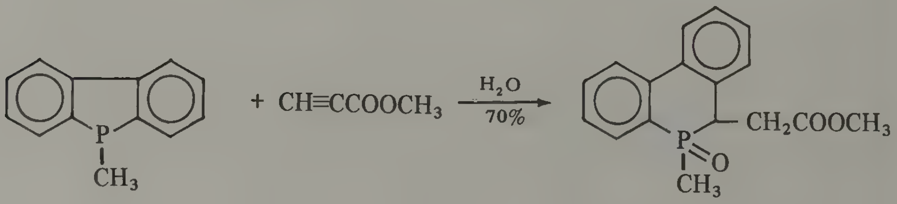


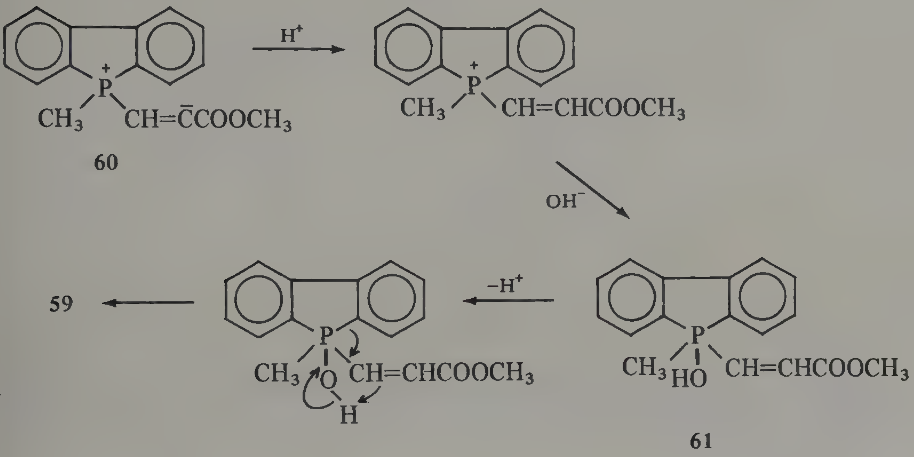
58

Far more useful, and employing novel chemistry, are some processes that effect ring expansion of the readily prepared dibenzophosphole system (Section 2.10). The first of these[94] depends upon a 1,2-aryl migration from a pentacovalent (phosphorane) intermediate, first discovered in the reaction of triarylphosphines with acetylenic compounds (moist). To accomplish ring expansion by this reaction, one of the benzo groups has to serve as the migrating aryl.

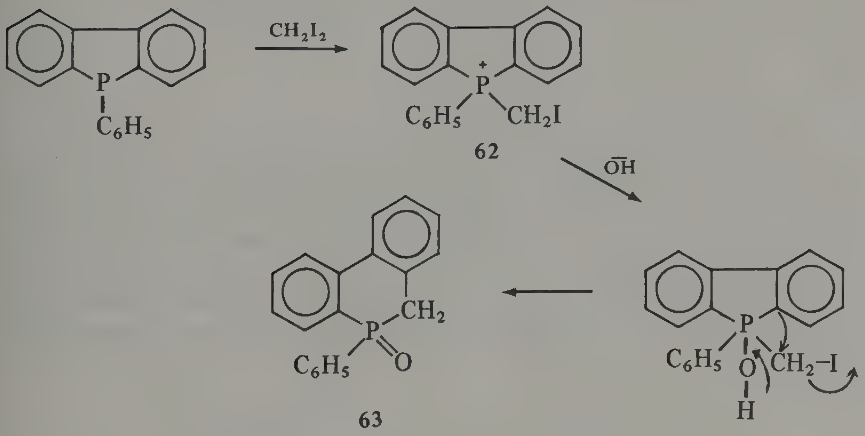


59

To account for this rearrangement, it is proposed that the initially formed dipolar adduct **60** is hydrated to a hydroxyphosphorane; formation of phosphoryl may be the driving force that displaces aryl from phosphorus.

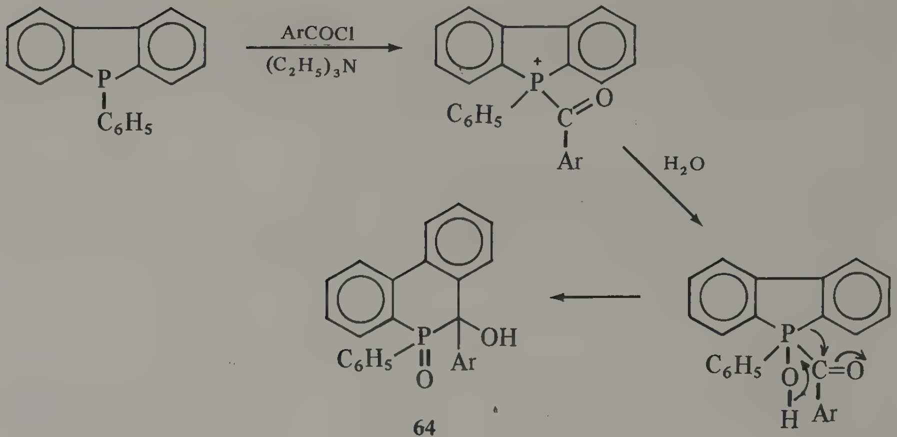


A hydroxy phosphorane intermediate is also involved in a second 1,2-aryl rearrangement[95] that occurs when an iodomethyl group is present; here the loss of I⁻ allows the aryl migration to occur as phosphoryl is formed.



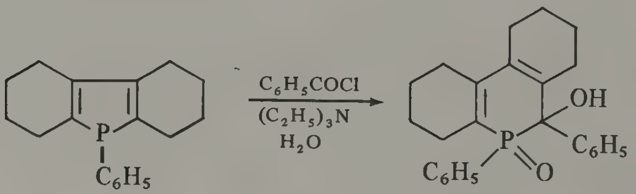
The yield of **63** from **62** is 58%. In both rearrangements, various substituents can be tolerated on phosphorus.

Finally, it has been demonstrated that a quite similar 1,2-aryl shift to an acyl carbon in a hydroxyphosphorane intermediate takes place, again acting as a useful ring-expansion device.[96]



64

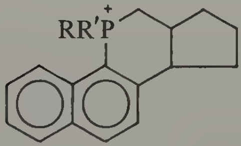
Compound **64** has been formed in 65% yield, whereas the P-CH_3 and P-C_2H_5 analogs can be obtained in excess of 90% yield. A similar process[97] provides the partially reduced compound **65**.



65

In all of the above rearrangements, the P(V) intermediate adopts the usual trigonal bipyramidal structure. The 5-membered ring is bonded at an apical and an equatorial position; it is from the apical position that aryl migration is believed to occur. Relief of ring strain in the 5-membered ring is also considered to be a driving force in the aryl migration.

Tetracyclic systems containing phosphorinane rings have only recently been constructed. These systems are of special interest in that they have the skeleton of steroids.



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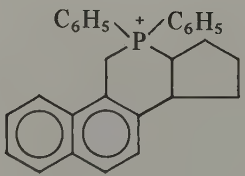
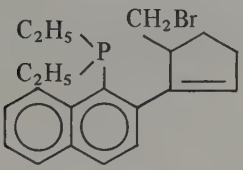


67

Structure 66 ($R = C_6H_5$, $R' = C_2H_5$) was prepared[98] by the well-known quaternization route (of 68), whereas a modification of the PPA-promoted cyclization of an alkenyl-phosphonium salt (69) was used to produce 67 in 25% yield.



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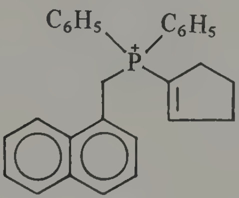
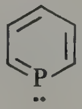


69

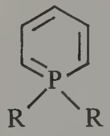
3.8 CONSTRUCTION OF THE PHOSPHORIN SYSTEM

Some of the more ingenious work in synthetic organophosphorus chemistry of recent years has involved the creation of the fully unsaturated—hence, in principle, aromatic—phosphorin system. First attained in P(III) form by Märkl[99] in 1966, the system attracted immediate interest because of its analogy to pyridine and because of the surprising stability exhibited by Märkl's compound (the 2,4,5-triphenyl derivative, an air-stable yellow solid with a melting point of 172°-173°). No true example of a C-P double bond was known prior to this time, which of course had contributed to the feeling that the phosphorin system could not exist. An enormous amount of effort has since gone into the development of new syntheses and a study of the chemical and physical properties of the system, mostly from the standpoint of ascertaining the presence or degree of aromaticity associated with this 6 π-electron arrangement. In this section, only methods that have been useful for constructing the ring will be considered; the properties of the system, which can indeed be described as aromatic but with special character donated by the P atom, are considered in Chapter 8.

Two types of phosphorins are encountered, depending on the number (3 or 5) of covalent bonds at phosphorus. A system of nomenclature is in use to define the two types, employing the prefix "λ" to indicate the degree of covalency.

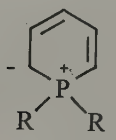


λ^3-Phosphorin



λ^5-Phosphorin

Their properties do differ, a result of the presence of ylide character in the λ^5-system.

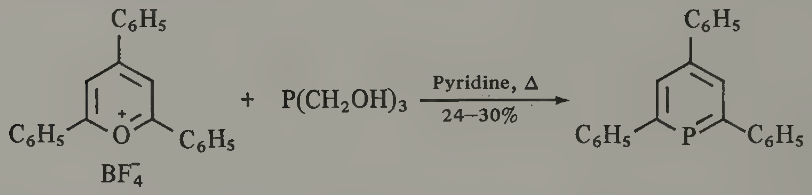


The λ^5-system had actually been obtained for the first time in 1963, also by Märkl,[4] but the λ^3-system is more curious because of its direct analogy to pyridine. A few benzo derivatives are also known, and the principles behind their syntheses are also described.

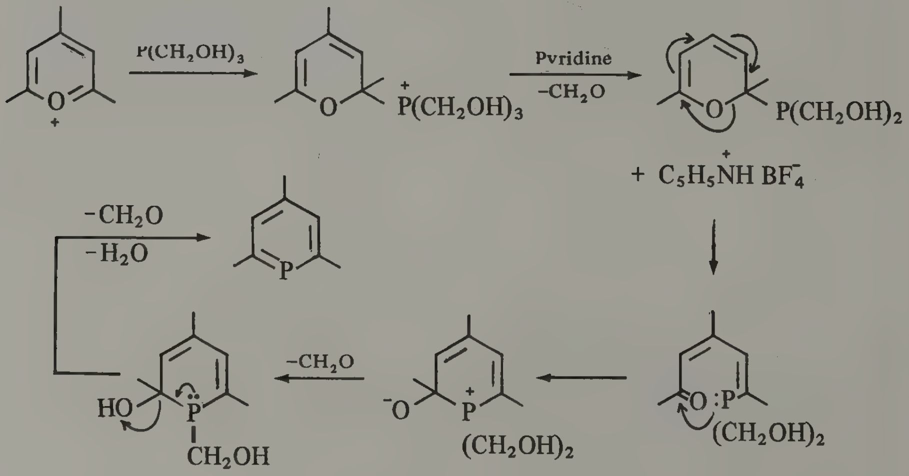
3.8.1 λ^3-Phosphorins

It is remarkable how simple the construction of this ring system has turned out to be. There are basically four approaches that have gained acceptance, all but one of which can be attributed to Märkl's pioneering efforts.

Märkl's first synthesis involves a one-step reaction of pyrylium fluoborates with phosphine[100] or the phosphine donors $P(CH_2OH)_3$,[99] $P(Si(CH_3)_3)_3$,[101] or $PH_4^+I^-$.[100] A key point for the successful use of $P(CH_2OH)_3$, the first to give a phosphorin, is to conduct the reaction in pyridine as solvent. The pyrylium salts all bear substituents at the 2, 4, and 6 positions, as in the synthesis of the famous 2,4,6-triphenylphosphorin:

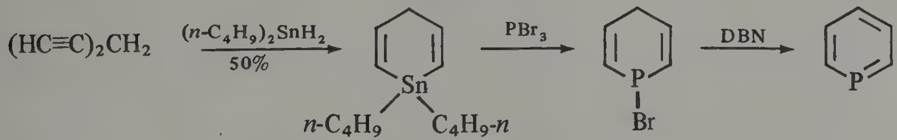


The mechanism no doubt involves a complex series of steps, which Märkl formulates[102] as follows:

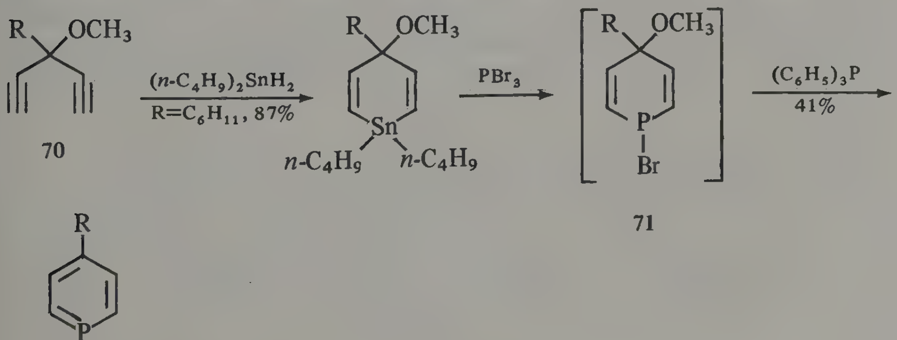


The use of PH_3 or $PH_4^+I^-$ requires operation in pressurized vessels, but better yields (50% or more) can be obtained. A large number of trisubstituted phosphorins have been obtained by this route; most of them are triaryl derivatives, but the important 2,4,6-trimethyl and 2,4,6-tri-*t*-butyl have been prepared. The former, which is a distillable liquid, became available after the pressurized PH_3 technique was introduced; $P(CH_2OH)_3$ had failed to react with the pyrylium salt, possibly due to steric crowding by CH_3 on approach of this relatively large nucleophile to the 2-position.

Just as stirring as the first synthesis of a triarylphosphorin was the achievement of the parent phosphorin molecule (phosphabenzene), a substance once no doubt thought by many to have no possibility of existence. Again the route involved in this dramatic work by Ashe[103] was remarkably simple. The ring is closed by twofold interaction of PBr_3 with a cyclic tin compound in a truly remarkable PX-metallation reaction; the product is the phosphinous bromide that retains the original cyclic structure of the tin compound. The product merely needs to lose HBr to form phosphorin. This is expedited by directly adding the base diazabicyclononene (DBN) to the initial reaction mixture



Phosphorin is a liquid that can be purified by gas chromatography at 110°; it is stable at room temperature if protected from air oxidation and is not affected by mild acids or base.[104] The method is not limited to the synthesis of the parent; 1,4-hexadiyne may be used[105] to generate the requisite dihydrostannabenzene with a 2-methyl group, and this can be converted to 2-methylphosphorin by heating with PBr_3 in CCl_4. Loss of HBr is spontaneous in this case, giving 2-methylphosphorin in 45% yield. The method was much less satisfactory as a route to 2,6-dimethylphosphorin; the yield is characterized simply as "very modest." A difficulty with this synthesis is that an isomeric (5-membered ring) tin compound can be formed in the diyne condensation step; this appeared to be the only product formed when 1-phenyl-1,4-pentadiyne was reacted with dibutyltin dihydride, thus



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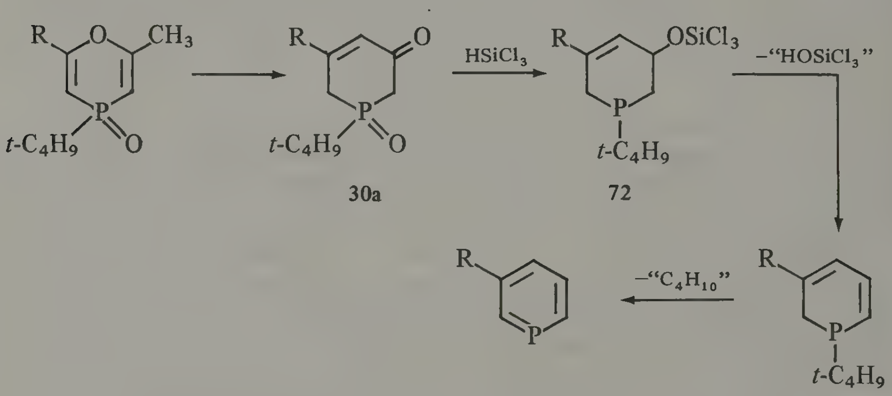
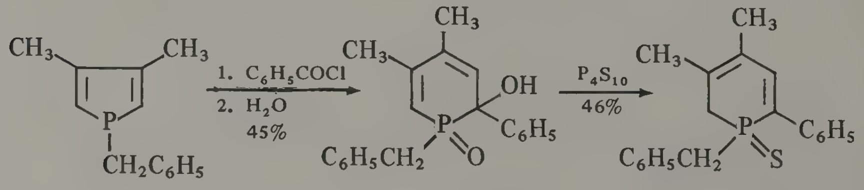
negating the phosphorin synthesis. This problem does not occur when a 3,3-disubstituted 1,4-diyne (**70**) is used,[106] and when one 3-substituent is OCH_3 the dihydrostannabenzene that forms can be reacted with PBr_3 to give a dihydrophosphorin (**71**) that can aromatize by loss of Br and OCH_3. Apparently the P-Br bond is cleaved to produce Br^+, whose removal is assisted by triphenyl phosphine (forming $(C_6H_5)_3\overset{+}{P}Br$). There no doubt will be other applications of the dihydrostannabenzene route to phosphorins, and many new types of derivatives might become available. Märkl has already attempted to prepare a 4-aldehyde derivative by a procedure that was successful for making arsabenzaldehyde, but without success.[102]

A third technique for phosphorin synthesis makes use of the unsaturated 3-ketophosphorinane system (as in **30**), discussed in Section 2.4, that results from phosphapyran derivatives. Märkl and Matthes attempted[107] to reduce this oxide with excess $SiHCl_3$, and although this was accomplished a second reaction also occurred that provided an intermediate (possibly 72) capable of decomposition on distillation to provide phosphorins! This reaction now stands as an important route to 3-substituted phosphorins, which cannot be made by either the pyrylium salt or dihydrostannabenzene routes. Thus, 3-phenylphosphorin was prepared in 30% yield from **30a**, R = C_6H_5, by this method.



The most recent phosphorin synthesis[108] starts with a phosphole and depends on the acylation-hydration sequence seen for dibenzophospholes[96] in Section 3.7 for ring expansion to a dihydro phosphorin (73). Heating with P_4S_{10} effects the loss of "OH" in an uncertain way and replacement of P = O with P = S. The product is desulfurized and the P-benzyl group eliminated as toluene.



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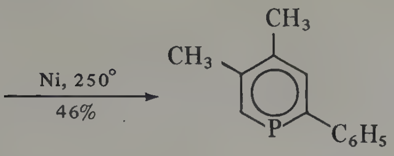
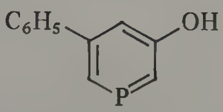


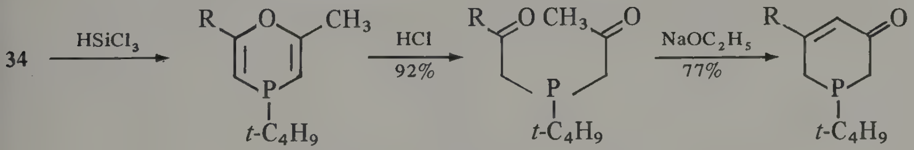
Although only one phosphorin has as yet been produced by this method, it is of value because it provides a substitution pattern not easily obtained by the other routes.

Again working from the phosphapyran, Märkl et al.[109] devised a technique that led to the first functionally substituted phosphorin, the 3-hydroxy derivative **74**.



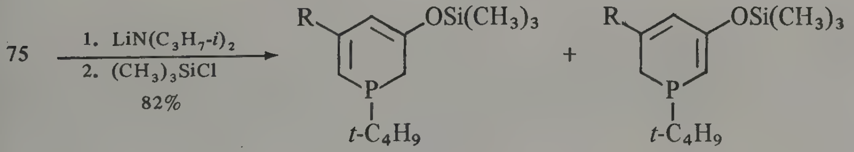
74

This heralds the beginning of an entirely new aspect of phosphorin chemistry, in which the many familiar functions of benzene or pyridine chemistry are to be installed on the phosphorin ring. The 3-hydroxy derivative, a low-melting distillable solid, was stable in that form rather than the ketone, and is, in effect, a phosphaphenol. This striking observation certainly will stimulate synthetic efforts to achieve other aromatic compounds. The synthesis from the phosphapyran **34**, R=C_6H_5, requires first the formation of the P(III) counterpart of 3-phosphorinanone **30**, which was achieved as follows:

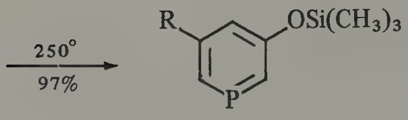


75

Attempts to aromatize by thermal cleavage of the butyl group of **75** were unsuccessful. This problem was overcome by conversion to a siloxydiene mixture (**76**-**77**) that on pyrolysis did undergo the elimination and gave the phosphorin **78** in 97% yield as a distillable liquid.

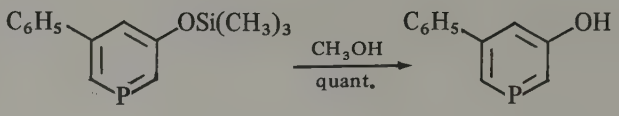


76 **77**



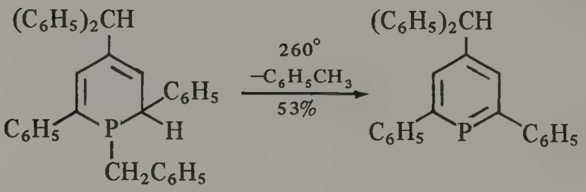
78

Conversion to the 3-hydroxyphosphorin was accomplished by boiling with neutral methanol.

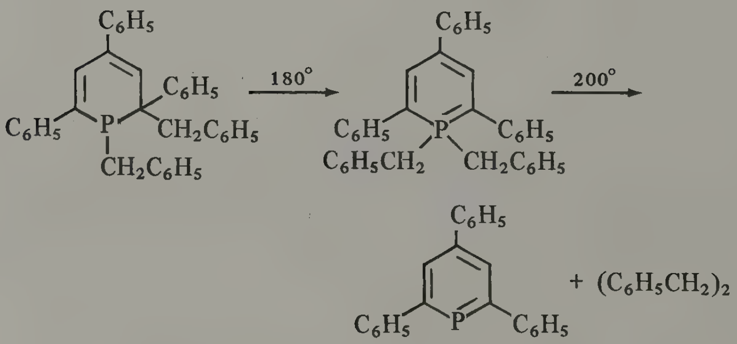


74

The final synthetic method to be considered depends again on a pyrolytic elimination to install the third double bond. The general principle requires that a good radical leaving group (e.g., benzyl or *t*-butyl) be present at the 1- or 2-positions (or 1,1- and 1,2-positions). Several such compounds are known, two examples of which are shown below:



(Ref. 110)

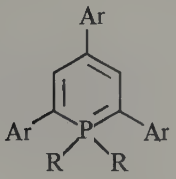


(Ref. 111)

Although not adding much versatility to the existing phosphorin syntheses, the general principle has found particular value in preparing "phosphanaphthalene", as will be seen.

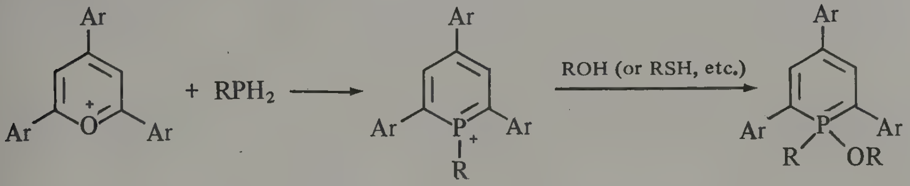
3.8.2 λ⁵-Phosphorins

The many derivatives of this system are primarily those with the 2,4,6-trisubstitution pattern, which are much more stable than the less highly substituted forms. The two groups on phosphorus can either be both alkyl or aryl, both based on heteroatoms, or a mixture of the two types.

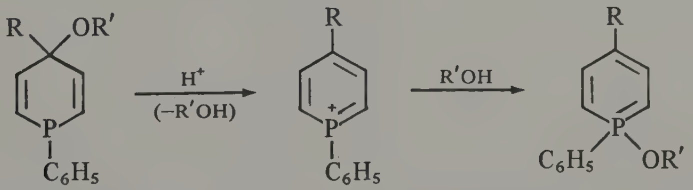


R = alkyl, aryl, OR, NR_2, SR, halogen

The primary synthetic route now in use depends on transformations of the λ^3-phosphorins as starting materials, because these are so easily prepared. The only major ring closure process is that where the pyrylium ion again is used to provide the five carbons of the ring, this time in reaction with a primary phosphine (or its equivalent)[112]:



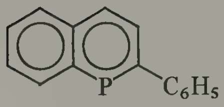
A rearrangement reaction[113] that produces monosubstituted (C-4) λ^5-phosphorins from dihydro-λ^3-phosphorins also has some utility:



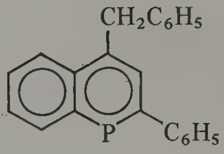
The starting dihydrophosphorin derivatives are readily prepared[114] by adding $C_6H_5PH_2$ to 3,3-disubstituted diynes under phase transfer conditions with a KOH catalyst enhanced by the presence of [18]-crown-6. Because the many routes based on λ^3-phosphorins as precursors are highly specialized, and as some are based on chemical properties to be considered in connection with the discussion of aromatic character, no further description of them will be given in this section. A review of the considerable amount of work done prior to about 1973, and an extensive list of known structures, is available.[115]

3.8.3 Benzophosphorins

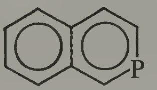
There is a distinct diminution of the stability of the phosphorin ring on fusion of one or two benzo groups, and in all but one reported case it has proved necessary to add the stabilizing feature of extra substitution in the heterocyclic ring in approaches to these compounds. At this time, the following structures have been isolated as stable and characterizable substances:



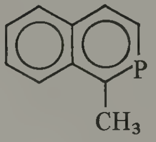
79,[116] mp 101°-102°



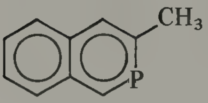
80,[117] mp 86°-87°



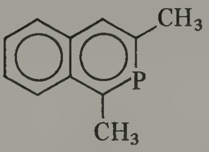
81[118], mp 82°-84°



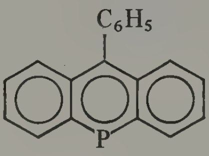
82[118], (impure)



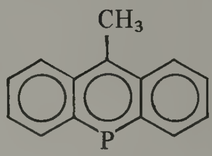
83,[118] mp 72°-74°



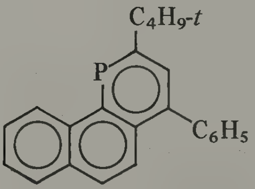
84,[118] bp 70° (10^{-2} mm)



85[87], mp 173°-176°

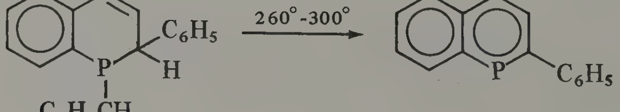


86[86], mp 120° dec

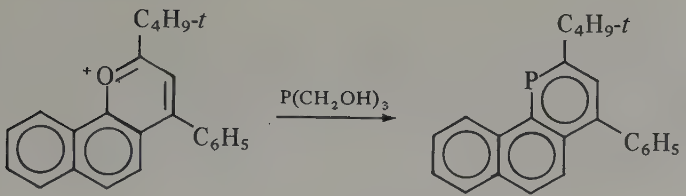


87,[119] mp 135°-136°

Two routes familiar from monocyclic phosphorin synthesis have made possible some of these structures. The technique of pyrolysis of a dihydrophosphorin derivative provided the 1-phosphanaphthalene, 79, whereas the pyrylium salt method led to 1-phosphanthrene 88.

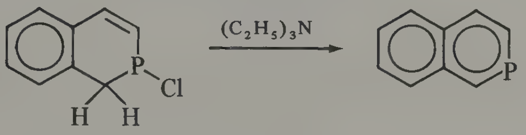


79

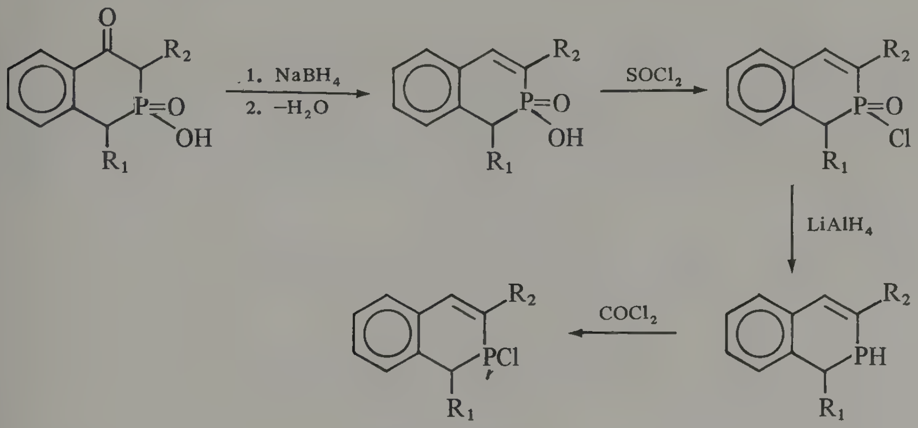


88

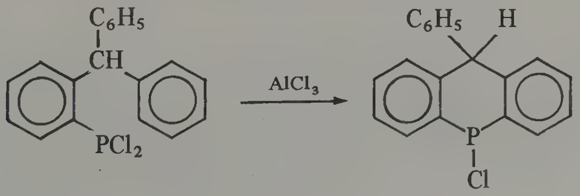
A new approach depends on dehydrohalogenation of a phosphinous halide to install the third double bond of the phosphorin ring in a final step, as in the illustration below,[118] which provided 2-phosphanaphthalene **81**:



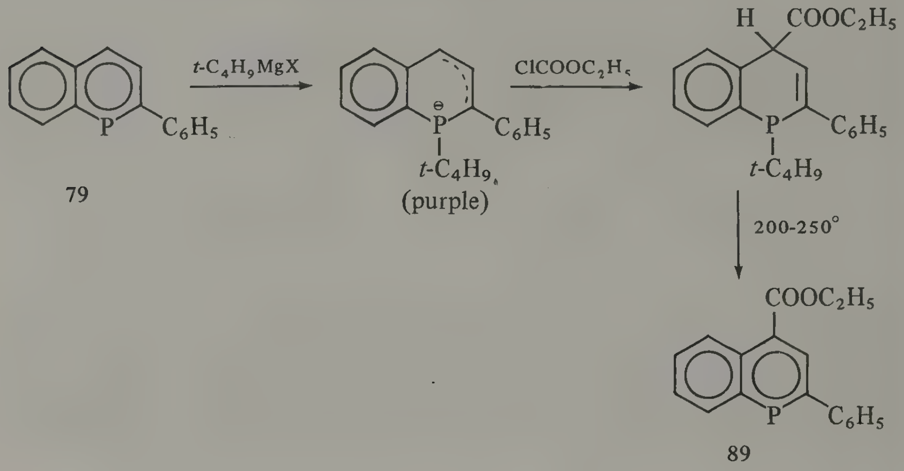
The method was useful not only for all of the 2-phosphanaphthalenes **81-84**, but also for phosphanthracenes **85** and **86**, as well as for some unstable compounds not shown (e.g., 9-phosphaphenanthrene[120]). The synthesis of the precursors of the phosphinous halides depends on conventional chemistry; the 3-phospha-2-tetralones prepared by the method of Henning[82] were useful for the precursors to **81-84**:



A Friedel-Crafts ring closure provided the precursor to **85**:

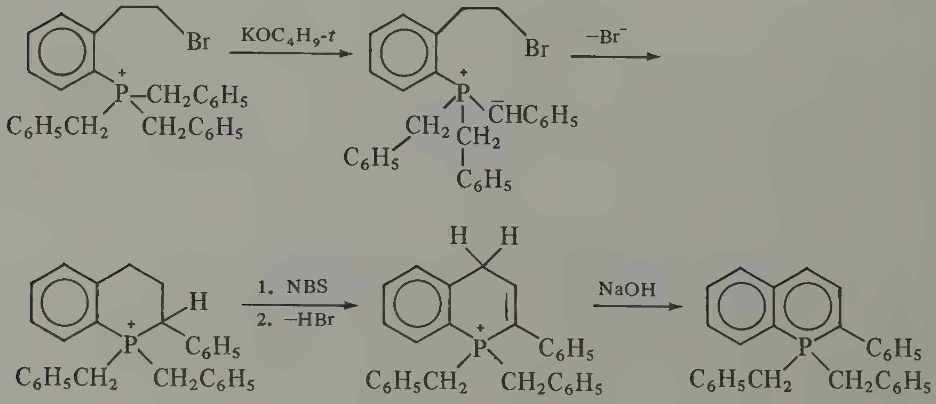


Just as the creation of a "phosphaphenol" stands as a major event in phosphorin chemistry, the construction of a "phosphanaphthoic acid" derivative is a turning point in the multicyclic phosphorin area, as it convincingly shows that functional group chemistry can be a reality in this field, needing only further investigation. The compound **89** was achieved in another sequence performed by Märkl and Heier[117] on the 2-phenyl-1-phosphanaphthalene (**79**).

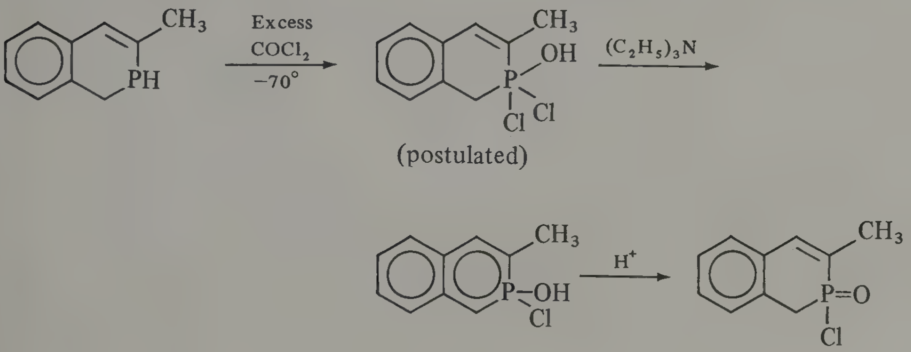


The attack at the 2-position by a Grignard reagent is a well-known property of phosphorins (Section 8.4), as is the alkylation of the resulting delocalized anion. The final step will be recognized as a form of the familiar pyrolysis procedure (the same sequence was used to install the 4-benzyl group in **80**). The product (**89**) was an orange-yellow oil, purified by Kugelrohr distillation at 120°-140° (0.1 mm).

λ^5-Benzophosphorins are also known, and a typical synthesis[121] is shown below. The final step emphasizes the ylide character of this system.



The 2-phosphanaphthalene system[122] supports a structural feature at P that is unknown in λ^5-phosphorins; P may bear the hydroxy group as in the structure **90**. Normally this group rearranges to the highly stable P=O structure, and indeed acid was found to isomerize **90** to **91**.

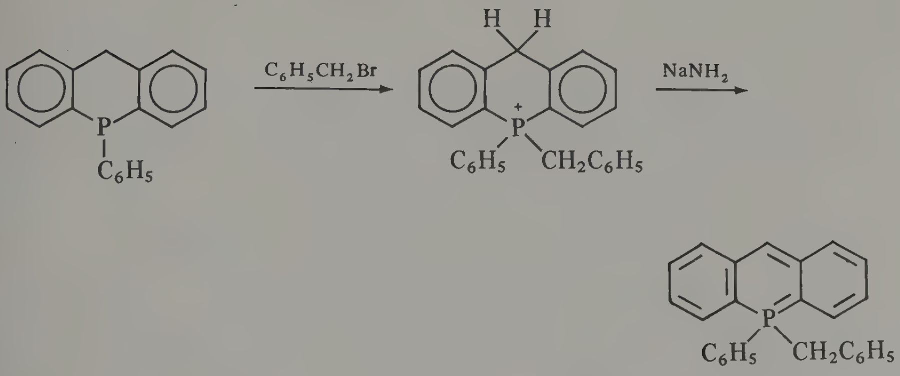


(postulated)

90 **91**

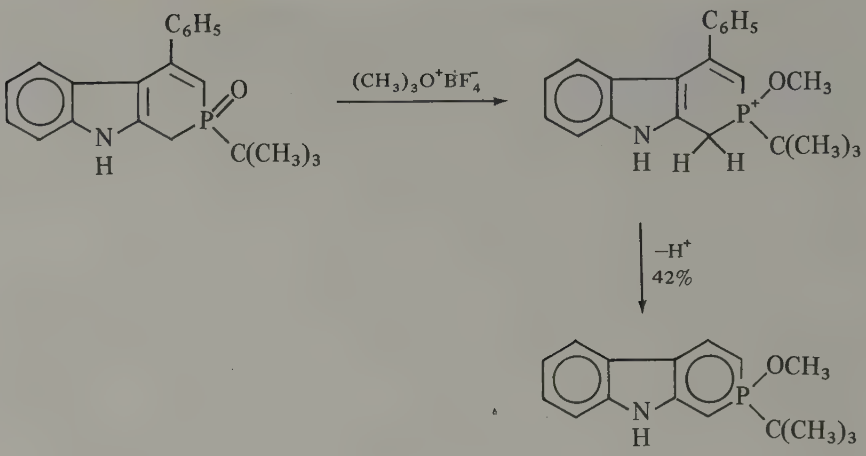
The conversion of a secondary phosphine to a phosphorane with excess phosgene is reported in this paper as a new observation.

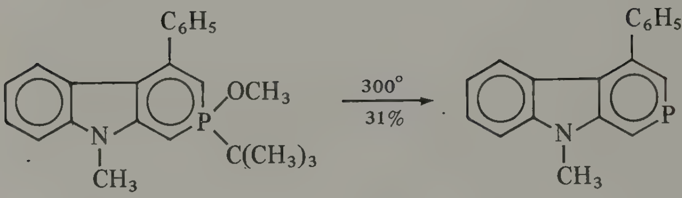
Tricyclic λ^5-phosphorins are represented[123] by **92**, a stable substance prepared by a method also useful for making monocyclic members of the λ^5-family.



92

The first multicyclic phosphorin derivatives with a heteroatom present were reported in 1979,[49] again opening an entirely new area of investigation. Both λ^3 and λ^5 derivatives in the phosphorino-indole system have been obtained as stable compounds, starting with the products of Fischer indolization of the unsaturated 3-phosphorinanones (Section 3.4).





Many new developments in this field can be expected in the future.

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chapter four

Small and Large Rings Containing Phosphorus

Although the chemistry of 5- and 6-membered rings has reached a mature stage of development, most of the other ring systems are in relatively primitive condition, and new synthetic methods are badly needed. The 4-membered (phosphetane) ring is in an intermediate position; one very valuable synthetic method exists for its construction, and the compounds have been of profound value as models for spectroscopic studies and for tests of concepts for reactions passing through the pentacovalent state. Even here, however, the major synthetic method is of limited scope, and produces phosphetanes only with C-methyl substituents (from 2 to 5) that can obscure some of the true properties of the parent ring. Furthermore, only one phosphetane is presently known with functionality other than that at phosphorus (a 3-carboxy derivative). The 3-membered ring exists in only about eight stable compounds, and the known larger rings (7-9 members) are in not much richer supply. Yet all offer fascinating opportunities for studies of bonding, conformation, and even delocalization phenomena in unsaturated systems.

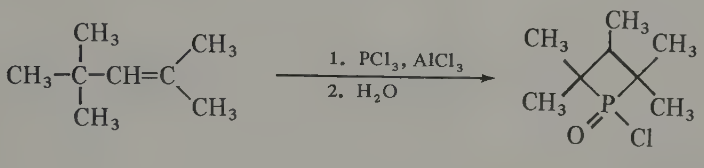
With its superior stage of development, the phosphetane system is chosen for the initial discussion in this chapter.

4.1 PHOSPHETANES

4.1.1 The Olefin-PX_3-$AlCl_3$ Process

In 1962, there appeared a paper[1] that set the stage for the creation of phosphetane chemistry. It was noted that certain olefins reacted with a mixture of PCl_3 and $AlCl_3$ to form saturated compounds with C-P bonds, and in subsequent work in the same laboratory[2] it was proven that the compounds were based on the phosphetane ring. The first example of a phosphetane formed by this new method was the

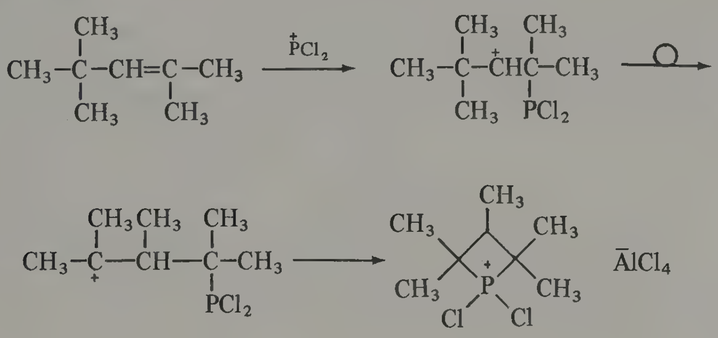
2,2,3,4,4-pentamethyl derivative of the phosphinic chloride (1); the cyclization reaction is remarkably simple and consists merely of stirring a 1:1:1 mixture of 2,4,4-trimethyl-2-pentene, PCl_3, and $AlCl_3$ in methylene chloride at 0°-10° for about 1 hr. The product is hydrolyzed at a temperature below 25° and the solid, recrystallizable phosphinic chloride is obtained in 62% yield. The acid and methyl ester were easily formed from the chloride.



1

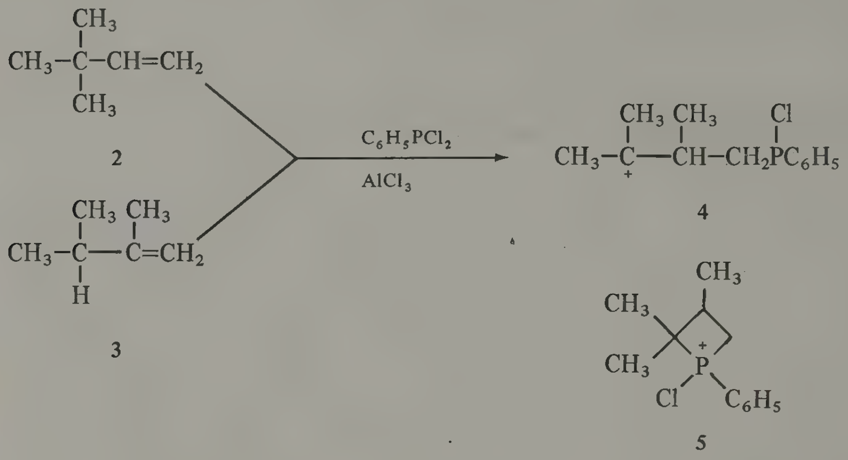
It was not until 1967 that another study (stereochemistry) of this product was reported[3]; in the same year, it was also demonstrated[4,5] that phosphonous dichlorides could participate in the process to form tertiary phosphine oxides. Other olefins were also employed successfully.[5] Several other laboratories recognized the novelty of the system and new contributions have appeared regularly over the last decade.

It is essential to recognize the basic mechanism of this unusual reaction before discussing its extensions and stereochemistry. McBride et al.[2] assigned an ionic mechanism that was presumed to be initiated by the formation of the species $\overset{+}{P}Cl_2\ \overset{-}{Al}Cl_4$. A carbonium ion is formed that undergoes an ordinary 1,2-shift to a more stable tertiary structure. Intramolecular alkylation on phosphorus then forms the phosphetane ring.

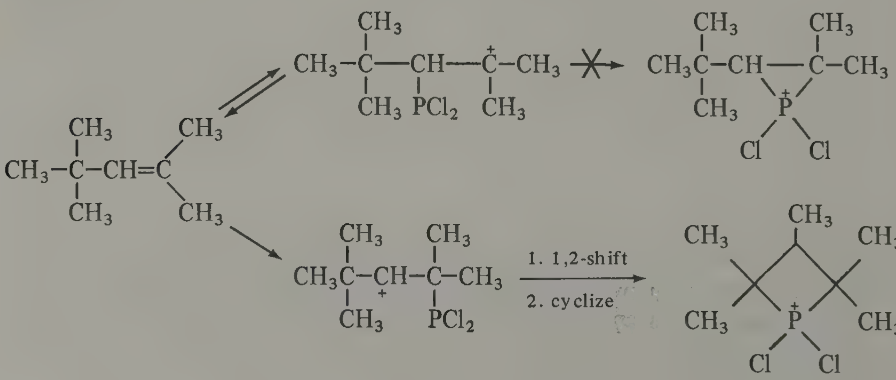


The key feature permitting the cyclization is the 1,2-shift, which creates a reactive 3-carbon fragment, and all olefins since discovered to form phosphetanes have of necessity had a branched carbon next to the double bond. This is the cause of the limitation of the method to multimethyl derivatives; the shift only occurs if a tertiary carbonium ion can result.

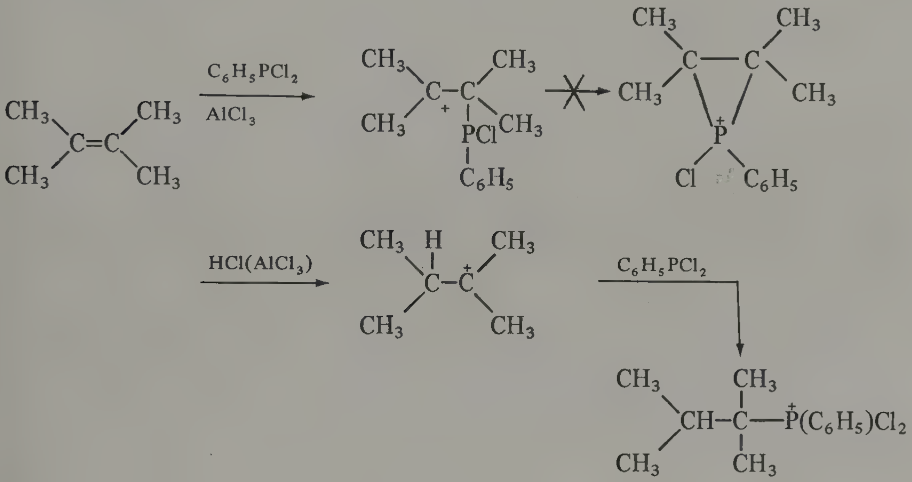
Support for this ionic mechanism comes from the observation that the two different olefins 2 and 3 can form the same phosphetane; olefin 2 undergoes a methyl shift, and 3 a hydride shift, to form the same carbonium ion (4) and, hence, phosphetane (5).



The structure of the initially formed carbonium ion requires clarification. From a 1-alkene, attack at the 1-position should be favored, giving a secondary or tertiary carbonium ion. However, for a 2-alkene, two sites of attack are possible and the one that seems favored is *not* the one that leads to the most stable carbonium ion. It has been assumed[2] that steric congestion interferes with the attack at the 3-position, which would give the most stable carbonium ion, and this early view has never received any additional comment. An alternative might be that attack occurs at both the 2- and 3-positions; the species from the former cannot easily stabilize itself by an intramolecular process (forming a phosphirane) and returns olefin to the medium, whereas the latter species rearranges and cyclizes readily to the phosphetane.

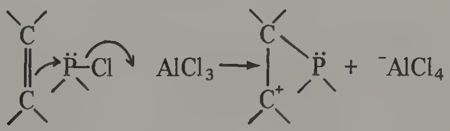


No phosphirane has ever been observed as a product of such reactions, even though one was specifically sought[6] by using an olefin that was biased against phosphetane formation. In this case, *no* cyclic product was observed; the product **6** was accounted for[7] by quite a different mechanism, involving protonation of the olefin by protonic species always associated with $AlCl_3$, followed by alkylation of phosphorus.



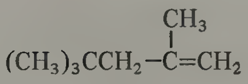
6

In this study,[7] it was observed that there is no direct evidence to support the popular concept that P(III) halides form P^+ ions with $AlCl_3$, although several reaction mechanisms are conveniently and repeatedly explained by assuming that such ionization occurs. ^{31}P NMR evidence strongly supported the formation of a nonionic complex with $AlCl_3$ and RPX_2 or R_2PX, but no change whatsoever was shown to occur with PCl_3. Conductance measurements by other workers[8] have led to the same conclusion. It therefore seems preferable to express the initial step of the olefin reaction in a somewhat different way, giving a role to $AlCl_3$ that assists in the attack of PCl_3 by removal of Cl^-.

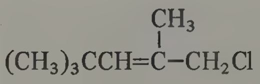


In the case where molecular complexes are formed from organic P(III) halides, it can be assumed that complexation has increased the electrophilic character of P, with stabilization of released Cl^- also of importance.

The olefins known to form phosphetanes, and the resulting substitution patterns, are given in Table 4.1. Tried unsuccessfully[9] were the olefins:

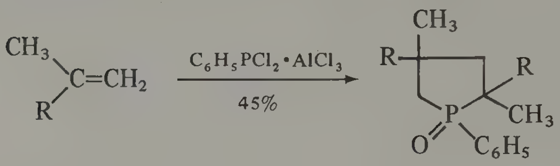


$(CH_3)_3CCH_2-\overset{CH_3}{\overset{|}{C}}=CH_2$



$(CH_3)_3CCH=\overset{CH_3}{\overset{|}{C}}-CH_2Cl$

Two olefins reacted with dimerization to give 5-membered rings, as in the example below[11]:

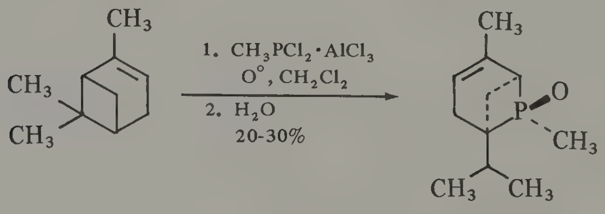


R = CH_3, 45%

R = C_6H_5, 5%

Several other olefins were used in the very first study[1] and, although C-P bonds were formed, the products could not be recognized as cyclic. With better spectroscopic techniques now available, it could be beneficial to reexamine these olefins, which included 2-pentene, 2-methyl-2-butene, 4-methyl-2-pentene, cyclohexene, 11-tricosene, and methyl oleate, to determine the nature of the C-P compounds formed.

One example[14] of the use of a cyclic olefin has been reported. α-Pinene, notorious for undergoing carbonium ion rearrangements, indeed provided a single stereoisomer of phosphetane 7, which has the unusual feature of a 3-carbon bridge from the 2,4-positions of the phosphetane ring.



7

The structure was established by X-ray analysis, which showed the internal C-P-C angle to be smaller (76.9°) than usual, with remarkably large puckering in the 4-membered ring (see Chapter 8). To account for the structure, the mechanism below was proposed:

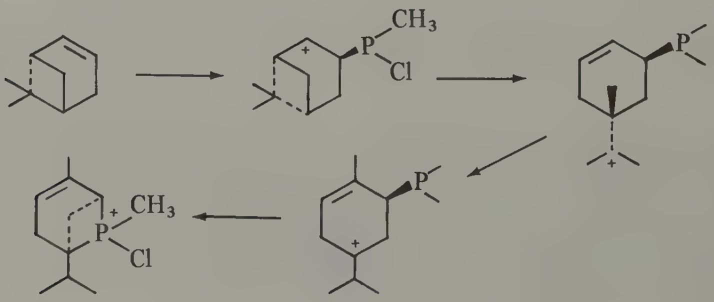
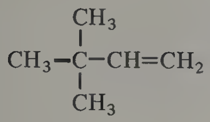
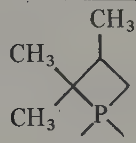
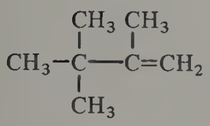
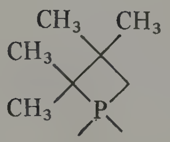
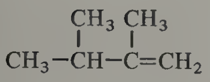
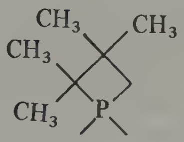
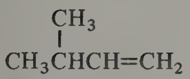
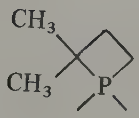
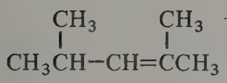
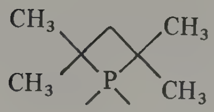
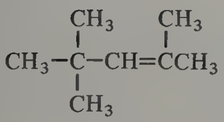
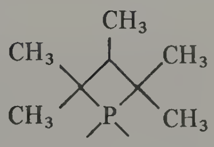
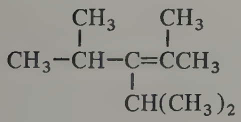
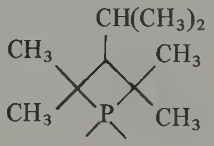
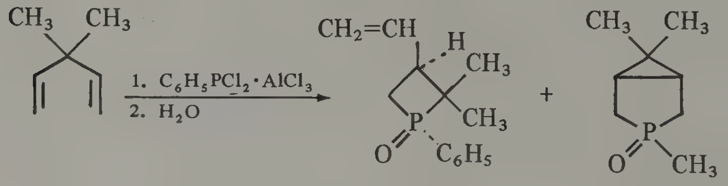


TABLE 4.1 Phosphetanes Formed from Olefins

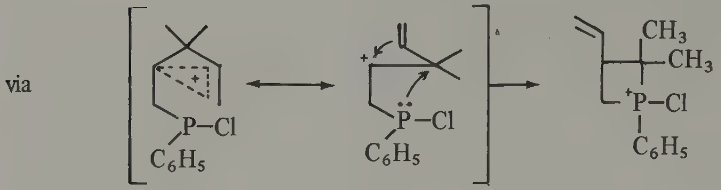
Olefin	Substitution Pattern	Illustrative References
 $CH_3-C(CH_3)_2-CH=CH_2$		9,10
 $CH_3-C(CH_3)_2-C(CH_3)=CH_2$		5
 $CH_3-CH(CH_3)-C(CH_3)=CH_2$		5
 $CH_3CH(CH_3)CH=CH_2$		11
 $CH_3CH(CH_3)-CH=C(CH_3)CH_3$		19
 $CH_3-C(CH_3)_2-CH=C(CH_3)CH_3$		2,3,9
 $CH_3-CH(CH_3)-C(CH(CH_3)_2)=C(CH_3)CH_3$		13

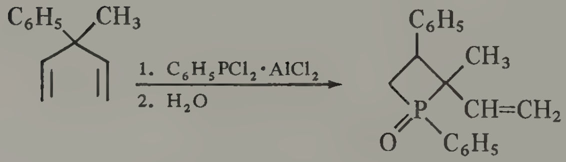
Also of much interest are recent studies where various types of dienes have been used under the standard conditions. Although a phosphetane derivative was obtained in only one instance, several phosphorus heterocycles of novel structures did result and they are summarized briefly.

(1) Phosphetanes **8** and **10** with the feature of C-vinyl and C-phenyl substitution were formed[15] from 1,4-pentadienes bearing 3,3-substituents. Their structures and proposed pathway of formation are shown below:

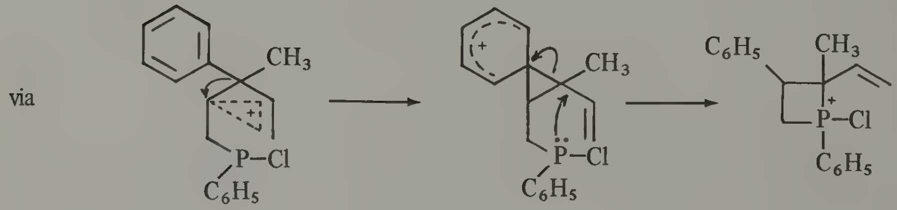


8, 20-25% **9**, 20-25%



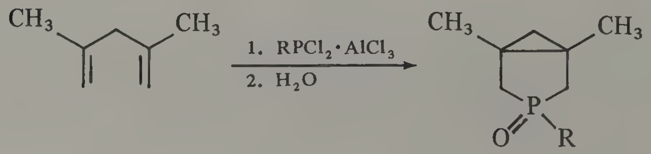


10, 5%



These are the first instances of groups other than alkyl migrating in such reactions.

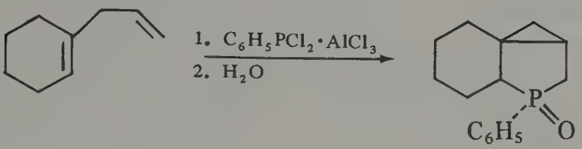
(2) The alternative pathway, which produces only a cyclopropane structure such as **9**, was followed when the diene carried no 3-substituent but was 2,4-disubstituted[16]:



(syn, anti)

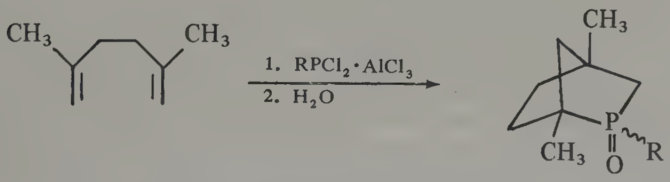
With the parent diene, only a phosphorinane was isolated.

(3) With one double bond of the 1,4-diene incorporated in a ring, the only cyclic product was of the cyclopropane type[17]:



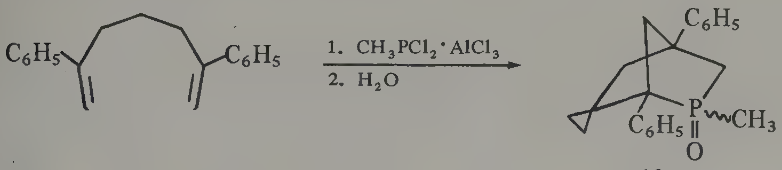
The mechanism of this reaction has been considered in Chapter 2.

(4) The 1,5-hexadiene system produces unique bridged structures such as 11.[16]



11

(5) 1,6-Dienes give similar bridged structures (12), but 1,7-dienes cyclize without incorporation of phosphorus[18]:

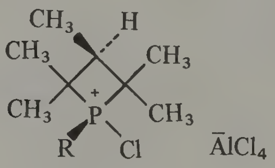


12

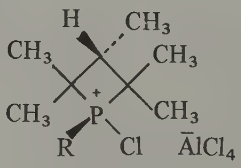
The P(III) compounds as yet known to participate in the olefin reaction are PCl_3, PBr_3, $C_6H_5PCl_2$, CH_3PCl_2, and $C_2H_5PCl_2$. A failure occurred[19] with $(CH_3)_3CPCl_2$, but other less highly substituted phosphonous dihalides should be participants in the reaction. In principle, phosphinous halides (R_2PX) should also be useful as a direct source of quaternary phosphetanium ions, but no use seems to have been made of them.

The conditions preferred for performing the reaction have been recently studied in detail.[9] The original[2] ratio of olefin-PCl_3-$AlCl_3$ (1:1:1) was confirmed, with the discovery that (1) excess $AlCl_3$ causes polymer formation, (2) excess PCl_3 gives chlorination in an allylic methyl group presumably by a radical mechanism, and (3) only this substitution reaction occurs if no $AlCl_3$ is present. The choice of the Lewis acid catalyst is important. $AlCl_3$ favors the ionic mechanism, and no competition from the radical (substitution) reaction occurs. With $ZnCl_2$, the substitution is not suppressed, and this is the only pathway followed. $FeCl_3$ causes only polymer formation. The solvent of choice remains CH_2Cl_2, as originally specified[2]; polymer formation is a complication, or the only result, with solvents such as hexane, toluene, ethylene dichloride, or dibromide. The reaction is quite rapid; it is generally conducted by mixing the reactants at 0°, stirring for 1 hr, and then hydrolyzing the initial product.

It will be noticed that the first product is of the same structure at phosphorus as the McCormack diene-P(III) halide cycloadduct, and differs only in that the counterion is $\bar{A}lCl_4$ rather than $\bar{C}l$. From this stage on, then, the workup of the products and their transformations is very similar for the two products. Thus, the chlorophosphetanium ions from the use of RPX_2 may be hydrolyzed to tertiary phosphine oxides; the dichlorophosphetanium ions (from PX_3) may be partially (and cleanly) hydrolyzed to phosphinic chlorides or completely hydrolyzed to phosphinic acids. Here the similiarities end; the chemistry of phosphetanes has developed along quite different lines than those already discussed for the phospholenes. The phosphetane ring has reasonable stability, although a few cases are known where C-P cleavage occurs, and is preserved in many reactions occurring at P. In fact, reactions at P represent the dominating chemistry for phosphetanes; there are no instances of reactions occurring on ring carbons. Interest in these reactions stems from the fact that, in some of the salts (e.g., 13, R=CH_3 or C_6H_5) and derived structures, *cis, trans* isomerism is present, and much can be learned about the mechanism and stereochemistry of nucleophilic substitution at phosphorus from studies with a particular isomer. The 2,2,3,4,4-pentamethyl derivative has been the most popular system for study.



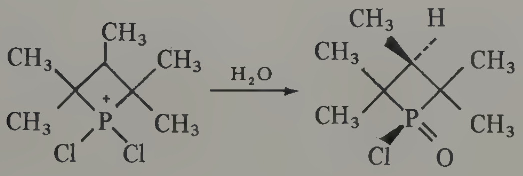
13a, cis



13b, trans

Because the non-nucleophilic $\bar{A}lCl_4$ ion does not allow equilibration through a pentacovalent intermediate in the way that $\bar{C}l$ would were it the counterion,[19] these salts are stable and spectroscopically distinguishable, and thus differ from the McCormack cycloadducts. However, as with the McCormack adducts, hydrolysis conditions can change the isomer ratio drastically. The isomer ratio in the salt is, for the most part, retained[19] on hydrolysis by addition of the salt to water, which implies that displacement of $\bar{C}l$ from P occurs with retention of configuration. However, the reverse order of addition allows unreacted salt to be contacted by $\bar{C}l$ formed early in the hydrolysis, and this causes some equilibration of the ions. Hydrolysis then proceeds faster with one isomer (presumably trans) than the other. The isomer mixtures can be separated by fractional crystallization[5] with some success or by column chromatography.[20] Although, as will be seen, ^1H and ^{13}C NMR spectroscopy are quite adequate for proving the structure of such isomers, X-ray analysis has also been performed on several derivatives (Ref. 21 and citations therein), and the entire stereochemical basis of phosphetane chemistry is on firm ground.

With the PCl_3 products (e.g., **13**, R=Cl), cis, trans isomerism is absent, yet partial hydrolysis to the phosphinic chloride proceeds with the sole production of the trans isomer (**14**), as established by X-ray analysis.[22] The same is true for the use of PBr_3.[23] This has made readily available a substance of known stereochemistry for the study of displacement and other reactions on phosphorus, which has added immeasurably to our mechanistic knowledge.

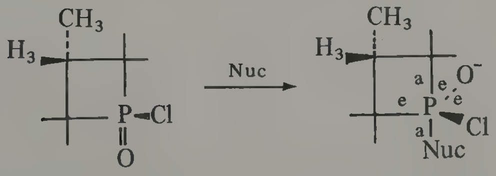


14 (trans)

Synthetic reactions in which the phosphetane ring is preserved may be classified as nucleophilic substitution at P(IV) or at P(III), interconversion of P(III) and P(IV), addition of two ligands to P(III) to form P(V) derivatives, and nucleophilic addition to P(IV) to create P(V). Each classification is discussed separately below.

NUCLEOPHILIC SUBSTITUTION AT P(IV) There have been so many studies of this process that only selected references will be supplied. Synthetically, the halogen of phosphinic or thiophosphinic halides may be displaced by reaction with water, alcohols, thiols, amines, azide ion, or organometallics (Mg or Li). Only for alcohols[24] is there any departure from the well-established stereochemical rule[20,25] in this series that these reactions proceed with *retention* of configuration, even though inversion is the result of substitution at noncyclic P(IV). Indeed, this unusual stereochemical result has played a major role in the development of ideas about the intermediacy of pentacovalent structures, their tendency to undergo stereoisomerization by pseudorotation, and the way in which groups add to and depart from phosphorus. The general process is pictured as follows:

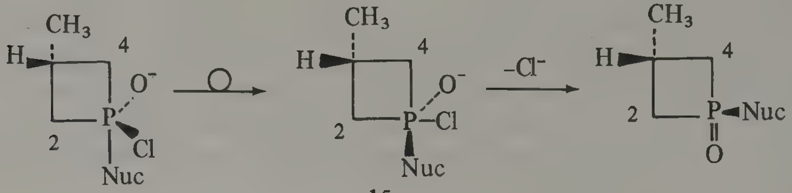
1.



The nucleophile attacks in order to occupy an apical position of the trigonal bipyramid. The 4-membered ring, with its internal C-P-C angle of about 80°, fits best in an apical-equatorial arrangement (90°) rather than equatorial-equatorial

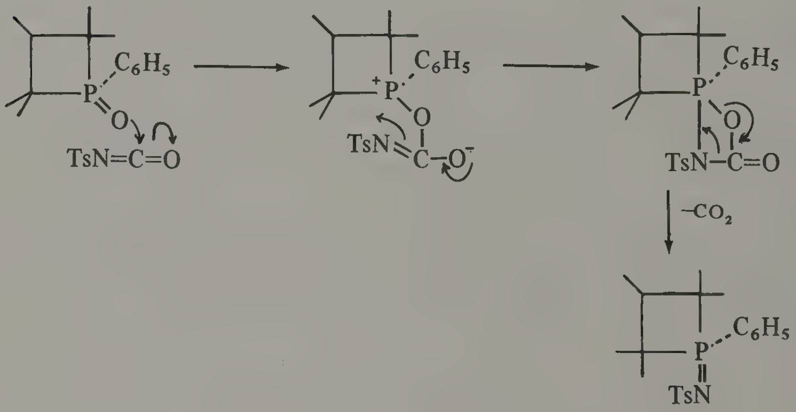
(120°). This forces the more electronegative O and Cl atoms into disfavored equatorial positions.

2.

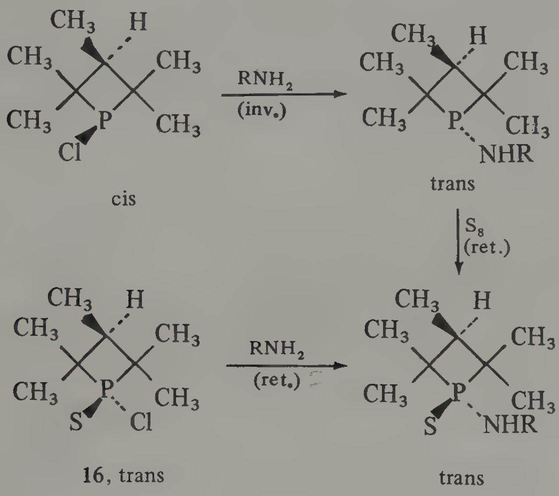


15

Pseudorotation with O⁻ as pivot can lead to a structure (15) where Cl is apical and from which it can depart to regenerate the P(IV) condition. In doing so, the 3-CH_3 remains on the same face of the 4-membered ring as oxygen, thus providing the trans relation (retention) to the newly attached nucleophile. (The exception that occurs with alcohols has been explained on the basis of an increase in apicophilicity, or decrease in equatoriophilicity, of phosphoryl O relative to Cl through hydrogen-bonding and its interference with p_π-d_π bonding.) Other displacements on P(IV), such as of carbanions from quaternary phosphetanium salts with $\bar{O}H$,[26] or of a P-alkoxy group from positive phosphorus,[27] are assigned a similar mechanism. A newly discovered[28] reaction with tosylisocyanate that replaces phosphoryl oxygen by a tosylimino group with retention can be interpreted as involving intramolecular nucleophilic attack at P(IV), followed by collapse of the P(V) intermediate.



NUCLEOPHILIC SUBSTITUTION AT P(III) Phosphinous chlorides in the phosphetane series are available from various routes, as seen in the next subsection, and have their normal reactivity. Displacement of chlorine has been definitively described[25] as proceeding with inversion of configuration when such nucleophiles as $\bar{O}CH_3$ or RNH_2 are employed. The proof rests upon the established trans stereochemistry in the P(IV) chloride (e.g., **16**) and the conversion of the displacement products to P(IV) derivatives also of known stereochemistry. An example of this approach follows:



cis

trans

16, trans

trans

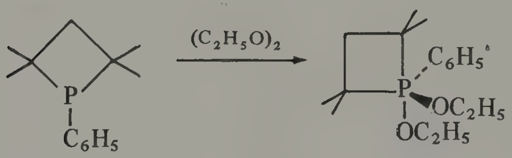
Particularly useful are displacements by organometallics (RMgX or RLi) to produce tertiary phosphines of known stereochemistry.[11,25]

P(IV)-P(III) INTERCONVERSIONS Tertiary phosphine oxides or sulfides of phosphetanes can be reduced to phosphines with the usual silane reagents in stereospecific fashion (retention).[20,25,29] Reductions of P(IV) chlorides are also known and are important sources of phosphinous chlorides. Phosphinic chlorides have been reduced[25] to secondary phosphines with $HSiCl_3$ or phenylsilane and hydrogen then replaced on P with Cl_2. Sulfur from thiophosphinic chlorides (from P_2S_5 and the oxychloride[11]) can be removed with triphenylphosphine, giving the phosphinous chloride.[11] The most direct route to the phosphinous chlorides, reduction with, for example, $(C_6H_5)_3P$ as for the McCormack adducts, seems not to have been tried. Oxidation (commonly with H_2O_2) of phosphines or phosphinous chlorides occurs with retention, as does sulfuration and quaternization.

P(III) TO P(V) CONVERSIONS The 4-membered ring is currently of great importance in studies of the structure of stable species with the pentacovalent state. For some time, it was believed that the small internal C-P-C angle would only be compatible with apical-equatorial positioning in the trigonal bipyramid, and that pseudorotations involving a ring positioned diequatorially would have a prohibitively high energy barrier. This generality frequently competes with another, that the most electronegative groups occupy the apical positions. However, results of several dynamic NMR (DNMR) studies that have been conducted recently require an explanation based on passage through the ring-diequatorial form, and the culminating experiment has been an X-ray analysis that shows the phosphetane ring quite reasonably positioned in a distorted but nevertheless recognizable trigonal bipyramid. Another major result has been the recognition of a rectangular pyramid, with the 4-membered ring in the rectangle plane!

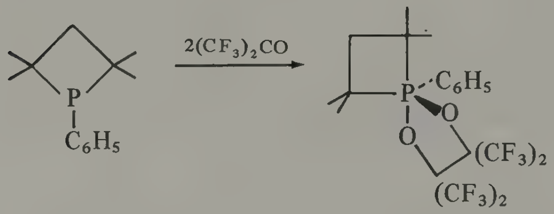
The P(V) state has been achieved synthetically for phosphetanes by several routes. These are summarized below, with comments on the significance of DNMR or X-ray analyses. A more detailed discussion of these experiments is not within the scope of this chapter.

1 (Ref. 30)



Pseudorotation seen from DNMR to pass through ring-diequatorial

2 (Ref. 31)

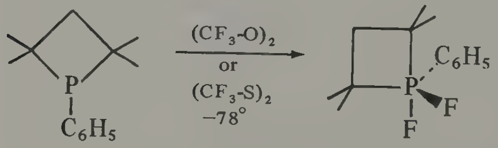


Passage through ring diequatorial, oxygens axial-equatorial (or diequatorial in a square planar form; see also Ref. 36) has free energy of activation at 155° of 20.1 kcal/mole, compared to the 15 calculated for reaction (1).

3 (Ref. 32)

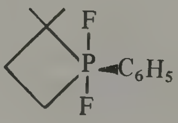
Extension of reaction (2) to other phosphetanes; new free energy of activation developed, one as low as 9 kcal/mole (P-OC_6H_5). Relative apicophilicities established.

4 (Ref. 33)



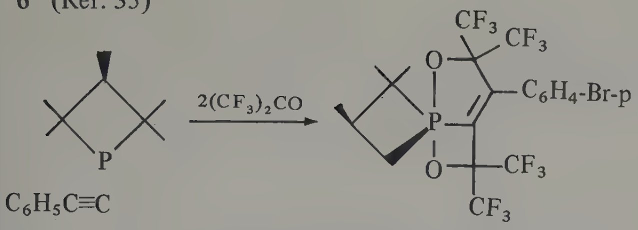
Equilibration at low temperatures involves diequatorial ring.

5 (Ref. 34)



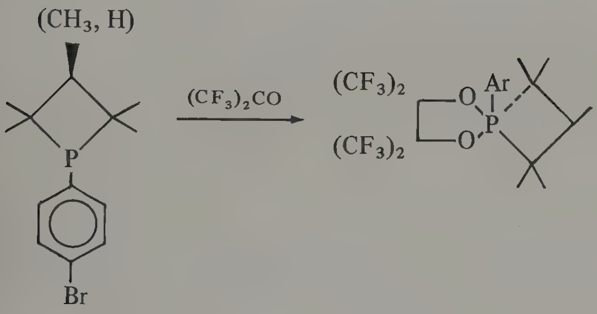
Extension of reaction (4) to other phosphetanes, with confirmation of diequatorial ring being achieved at low temperatures:

6 (Ref. 35)

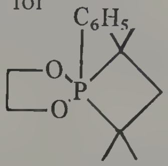


By X-ray, the 4-membered ring is diequatorial; internal C-P-C angle = 82.9°, in a distorted trigonal bipyramid.

7 (Ref. 36)

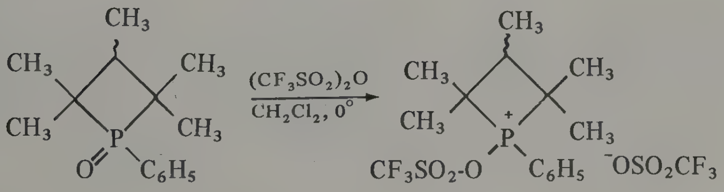


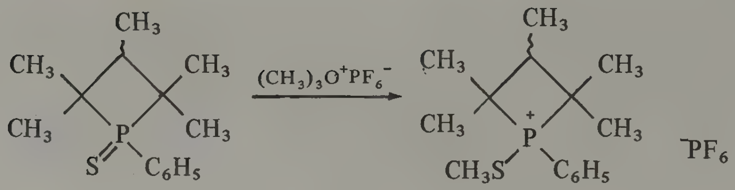
The 4- and 5-membered rings are co-planar by X-ray, in the base of a rectangular pyramid. Both rings are therefore diequatorial; the phosphetane internal C-P-C angle is 78.1°. A similar structure was found[37] for



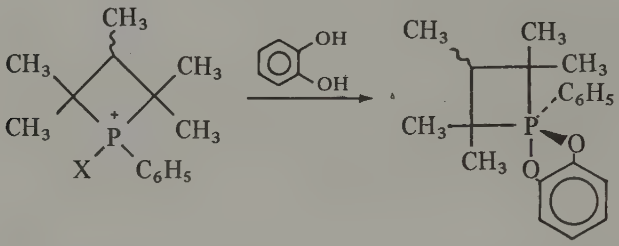
This fascinating area will surely continue to receive attention in years to come.

P(IV) TO P(V) CONVERSION Additions of nucleophiles to P(IV) in order to create stable, pentacovalent species are not well known processes in phosphorus chemistry, but recently announced techniques allow such conversions in the phosphetane (and other) series. To utilize oxides or sulfides in such processes, it is generally required that alkylation or acylation take place on O or S, followed by attachment of the nucleophile to P. Displacement of the alkylated O or S follows. Potent agents are required to bring out nucleophilicity in P=O or P=S groups, but the reagents $(CF_3SO_2)_2O$ and $(CH_3)_3\overset{+}{O}BF_4^-$ have been found useful for this step[38]:

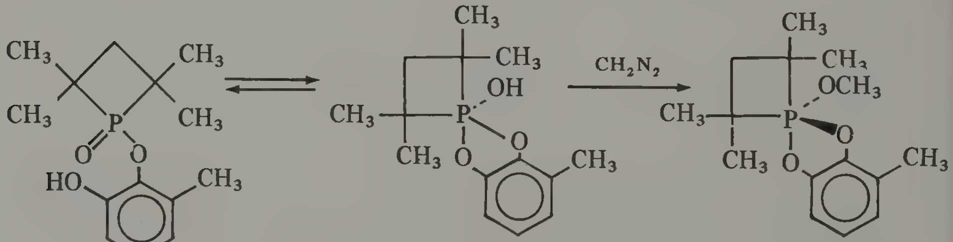




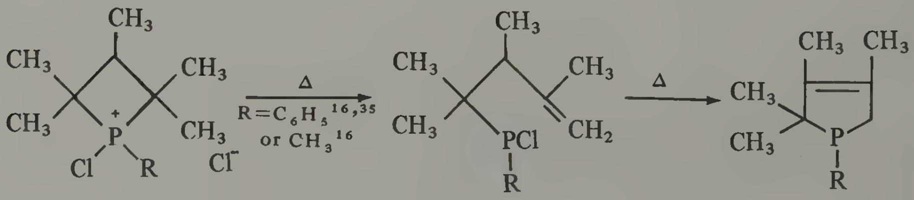
These salts are then reacted with catechol to create the P(V) state:

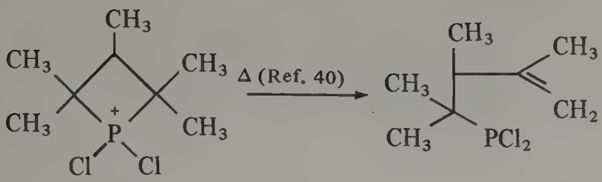


It has also been shown[39] that a free hydroxy on a catechol phosphinate may add to the phosphoryl group in a reversible reaction that supplies P(V) with a hydroxy group. Alkylation on oxygen then traps the product in the P(V) form:

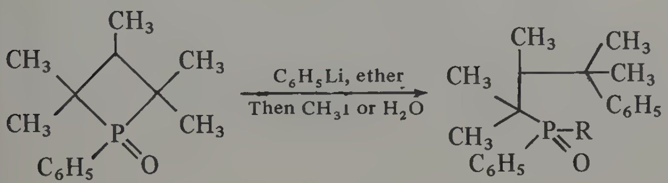


Research in the phosphetane field is not without some difficulty due to ring cleavage. Heating a chlorophosphetanium chloride can lead to linear P(III) chlorides.



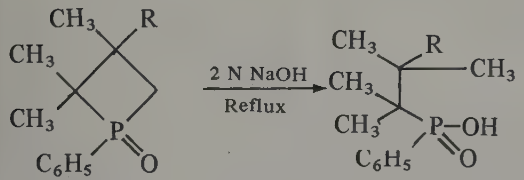


Both phosphine oxides and phosphonium salts are sensitive to strong bases, as seen in the illustrative reactions below:

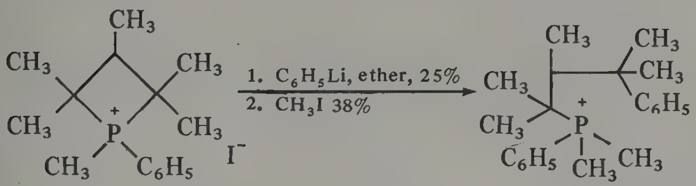


17

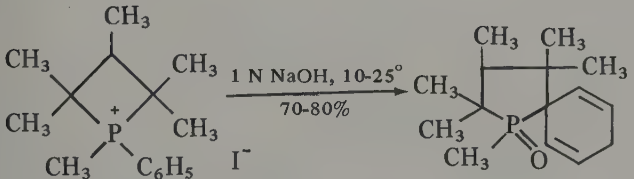
R=CH_3[20,41] or H[20]
(81%)



R=CH_3, 44%[42]
R=H, 88%[42]

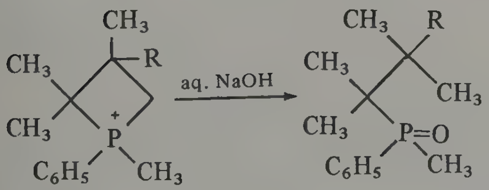


Ref. 41

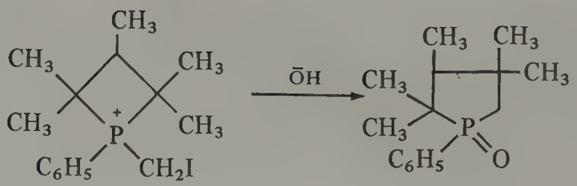


18

Refs. 4, 20, 43



R=H, Ref. 10
R=CH_3, Ref. 42

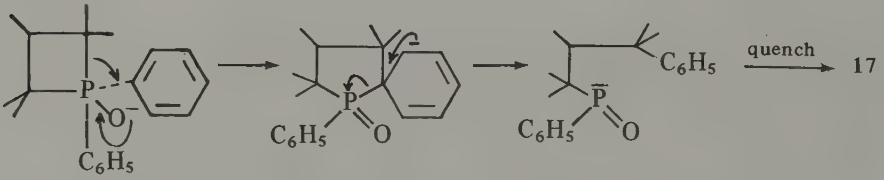


19

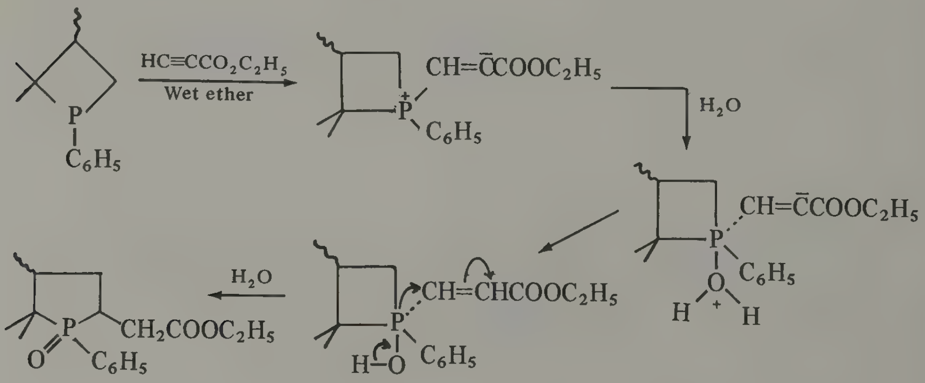
Ref. 4

Other related ring-openings[42] of salts occurred with the nucleophiles $\bar{N}H_2$ and $\bar{C}N$ under mild conditions. All of these reactions have in common the initial formation of a pentacovalent intermediate; because the ring occupies one apical position and the nucleophile the other, there is no grouping in position to depart readily and complete a substitution process. Furthermore, phenyl is a group of low apicophilicity and the alternative of ring-expansion then becomes a possibility.

Ring-opening may occur as a follow-up to the rearrangement, as in the formation of 17.

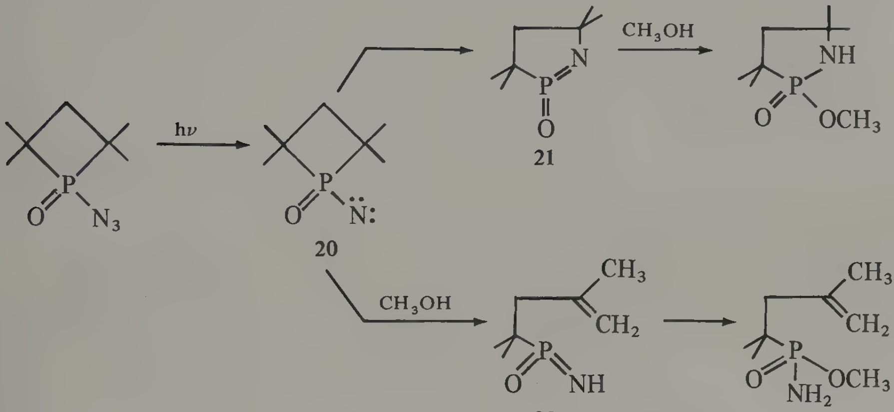


Even P(III) forms can undergo ring-opening with the proper reagents[20,42]:

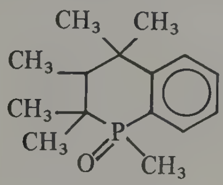


Similar reactions have been noted for 5-membered rings, where expansion to 6-membered rings occurs (Chapter 3).

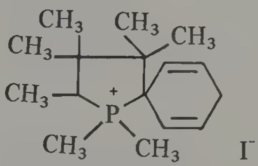
Finally, ring expansion or opening occurs on irradiation of phosphinic azides in CH_3OH, probably through nitrene (20) and metaphosphonimidate (21, 22) intermediates.[44,45]



The structure of the spiro compound 18 requires comment. Spectroscopy seems to have given a definitive picture of its structure,[4] easily supported by mechanistic considerations. Furthermore, aromatization with Pd-C gave a phosphinoline (23)[43,46] whose structure was established by X-ray analysis.[47] However, an X-ray analysis[48] of a salt derived from compound 18 suggested that the ring methyls are misplaced and the proper structure should be 24.



23



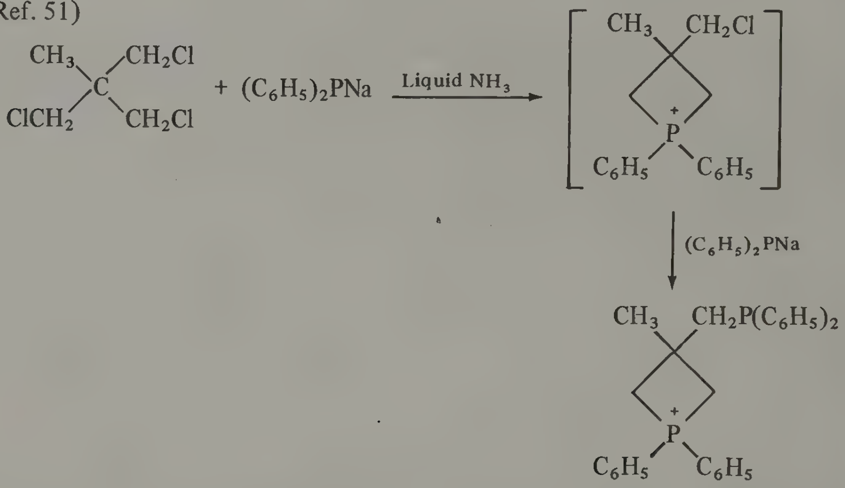
24

This discrepancy has attracted some attention,[49] for the revised structure, if correct, presents a serious challenge to the proposed mechanism. However, the X-ray result must first be reexamined in order to clarify this situation.

4.1.2 Other Routes

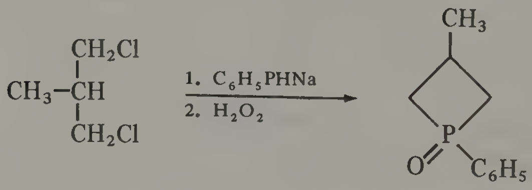
Very few phosphetanes have been made by processes other than the olefin-PX_3 reaction, and no other general route exists at this time. This synthetic deficiency has left many properties of the ring system unexplored, and there is a clear need for new approaches to phosphetanes. With further development, the simple reaction of 1,3-dihalides with metallic phosphides could prove useful in obtaining phosphetanes with fewer C-methyl substituents than the olefin route provides. This reaction as a source of 1H-phosphetane (not well characterized) was claimed first in a patent,[50] but several examples now exist where substituted phosphetanes have been prepared:

1 (Ref. 51)



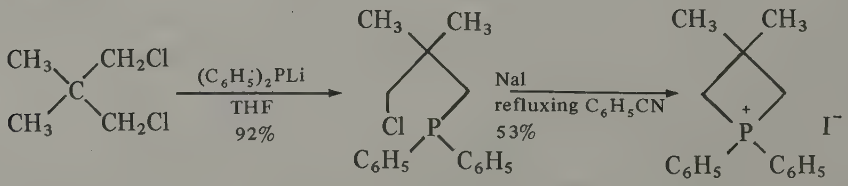
This compound was prepared primarily for study as a metal coordinating reagent; yield information was not provided.

2 (Ref. 52)



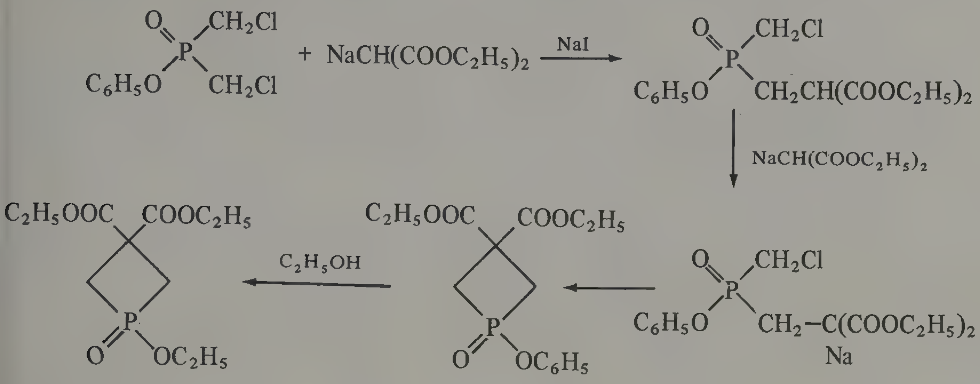
No experimental details have been published for this synthesis, which is included in a review article.

3 (Ref. 53)



The intermediate chloride was a distillable liquid; cyclization was conducted with a 20-hr addition period to a dilute solution of NaI in benzonitrile as solvent.

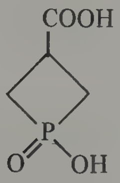
A different approach to phosphetanes based on malonic ester chemistry has been published by one laboratory.[54] The method is notable because it has produced the only phosphetanes possessing a functional group on a ring carbon.



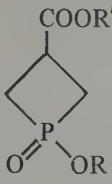
26 (60.5%)

25

Iodide ion greatly speeded up the alkylation reaction; cyclization resulted from the formation of the salt of the alkylation product. The phenyl phosphinate was quite superior to the ethyl ester, which formed noncyclic products. Ester exchange was then employed to obtain the distillable ethyl ester. Ester 26 was hydrolyzed with dilute HCl to produce the carboxy phosphinic acid 27 (67%) that was converted by conventional reactions to various ester derivatives (28-30).



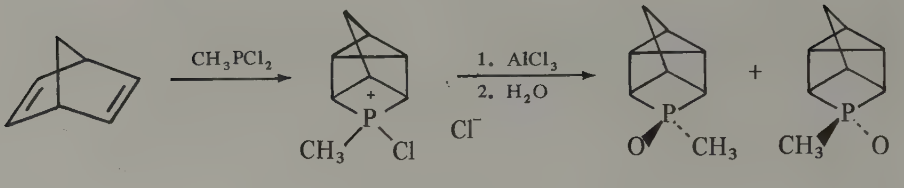
27



28, $R=H, R'=C_2H_5$
29, $R=R'=C_2H_5$
30, $R=R'=CH_3$

No further papers seem to have appeared on this synthetic method or transformation of its products, although entry to quite valuable products could result from further study. The products have good stability, although ring-opening by attack of ethoxide on phosphorus was noted.

One example of a bridged-ring system containing a phosphetane unit was noted in Chapter 2, where the reaction of norbornadiene with CH_3PCl_2 was described.[55] The reaction has recently been reexamined[56] and conditions developed for obtaining the product (31) in the stereoisomeric forms. This is accomplished by preventing the equilibration of the adduct through the pentacovalent form, a feature of McCormack cycloadduct chemistry (Chapter 2).

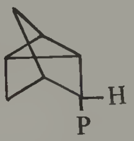


Exo, Endo 31a (endo) 31b (exo)

Trichlorosilane reduction occurred with inversion of configuration, apparently through epimerization by the HCl formed.

32

The phosphetane ring of **31a** is quite sensitive to opening with base (90% in 75 min at room temperature with 5 N NaOH); salts derived from phosphine **32** rapidly ring-opened with 0.001 N NaOH. The products are based on the ring system **33**.

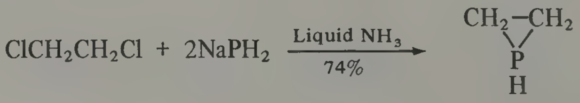


33

The additional strain imposed in the 4-membered ring by the bridging is readily apparent from X-ray analysis[57] of a salt, which shows much greater puckering and a significantly smaller C-P-C angle than normal. This strain can be associated with the greatly increased sensitivity of the ring.

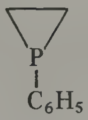
4.2 PHOSPHIRANES

Phosphirane was first mentioned in a patent in 1963,[50] but for such a novel substance the characterization provided was considered incomplete and its existence was treated with some skepticism.[58] However, the method used was subsequently described in detail[59] and the case for its existence convincingly defended. The method is remarkably simple:

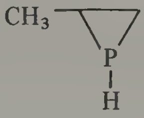


Phosphirane is a distillable (bp 36.5°), gas-chromatographable liquid, but its stability is modest and a sample stored at 25° for 24 hr completely decomposed with the formation of the isomeric ethylphosphine and of ethylene. A solution in methanol was more stable. Spectroscopic characterization provided, among other data, the ^{31}P NMR shift that is the most upfield ever observed, save for the element itself (δ −341; P_4 −488). The ring protons were made difficult to recognize because the pyramidal stability of phosphorus created an AA′BB′MX spectrum. The most abundant peak in the mass spectrum was the molecular ion. This striking report was soon followed by another[60] that extended the method of preparing P- or C-substituted phosphiranes (**34-37**) of quite good stability, and the field of monocyclic phosphirane chemistry is now on firm ground. The C-substituted derivatives **36** and **37** exist as cis, trans isomers, which attests to the pyramidal stability and slowness of proton exchange in these secondary phosphines.

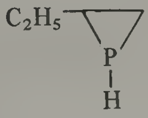
34 (30%)



35 (60%)



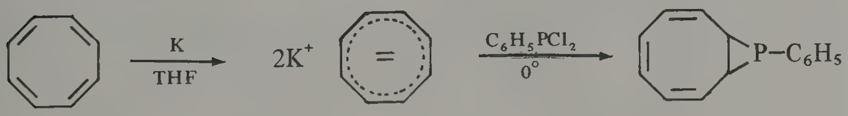
36 (30%)



37 (25%)

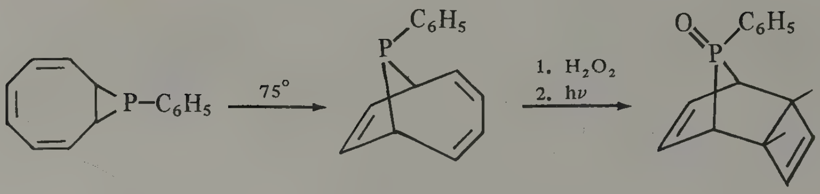
1-Phenylphosphirane is particularly stable and easy to prepare and most subsequent work in the phosphirane field has been accomplished with it. Its synthesis merely consists of preparing a liquid ammonia solution of C_6H_5PHNa (2 moles) from $C_6H_5PH_2$, and then slowly treating the solution with ethylene dichloride (1 mole). Salt precipitates immediately, and after the ammonia is allowed to evaporate a white solid remains. The product is extracted with ether and distilled at 44°-48° (1.5 mm).

The only other P(III) phosphirane known at present is the remarkable bicyclic **38**, the product of a unique reaction between the dianion of cyclo-octatetraene[61] with phenylphosphonous dichloride.



38

Although it can be sublimed *in vacuo*, the solid **38** becomes oily on standing and darkens on exposure to air. A chloroform solution heated to 70° permits rearrangement to another valuable heterocyclic system (**39**) on which considerable work has been done. As noted in Chapter 2, **39** is a source of the intriguing phosphabicyclo [2.2.1] heptane system as incorporated in **40**.

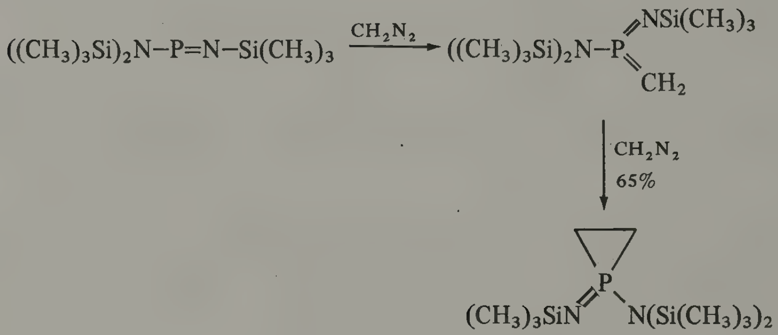


39, m.p. 85.5°-86.5°

40

Both for the monocyclic and bicyclic phosphiranes it was noticed that reagents that converted P(III) to P(IV), such as HCl, CH_3I, or oxidation, led to very unstable products, in no case resulting in a recognizable derivative. However, three special types of stable P(IV) derivatives have been reported:

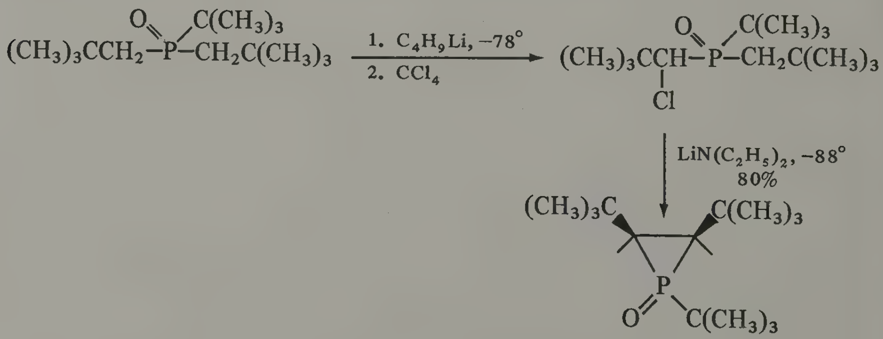
1 (Ref. 62)



41

Although sensitive to water, **41** is a thermally stable, distillable liquid, bp 67°-68° (0.1 mm). Its ^{31}P shift remains on the high-field side (δ −66.9) but is no longer as spectacular as the value for the P(III) compounds.

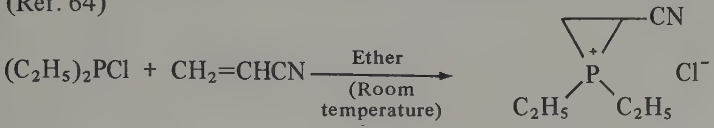
2 (Ref. 63)



42

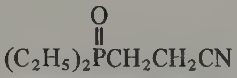
Compound **42**, a crystalline solid of mp 119°-120°, is stable to concentrated HCl, but undergoes ring-opening with lithium piperidide, or loss of the P fragment on refluxing in benzene. Its ^{31}P shift is also at high field (−1.3) for a phosphine oxide, but by no means as striking as the P(III) value.

3 (Ref. 64)



43

This product is obtained as a crystalline solid, giving the proper P and Cl analysis. Infrared spectroscopy shows the CN group to be present, and no olefinic protons occur in the NMR spectrum. Hydrolysis with NaOH gives the open-chain phosphine oxide **44**.



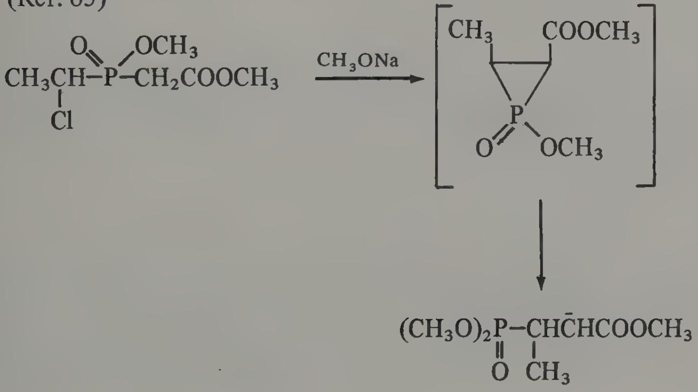
$$(C_2H_5)_2\overset{\overset{O}{\|}}{P}CH_2CH_2CN$$

44

The case for **43** being cyclic, however, is not strong, and reexamination by ^{31}P and ^{13}C NMR would be very desirable. If it can be convincingly established that a phosphirane has been formed, this method of synthesis could become of great value.

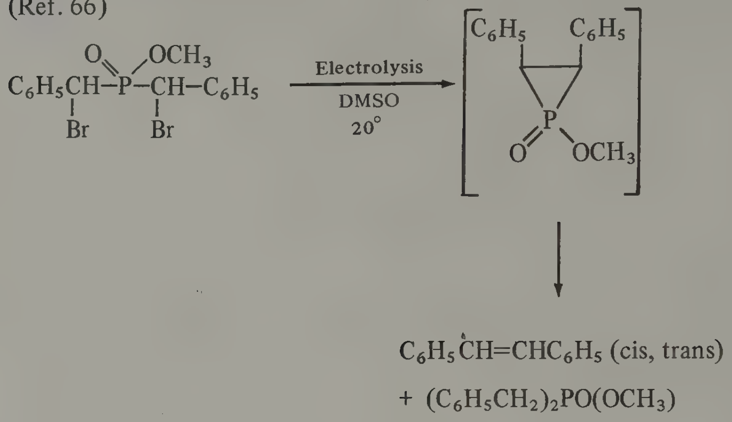
With the exception of **43**, the stable P(IV) phosphiranes are characterized by having sterically large groups attached to the ring. These may be essential for stability, as other workers have performed reactions that seem to have provided P(IV) derivatives only as transient intermediates. Only from the nature of the final products has the intermediacy of the phosphirane been detected:

1 (Ref. 65)

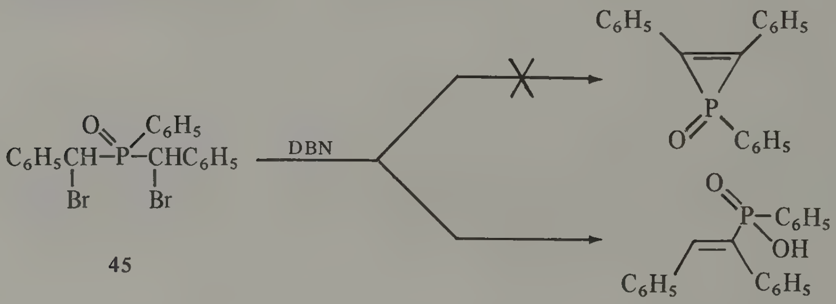


Here it is proposed that the phosphirane undergoes ring-opening by nucleophilic attack on phosphorus.

2 (Ref. 66)



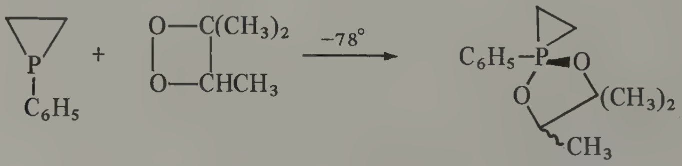
Fragmentation of the phosphirane is assumed to occur under the reaction conditions. In both of these reactions, the phosphirane intermediate is a great help in accounting for the formation of new C-C bonds. An earlier claim[67] that dibromide **45** reacted with the base DBN to form a phosphirene has been challenged,[68] and it is now believed that the phosphorus species actually prepared and studied was the vinylphosphinic acid **46**.



45

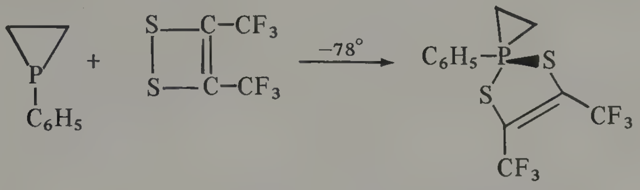
46

A recent discovery in phosphirane chemistry is the fact that P(V) forms can be created at low temperatures, and at least in one case[69] are sufficiently stable that they can be detected spectroscopically:



47, δ ^{31}P −87

On warming, the ^{31}P signal is lost and ethylene is formed. The usual trigonal bipyramid geometry can be badly distorted in this compound, which can even acquire square pyramid structure. A dithio compound **48** has also been prepared[70] at −78°, and has been detected by its decomposition products.



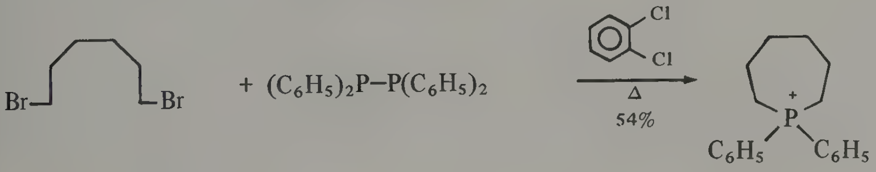
48

4.3 RINGS OF SEVEN OR MORE MEMBERS

This area of heterocyclic phosphorus chemistry lacks the coherency brought about by dominating synthetic methods; although a number of derivatives of the 7- , 8- , and 9-membered rings have been prepared, methods have, for the most part, been rather specific and have not yet led to structures in much variety. Frequently, a multistep synthesis of the starting material for ring-closure must be performed. Nevertheless, several methods do exist for the synthesis of monocyclic derivatives and, with further development, they could add greatly to knowledge in this area. Benzo derivatives are also known and approaches to them will constitute the final topic.

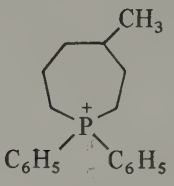
4.3.1 General Approaches to Monocyclic Systems

In 1963, Märkl[71] described a one-step procedure starting with acyclic materials to effect formation of the phosphepane system:

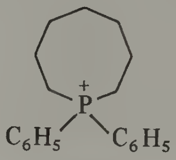


49

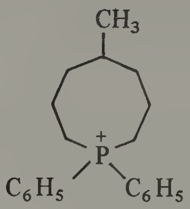
This reaction has already been discussed in Chapter 3, for it is a source of phosphorinanes as well. Although Märkl also showed[72] that the same dihalide reacted with potassium diphenylphosphide to produce the phosphepanium salt (**49**), this method has not been further developed. The approach via the diphosphine, however, was later shown[53, 73] to be useful for the synthesis of C-substituted phosphepanes as well as phosphocanes, and, in addition to **49**, the structures below are now known:



50, 85%[73]



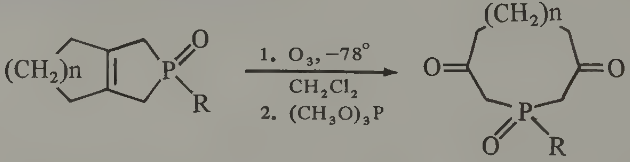
51, 20%[73]



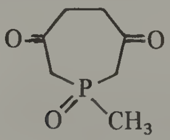
52, 34%[73]

As usual, base treatment is able to displace one phenyl group and form the tertiary phosphine oxides and, from these, phosphines have been prepared by phenylsilane reduction. The initial cyclizing reaction is easily carried out in refluxing *o*-dichlorobenzene and employs a 1:1 ratio of the two reactants. A major difficulty is the procurement of the requisite dihalides. The synthesis of **52**, for example, required six steps, starting from 4-methylcyclohexanone. Nevertheless, the method has the potential of providing many other cyclic derivatives, hopefully some with functional groups on a ring carbon.

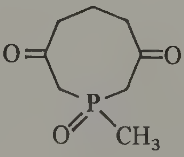
The other method[74] has the advantage of directly producing rings of 7-9 (possibly more) members with two keto functions present. It has already received some mention in Chapter 2, because the immediate precursor of the large rings is always a bicyclic phospholene derivative.



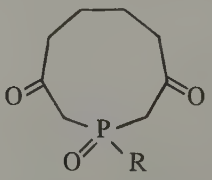
Details of the McCormack phospholene syntheses from 1,2-dimethylene cycloalkanes were described in Chapter 2. The ring-opening ozonolysis is smoothly accomplished at −78°, and yields are frequently in the 80-90% range. In every case, the diketones are white, crystalline solids. With R=alkyl or phenyl, the compounds are quite stable but with R=OH there is a tendency, even in the solid, for intramolecular aldol condensation to occur (vide infra). Structures prepared to date include the following:



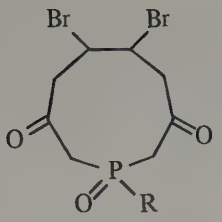
53, 90%[74]



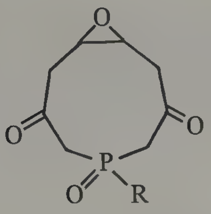
54, 83%[74]



55, R = CH_3, 94%[74]
R = OH, 84%[74]
R = C_6H_5, 85%[75]

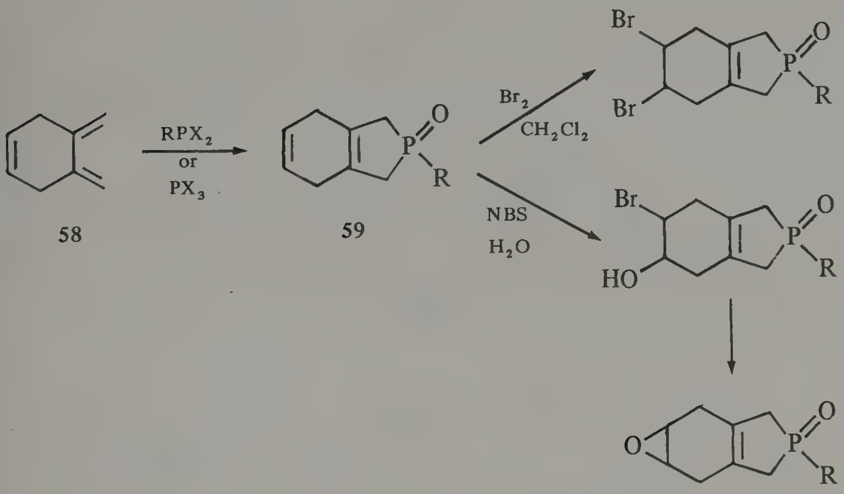


56, R = CH_3, 88%[75]
R = OH, 69%[75]
R = C_6H_5, 89%[75]



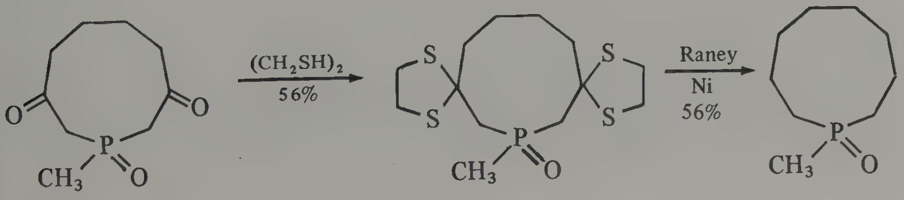
57, R = C_6H_5, 95%[75]

The multisubstituted derivatives **56** and **57** were derived from the bicyclic phospholene derivative **59**, itself prepared from triene **58**.

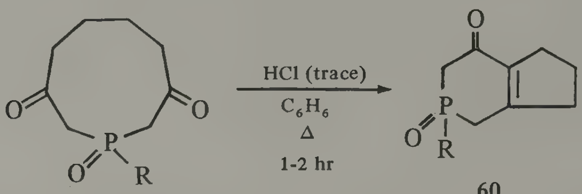


There is no doubt that other derivatives could be prepared from phospholene **59**, taking advantage of an apparent greater reactivity of the cyclohexene double bond than of the 3-phospholene double bond to electrophilic addition.

The diketones also can be converted to the parent heterocycle, as in the example below.



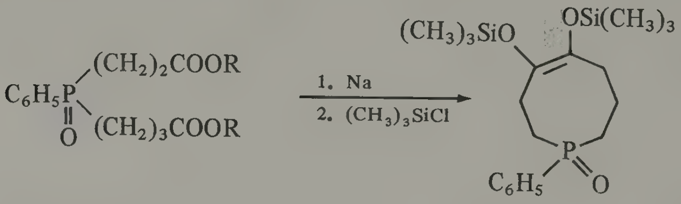
The 9-membered diketones are quite prone to undergoing intramolecular aldol condensation with acidic or basic reagents, however, and this can be a complication in utilizing them in synthetic operations. The aldol products (**69**) in Chapter 3 have a novel structure, and remain to be exploited as precursors of bicyclic phosphorinanes.

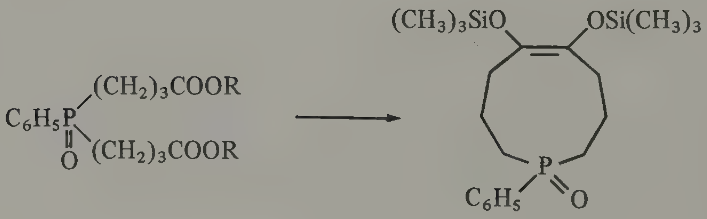


60

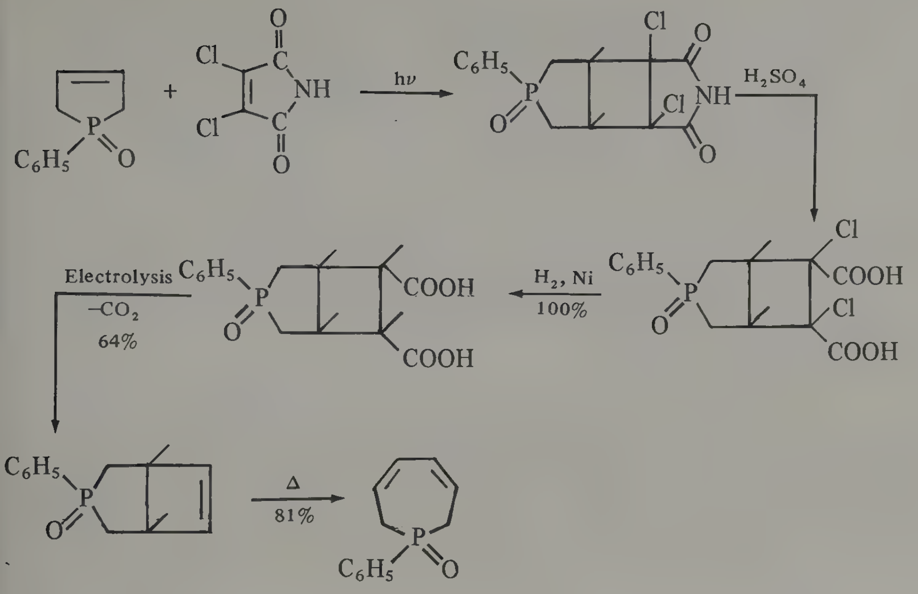
Aldolization has been the major result of attempts to add C_6H_5MgBr to the diketone **55** ($R = CH_3$), or to prepare enol ethers in the presence of triethylamine at room temperature or pyridine at 115°. This complication should not occur with the smaller rings, but these reactions have not yet been attempted.

The acyloin condensation of diesters, so useful for preparing large-ring carbocyclic systems, has been reported[76] to be applicable to phosphorus heterocycle synthesis, but the silylated products have not responded to attempted reactions to convert them to other derivatives.



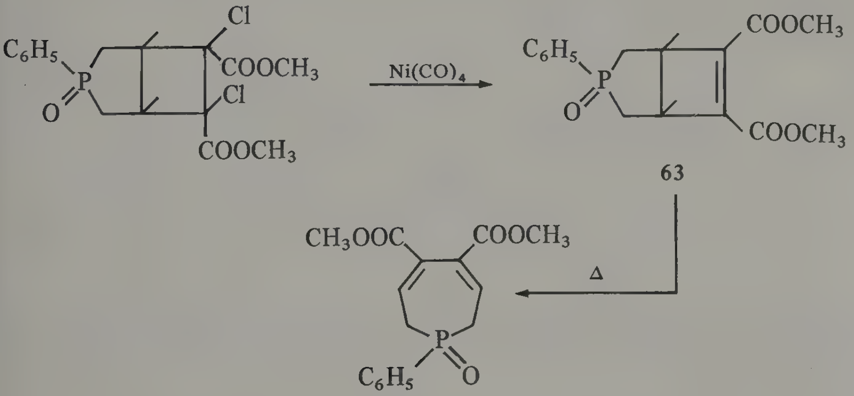


Unsaturated derivatives of the 7-membered system have been obtained by Märkl by two different methods. In his first study,[77] he formed the fully unsaturated (phosphepin) ring, a system of special interest because of its potential for cyclic delocalization via the d orbitals of phosphorus. This subject is developed in Chapter 8. The 1-phenyl-1-oxide (**62**) was a crystalline solid of reasonable stability. The sequence begins with a [2+2] cycloaddition of a 3-phospholene oxide:

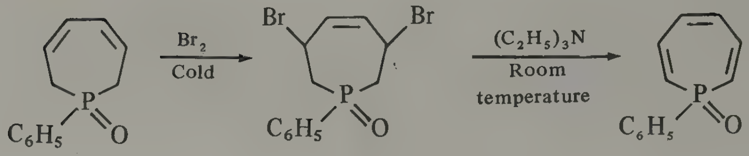


61 62

The key step is the electrocyclic, conrotatory ring opening of **61** by refluxing in diphenyl ether. This represents a novel and valuable way to attain a 7-membered ring with phosphorus and was found also to occur with the diester derivative (**63**).

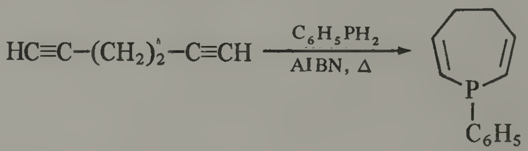


To complete the synthesis of the phosphepin (**66**), compound **64** was treated with one mole of bromine, and the 1,4-adduct (**65**, stereoisomers) then subjected to dehydrohalogenation.

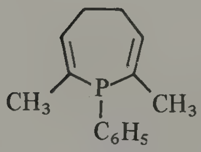


64 65 66

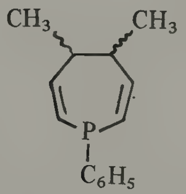
Märkl later[78] showed that the radical-promoted phosphine-diyne condensation approach used previously for preparing phospholes (Chapter 2) could be extended to the construction of the 7-membered ring, and he prepared three dihydrophosphepins (**67-69**) by this route.



67, 33%

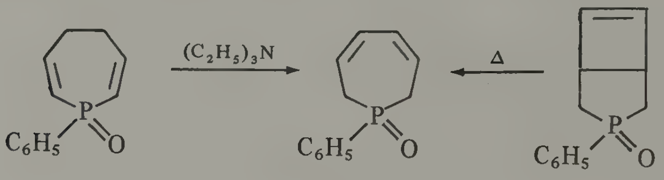


68, 28%



68, 24% (isomer mixture)

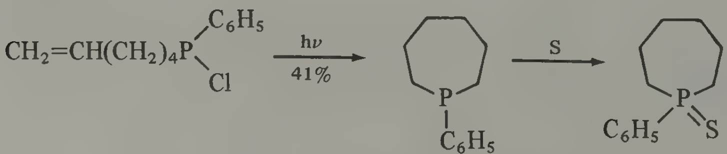
The phosphines readily formed salts and oxides. The oxide of **67** was found to be readily isomerized with base to **62**, identical to the product of the electrocyclic ring-opening of the bicyclic **61** prepared in the earlier work.[77]



62 61

Other routes that have been used to prepare specific monocyclic compounds are outlined below.

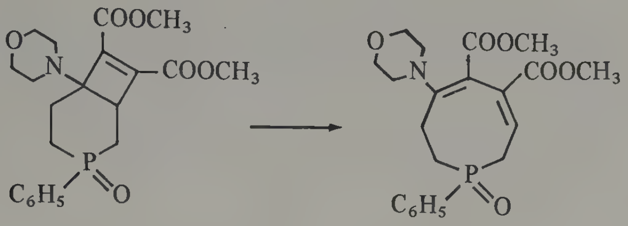
1 (Ref. 79)



(Crude)

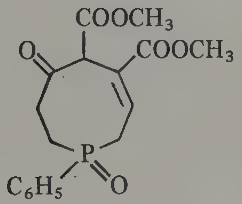
This method is an extension of a reaction used to prepare 5- or 6-membered rings. It has not yet been used for preparing other homologs.

2 (Ref. 80)

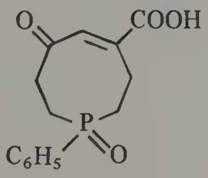


70 **71**

Compound **70** was prepared by the condensation of the enamine of the 4-phosphorinanone with dimethyl acetylenedicarboxylate (Chapter 3). As a cyclobutene, it undergoes electrocyclic ring opening, giving a tetrahydrophosphocin (**71**). Two other derivatives have been prepared from **71**, ketoester **72** by mild hydrolysis of the enamine function and ketoacid **73** by stronger hydrolysis and decarboxylation.

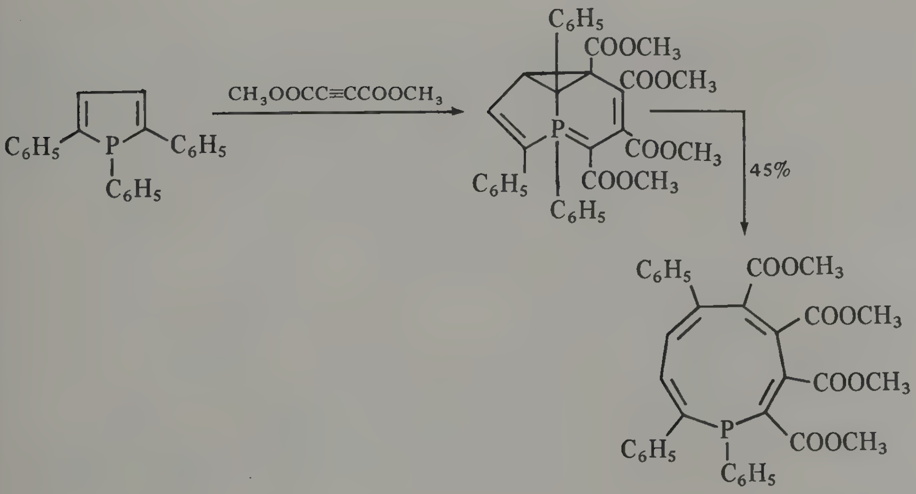


72



73

3 (Ref. 81)

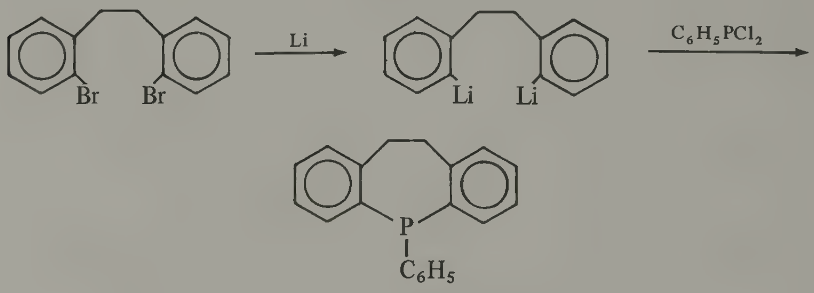


74

Although hardly classifiable as a versatile synthetic method, this reaction is of importance as it has produced a very unusual compound that contains the potentially aromatic ($4n+2$, $n=2$) phosphonin system. The ring is too highly substituted in 74 to reveal much about the electronic characteristic of the system, and little attention has been given to this matter. Nevertheless, it does serve to indicate that the phosphonin ring can exist, and it would be of great interest to determine if cyclic delocalization is present. This has been established[82] for heteronins with nitrogen or oxygen; no monocyclic sulfur derivatives have yet been prepared.

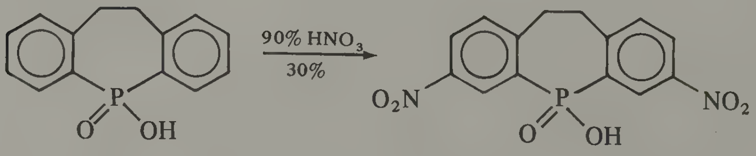
4.3.2 Benzo Derivatives

For the 7-membered rings, a number of benzo derivatives are known, but only one type of fused ring system has been reported for each of the 8- and 9-membered rings. The first benzo derivative prepared (75[83]) was that of the phosphepin system, and even now most of the known multicyclic systems contain this ring. Mann's synthesis[83] was quite direct:



75, 23%

The product was difficult to purify, and later workers[84] found it easier to oxidize the crude phosphine to the readily crystallizable phosphine oxide and then remove the oxygen with trichlorosilane. So prepared, the phosphine was more easily crystallized. In this study, it was shown that the P-phenyl group could be cleaved by fusion with NaOH, forming the phosphinic acid 76 in 92% yield. Entry to other members of this multicyclic system is possible from this acid, for it was shown that dinitration occurred smoothly (87%) to produce compound 77.

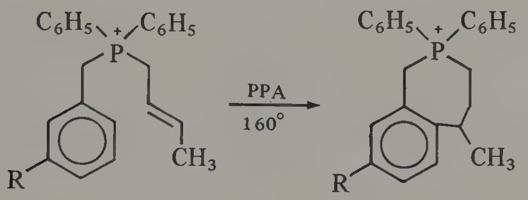


76

77

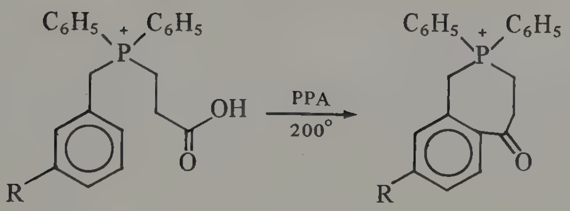
Acid **76** was also converted[85] to the secondary phosphine oxide by the sequence (1) $SOCl_2$, (2) $LiAlH_4$, and it is apparent that much useful chemistry can be performed on this system.

The Berlin methods of ring closure by carbonium ion attack on aryl groups that form 5- or 6-membered rings can also be extended to form 7-membered rings.



Ref. 86

R = H, 30%
R = CH_3, 24%



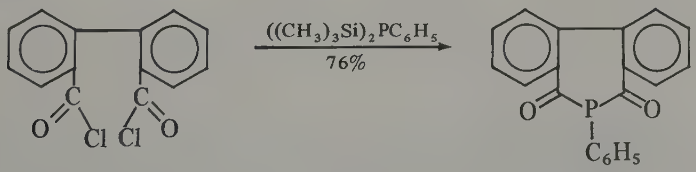
Ref. 87

R = H, 64%
R = CH_3, 34.5%
R = Cl, 40%

Because the phosphonium salts are prepared by quaternization of readily available starting materials, the methods are quite attractive for access to the benzo[c]phosphepin system.

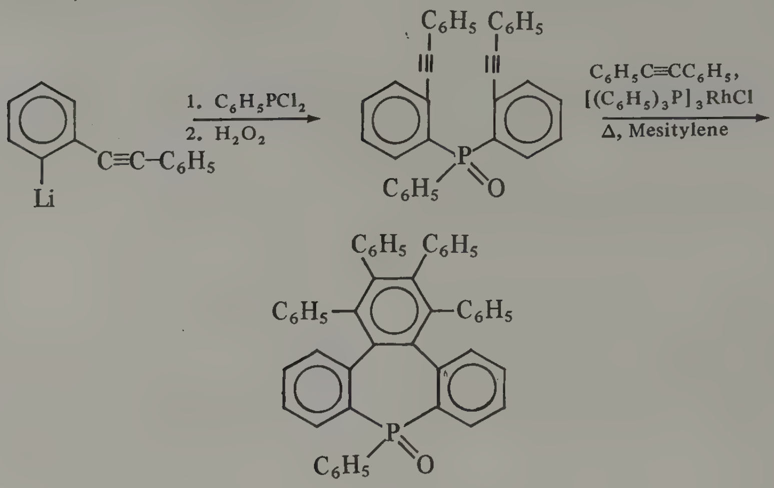
Other, less-developed approaches to 7-membered rings include the following:

1 (Ref. 88)



The product is a stable, yellow solid. A study of its chemical reactivity could produce other novel heterocycles.

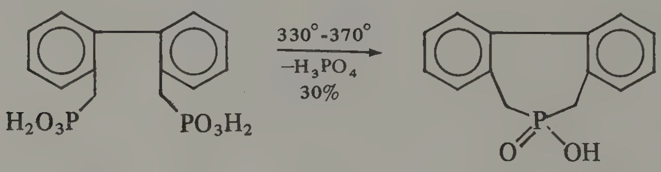
2 (Ref. 89)



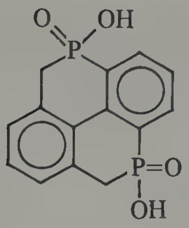
78 (10-20%)

The reaction involves condensation of the two acetylenic groups of the phosphine oxide with that of tolane to create the benzo group at the 4,5-position of the phosphepane ring. The product is of stereochemical interest (see Chapter 8) because the nonplanarity of the central ring allows it to exist in stereoisomeric forms. Both isomers can be obtained from the cyclization, the former as specified above, the latter from operation at a lower temperature. They are interconvertible thermally, with $\Delta G^{\neq} = 31.1$ kcal/mole. Both the phosphines and quaternary salts were prepared in this series and the isomer stability was retained. A slight reduction in $\Delta G^{\neq}$ (by about 2 kcal/mole) for the salt was suggested as a possible indication of stabilization of the planar transition state of the interconversion by cyclic electron delocalization (see Chapter 8), but an effect this small could easily be associated with other factors.

3 Ref. 90:

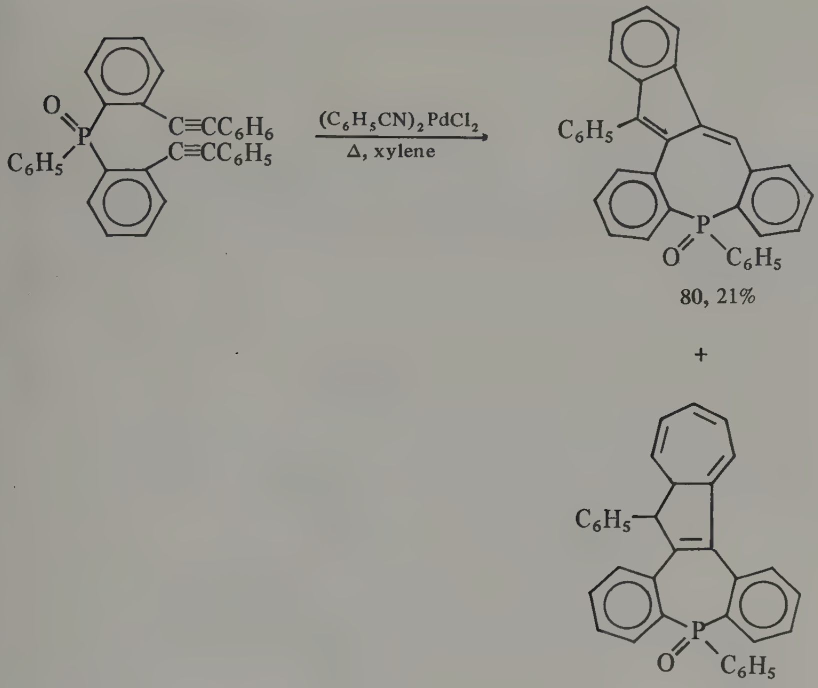


The starting bis(phosphonic acid) is available from the Arbusov reaction on 2,2′-bis(chloromethyl)biphenyl. The product is accompanied by a tetracyclic structure 79 (10%) that was removed by its relative insolubility in ethanol compared to the phosphepane derivative.



79

The same bis-acetylenic compound that Winter used to prepare tribenzophosphepin 78 can be cyclized directly with a Pd(II) catalyst to form an 8-membered ring.[91a]



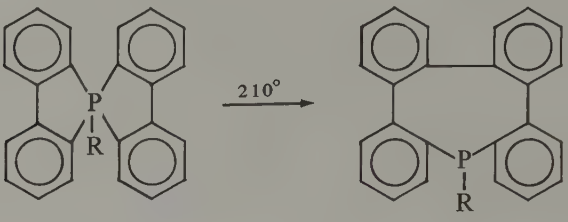
80, 21%

+

81, 4.7%

The structure was established by X-ray analysis.[91b] A smaller amount of a phosphephin (**81**) was also formed. These compounds are primarily of stereochemical interest; the method of formation is quite specific and not readily extended to other derivatives.

The tetrabenzophosphonin system (83) is the only multicyclic derivative known for the 9-membered ring. It was first prepared by Wittig[92] and later by Hellwinkel[93] in a remarkable thermal rearrangement of the dispirophosphorane 82.

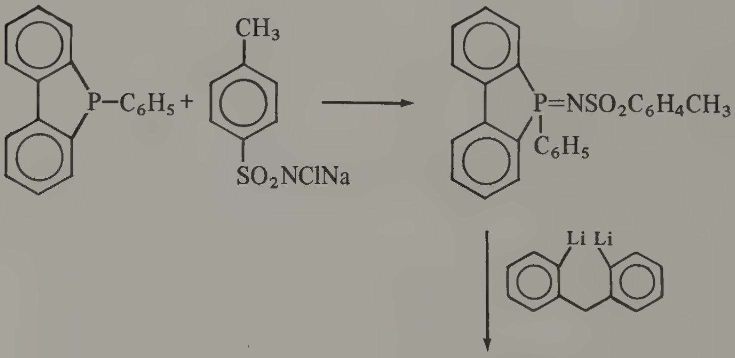


82

83

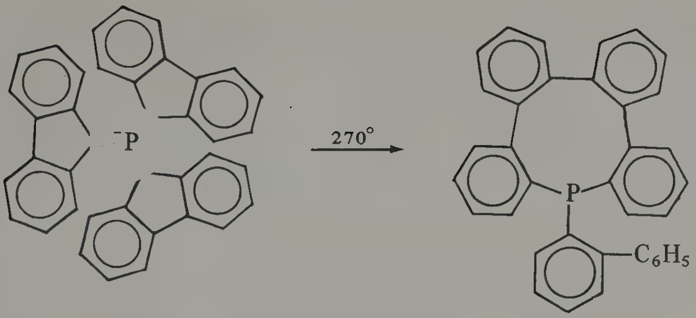
R = C_6H_5 (86%)[92]
R = CH_3[93]

The products, several examples of which are known,[92] are more properly considered chemically as tertiary aromatic phosphines, as the resemblance to a phosphonin is only formal. The usual high nucleophilicity to alkyl halides is retained. The preparation of the phosphoranes is of interest, since it starts with dibenzophosphole.



82 (77%)

Hellwinkel[93] also found that the phosphonin ring resulted from thermal rearrangement of the intriguing hexacoordinate anion 84.



84

An excellent summary of the fascinating properties of the penta- and hexa-covalent compounds, especially their stereochemistry, is provided by Mann.[94]

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94 Ref. 58, pp. 88-89, 156-158.

chapter five

^{31}P NMR Spectroscopy of Cyclic Compounds

Phosphorus chemistry is fortunate in being based on an element that has outstanding properties for nuclear magnetic resonance experiments. With a spin quantum number (I) of 1/2, and with only one isotope (^{31}P) occurring naturally, it has been a relatively easy matter to record NMR spectra for phosphorus compounds, and this has been practised from the very beginning of the NMR era. The sensitivity of the ^{31}P nucleus is only 0.0663 that of ^{1}H, but the vast majority of phosphorus compounds have only one such nucleus, and signals of useful intensity can be obtained from solutions of not unreasonable concentration. The advent of proton-decoupling and the Fourier transform technique has been of immense significance in ^{31}P NMR, the former in providing very sharp singlets (unlike the broad, complex multiplets resulting from ^{1}H coupling), the latter in reducing further the minimum concentration required (to 10^{-2} M or less). However, because of their general lack of availability, only about two dozen heterocyclic compounds containing C-P bonds were included in the extensive tables of ^{31}P NMR spectra published in 1967.[1] Since then, however, hundreds of heterocycles have been examined, and applying the technique is virtually standard practice in this area of research.

For years, ^{31}P chemical shifts in general were mostly considered as just another characterizing physical property of organic compounds, and little use was made of them in terms of rationalizing the organic structure present with the magnitude of the shift. To be sure, reasonably distinct ranges of shifts have been associated with particular phosphorus functional groups for some time and, with respect to a given function, it is frequently found that there can be assigned to each substituent on phosphorus standard increments that on addition give a reasonable prediction of the actual value. Nevertheless, the underlying cause for the increment associated with a particular substituent, and the reasons why variations occur even with seemingly very similar groups, has until recently received little consideration. In heterocyclic chemistry, it is just this type of variation that is important, for it is now known with certainty that in many cases steric influences are at play; once understood they can lead to great structural predictive values for ^{31}P NMR spectroscopy. This chapter is constructed with this in mind, to develop the empirical concepts of interpretation of organic structural influences on ^{31}P shifts, and especially to show how these shifts can be informative about the stereochemistry and bonding of ^{31}P in a given molecule. No effort will be made to discuss the fundamental theory of ^{31}P NMR shifts; this has been done in the widely used review of 1967,[1] and more recently (1971) by Van Wazer.[2] Suffice it to say that theory is not yet able to handle many of the effects commonly seen in organic compounds, and the empirical approach, so successful in ^{13}C NMR, is better able to aid in spectral interpretation.

The literature has been surveyed for the publication of ^{31}P NMR chemical shifts of heterocycles, and where applicable for ^{31}P-^{31}P coupling constants. The results of the survey are provided in Tables 5.1-5.12 in Section 5.9 as follows:

5.1 Phosphiranes and Phosphetanes
5.2 Phospholanes
5.3 3-Phospholenes
5.4 2-Phospholenes
5.5 Phospholes and Dimeric Derivatives
5.6 Multicyclic Derivatives of Phospholenes and Phospholanes
5.7 Phosphorinanes
5.8 Multicyclic Phosphorinane Derivatives
5.9 Phosphorins and Benzophosphorins
5.10 Rings of Seven or More Members
5.11 Bridged Ring Systems
5.12 Systems with Two or More P atoms
5.13 Rings with O, N, or S

No claim is made that all published ^{31}P data have been located and included in these tables, although it is probable that 90% or more do appear there. The tables dealing with derivatives based on 5- and 6-membered rings are closer to being complete. The literature through 1978 has been surveyed and a few 1979 reports are also included. The references to the tables are collected and numbered separately from those in the body of the chapter. Again those systems lacking a C-P bond are excluded from consideration.

Since references are associated with all entries in the tables, these are not repeated in the text when examples are taken from the tables for discussion. Occasional references are also made to ^{31}P shifts of noncyclic compounds; unless otherwise referenced, shifts for these compounds are given in Ref. 1.

5.1 TECHNIQUES IN ^{31}P NMR

Modern instrumentation makes use of ^{1}H decoupling, with the Fourier transform treatment of the response from pulsed irradiation. Frequently the magnet systems require locking on an internal deuterium (sometimes ^{19}F) nucleus, and for this reason it is now common to find that the preferred solvent is $CDCl_3$, D_2O, DMSO$-d_6$, C_6D_6, etc. A solution that contains 10-20% of the species being measured gives a strong signal in a reasonable collection time. It is extremely important to report the solvent used, particularly for phosphine oxides, where hydrogen bonding solvents can cause downfield shifts of as much as 10 ppm relative to nonbonding solvents. Phosphine oxides are frequently hygroscopic, making it difficult to insure that an anhydrous medium, free of the deshielding of hydrogen bonding, is in use. There consequently can be marked differences from reported chemical shifts for such compounds, even when the specified medium is used.

Chemical shifts have been referenced to a number of standards, but it is now the general practice to use 85% H_3PO_4 (usually in an external capillary or a separate tube for the superposition of a signal on a measured spectrum). Other substances used in the past and on occasion at present are

Trimethyl phosphite, $(CH_3O)_3P$, 139.6 ppm downfield from 85% H_3PO_4
Phosphorous anhydride, P_4O_6, 112.5 ppm downfield from 85% H_3PO_4

The use of 85% H_3PO_4 has a major disadvantage, in that its signal falls near the midpoint of the wide range of ^{31}P shifts. In ^{1}H and ^{13}C NMR, agreement is nearly universal on the use of a reference at the extreme upfield end of the range, and on the adoption of a positive sign for shifts downfield of the reference. With H_3PO_4 as reference ^{31}P NMR shifts require both positive and negative signs, and the independent convention was early adopted of designating downfield shifts with negative signs, and those upfield of the reference as positive. Recent efforts to standardize a common system for expressing NMR shifts for *all* nuclei downfield of a reference as positive have taken hold of ^{31}P NMR spectroscopy as well, and in 1977 the journal *Phosphorus and Sulfur*[3] took the editorial position of *requiring* the use of the convention of the common system in its papers. This usage is now spreading, no doubt to the regret of some and making it necessary to be very cautious when reading the current literature to determine which convention the author is using. It is more essential than ever, then, that current authors state the reference and the sign convention in their articles to aid in the use of their data. In this book, the *new* convention is used consistently; this is true of the compilation of published data in the tables of this chapter, which required revision of the reported signs. Published data referenced to another standard have been recalculated to H_3PO_4 as zero.

^{31}P NMR shifts are generally expressed to the nearest 0.1 ppm, and some authors are now publishing the computer printout values to the nearest 0.01 ppm. However, in practice, it is very difficult to reproduce a published value even to a few tenths of a ppm. Solvent and concentration effects no doubt are involved in this, and it is now known that, for some classes of phosphorus compounds, temperature effects can be substantial[4] (as much as 0.6 ppm/10°).

In the practice of ^{31}P NMR, only occasional use is made of coupling with ^{1}H, and in fact most spectra currently being obtained have been purposely decoupled. This is not to say that ^{1}H-^{31}P coupling is of no value; it is simply easier to determine the effect on a ^{1}H NMR spectrum. On occasion, however, a proton-coupled spectrum can lead to a solution of a problem. An excellent example is the recognition of a P-H bond, where the direct coupling constant is so large (several hundred hertz) that the result is unambiguous. Two and three bond couplings are much smaller (1-40 Hz).

Lanthanide shift reagents can influence ^{31}P,[5] and substantial differences have been observed in both P(III) and phosphoryl compounds. In a practical sense, there would be utility in this technique only for compounds where two or more ^{31}P nuclei are present. However, cases can be visualized where it could be quite helpful, for it is possible to have second-order NMR spectra for coupled ^{31}P nuclei that could be simplified by selective complexation of one nucleus.

Spin-lattice relaxation phenomena have become quite useful in ^{13}C and ^{1}H NMR spectroscopy since the advent of pulsed Fourier transform techniques. ^{31}P relaxation, however, has been studied so far in only a handful of organophosphorus compounds.[6] An attempt has recently been made to use the technique to aid in the solution conformational analysis of 1,3,2-dioxaphosphepanes, but without useful results.[7] It is premature to judge the utility of the technique in the study of phosphorus heterocycles; much more work needs to be done before it will become clear if structural studies will be aided by the measurement of T_1.

5.2 CHEMICAL SHIFTS OF THE MAJOR PHOSPHORUS FUNCTIONAL GROUPS

The most important influence on the ^{31}P shift is derived from the number and nature of the atoms directly attached to phosphorus. Although the range of ^{31}P shifts is quite large, overlap does occur, and one must be very cautious in assigning a phosphorus structure to an unknown solely on the basis of its ^{31}P NMR shift. Nevertheless, useful generalities do exist and are summarized below for the more commonly encountered functions, especially those of heterocyclic chemistry. In this compilation, which is based on the data of Ref. 1, only noncyclic compounds with saturated, unsubstituted alkyl groups or phenyl groups are represented.

RPH_2	−110 to −165	$RPO(OH)_2$	+15 to +30
R_2PH	−40 to −100	$RP(O)(OR)_2$	+15 to +40
R_3P	+20 to −62	$R_2P(O)(OH)$	+25 to +50
$RPCl_2$	+161 to +200	$R_2P(O)(OR)$	+25 to +50

R_2PCl	+80 to +120	$RPOCl_2$	+35 to +65
$RPBr_2$	+150 to +195	R_2POCl	+40 to +75
$RP(OR)_2$	+150 to +200	$R_3\overset{+}{P}H$	0 to −5
$R_2P(OR)$	+90 to +125	$R_4\overset{+}{P}$	+20 to +45
$R_3P(O)$	+20 to +50	R_5P	−85 to −100
$R_3P(S)$	+30 to +60		

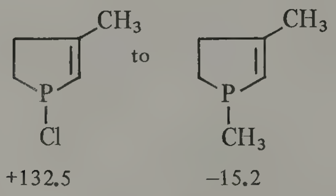
To understand why a group has a particular shift range is not always easy, and there are conflicting views in the literature on the direction of shifts when changes are made in the fundamental parameters of electronegativity of attached atoms, hybridization and bond angles, and d_π-p_π bonding from back-donation of lone pairs on attached atoms. The direction of the effect of increased electronegativity (deshielding) and increased d-orbital utilization (shielding) as expressed by Murray et al.[8] seems to work well in the empirical approach, although the opposite directions had been assumed for these effects in earlier theoretical work.[11] Then the electronegativity effect is consistent between ^{31}P and ^{13}C NMR. The direction of the back-bonding effect has also been supported in recent work by Albright et al.[9] The interplay among these (and perhaps other) effects needs to be considered in developing a feeling for the direction of shift changes as modification of the functionality about ^{31}P is made. Some useful generalizations develop from such considerations.

First, increasing the electronegativity of the directly attached atoms decreases the electron density on P and, other effects being equal or nearly equal, causes deshielding. This is especially clear in P(III) compounds, where complications of d-orbital utilization are less prominent. The series below illustrates the magnitude by which electronegativity changes can influence shifts.

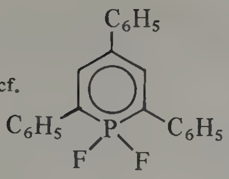
PCl_3	CH_3PCl_2	$(CH_3)_2PCl$	$(CH_3)_3P$
+219	+192	+94	−62

The important parameter of bond angle remains reasonably constant [PCl_3 100.1°, $(CH_3)_3P$ 98.6°] in this series. The electronegativity effect is well known in the heterocyclic series, as a few examples will make clear.

cf.

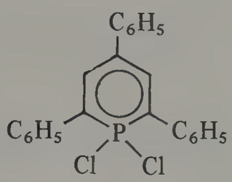


cf.



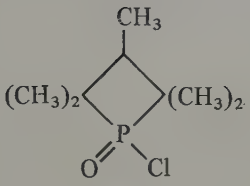
+73.0

to



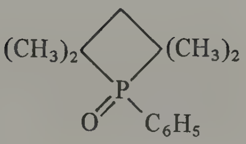
+17.0

cf.



+80.7

to



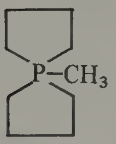
+51

Second, increase in covalency from P(III) to P(IV), where the starting three ligands to phosphorus remain the same and do not carry lone pairs that can be backdonated to P, almost invariably causes strong deshielding, as in the series below.

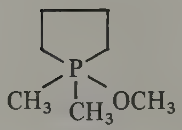
$(CH_3)_3P$	$(CH_3)_3P{=}O$	$(CH_3)_3P{=}S$	$(CH_3)_4\overset{+}{P}I^-$
-62	$+36$	$+59$	$+25$

Several factors are involved here. The fourth atom may be strongly electronegative, thus contributing to the deshielding. Or it can be argued that a lone pair provides strong shielding, which is lost on bonding. The change in bond angle from about 95°-100° in P(III) to about 103°-108° in P(IV) is also an important factor, and in fact has led to a broader generality that a relative contraction of bond angles is a cause of shielding. This notion is quite useful for simple systems where the organic ligands remain constant, but is *not* useful, as will be seen, to explain shift effects in a given P(III) or P(IV) state that accompany structural changes within an organic ligand.

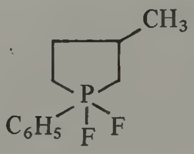
Finally, an increase in the relative degree of occupation of d-orbitals in P(IV) derivatives is associated with shielding. This is especially valuable in accounting for the pronounced upfield shifts of the pentacovalent phosphoranes, which have dsp^3 hybridization. These compounds have very negative shift values when only organic ligands are present, and even replacement by one or two electron-attracting oxy functions does not shift values downfield of that for H_3PO_4. However, continued increases in electronegativity can cause this line to be crossed.



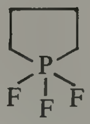
−91.7



−69.1

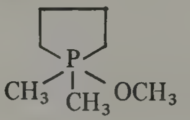


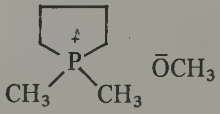
−2.3



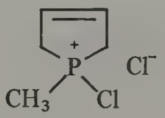
+29.6

A decision on ionic *versus* pentacovalent character in a substance is frequently possible on the basis of the high-field positions adopted by the latter. For example, the methoxy phosphorane derivative above conceivably could be ionic:

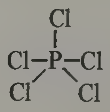




Were this true, a large positive shift (about +48, as in the phosphonium iodide) would have been observed for the phosphonium ion. On the other hand, ionic character was clearly established for the McCormack cycloadducts by their markedly downfield signals relative to the high-field value for the pentacovalent form of PCl_5 as a model.



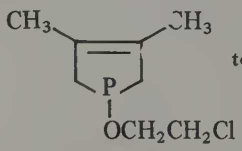
+112



−80

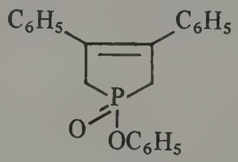
The d-orbital concept is helpful in explaining some other effects that are noted on the P(III)→P(IV) conversion. Thus, oxidation of a phosphonite to a phosphonate, or a phosphinite to a phosphinate, causes strong shielding, unlike the case of oxidation of phosphines:

cf.

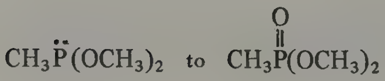


+134

to



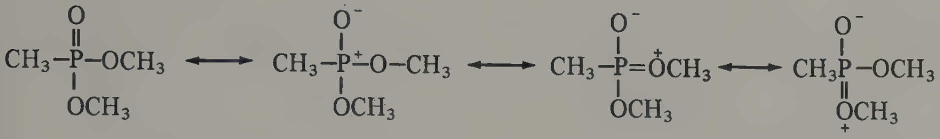
+60.8



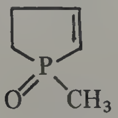
cf. $CH_3\overset{\cdot\cdot}{P}(OCH_3)_2$ to $CH_3\overset{O}{\overset{\|}{P}}(OCH_3)_2$

+182.5[10] +32.3[11]

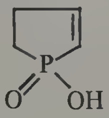
The change to the polarized P(IV) state enhances the utilization of d-orbitals for back-donation (π bonding) by the various oxygens.



The back-donation concept helps to explain the lack of strong deshielding that accompanies replacement of alkyl by hydroxy, as in the following:



+67



+76.8

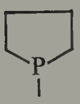
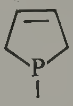
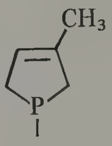
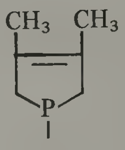
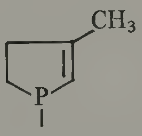
The deshielding due to the increased electronegativity of –OH is largely offset by the shielding of increased d-π bonding. Similarly, phosphine sulfides have values very close to (even downfield of) phosphine oxides; the deshielding by the increase in electronegativity in the oxide is offset by the increased π bonding of this atom relative to sulfur. The form $R_3\overset{+}{P}\text{-}S^-$ is probably more important in the sulfides.

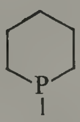
5.3 INFLUENCES OF ALKYL SUBSTITUENTS ON ^{31}P NMR SHIFTS

At first glance, there appears to be no regularity in the way structural changes of an alkyl group affect ^{31}P NMR shifts, as seen in the series below.

$(CH_3)_3P$	$(CH_3CH_2)_3P$	$(CH_3CH_2CH_2)_3P$	$((CH_3)_2CH)_3P$
−62	−21	−33	+19

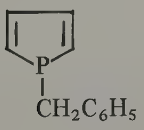
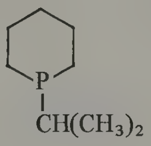
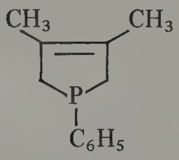
One thing that did emerge from early considerations of structure-spectra relations was that a given alkyl group always made a constant contribution to the ^{31}P shift of a particular phosphorus function. Tables of increments for the various alkyls have been compiled for tertiary phosphines,[12] secondary phosphines,[13] primary phosphines,[14] and phosphonium salts.[15-17] The treatment by Grim of the data for tertiary phosphines[12] is particularly useful in the heterocyclic series. Grim assigned a "Group Contribution" (GC) to each alkyl, which could then be added as dictated by a particular phosphine to give a close approximation of the actual ^{31}P chemical shift. Some of Grim's GC values (in ppm) follow: CH_3, −21; C_2H_5, −7; n-C_3H_7, −11; i-C_3H_7, +6; n-C_4H_9, −11; i-C_4H_9, −15; t-C_4H_9, +23; *cyclo*-C_6H_{11}, +2; benzyl, −4; phenyl, −3. Thus, one can calculate for $(i\text{-}C_3H_7)_2PC_6H_5$ a value of $2(+6) + (-3) = +9$, to be compared to the experimental value +10. It was later[18] shown that the concept worked equally well for some heterocyclic phosphines; the entire ring was assigned a GC, which could be added to the Grim GC for the P-alkyl substituent.



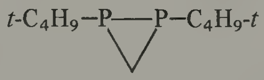
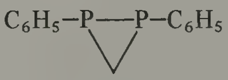
GC = −11 −21 −14.3 −29 +6.6 +12 −32

No doubt other rings could be similarly characterized. The agreement with experimental values is quite good:

Calc.	+8	−26	−32
Expt.	+8.0	−25.4	−34.5

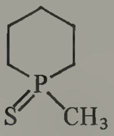
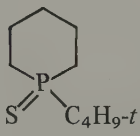
The GC values for the alkyls can be used qualitatively to account for ^{31}P effects in other ring systems. Thus, t-C_4H_9 (GC = +23) derivatives can be expected to absorb strongly downfield relative to, for example, the corresponding phenyl (GC = −3) compound, and this is seen even in the unusual case below:

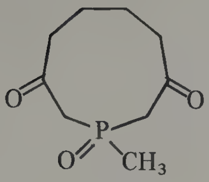
−91.7 −122

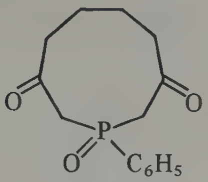
$\Delta\delta = 30.8$ ppm; calc. $\Delta\delta = 2(23-3) = 40$ ppm

The relative GC concept can be extended to P(IV) functions with alkyl substituents in a qualitative way. However, P-phenyl derivatives are generally upfield of P-alkyls, the opposite of what would be expectated from GC values in phosphines. This interesting observation may have either a steric or a π-bonding explanation, as will be discussed later.

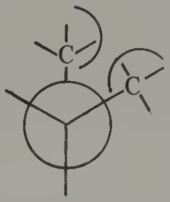



+33.9 +57.0

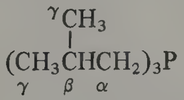

+32.6


+25.4

Nevertheless, this empirical approach does not help in understanding *why* ^{31}P shifts respond to structure changes in the way they do. Grim did notice that his GC values for phosphines could be considered as being composed of contributions from each type of carbon present (α, β, γ with respect to ^{31}P); however, the significance of this observation did not become apparent until it was recognized[19] not only that many phosphorus functionalities had ^{31}P shifts that were additively influenced by the numbers of each type of carbon but, more importantly, that the relative influence of each type of carbon was exactly the same as is so well known in ^{13}C NMR (as well as in ^{15}N NMR). Thus, increasing the number of carbons α- or β- to ^{31}P causes strong deshielding, but increasing the number of γ-carbons causes *shielding*. This immediately reveals that a steric component is present in ^{31}P shift effects, for the γ-shielding effect of ^{13}C NMR of alkanes is generally accepted to arise from steric compression in gauche conformations, as shown below.



The consequence of the compression is to shift electron density towards the γ-related carbons, thus increasing the shielding. It then became easy to understand why, for example, *i*-butyl groups cause shielding relative to *n*-butyl (greater number of γ-carbons), or why *t*-butyl causes more deshielding than *n*-butyl (greater number of β-carbons).


$(\underset{\gamma}{CH_3}\overset{\overset{\gamma}{CH_3}\,|}{\underset{\beta}{C}}H\underset{\alpha}{CH_2})_3P$ 6 γ-carbons, $\delta = -40$

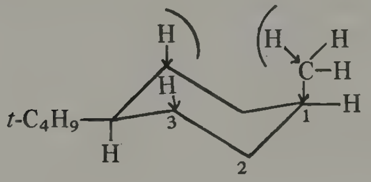
$(CH_3\underset{\gamma}{CH_2}\underset{\beta}{CH_2}\underset{\alpha}{CH_2})_3P$ 3 γ-carbons, $\delta = -32.3$

In developing this approach to ^{31}P NMR, a parent value was assigned to the methyl derivative of a particular phosphorus function, and then increments were applied for each additional carbon β- and γ- to phosphorus. Some examples of these values follow:

Compound	δ, CH_3 Parent	β-Constant	γ-Constant
R_3P	-62	+13.5	-4
R_2PH	-99	+22	-10
R_3PO	+36.2	+4	-1
R_4P^+	+25.3	+3.7	-1.5

Although the magnitude of the β and γ constants varies considerably, the deshielding-shielding relation holds for the entire series of functions.

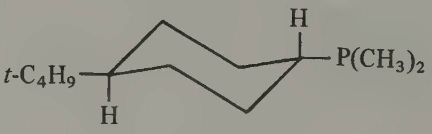
If the analogy to ^{13}C NMR (which has been applied successfully also in explaining effects in 1,3,2-dioxaphosphorinanes[20]) is continued, steric compression would be expected to be enhanced in rigid cyclic systems, either where P is a member of the ring or a substituent on the ring. This follows, for example, from the upfield ^{13}C shifts involved in the crowding when axial cyclohexane conformers are compared to equatorial conformers.[21]



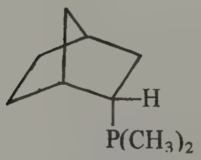
δ CH_3	17.5	22.8
δ C-1	27.0	32.6
δ C-2,6	33.0	36.0
δ C-3,5	21.4	27.7

For tertiary phosphines, this expectation is generally realized when P is exocyclic, as in the isomer pairs below.[22,23]

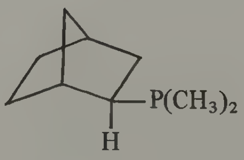
−45.8



−42.5

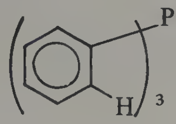


−47.4

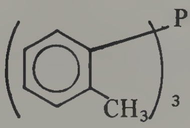


−43.2

Steric crowding is, of course, enhanced in γ-eclipsed conformations, and this no doubt is involved in the pronounced upfield shift on substituting *ortho*-H by CH_3 in triphenylphosphine.[24]

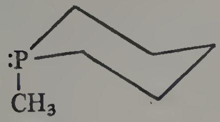


−6

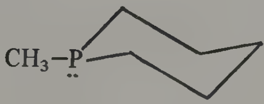


−32.6

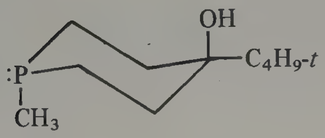
When P is in the ring, shielding can also result from steric compression, but just as in ^{13}C NMR the effect is less reliable if the compression does not directly involve this atom. Thus, the conformers of 1-methylphosphorinane measured at low temperature[25] have the expected relative difference in their shifts, with axial upfield of equatorial by 3.1 ppm from the increased crowding, and so do some rigid 4-phosphorinanol isomers.



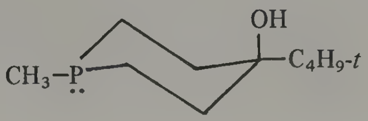
vs.



, Δδ 3.1 ppm

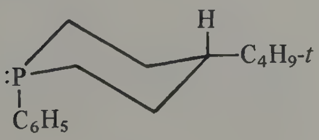


−67.3



−57.7

However, it has recently been noted[26] that the opposite relation holds for some P-phenyl derivatives:



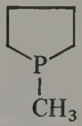
−32.9

−38.6

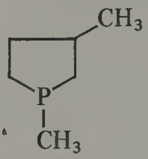
In this particular case, some ring distortion in the cis isomer may cause a significant difference in other nonbonded interactions, and this is supported by the observation of ^1H NMR signals for the *t*-butyl groups that differ by 0.12 ppm. For the 1-phenyl-4-*t*-butyl-4-phosphorinanols, these signals are separated by 0.20 ppm.[27] In contrast, where methyl replaces phenyl, the difference is only 1 Hz at 60 ppm.[28]

This provides a cautionary note to the use of ^{31}P shifts as a sole indicator of cis, trans geometry in phosphorinanes.

Shielding by γ-carbons can only be expected when steric crowding results, and it should not be assumed that all γ-carbons will be oriented to produce this effect. A case in point is the replacement of a β-hydrogen by methyl in the phospholane system. The averaged dihedral angle relating 3-CH_3 to P will be much larger than the 60° of a gauche conformation, thus weakening the steric interaction.



−32

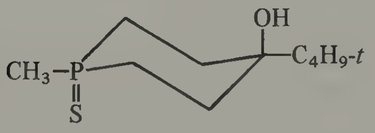


−33.4, −33.8
(cis and trans)

When a second β-H (at C-4) is replaced by *cis*-CH_3, the ring conformation changes to alleviate the 3,4-dimethyl crowding; the new conformations are not known with certainty, but would appear to possess greater crowding at P (δ −41.6 and −55.4, isomers unassigned).

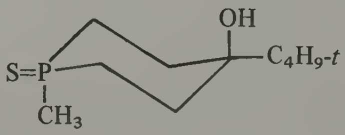
The γ-constants applied to ^{31}P are noticeably smaller for P(IV) functions than for P(III), and there are indications that effects other than simple steric compression play a role with these functions. Thus, although some phosphorinane sulfides show the expected effect (assuming crowding is greater for axial P-CH_3 than axial P=S), phosphorinane oxides do *not*.

cf.



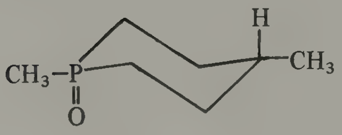
+31.9

to



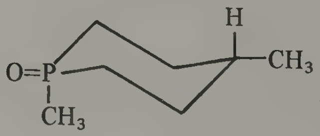
+29.4

cf.



+38.7

to

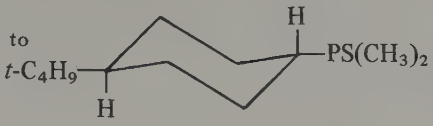


+40.9

Thus, cis, trans structural assignment on the basis of ^{31}P shift effects is unreliable in P(IV) forms. In cycloalkanes with exocyclic P(IV) substituents, and even with the highly polar P(III) groups PCl_2 and $-P(OCH_3)_2$, the crowding effect is less important, and in some cases is overwhelmed by another influence. Some examples[22, 23] are shown below:

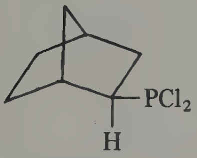
cf.

to

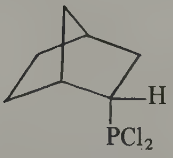


+43.3 +42.5

cf.



to

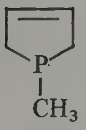


+187.5 +196.8

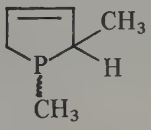
A possible explanation for the second effect receives comment in a later section.

The β-deshielding effect is also a useful concept, and helps account for shifts in heterocyclic systems. No clearcut explanation has yet emerged for the origin of β-deshielding in ^{13}C or ^{31}P NMR, and it must be considered an empirical observation. In cyclic phosphorus compounds, unless sp^2 carbons are being substituted, the replacement of β-H by a β-alkyl group can produce cis, trans isomers, and it turns out that, whereas both isomers show deshielding, there is quite a distinct difference in the size of the effect. In general, cis substitution causes more deshielding than trans for P(III), as well as several P(IV) forms. The effect can be a very useful indicator of cis, trans geometry when both isomers are available. It may originate from the different steric environment that will result for the P atom and its substituents or lone pair in the two different conformations adopted by the isomers.

cf.

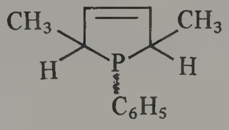


to



cf.

to



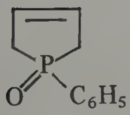
–41.6

cis –16.7
trans –28.2

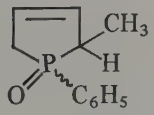
–25.3

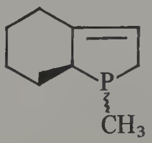
cis +15.1
trans +8.5

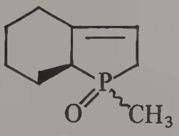
cf.



to





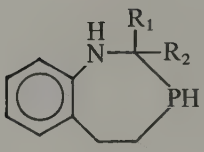


+54.2

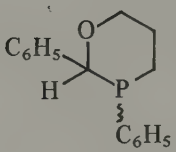
cis +72.9
trans +55.8

cf. cis –26.2
to trans –28.6

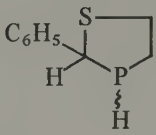
cf. cis +77.1
to trans +70.5



cf. $R_1 = R_2 = H$, −72.4, to
$R_1 = CH_3$, $R_2 = C_2H_5$, −21.7 and −31.4
(isomers unassigned)

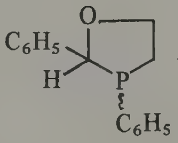


cf. cis −22.6
to trans −33.7



cf. cis (H, C_6H_5) −5.6,
to trans (H, C_6H_5) −15.6

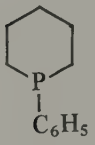
However, cis substitution necessarily creates a steric crowding situation with the P-substituent and the resulting shielding can more than compensate for the deshielding β-effect. Thus, in the system below the cis, trans isomers show reversal of the usual effect, and indicate the need for caution in the use of the β-effect for isomer assignments.



cis −7.5
trans −4.0

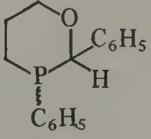
Polar substituents on α-carbons of alkyl chains attached to P would be expected to introduce some extra deshielding (along with the β-effect) because of their electron-withdrawing inductive effects [cf. $(CH_3)_3P$, −62, to $(HOCH_2)_3P$, −31], but in phosphorus heterocycles there are presently not available sufficient data to assess the importance of this effect when polar atoms replace carbon. In the following examples, if allowance is made for the deshielding effect of β-phenyl in the heterosubstituted rings, then there is little difference from the parents. This suggestion that a ring heteroatom β- to phosphorus has only a small effect could be extremely useful in predicting the ^{31}P shift of a new heterosubstituted system.

cf.



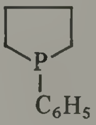
−34.3

to



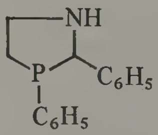
cis −22.6
trans −33.7

cf.



−15.3

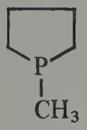
to



−2.9 (isomer unspecified

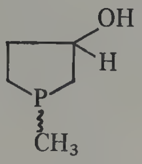
Polar atoms on β-carbon are more common in phosphorus heterocycles both as members of the ring and as exocyclic substituents. A number of examples suggest that generally upfield shifts can be expected from such substitutions, speaking against a through-the-chain inductive origin for the effect. Conformational differences are surely induced in the rings by such substitutions and will have a definite effect on δ ^{31}P.

cf.



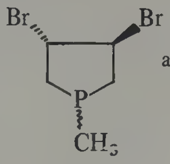
−32

to



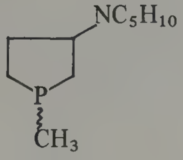
cis −38.8
trans −40.3

and



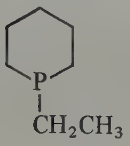
−41.5

and



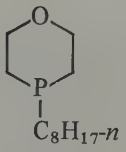
−39.2

cf.



−38.6

to



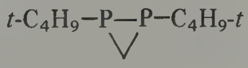
−52

5.4 THE EFFECT OF RING SIZE ON ^{31}P SHIFTS

5.4.1 The P(III) Series

Enough data are available to establish some important tendencies on variation of ring size. The series begins with an extraordinary value for the three-membered ring; the shielding places the ^{31}P shifts at the extreme upfield end of the known range of shifts, far beyond other P(III) values. Far upfield shifts are found also in the diphosphiranes.

H, −341
CH_3, −251
C_6H_5, −234

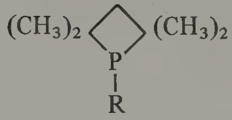


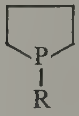
$t\text{-}C_4H_9\text{–}P\text{–}P\text{–}C_4H_9\text{-}t$

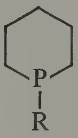
−168.8

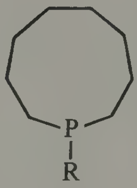
The peculiar bonding required for the formation of a three-membered ring may well be at play here, although it has been suggested for similar high-field shifts in the ^{13}C NMR of cyclopropanes[29] that a ring current produces the shielding. The ^{15}N resonance of ethyleneimine is the most upfield value known for a neutral nitrogen compound,[30a] and ^{17}O in oxiranes is similarly far upfield,[30b] no doubt for a common reason.

Addition of one more atom to the ring completely changes the picture; although there are few data for phosphetanes, there is known one P(III) form that suggests that no major abnormality will be found for this system. This form, unfortunately, is complicated by a plurality of (deshielding) methyls on the α-carbons, but if some allowance is made for this fact it appears that the parent ring will fall somewhere close to the 5- and 6-membered rings, delineating clearly the unique position of the phosphiranes.



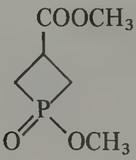




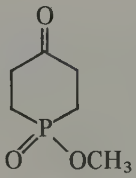


R = C_6H_5	+4.4	−15.3	−34.3	--
R = CH_3	--	−32	−53.7	−33.8

There is a definite difference in endocyclic C-P-C angle in these ring systems, as can be seen for the oxides by the following data taken from Section 8.2 and Table 8.1 of Chapter 8: phosphetanes, 79.4°-82.5°; phospholanes, 94.8°; phosphorinanes, 99.8°; phosphonanes, 106.3°. Although this property may figure in establishing the shift, it clearly is not the dominating effect. It would be extremely desirable to obtain a phosphetane for ^{31}P measurement that was free of α-methyls in order to confirm the suggestion that the parent value may be in the same range as the value in the phospholane or phosphorinane. Indeed, a phosphinate in the phosphetane series is known without these α-methyls, and its ^{31}P value is quite similar to that of a phosphorinane.



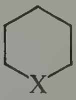
+36.6



+46.9

The 6-membered ring is seen to stand out with a more shielded ^{31}P than is observed for the 5- and 9-membered rings. The suggestion has been made[19] that this is the result of the fixed γ-gauche relation between P and C-4 in the phosphorinanes, causing shielding relative to the other rings. The effect is found also in P(IV) compounds, as will be discussed.

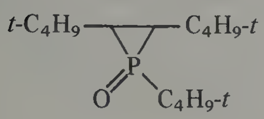
There is a suggestion of a parallel with ^{13}C NMR shifts for the first three members, depending on confirmation of the phosphetane value. The relative position of the 6-membered ring does not agree, but the model compounds being used are far less comparable than desired since the P- series carries a phenyl substituent.



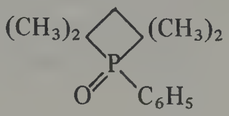
C_6H_5P	−234	−(10 to 30)	−15	−34
CH_2[19]	−2.6	23.3	26.5	27.8

5.4.2 The P(IV) Systems

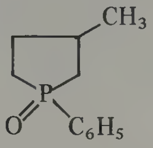
Saturated rings with from 3 to 8 members are known for oxides, but even with careful selection of models for which data are available there is as yet little consistency in the nature of the substitution present.



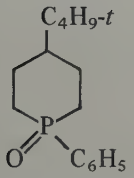
−1.3



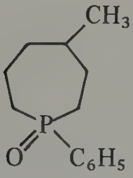
+51



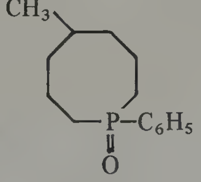
+56



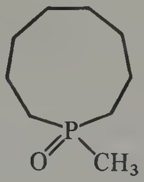
+30, +28.2
(isomers)



+40.4, +40.8
(isomers)



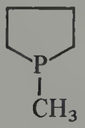
+39.5, +37.0
(isomers)



+48.9

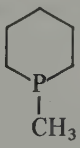
Most notable is the drastic reduction in the shielding of the phosphirane ring brought about by oxidation, even after allowing for the presence of *t*-butyl substituents. The relative Δδ for P(III) → P(IV) appears to be about 200 ppm for this ring, but only about 50-70 ppm for the 4- , 5- , and 6-membered rings. Again the 5- is significantly downfield of the 6-membered ring, a fact that needs further comment because of the great importance of these rings in phosphorus chemistry. The relation is consistent throughout many structural variations, both P(III) and P(IV), and is also well known in the cyclic phosphates[31] [where it has been attributed to diminished shielding by π bonding from O in the smaller ring, an effect not pertinent with P(III) forms]. The selection of compounds below illustrates the relation:

cf.



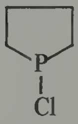
−32

to



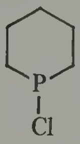
−53.7

cf.



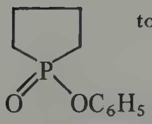
+126.6

to



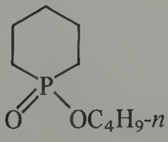
+108.0

cf.



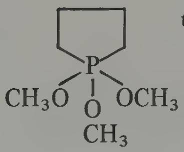
+76

to



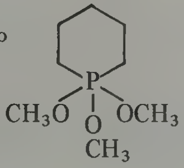
+46

cf.



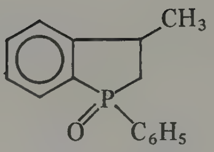
−69

to



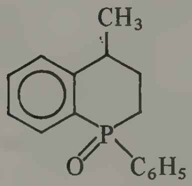
−91

cf.



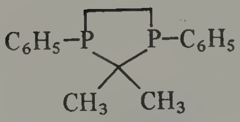
+48.5, +49.7
(isomers)

to



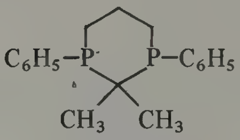
+23.5
(both isomers)

cf.



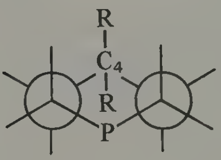
+22.2, +17.3

to



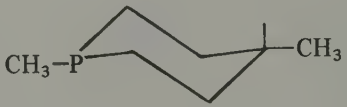
−2.0, −4.0

If the greater shielding in 6-membered rings is another manifestation of a γ-gauche interaction, it would be reasonable to expect some dependence of the ^{31}P shift on the nature of substituents at the gauche-related carbon (C-4), and there are some data pointing this way.



A single 4-substituent causes a change in the position of conformational equilibrium, since in general a C-substituent demands the equatorial position more strongly than does a P-substituent, but even allowing for this effect, there appears to be extra shielding associated with 4-substitution (an effect also known for the 1,3,2-dioxaphosphorinane system[20]). For example, the two 1,4-dimethyl derivatives have the preferred conformations shown below; both have shifts upfield of the 1-methyl compound (−53.7, averaged for a 2:1 axial-equatorial mixture[32]).

cis −61.9

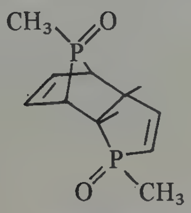


trans −55.7

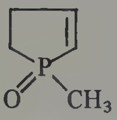
A 4,4-disubstituted phosphorinane (4,4-dimethoxy-1-methyl) has δ −59.7, again displaying an upfield shift not connectable with a conformational change.

5.5 SPECIAL CASES WHERE MOLECULAR GEOMETRY INFLUENCES ^{31}P SHIFTS

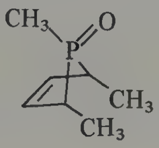
It has been the purpose so far to account for small changes in chemical shifts in a systematic way, isolating particular molecular features for consideration. Some important shift effects are known, however, that are not readily handled by this approach, and which seem to require new explanations. An excellent example is provided by the phosphole dimer structure, where the two different ^{31}P nuclei can have strikingly different shifts.



+91.4, +61.8



+67.0



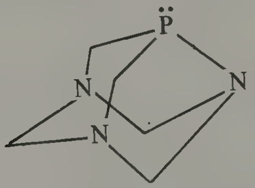
+58.2

^{31}P in the 2-phospholene ring of the dimer has a normal value of +61.8 compared to the monocyclic model, but the bridging P has an extraordinary low-field value of +91.4. A monocyclic model would be a *cis*-2,4-dimethyl-3-phospholene oxide, and that isomer with *trans*-1-methyl is known to have δ +58.2. What is the cause of this huge downfield shift in the dimer? Is it related to the contraction of the internal C-P-C angle imposed by the bridging, or to closer proximity of P to the double bond, or perhaps to some more subtle change in conformation or nonbonded orbital interaction? There will be other examples cited in this section where similar questions must be asked.

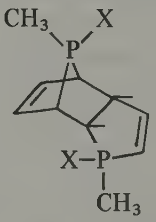
The importance of bond angle and hybridization differences has been already mentioned as having special significance in establishing the range of ^{31}P shifts for P(III) groups *versus* their P(IV) counterparts. However, *within* a P(III) or P(IV) family, bond angle differences are much less useful in explaining ^{31}P shift differences and a strong case against the continued use of this concept to explain large shift differences by small angle changes has been published.[20] There is, in fact, no agreement in the literature even on the *direction* of such an effect; for example, one paper on phospholes[33] proposes from the Letcher-Van Wazer theory that the *downfield* ^{31}P shift so characteristic of this system is due to the significantly reduced internal C-P-C bond (90.7° in 1-benzylphosphole[34]), whereas other papers[35] propose that *high-field* values for P(III) at the bridgehead of cage structures such as phosphatriptycene are due to reduction in the internal C-P-C angles with effective diversion of s-character into the lone pair. Bond angle differences within a family may very well have an influence on ^{31}P shifts, but a closer examination of the literature certainly does not provide a clear picture for predictive purposes as to what these influences are. The following points might be considered.

1 Triphenylphosphine has C-P-C angles of 103° (Ref. 36), and trimesitylphosphine has greatly expanded angles of 109.7° (Ref. 37a); the latter has a much more shielded phosphorus (δ −36.6[37b]) than does triphenylphosphine (δ −6[2]). This is exactly the opposite effect than would be predicted from the phosphatriptycene data, where increased shielding relative to triphenylphosphine is attributed to a *contraction* of the bond angles. The importance of steric effects in explaining such results will receive consideration at the end of this section.

2 The cage structure below has what may be the most upfield ^{31}P value (−100) ever recorded for a tertiary phosphine (excepting the phosphiranes). The bond angle argument was invoked to explain this effect, but in fact the bond angles reported [96.1° (Ref. 38) or 98±1° (Ref. 39)] do not show a really significant reduction from that of trimethylphosphine (99°). It is out of the question that this small change in bond angle could produce such an upfield shift from the −62 value for trimethylphosphine.



Similar arguments can be developed from other published data, but a return to the phosphole dimer structure will provide one final point. When the double bonds are removed from the dimers by hydrogenation, the ^{31}P shifts of the two resulting phospholane oxide rings are nearly identical, so much so that these coupled nuclei display the classic distortion of an AB system.[40] The bond angles will be but little changed in the reduced form relative to the unsaturated form with the bridging C-P-C angle retaining its contraction. The spectacular downfield shift of the unsaturated form therefore cannot be a direct result of a bond angle difference. Even more dramatic are the relative shifts for phosphines in this system; as seen below in the table of comparative data, the bridging P(III) is even downfield of the



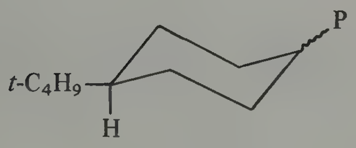
X	Bridging P	2-Phospholene P
Lone pair	+97.7	−1.5
O	+91.4	+61.8
S	+110.3	+62.0
$CH_3^+ I^-$	+98.3	+58.8

position for various P(IV) derivatives (a violation of a generality), and establishes the record for the most deshielded tertiary phosphine.

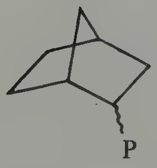
Again in the *saturated* phosphine, however, the two ^{31}P nuclei have very similar and quite ordinary chemical shifts (δ −18.0 and −21.7 for the above dimer system). The exact nature of the effect that is causing the deshielding in the original dimer structures remains unknown.

Whatever the cause of the shifts in the phosphole dimer system, they do reveal that profound influences can be felt on ^{31}P nuclei that cannot be explained by bond angle arguments, by electronegativity effects, by back bonding into d-orbitals, or by γ-gauche steric compression, and must depend on subtle changes in molecular architecture or nonbonded interactions. In some cases, especially based on R-O-P-OR systems, there appears to be a relation between torsion angles in the rotameric forms (gauche and trans), the bond angle at P, and the ^{31}P shift[41]; the smaller torsion angle in the gauche rotamer is related to a larger bond angle experimentally, and these forms have the upfield ^{31}P shifts. There are so many exceptions with C-P heterocycles, and other systems pointed out elsewhere,[42] regarding the direction of the ^{31}P shift with angle changes that this theory is not generally applicable in its present form. With refinement and study of specific cases where all involved parameters have been experimentally determined, it may become more useful. The P(III) state is especially sensitive to subtle effects and difficult to fit into general pictures; tertiary phosphines have been seen in these discussions to have ^{31}P shifts over the range of about +100 to −250 ppm! With this extraordinary sensitivity to effects that do not even involve a change in atoms directly attached to P, it is no wonder that there has been such difficulty in explaining trends in ^{31}P shifts observed among phosphines.

Heterocyclic compounds are not the only ones where unusual steric influences must act on ^{31}P shifts. In studies of various P functions on rigid cyclic systems, it has been observed that the most sterically compressed of two positions (e.g., axial or equatorial) does not always lead to the most upfield ^{31}P shifts. Some selected examples[22,23] of this situation are

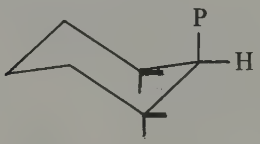


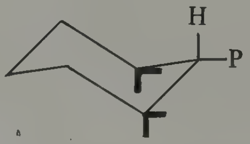
	axial	equatorial
PCl_2	+208.9	+194.6
$P(OCH_3)_2$	+192.6	+190.0
$PS(CH_3)_2$	+43.3	+42.5
$\overset{+}{P}(CH_3)_3$	+30.8	+29.6



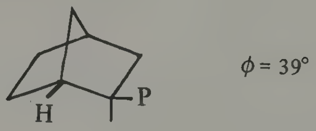
	endo	exo
PCl_2	+196.8	+187.5
$P(OCH_3)_2$	+192.4	+185.3
$PS(CH_3)_2$	+40.2	+42.9
$\overset{+}{P}(CH_3)_3$	+29.5	+30.1

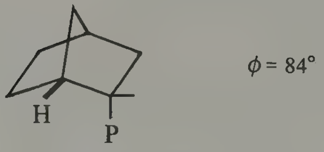
It has been proposed that a second shielding effect operates on P when equatorial in the cyclohexanes[42] or endo in the norbornanes[23] that overwhelms the shielding of steric compression. This second effect has been related in an empirical way in the cyclohexanes to the presence of a greater number of rigidly held C-H bonds in the β-position that are gauche to the C-P bond. There are two such bonds in axial isomers, but four in equatorial isomers. These are emphasized with heavy lines in the structures below.





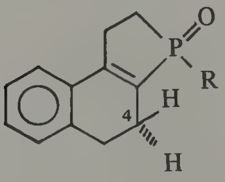
The effect only seems to operate on P(IV) or highly polar P(III) functions; the $(CH_3)_2P$– and H_2P– groups had the expected upfield signals for the crowded axial isomers (−45.8 and −131.3, respectively, compared to −42.5 and −111.6 for the equatorial isomers). In the norbornanes there is closer proximity of the P function to the β-CH bond on the 1-position in the exo than in the endo position,[23] thus providing greater shielding.



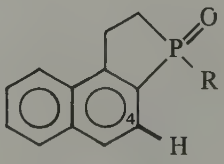


The exact nature of any interaction is yet to be defined, and again it is emphasized that the concept is strictly an empirical one at this time. Nevertheless, it appears useful in explaining some unpredicted chemical shifts in heterocyclic systems. Two examples are given below.

1 Aromatization of the central ring of various derivatives of structure **1** to form naphthalene derivatives (**2**) can be accompanied by a strong (5-10 ppm) upfield shift.

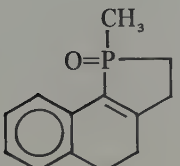


1, R = CH_3, δ +65.1

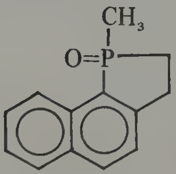


2, δ +56.1

It is not obvious why a change in conjugation from a styrenoid to a naphthalene system of unsaturation should lead to such a pronounced effect, because as will be seen in the next section cyclic phosphine oxides are not very sensitive to conjugative effects. Also pointing away from a conjugation effect is the observation that in the isomeric system little change accompanies the aromatization (cf. **3** to **4**).



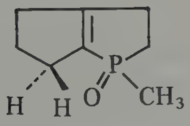
3, δ +63.0



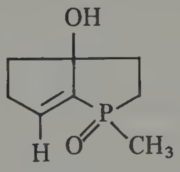
4, δ +61.6

There is, however, a conformational change near P in the conversion of **1** to **2** that is absent in **3** to **4**; this change occurs at the 4-position, and amounts to the replacement of two β-CH bonds that are gauche to P by one CH bond that is eclipsed. This is precisely the sort of effect noticed for the cyclohexane and norbornane compounds, where closer proximity of P to a β-CH was identified with shielding.

2 Movement of the double bond from the fusion position to the cyclopentane ring in the bicyclic system below produces a very strong shielding effect.

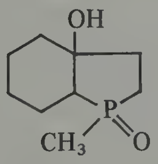


5, δ +63.2

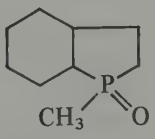


6, +32.0

Indeed, the value for **6** is the most upfield ever recorded for *any* 5-membered cyclic phosphine oxide. The OH group does not seem responsible for this effect, for no significant ^{31}P difference exists between structures **7** and **8**.



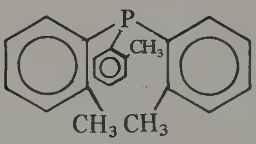
7, δ +68.8, +73.2 (isomers)



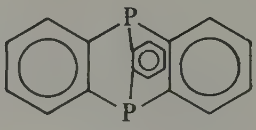
8, δ +78.8 (D_2O)

Because the double bond remains conjugated with phosphoryl in both **5** and **6**, an electronic effect can be ruled out. What remains as a possible effect is the same conformational change seen in the aromatization of **1**; at the β-carbon, two gauche C-H interactions are replaced by an eclipsing C-H interaction.

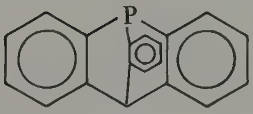
Tri(*o*-tolyl)phosphine has already been noted[24] to exhibit a pronounced shielding effect from the eclipsed relation of C-P to C-CH_3. Such eclipsing is present when phosphorus is installed in the triptycene framework, and this may well be involved in the pronounced upfield shifts noted for several such systems.



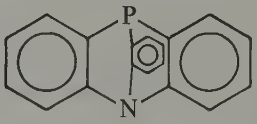
–32.6



–43



–64.8



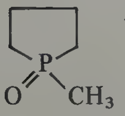
–80

The rigid geometry holds three bonds eclipsing the C-P bonds, and the increased shielding noted by several authors for these compounds must at least in part be attributed to this effect. The bond angle argument has been used to explain the shifts, and this is partly justified from the observation[43] that the diphosphatriptycene has C-P-C angles of 97° (cf. to 103° for triphenylphosphine). This argument would necessitate further substantial reduction in the C-P-C angle on replacing P by CH (to –64.8) or by N (to –80) and, in fact, for azaphosphatriptycene, an angle reduction to 93.3° is indeed achieved.[44] Nevertheless, with the skepticism already expressed about the predictability of bond angle influences on ^{31}P shifts it is proper to include consideration of the conformational situation in these structures.

5.6 CONJUGATIVE EFFECTS ON ^{31}P SHIFTS

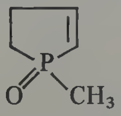
It is generally accepted by many authors (e.g., Ref. 45) that π-electrons on an adjacent double bond can interact with P(IV) forms to cause upfield ^{31}P NMR shifts (as well as other effects, such as decreasing the IR frequency of C=C stretching, increasing thermodynamic stability, etc.). One explanation for this phenomenon is that d orbitals share some of the electron density on the α-carbon, and that in general an increase in d-orbital utilization produces shielding. Vinyl phosphonium salts show a more pronounced effect than phosphine oxides, where π bonding from oxygen can compete with and reduce the π bonding from the double bond.[9] However, it is always difficult to make a single, specific change in going from one structure to another, closely related one. Installing unsaturation next to phosphorus necessarily changes nonbonded interactions and bond angles, and any chemical shift effect has to be considered as a consequence of several molecular changes. It is not too suprising, then, to find in heterocycles that the expected shielding effect of conjugation can be overwhelmed so that net *deshielding* takes over. This is particularly true of phosphine oxides, and the selected examples below show both effects. This is also true among phosphonium salts, although it is more common to find shielding than deshielding. Multiply unsaturated ions seem consistently to show an appreciable shielding effect.

cf.



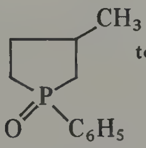
+65.8

to



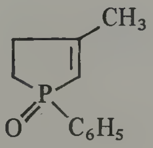
+67.0

cf.



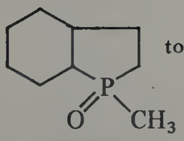
+56
(cis or trans)

to



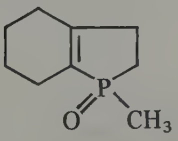
+60.5

cf.



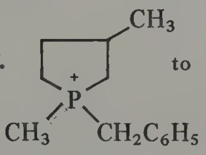
+78.8 and +82.8
(cis, trans)

to



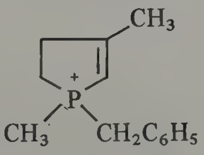
+76.5

cf.



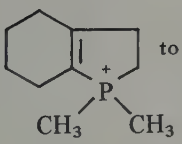
+51.1, +50.9
(cis, trans)

to



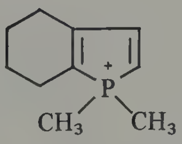
+59.5

cf.



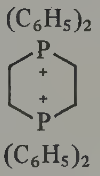
+52.8

to



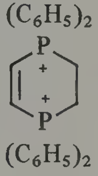
+41.1

cf.



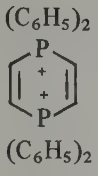
+14.4

to



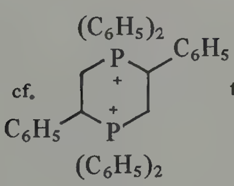
+2.8

and



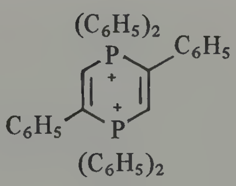
−16.0

cf.



+20.4

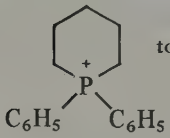
to



−3.5

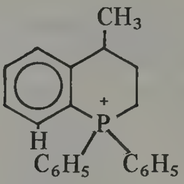
Fusion of a benzo group at the b-face of either a 5- or a 6-membered heterocycle should lead to a similar electronic effect and produce shielding but not without significant modification in the steric environment about P. Specifically, an eclipsing interaction (also shielding) develops with the ortho C-H bond, and it is not surprising to find for the few structures available that net shielding *is* the result of benzannelation.

cf.



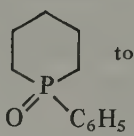
+16.5

to



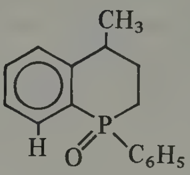
+10.7

cf.



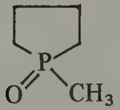
+42.3

to



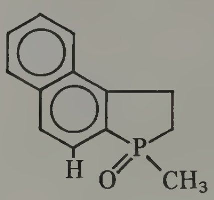
+23.5

cf.



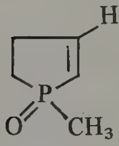
+65.8

to

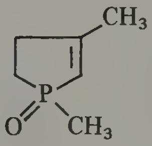


+56.1

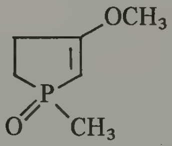
The placement of electron-releasing groups on the β-carbon of a conjugated double bond might be expected to emphasize the shielding of conjugation, and pertinent data are available in the 2-phospholene series to consider this possibility:



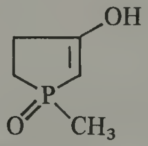
+67.0



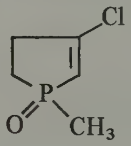
+66.8



+62.0



+60.5

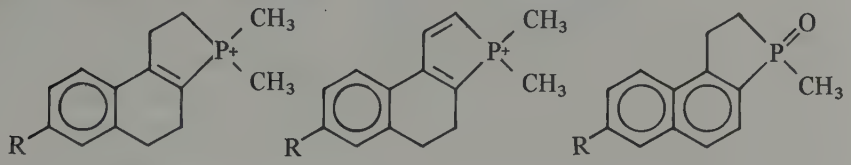


+59.7

A quite similar trend can be seen in related 2-phospholene sulfides. The structural variation does seem to produce a weak effect in the expected direction but it is surprising to find the largest effect with the chloro compound. Thus caution is required in interpreting the effect solely as one of electron release via resonance, as Cl is generally accepted to be a weaker releaser than alkoxy.

An approach that would aid in determining the origin of these upfield shifts would be to separate the electron-releasing group from the 2-phospholene unit by an aromatic ring. Conformational differences would then disappear. Three types of structures have been prepared where the methoxy group is so placed, and in each a very small shielding effect persists. The interaction of electron donating groups on benzene with directly attached phosphonium groups has been studied by Schiemenz,[46] who found no substantial indications of conjugative effects, and by

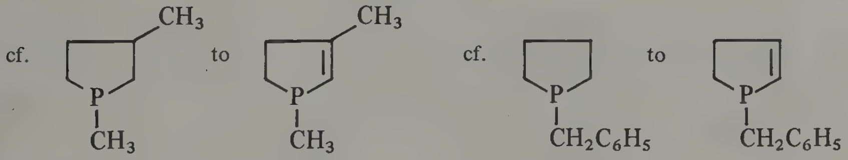
Grim and Yankowsky,[47] who did find a spread of values in the series $(X\text{-}C_6H_4)_3\overset{+}{P}CH_3$ from +24.6 for X = 4-CF_3 to +18.8 for X = 4-OCH_3.



R = H, +56.0 +48.3 +56.1
R = CH_3O, +55.3 +46.4 +55.2

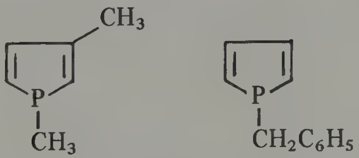
Exploration of the effect of the chlorine atom and an amino function in this tricyclic series would now be of interest to see if the trend from the monocyclics is reproduced.

In the P(III) condition, the possibility of conjugation via p_π-p_π overlap, as in enamines, needs to be considered; in this valence state, d orbitals are generally considered to be more diffuse and of less importance for secondary bonding. Again the phospholenes provide data to explore the point. Some selected examples (of several) show that pronounced deshielding takes place.



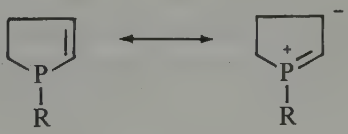
–33.4, –33.8 –15.2 –14.4 0.0

Some phospholes show an enhancement of the downfield shift:



–6.9 +11.5

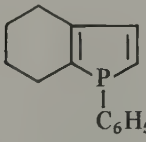
It is quite reasonable on an intuitive level that electron release from P(III) would cause deshielding, and this notion has been useful in explaining downfield shifts of ^{15}N when an amino group is attached to sp^2 carbon.[48] The resonance structure below provides the basis for understanding why p_π-p_π overlap can cause deshielding in 2-phospholenes.



Thus, the increased positivity of phosphorus could constitute a deshielding effect. An alternative is to consider the double bonding developing on P as responsible for the effect; it is an established fact in the P(II) condition, as will be noted in the next section, that very strong deshielding accompanies C-P multiple bonding. There are few models, however, that contain the full multiple bonding corresponding to the dipolar canonical form for the phosphole. That the multiple bonding in 2-phospholenes and phospholes is associated with deshielding is clear from the data provided, but these ^{31}P data alone do not *prove* that the delocalization has taken place in the manner indicated, although this is a perfectly reasonable explanation. The usual array of other influences acting on ^{31}P needs to be remembered, and the ^{31}P effect should be evaluated along with other consequences of any delocalization.[49,50] In point of fact, the bulk of the experimental evidence in phospholes does indicate the presence of some p_π-p_π delocalization (see Chapter 8), and by analogy in 2-phospholenes as well, although objections to this view have been raised.[50]

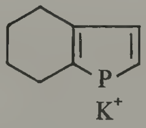
When the electron density on P is increased by removal of the exocyclic substituent and generation of an anion,[51] there is a marked increase in the deshielding.

cf.



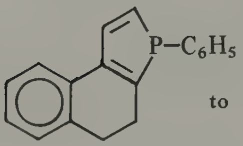
δ +10.5

to



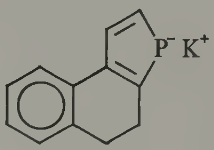
δ +73.3

cf.



δ +12.8

to

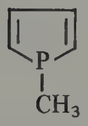


δ +81.7

These phosphole anions give the most downfield ^{31}P shifts ever recorded for the R_2P^- species, the previous low having been seen for $[(CH_3)_2CH]_2PK$ (+23.2). In fact most anions show values upfield of H_3PO_4. Because the phosphole anion is isoelectronic with the aromatic system thiophene, it is reasonable to associate the deshielding effect with the greater delocalization of this 6π-electron system. The effect should be general and apply to other nuclei as well in the 5-membered heterocycles. This is indeed the case, as is seen by comparing ^{33}S in thiophene[52] (−220 ± 6 downfield from CS_2) to tetrahydrothiophene (+89 ± 38 upfield). The same is true for ^{15}N and ^{17}O in similar heterocycles. The increased order of the C-S bond best accounts for this effect, implying that this explanation probably holds for the phosphole system.

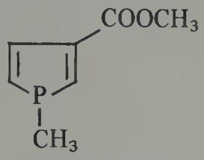
If p_π-p_π conjugation is involved in the phospholes, electron-withdrawing substituents on the β-carbon should enhance it, and this is indeed displayed in the case below.

cf.



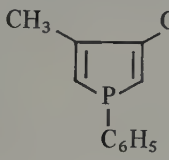
−8.7

to

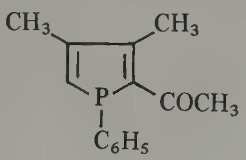


+3.0

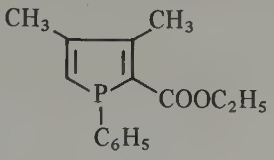
Such groups attached to the α-carbon would cause a less direct electronic effect, but a definite deshielding would result by its action as a β-substituent to P.



−2.5

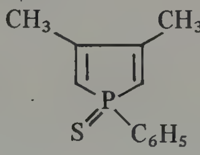


+5.0

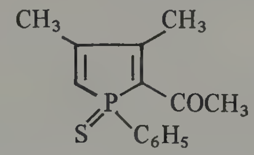


+5.0

Deshielding is also seen, but to a smaller extent, in P(IV) phospholes.

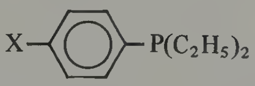


+46.1



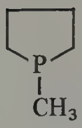
+48.0

Little information is available on the effect of such substituents on noncyclic aromatic phosphines. For the series

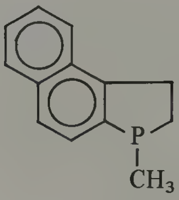


values were the following[53]: X = H, −16.8; F, −16.2; Cl, −15.9; Br, −16.0; $-OCH_3$, −17.6; $N(CH_3)_2$, −19.1. The last two do suggest that electron release via resonance can cause a small upfield shift. A similar effect is seen in triarylphosphines,[54] where there was found a spread of shifts from the extremes for 4-CF_3 (−6.0) and 4-$(CH_3)_2N$ (−11.5). These data were roughly correlated with Hammett σ_{para}.

Benzannelation at the b-face might also be expected to lead to deshielding by the electron delocalization mechanism, but the introduction of an eclipsing C-H bond at the ortho position would be suspected to lead to shielding. The only comparison possible at this time is between the structures below.



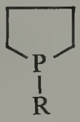
–32

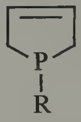


–18.6

The deshielding seen is of the same magnitude as that of introduction of a double bond, suggesting the importance of the electronic effect.

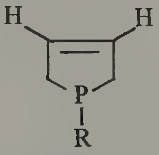
That installation of double bonds in cyclic systems can influence ^{31}P shifts even when not in the conjugated position is revealed by data such as the following:

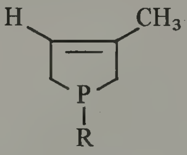


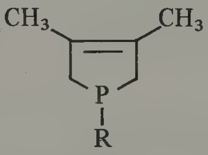


R = CH_3	–32	–41.6
R = C_6H_5	–15.3	–25.3
R = $C_6H_5CH_2$	–14.4	–23.5

The effect is not present in noncyclic P(III) structures, and it may be a consequence of a conformational change (vide infra) rather than of a through-space influence of the π-electrons. Reinforcing this idea is the irregular result of adding methyls to the sp^2 carbons; one methyl causes deshielding, but two methyls cause shielding, *both* relative to the unsubstituted phospholene:

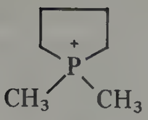




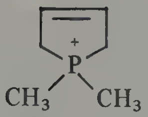


R = CH_3	–41.6	–33.5	–50.3
R = C_6H_5	–25.3	–18.6	–34.5
R = Br	+111.4	+120.5	+104.0

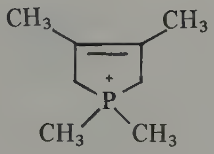
In P(IV) forms, any shielding effect of installing the double bond is less pronounced (as in the salts **9** and **10**) or overcome by a deshielding effect (oxides **12** and **13**). Nevertheless, the trend on methylation of the double bond is just the same as that seen for the phosphines. This is evident from the data for the oxide series **14-16**.



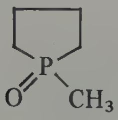
9, +47.8



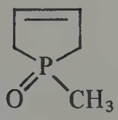
10, +45.0



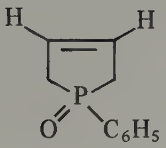
11, +36.6



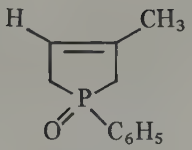
12, +54.2



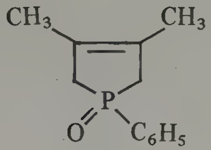
13, +65.5



14, +54.2

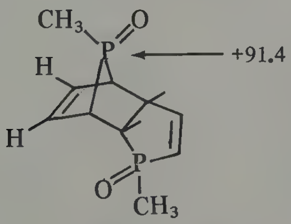


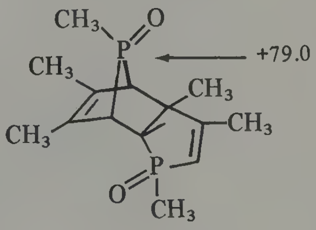
15, +55.4



16, +46

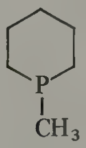
In noncyclic salts[55] and phosphine oxides,[56] instances have been reported where small shieldings occurred in the β,γ-unsaturated compound relative to saturated derivatives. Homoallylic d_π-p_π overlap has been proposed[55] as a possible origin of the shielding in salts. Some of the data for the cyclic oxides seen above reveal, however, that another effect, acting in the opposite direction, must also be operative, because net deshielding is observed. The extreme in this deshielding action seems to occur in the 3-phospholene structure when rigidly incorporated in the phosphole dimer framework. As already noted, both P(III) and P(IV) forms have truly remarkable downfield values. Even here, however, the dimethylation shielding effect can be detected, as noted in the structures below.



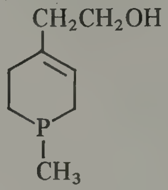


That adjacent methyls can cause a conformational distortion of the ring was first proposed[57] to account for marked modification of the delocalization properties of phospholes (see Chapter 8) when so substituted. There are insufficient structural data at present to investigate further the idea that a conformational change lies behind these various substitution effects. As is discussed in Chapter 8, however, it is clear that P will be in a different steric environment in a 3-phospholene (at the flap of the envelope conformation) than in a phospholane (in the plane of the envelope); different nonbonded interactions are certain to be present, and thus account for the difference in chemical shifts. C-Methylation can very well influence the population of the various conformations open to the saturated ring in the attempt to minimize nonbonded interactions.

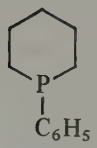
Installation of a β,γ double bond in 6-membered rings with P(III) also produces a marked shielding effect. Data for exact counterpart structures are not available, but the effect is strongly suggested from the following comparisons:



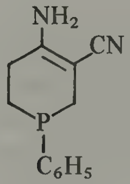
−53.7



−70

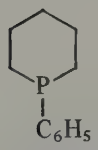


−34.1

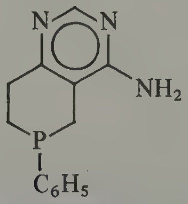


−46.9

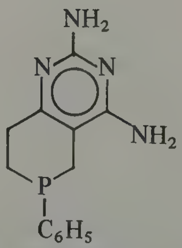
Again a conformational change is the suspected cause. The extensive series of phosphorino[3,4-e]pyrimidine derivatives prepared by Berlin also shows such shielding, at the same time revealing that an electron density increase in the fused ring seems somehow to enhance the effect.



−34.3

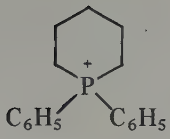


−44

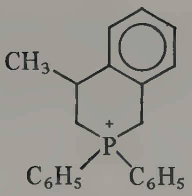


−51.9

Less information is available on benzo[c] fusion; the only comparison possible is between 17 and 18, with the latter slightly influenced by a β-CH_3 group.

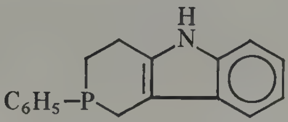


17, +16.5



18, +17.7

Fusion of a 5-membered ring would not necessarily produce the same conformational change, possibly accounting for the relative deshielding seen in phosphorinoindole derivative **19**. An explanation for this reversal of an effect is not obvious at present.

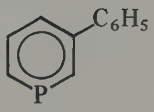


19, –25.8

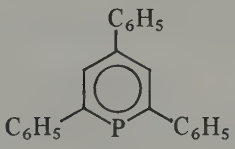
5.7 P(II) SYSTEMS

The extremely important family of the aromatic phosphorins has phosphorus in the rare multiply-bonded dicoordinate state, which is characterized by remarkably downfield ^{31}P NMR shifts. This is seen also in the noncyclic derivative **20**.[58]

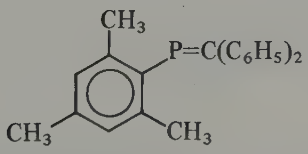
+211



+209



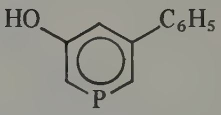
+178.2



20, +233

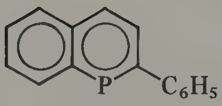
Similar deshielding of ^{15}N in pyridines (C_5H_5N, +315) relative to saturated amines (C_4H_8NH, +10) is known.[30]

C substitution of phosphorins leads to shifts predictable in direction from consideration of ^{13}C effects in benzene derivatives, but naturally of different magnitude. Thus, the shielding in 2,4,6-triphenylphosphorin (29.8 ppm) relative to phosphorin can be viewed as the consequence of ^{31}P being in the ortho position relative to two phenyl substituents and para to a third; in benzene, a phenyl substituent causes shielding of both ortho (1.1 ppm) and para (1.2 ppm) positions. Similarly, the hydroxy phosphorin 21 has a relatively deshielded ^{31}P, just as is true for ^{13}C at the meta position of a phenol (1.4 ppm).

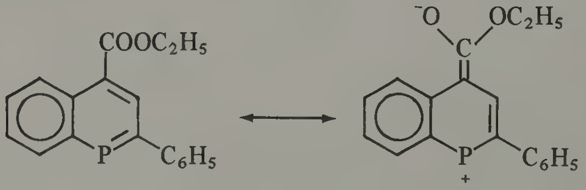


21, +212.8

Resonance with electron-withdrawing groups produces strong deshielding of ^{13}C at the para position, and this effect is present also in a phosphorin. Thus placement of an ester group on benzophosphorin 22 (+197) causes a shift to +221 in 23.



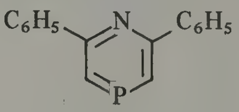
22



23

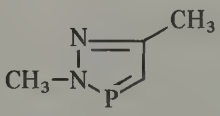
Such substituent effects show remarkable additivity in benzenes and pyridines and, once sufficient data are accumulated, this may prove to be true for phosphorins as well.

An azaphosphorin (24) has been reported to have a chemical shift of +245.4, a value perhaps reflecting the electron attraction of the pyrido-type nitrogen.

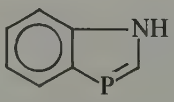


24

Three azaphosphole derivatives are known with the P(II) feature.

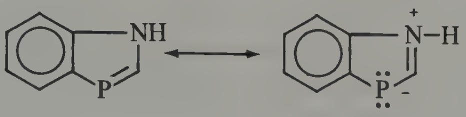


25, +228.9



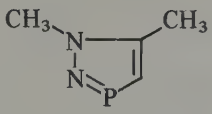
26, +77.2

Compound **25** has a shift in the expected -P=C region, although the presence of an electronegative N on phosphorus surely contributes to the deshielding. Compound **26** has a deshielded ^{31}P but by a less spectacular size. It is proposed here that this might be attributable to electron release from the indole-like nitrogen, causing the phosphorus to develop a more P-C single-bonded character.



26a

Canonical form **26a** has the structure of a phosphide ion, a dicoordinate species that as noted generally has ^{31}P shifts upfield of H_3PO_4. A diazaphosphole with a P-N double bond has a very deshielded ^{31}P also:

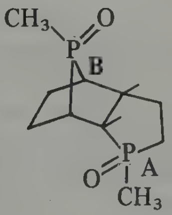


+223.0

It is obvious that some fascinating shift effects will continue to be uncovered as new phosphorus aromatics are prepared.

5.8 COUPLING BETWEEN TWO OR MORE ^{31}P NUCLEI IN RINGS

When two nonequivalent ^{31}P nuclei are present in a cyclic structure, substantial spin-spin splitting can be observed if the atoms are separated by one, two, or three bonds. Definite ranges have been observed for the magnitude of these coupling constants. When the chemical shifts of the coupled ^{31}P nuclei are well separated, typical first-order coupling patterns are seen. However, chemical shifts differing by only 1-2 ppm show definite second-order characteristics; a classic example of an AB spectrum is found in the case of the reduced phosphole dimer **27**, where



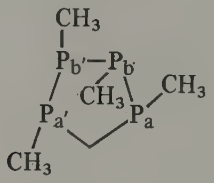
27

δ_{P_A} = +67.1 and δ_{P_B} = +68.8. The chemical shift difference (61.9 Hz) is only about 1.5 the size of the coupling constant (43 Hz) and, just as in ^{1}H NMR spectroscopy, this leads to distortion of the signals.

Structures with more than two ^{31}P nuclei in cyclic systems have also become available in recent years, and they provide several examples of P-P coupling. These structures are portrayed in Table 5.11.

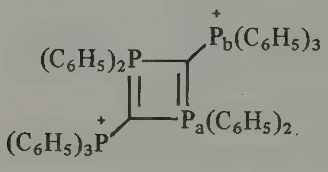
Most of the coupling information now available concerns directly bonded ^{31}P nuclei, where very large coupling constants are found. Only a few of the several possible combinations of different phosphorus functionalities have been tested, and no doubt each will have its own range of values. In a general sense, however, it appears that most P(III) as well as P(IV) forms will have $^1J_{PP}$ values falling in the range of 170-300 Hz (one salt has a value of 503 Hz).

$^2J_{PP}$ is much smaller, although very little information is available. An excellent example of its occurrence is found in the tetraphospha system 28, which displays a complex AA′BB′ spectrum. The spectrum has been completely worked out,



28

and provided the couplings $^1J_{ab}$ = 23.66, $^1J_{bb'}$ = 264.2, $^2J_{ab'}$ = 2.5 and $^3J_{aa'}$ = 23.2 Hz. That ^{2}J is smaller than ^{3}J is not surprising, as this is true for some phosphorus functions in coupling both to ^{1}H and to ^{13}C. A ^{2}J value of 7.4 Hz is reported for coupling of a ring phosphorus (P_a) of 29 with exocyclic ^{31}P.



29

Three-bond coupling is of more interest because its magnitude may be under dihedral angle control, as is true of ^{31}P coupling to ^{1}H and ^{13}C. The recognition[59] of three-bond coupling in phosphole dimer derivatives has provided a rich source of compounds, and at least for the particular dihedral angle imposed in this rigid system (about 170°) these compounds allow assignment of values for several different P functions as follows[40,59].

35-40

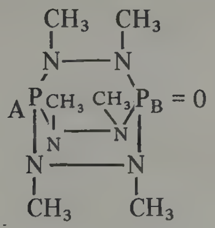
35-45

40-50

25

Because the $^3J_{^{13}C-^{31}P}$-dihedral angle relation is totally different for P(IV) functions (giving normal Karplus plots) than for P(III) functions (giving plots with minima near 110°; see Chapter 6), it will be interesting to see if P-P coupling is under similar functionality control.

The rarity of structures with two different P atoms three bonds apart justifies inclusion of the system typified by **30** in the discussion, even though there are no carbon atoms in the rings. A number of such caged derivatives were made[60] with differing functionalities on P; $^3J_{PP}$ varied from 74.4 to 132.1 Hz in this system with $\phi = 0°$.



30

$\delta\ P_A = +5.6$, $\delta\ P_B = +96.1$,

$^3J_{PP} = 84.3$ Hz

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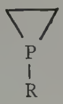
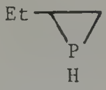
5.9 TABLES OF ^{31}P NMR DATA

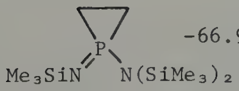
TABLE 5.1 Phosphiranes and Phosphetanes[a]



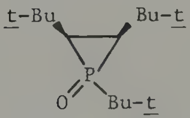
R=H, -341[1]
R=Me, -251[1]
R=Ph, -234[1]



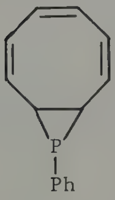
cis,trans
-288, -271[1]



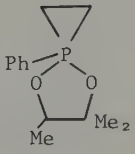
-66.9 (C_6H_{12})[2]



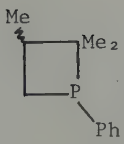
-1.3[3]



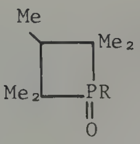
-181[4]



-87[5]



+3.3, +27.9[6]
(neat, isomers)



R=Cl, +80.7[7]*
R=Br, +86.1[7]
R=OH, +57.6[7]
R=OMe, +55.1[8]

TABLE 5.1 continued

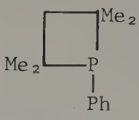
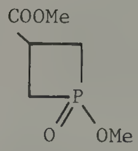
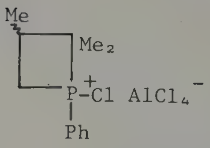
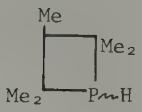
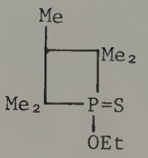
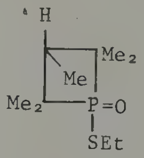
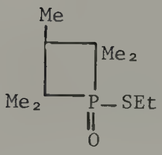
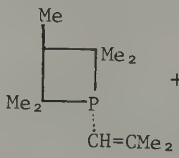
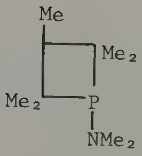
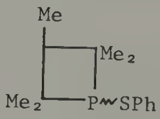
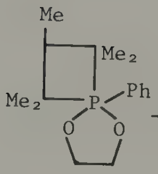
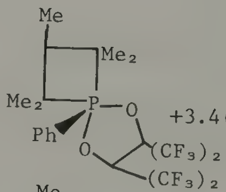
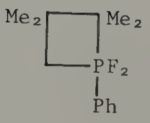
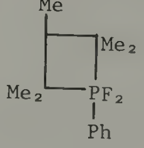
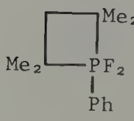
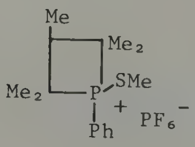
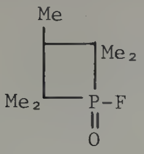
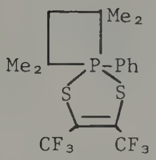
	P(III), +4.4 (CH_2Cl_2)[9] oxide, +51 (CH_2Cl_2)[9]		+36.6[10]
	+98.6,+86.5(CH_2Cl_2)[6] (isomers)		+23[b](C_6H_6)[11]
	+120.6(C_6H_6)[11]		+74.5[12]*
	+74.6(C_6H_6)[11]		+32.5(C_6H_6)[13]
	+106(C_6H_6)[13] oxide,+74(C_6H_6)		+99(C_6H_6)[13] sulfide, +118 ($CHCl_3$)
	-14.1(C_6D_6)[14]		+3.4(C_6H_6)[13]*
	0.0[11]		-2.9(C_6D_6)[14]
	(-100°) +3.0, -30[15] (isomers)		+82.7[16] (cis and trans)

TABLE 5.1 continued

	+65.6(CDCl$_3$)[17]		+17.5(CH$_2$Cl$_2$)[18]

[a] References bearing an asterisk have data for similar compounds.

[b] Value is unusually low-field for a sec. phosphine and needs confirmation.

TABLE 5.2 Phospholanes[a, b]

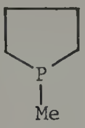
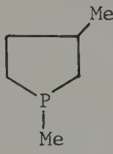
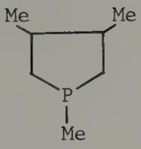
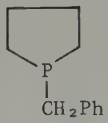
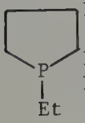
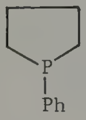
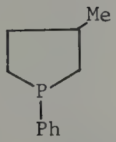
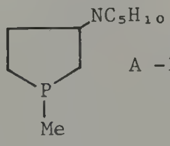
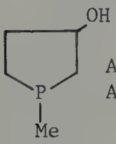
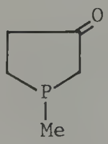
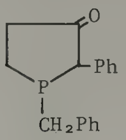
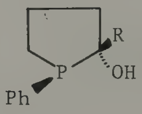
	A -32(neat)[19] B +65.8(CDCl$_3$)[20] D $-$Me,I$^-$ +47.8 (MeOH)[20]		A -33.4 and -33.8 (neat)[19] B (cis)+62.6[21] B (trans)+63.3[21] D $-$CH$_2$Ph(cis),Br$^-$ +51.8[21] D $-$CH$_2$Ph(trans), Br$^-$ +51.8[21]
	A -41.6 and -55.4(neat)[19] B (cis,cis) +65.3(CDCl$_3$)[22] B (trans,trans) +73.0(CDCl$_3$)[22]		A -14.4(neat)[19]
	D $-$Et,ClO$_4^-$, +58.8 (CHCl$_3$,TFA)[23] D $-$Et,I$^-$, +59.5[24] D $-$Et,ClO$_4^-$, +51.4 (CHCl$_3$)[23]		A -15.3[25] D $-$Me, +44.3(CHCl$_3$)[23] D $-n$-C$_3$H$_7$, +49.1 (CHCl$_3$)[23] D $-n$-C$_4$H$_9$, +49.2 (CHCl$_3$)[23] D $-$Ph, +44.3(CHCl$_3$)[23]
	B +56(neat)[20] D $-$Me(cis)+43.6 (H$_2$O)[26] D $-$Me(trans) +43.8(H$_2$O)[26]		A -39.2(CDCl$_3$)[27]
	A (cis)-38.8[28] A (trans)-40.3[28]		A -45.7(C$_6$H$_6$)[27] B +51.0(CHCl$_3$)[27] C +42.4(CDCl$_3$)[29]

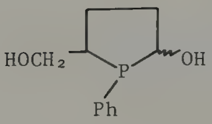
TABLE 5.2 continued



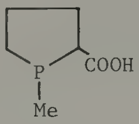
B +59.8 (CDCl$_3$, TFA)^{30*}



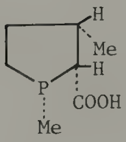
B, R=H, +55.1 (CHCl$_3$)^{31}
B, R=Me, +59.8 (CHCl$_3$)^{31}



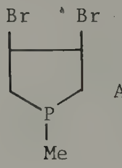
B +53.9 (MeOH)^{31}



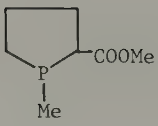
B (cis Me, COOH) +76.1(D$_2$O)^{32}
B (trans Me, COOH) +77.1(D$_2$O)^{32}



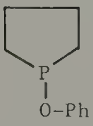
B +77.2 (D$_2$O)^{32}



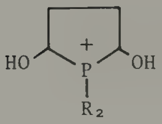
A −41.5(C$_6$H$_6$)^{33}



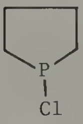
A (cis) −7.5^{32}
A (trans) −18.4^{32}



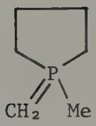
B +76.7^{34}



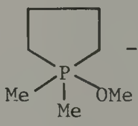
D -Bu-n, Cl$^-$ +46^{35}
D -C$_8$H$_{17}$-n, Cl$^-$ +44^{35}



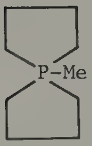
A +126.6



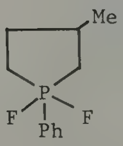
+24.9 (neat)^{36*}



−69.1 (PhMe)^{37}

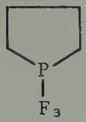


−91.7^{38}



−2.3 (neat)^{17}

TABLE 5.2 continued

	+29.6[39]		+61.2 ($CHCl_3$)[40]

[a] References bearing an asterisk have data for similar compounds.

[b] Capital letters define the P function: A, P(III); B, oxide; C, sulfide; D, salt.

TABLE 5.3 3-Phospholenes[a]

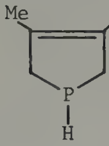
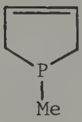
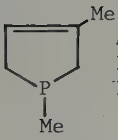
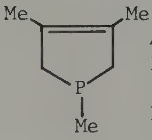
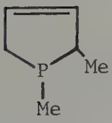
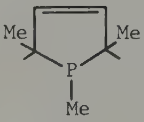
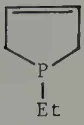
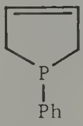
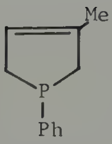
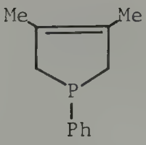
	B +44.4(H_2O)[20] B +39.8($CDCl_3$)[20]		A -41.6(neat)[19] B +65.5($CHCl_3$)[41] C +54.8($CDCl_3$)[26] D -Me,I^-,+45.0(D_2O)[17] D -Cl,Cl^- +112 ($CDCl_3$)[42]
	A -33.5(neat)[19] B +74.7[40] D -Me,I^-, +47.1 ($CDCl_3$)[43]		A -50.3(neat)[19] B +60.0,+67.2 (neat)[22] D -Me,I^-, +36.6 ($CDCl_3$)[20]
	A (<u>cis</u>)-16.7 (neat)[19] A (<u>trans</u>)-28.2 (neat)[19] C (Me <u>cis</u>) +63.4 ($CDCl_3$)[26] D -Cl, Cl^- +121 ($CDCl_3$)[40]		A (<u>trans</u>,<u>trans</u>) -8.9(neat)[19] B (<u>cis</u>,<u>cis</u>) +61.5[22] B (<u>trans</u>,<u>trans</u>) +58.2[22] D -Cl, Cl^- +125[44]
	B +71.3[34]		A -25.3(neat)[19] B +54.2(neat)[45]
	A -18.6(neat)[46] B +55.4($CDCl_3$)[47] D -Br,Br^- +89 ($CDCl_3$)[42]		A -34.5[19] B +46[48] C +45[48]

TABLE 5-3 continued

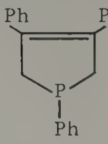
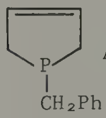
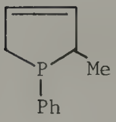
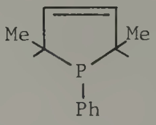
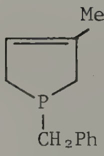
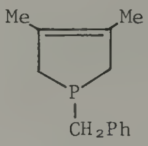
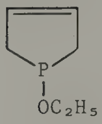
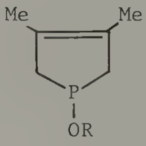
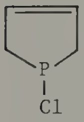
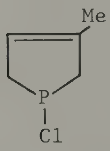
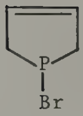
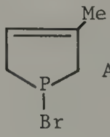
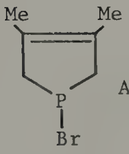
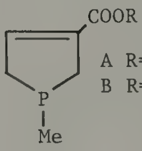
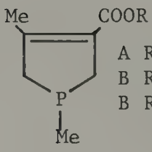
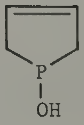
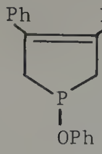
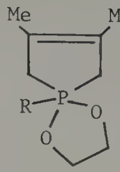
	B +48(CHCl$_3$)^{49}		A −23.5(neat)^{19}
	A (trans)−9.2 (neat)^{19} D −Br,Br$^-$ +81 (CDCl$_3$)^{44}		A (cis)+15.1 (CDCl$_3$)^{50} A (trans)+8.5 (CDCl$_3$)^{50} B (cis)+72.9 (CDCl$_3$)^{50} B (trans)+55.8 (CDCl$_3$)^{50}
	A −18.7(neat)^{19}		A −29.9(neat)^{19}
	B +68(neat)^{51}		A R=CH$_2$CH$_2$Cl, +134^{52*}
	B +84.0(neat)^{53}		A +127.5^{54}
	A +111.4(neat)^{54}		A +120.5(neat)^{46}
	A +104.0(neat)^{19}		A R=Me,−33.5^{32} B R=H,+70.9(D$_2$O)^{32}
	A R=Me,−46.1^{32} B R=H,+67.3(D$_2$O)^{32} B R=Me,+68.9(D$_2$O)^{32}		B +75.1(D$_2$O)^{53}

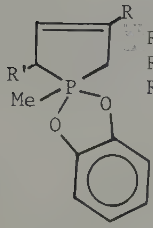
TABLE 5-3 continued



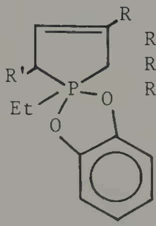
B +60.8[34]



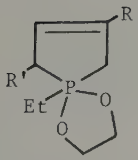
R=Me,+14.0($CDCl_3$)[16]
R=Ph,+7.8($CDCl_3$)[16]



R,R'=H,+16.7[55]
R=Me,R'=H,+15.2[55]
R=H,R'=Me,+15.2[55]



R,R'=H,+18.4[56]
R=Me,R'=H,+16.9[56]
R=H,R'=Me,+19.0[56]



R,R'=H,+3.5[56]
R=Me,R'=H,+8.1[56]
R=H,R'=Me,+2.7[56]

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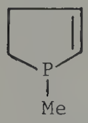
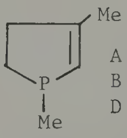
[a] Capital letters define the P function: A, P(III); B, oxide; C, sulfide; D, salt.

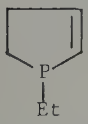
TABLE 5.4 2-Phospholenes[a]



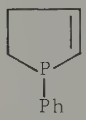
B +67.0($CHCl_3$)[41]
C +65.5($CDCl_3$)[29]



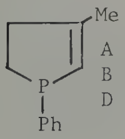
A -15.2(neat)[19]
B +66.8($CHCl_3$)[20]
D -Me,I^- +54.5 ($CDCl_3$)[43]



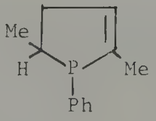
B +72.5[34]



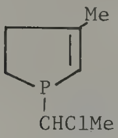
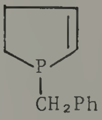
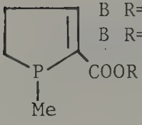
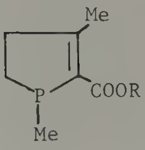
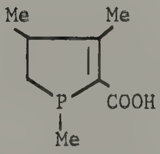
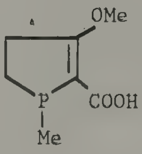
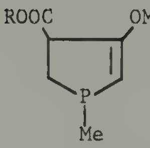
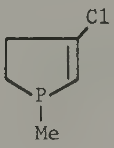
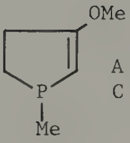
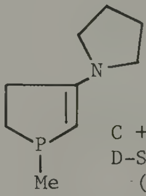
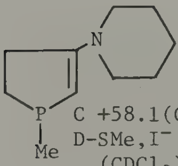
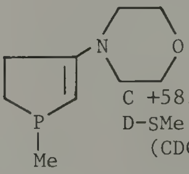
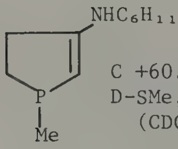
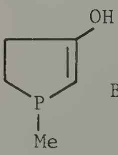
B +58.6(neat)[30]

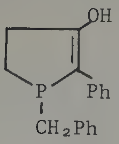


A +4.0(neat)[19]
B +60.5($CDCl_3$)[47]
D -Cl,Cl^-($CDCl_3$)[42]

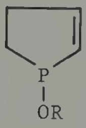


A (cis)+11.4 ($CDCl_3$)[50]
A (trans)+24.2 ($CDCl_3$)[50]
B (cis)+63.1 ($CDCl_3$)[50]
B (trans)+57.4 ($CDCl_3$)[50]

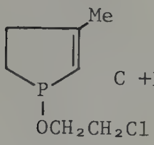
	B +74[52]		A 0.0(neat)[46]
	B R=H,+74.3(D_2O)[32] B R=Me,+70.9(D_2O)[32]		B R=H,+76.0 (D_2O)[32] B R=Me,+74.4 (D_2O)[32]
	B +70.8(D_2O)[32]		B +66.5(D_2O)[32]
	A R=Et,-19.3 and -17.5[32] B R=H,+69.7(D_2O)[32]		C +58.5($CDCl_3$)[29]
	A -14.4($CDCl_3$)[27] C +58.7($CDCl_3$)[19]		C +57.8($CDCl_3$)[57] D-SMe,I^- +69.8 ($CDCl_3$)[57]
	C +58.1($CDCl_3$)[57] D-SMe,I^- +71.0 ($CDCl_3$)[57]		C +58.7($CDCl_3$)[57] D-SMe,I^- +77.2 ($CDCl_3$)[57]
	C +60.1($CDCl_3$)[57] D-SMe,I^- +69.6 ($CDCl_3$)[57]		B +60.5($CHCl_3$)[27]



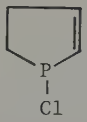
B +77.2(CDCl$_3$, TFA)^{30}



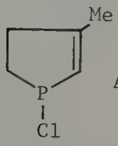
A R=CH$_2$CH$_2$Cl, +150^{52}
A R=*t*-Bu,+127^{52}
B R=H,+76.8^{53}
B R=Et,+69^{51}(neat)



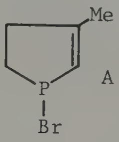
C +116^{52}



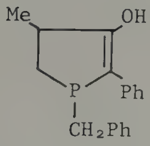
B +80.5(neat)^{53}



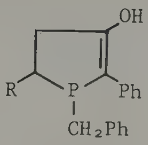
A +132.5(neat)^{54}



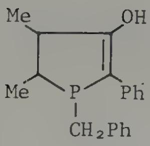
A +130.6(neat)^{46}



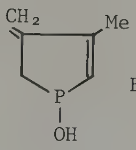
B +74.4 and +70.0(CDCl$_3$, TFA)^{30}



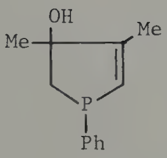
B R=Me,+77.6 (CDCl$_3$,TFA)^{30}
B R=Ph,+71.4 (CDCl$_3$,TFA)^{30}



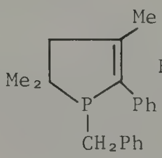
B +70.0 and +68.4(CDCl$_3$, TFA)^{30}



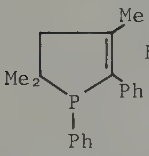
B +60.7^{58}



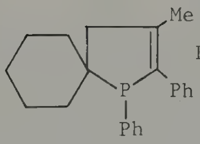
B +46.8^{58}



B +67.3 (CDCl$_3$)^{59}



B +64.5(CDCl$_3$)^{59}

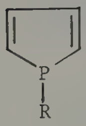


B +64.2 (CDCl$_3$)^{59}

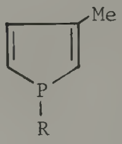
[a] Capital letters define the P function: A, P(III); B, oxide; C, sulfide; D, salt.

TABLE 5.5 Phospholes

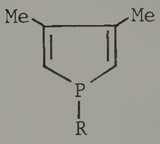
A. P(III) Derivatives



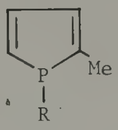
Me,-8.7(neat)[33]
$PhCH_2$,+8.0(neat)[60]
$PhCH_2CH_2$,+5.8(neat)[60]
p-$ClC_6H_4CH_2CH_2$,+5.9 (neat)[60]
n-Bu +5.5[61]
Ph +7.8[61]



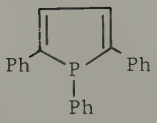
Me,-6.9(neat)[60]
$PhCH_2$,+11.5 (neat)[60]
t-Bu,+40.5 (neat)[62]
n-Bu,+8.5[61]
Ph,+9.5[61]



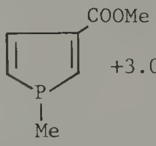
Me,-20.2(neat)[60]
$PhCH_2$,-3.0(neat)[60]
n-Bu,-6.5($CDCl_3$)[63]
t-Bu,+27.5($CDCl_3$)[62]
Ph,-2.5[63]



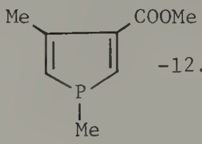
Me,-7.3 (neat)[60]



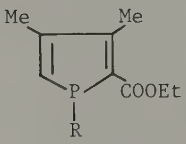
+3[64]



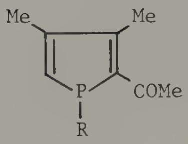
+3.0($CDCl_3$)[60]



-12.6($CDCl_3$)[60]

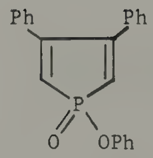


R=t-Bu, +34.3 ($CDCl_3$)[63]
R=Ph,+5.0 ($CDCl_3$)[63]

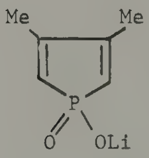


R=n-Bu,+6.8($CDCl_3$)[63]
R=t-Bu,+35.1($CDCl_3$)[63]
R=Ph,+5.0($CDCl_3$)[63]

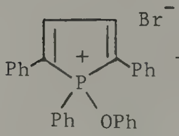
B. P(IV) Monomers



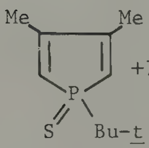
+46.6[34]



+45.0[34]



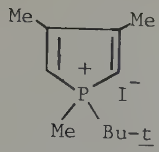
+74.6[65]



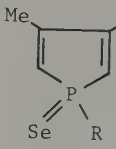
+70.5($CDCl_3$)[62]

TABLE 5.5 continued

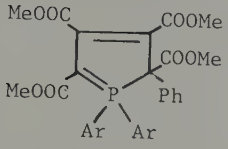
B. P(IV) Monomers (Continued)



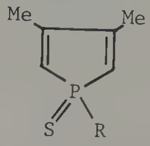
+52.8(CDCl$_3$)[62]



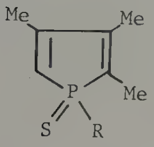
R=Me,+44.0[66]
R=*t*-Bu,+28.5
(CDCl$_3$)[62]



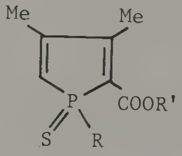
Ar=Ph,
+48.5
(CHCl$_3$)[67]
Ar=p-MeC$_6$H$_4$,
+48.5
(CHCl$_3$)[67]



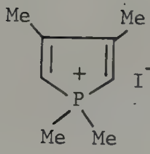
R=n-Bu,+52.2
(CDCl$_3$)[63]
R=*t*-Bu,+70.5
(CDCl$_3$)[63]
R=Ph,+46.1
(CDCl$_3$)[63]



R=n-Bu,+55.3
(CDCl$_3$)[63]
R=*t*-Bu,+73.8
(CDCl$_3$)[63]
R=Ph,+48.0
(CDCl$_3$)[63]

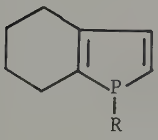


R=*t*-Bu,R'=
Et,+73.7
(CDCl$_3$)[63]
R=Ph,R'=Et,
+48.8
(CDCl$_3$)[63]
R=Ph,R'=H,
+53.2
(CDCl$_3$)[63]

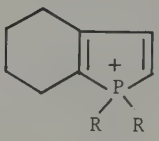


I$^-$,+34.4(D$_2$O)[43]

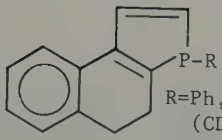
C. Multicyclic Phospholes and P(IV) Derivatives



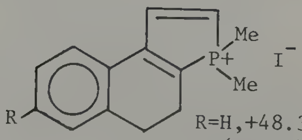
R=Ph,+10.5
(CDCl$_3$)[68a]
R=Me,−7.6
(CDCl$_3$)[68b]



R=Me,I$^-$ +41.1
(MeOH)[69a]
R=PhCH$_2$,Br$^-$
+50.1
(CDCl$_3$)[69a]



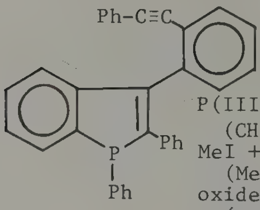
R=Ph,+12.8
(CDCl$_3$)[68a]
R=Me,−4.1
(CDCl$_3$)[69b]



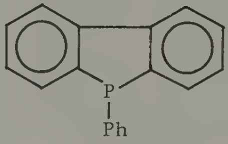
R=H,+48.3
(CDCl$_3$)[69a]
R=OMe,+46.4
(CDCl$_3$)[69a]

TABLE 5.5 continued

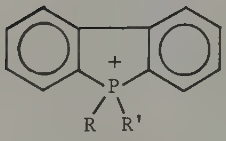
C. Multicyclic Phospholes and P(IV) Derivatives (Continued)



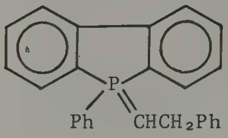
P(III)+2.4 ($CHCl_3$)[70]
MeI +31.4 (MeOH)[70]
oxide +39.9 (acetone)[70]



-10.2[71]

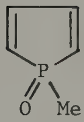


R=R'=Me,I$^-$,+27(TFA)[72]
R=Me,R'=Ph,I$^-$,+21.5[73]
R=Ph,R'=CH_2COOMe,+24[73]

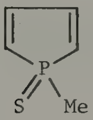


+17[73]

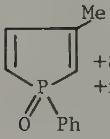
D. P(IV) Dimers[a]



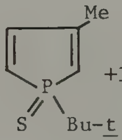
+91.4($CDCl_3$),
+61.8(35)[69]



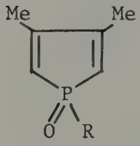
+110.3($CDCl_3$),
+62.0(41.5)[69]



+81.7($CDCl_3$),
+55.1(40)[69]



+134.5, +86.5[62]

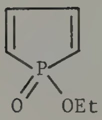


R

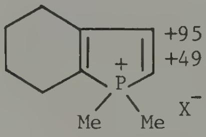
Me, +79.0($CDCl_3$), +56.8(40)[69]

t-Bu, +93.1, +74.4(40)[62]

n-Bu, +83.0, +61.5[61]



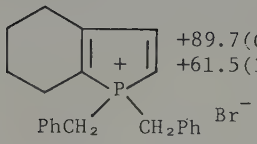
+83($CHCl_3$),
+70[51,74]



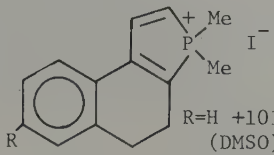
+95.1(MeOH),
+49.8(44)[69]

TABLE 5.5 continued

D. P(IV) Dimers[a] (Continued)

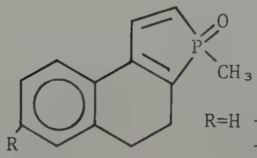


+89.7($CDCl_3$), +61.5(36)[69]



R=H +101.1 (DMSO), +57.5(38)[69]

R=OCH_3 +96.0 ($CDCl_3$), +52.6(44)[69]



R=H +89.0($CDCl_3$), +57.3(35)[69]

R=OMe +88.3($CDCl_3$), +56.5(36)[69]

---

[a] Of structure below, from monomer shown. The bridging P has the downfield signal; $^3J_{PP}$ is in parentheses. Some derived forms appear in Table 5.11.

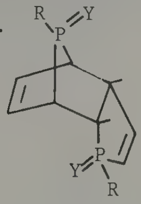
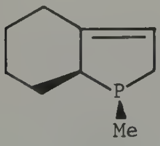
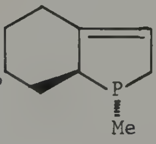


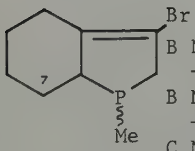
TABLE 5.6 Multicyclic Derivatives of Phospholenes and Phospholanes



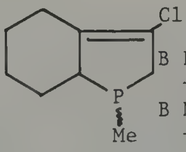
A −26.2(neat)[75]
B +77.1(D_2O)[75]
C +59.9($CDCl_3$)[29]



A −28.6(neat)[75]
B +70.5(D_2O)[75]
C +58.0($CDCl_3$)[29]

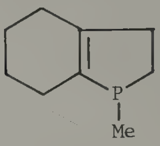


B Me,C-7*cis* +67.2[75]
B Me,C-7*trans* +61.6[75]
C Me,C-7*cis* +51.4[29]

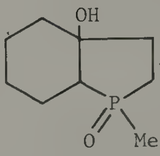


B Me,C-7*cis* +66.4(D_2O)[75]
B Me,C-7*trans* +60.7(D_2O)[75]

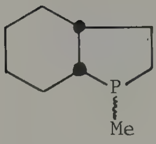
TABLE 5.6 continued



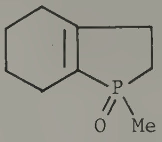
A −7.7(CDCl$_3$)[76]
B +76.5(D$_2$O)[75]
B +63.2(CDCl$_3$)[75]
D −Me,I$^-$ +52.8
(CDCl$_3$)[77]



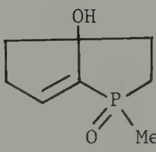
+68.8,+73.2
(CDCl$_3$)[78]
(isomers)



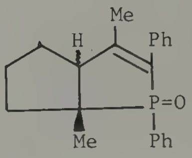
B +78.8 and
+82.8(D$_2$O)[75]



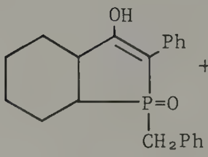
+63.2(CDCl$_3$)[78]



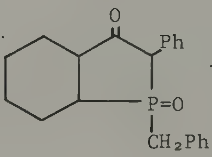
+32.0(CDCl$_3$)[78]



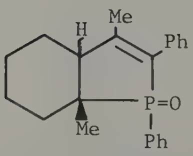
Me,Ph,cis,
+66.4
(CDCl$_3$)[59]
Me,Ph,trans
+64.0
(CDCl$_3$)[59]



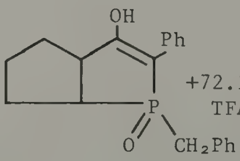
+72.3
(CDCl$_3$,
TFA)[30]



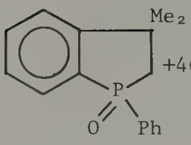
+56.8(CDCl$_3$,
TFA)[30]



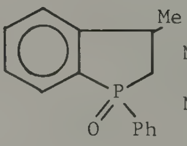
Me,Ph,cis,+62.0(CDCl$_3$)[59]
Me,Ph,trans,+59.7(CDCl$_3$)[59]



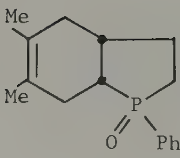
+72.3(CDCl$_3$,
TFA)[30]



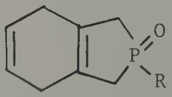
+46.7(CDCl$_3$)[79]



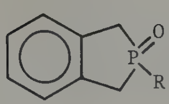
Me,Ph,cis
+48.5(CDCl$_3$)[79]
Me,Ph,trans
+49.7(CDCl$_3$)[79]



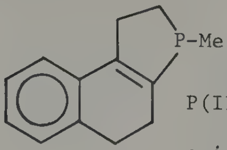
+58.9(CHCl$_3$)[80]



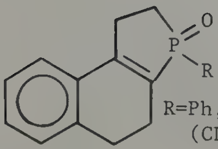
Me +58.1(CDCl$_3$)[81]
Ph +49.7(CDCl$_3$)[81]
OH +60.1(DMSO)[81]



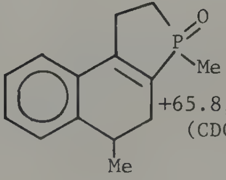
Me +73.3 (D_2O)[81]
OH +71.2 ($CDCl_3$)[81]



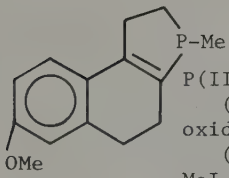
P(III) −5.8 ($CDCl_3$)[76]
oxide +65.1 ($CDCl_3$)[76]
MeI +56.0 (DMSO)[76]



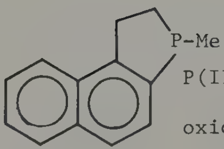
R=Ph,+58.6 ($CDCl_3$)[76]
R=OH,+74.8 (DMSO)[76]



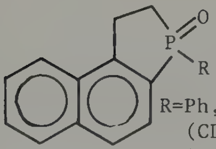
+65.8,+66.1 ($CDCl_3$)[76]



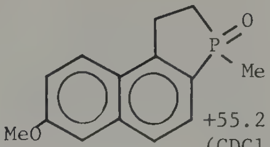
P(III) −5.9 ($CDCl_3$)[76]
oxide +66.4 ($CDCl_3$)[76]
MeI +55.3 (DMSO)[76]



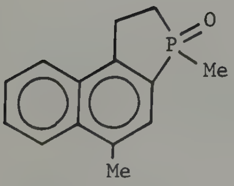
P(III) −18.6 ($CDCl_3$)[76]
oxide +56.1 ($CDCl_3$)[76]



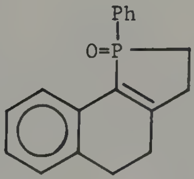
R=Ph,+55.3 ($CDCl_3$)[76]
R=OH,+70.3 ($CDCl_3$)[76]



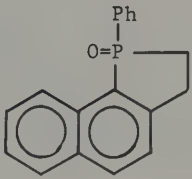
+55.2 ($CDCl_3$)[76]



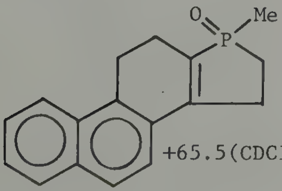
+55.9($CDCl_3$)[76]



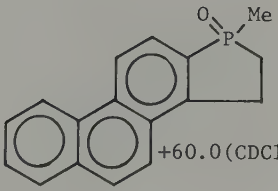
+57.4($CDCl_3$)[76]



+55.6($CDCl_3$)[76]

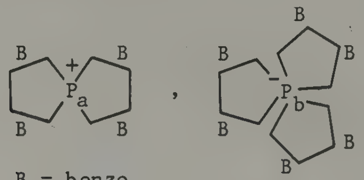


+65.5($CDCl_3$)[76]

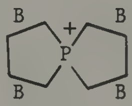


+60.0($CDCl_3$)[76]

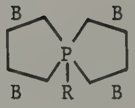
TABLE 5.6 continued



B = benzo
P_a +24, P_b -184(DMF)[82]



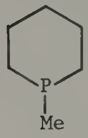
B = benzo
I^- +24[83]



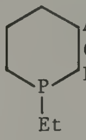
B = benzo
R = Me,-97(DMF)[83]
R = Ph,-85(DMF)[83]

[a] Capital letters define the P function: A, P(III); B, oxide; C, sulfide; D, salt.

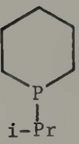
TABLE 5.7 Phosphorinanes[a]



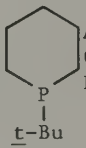
A -53.7(neat)[84]
C +33.9($CDCl_3$)[85]
D -Me,I^- +18.2(D_2O)[22]



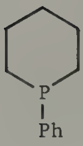
A -38.6(neat)[84]
C +39.3($CDCl_3$)[85]
D -Me,I^- +23.1(D_2O)[22]



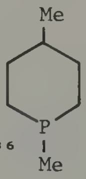
A -25.4(neat)[84]
C +48.1($CDCl_3$)[85]
D -Me,I^- +27.7(D_2O)[22]



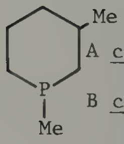
A -14.8(neat)[84]
C +57.0($CDCl_3$)[85]
D -Me,I^- +32.8(D_2O)[22]



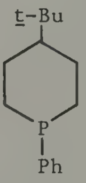
A -34.3(neat)[84]
B +42.3(D_2O)[22]
C +37.5($CDCl_3$)[85]
D -Et,ClO_4^-,+21.7 ($CHCl_3$)[23]
D -Ph,Cl^-,+16.5(MeOH)[86]



A *cis*-61.9,*trans*-55.7 (C_6H_6)[87]
B *cis*+40.9,*trans*+38.7 ($CHCl_3$)[87]
C *cis*+29.0,*trans*+30.8 ($CHCl_3$)[87]
D -Me,I^-,+17.2(H_2O)[87]

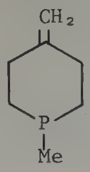


A *cis*-54.3,*trans*-55.4 (C_6H_6)[87]
B *cis*+40.6,*trans*+42.2 ($CDCl_3$)[87]
C *cis*+32.6,*trans*+30.5 ($CDCl_3$)[87]
D -Me,I^- +19.2(H_2O)[87]

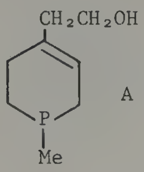


A *cis*-32.9,*trans*-38.6 (o-$C_6H_4Cl_2$)[88]
B *cis*+30.0,*trans*+28.2 (o-$C_6H_4Cl_2$)[88]

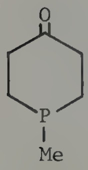
TABLE 5.7 continued



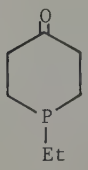
A −55.8[22]



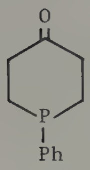
A −70[22]



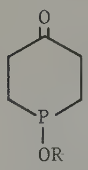
A −59.2(neat)[89]
B +38.4($CHCl_3$)[80]
C +29.9($CDCl_3$)[80]
D −Me,I^- +21.3 ($CHCl_3$)[80]



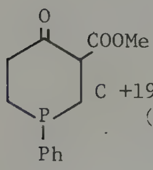
B +45.7($CHCl_3$)[85]
C +38.6($CHCl_3$)[85]
D −Me,I^- +25.7($CHCl_3$)[85]



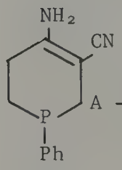
A −37.0(C_6H_6)[90]



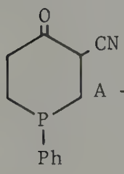
B R=H,+41(DMSO)[91]
B R=Me,+46.9($CDCl_3$)[91]



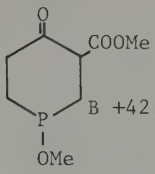
C +19.0,+19.3 (MeOH)[92]



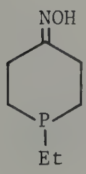
A −46.9($CHCl_3$)[93]



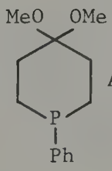
A −39.4,−43.7 (C_6H_6)[94]



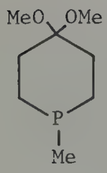
B +42.2($CDCl_3$)[91]



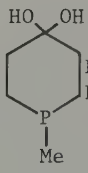
B +54(D_2O)[95]



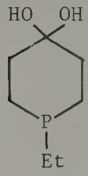
A −37.9(C_6H_6)[90]

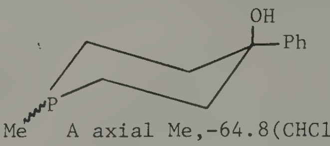


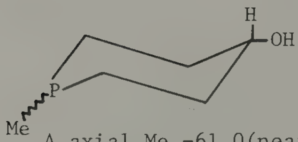
A −59.7(neat)[89]

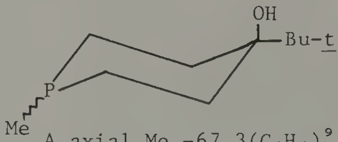


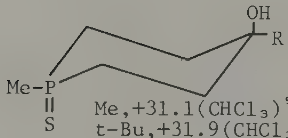
B +41.6(H_2O)[96]
D −Me,I^- +17.2(H_2O)[96]

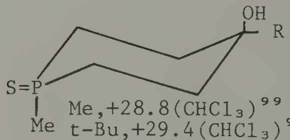

B +51.8(H_2O)[96]
D -Me,I^- +21.7(H_2O)[96]

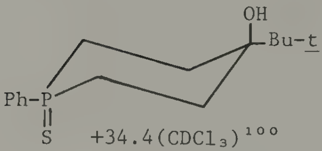

A axial Me,-64.8($CHCl_3$)[85]
A equat. Me,-57.0($CHCl_3$)[85]

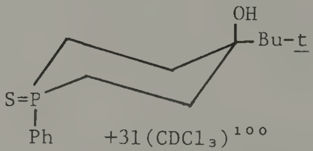

A axial Me,-61.0(neat)[97]
A equat. Me,-55.7(neat)[97]

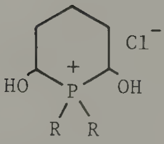

A axial Me,-67.3(C_6H_6)[98]
A equat. Me,-57.7(C_6H_6)[98]

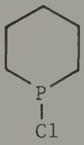

Me,+31.1($CHCl_3$)[99]
t-Bu,+31.9($CHCl_3$)[99]
Ph,+32.0(MeOH)[99]

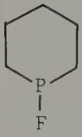

Me,+28.8($CHCl_3$)[99]
t-Bu,+29.4($CHCl_3$)[99]
Ph,+29.1(MeOH)[99]

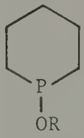

+34.4($CDCl_3$)[100]

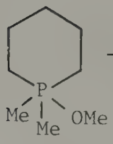

+31($CDCl_3$)[100]


n-Bu,+20[101]
i-Bu,+23[101]
n-C_8H_{17},+25[101]
c-C_6H_{11},+20[101]


A +108.0[25]


B +63.1(neat)[17]
C +117.8(neat)[17]


B R=n-Bu,+46.0[102]


-91.3[37]

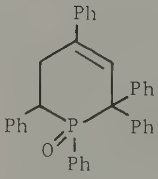
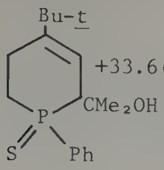
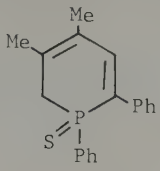
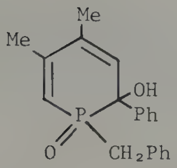
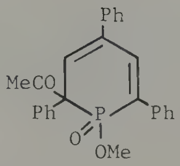

+30(DMSO)[103]

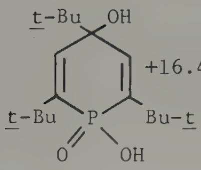
TABLE 5.7 continued

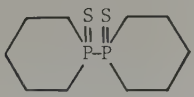

$+33.6(CDCl_3)^{100*}$


$+26.7^{104}$


$+29(CDCl_3)^{105}$


$+31(C_6H_6)^{106}$


$+16.4(C_5H_5N)^{107}$


$+37.5(CHCl_3)^{40}$

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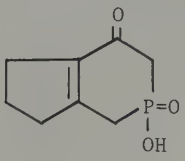
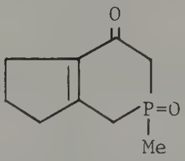
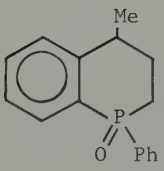
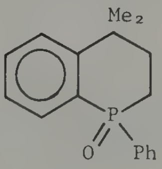
[a] Capital letters define the P function: A, P(III); B, oxide; C, sulfide; D, salt.

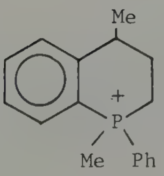
TABLE 5.8 Multicyclic Phosphorinane Derivatives*


$+46.8$ $(DMSO)^{108}$


$+42.3$ $(CDCl_3)^{109}$


cis and trans $+23.5^{79}$ $(CHCl_3)$


$+24.6(CDCl_3)^{79}$


PF_6^-, $+9.8$ (MeCN, $TFA)^{110}$

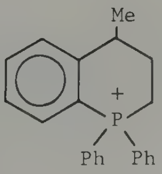
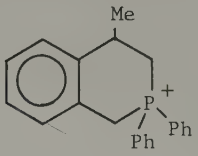
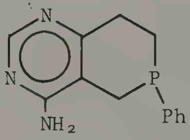

PF_6^-, $+10.7^{110}$ (MeCN, TFA)

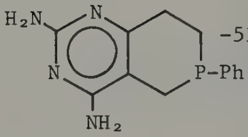
TABLE 5.8 continued



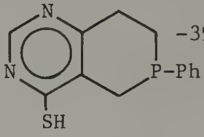
PF_6^-, +17.7 ($CDCl_3$, TFA)[110]



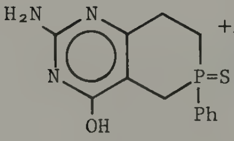
P(III),-44 (DMSO)[93*]
oxide,+29.0 (DMSO)[93]



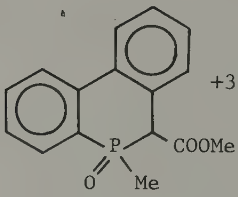
-51.9 (DMSO)[111]



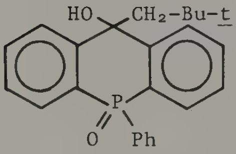
-39.6(DMSO)[93]



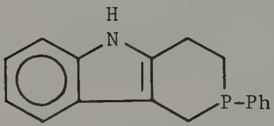
+31.4 (MeOH)[92*]



+33[112]



+13.4($CDCl_3$)[113]



P(III),-25.8(EtOH)[114]
2-$C_{10}H_7CH_2Cl$ salt,
+13.8[114](EtOH)

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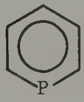
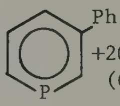
*References bearing an asterisk have data for similar compounds.

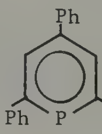
TABLE 5.9 Phosphorins and Benzophosphorins*



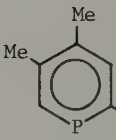
+211[115]



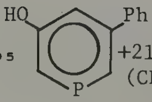
+209 ($CDCl_3$)[116]



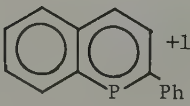
+178.2 ($CDCl_3$)[117]



+181 ($CDCl_3$)[105]

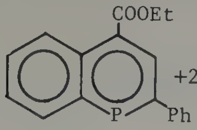


+212.8 ($CDCl_3$)[118]

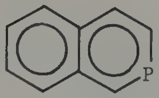


+197[117]

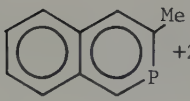
TABLE 5.9 continued



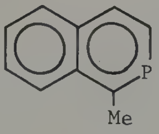
$+221(CHCl_3)^{119}$



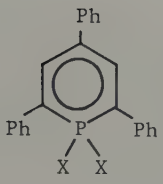
$+192(CDCl_3)^{120}$



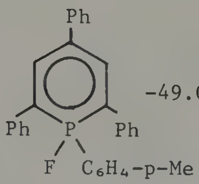
$+200(CDCl_3)^{120}$



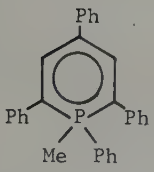
$+190(CDCl_3)^{120}$



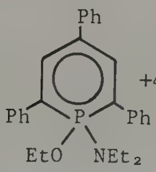
X=Cl,+17.0 $(C_6D_5)^{121}$
X=F,+73.0 $(C_6D_6)^{121}$
X=Me_2N,+42.5 $(C_6H_6)^{122}$



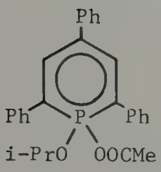
-49.0^{123}



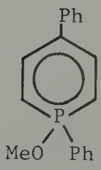
-6.5^{117*}



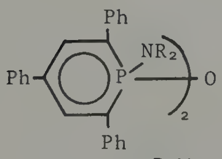
$+45(C_6H_6)^{124}$



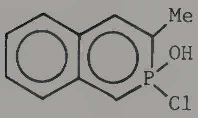
$+53(C_6H_6)^{122*}$



$+38.3(CDCl_3)^{125*}$



R=Me,+42.5$(C_6H_6)^{122}$
R=Et,+40$(C_6H_6)^{122}$



+27.1 $(C_6D_6)^{126}$

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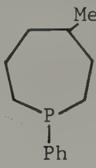
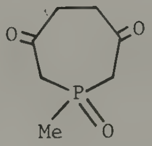
*References bearing an asterisk have data for similar compounds.

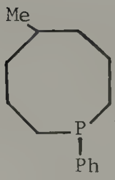
TABLE 5.10 Rings of Seven or More Members



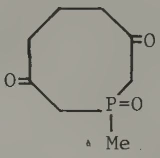
oxide, +40.7 and +40.4[127]
$PhCH_2Br$ salt, +29.5 and +29.6[127]



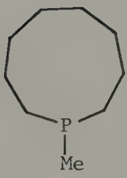
+29.8(DMSO)[102]



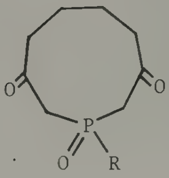
oxide, +39.5 and +37.8[128]
$PhCH_2Br$ salt, +28.6 and +27.2[128]



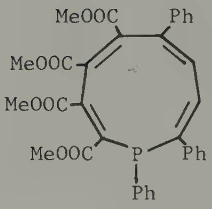
+29.0(DMSO)[108]



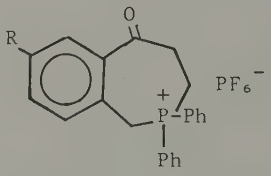
P(III), −33.8 ($CDCl_3$)[109]
oxide, +48.9 ($CDCl_3$)[109]
MeI, +31.9 ($CDCl_3$)[109]



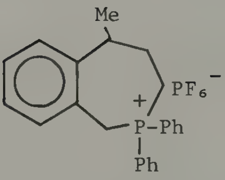
R=Me, +32.6 (DMSO)[108]
R=Ph, +25.4 ($CDCl_3$)[109]
R=OH, +26.5 (DMSO)[108]



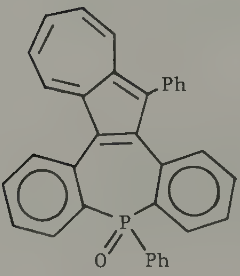
−35[64]



R=H, +21.5($CDCl_3$ and TFA)[129]
R=Me, +21.5($CDCl_3$ and TFA)[129]
R=Cl, +21.0(DMSO)[129]

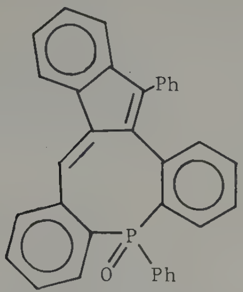


+14.2($CDCl_3$ and TFA)[110]



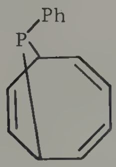
+21.8($CHCl_3$)[130]

TABLE 5.10 continued

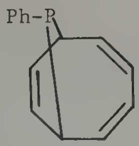


+23.5($CHCl_3$)[130]*

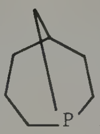
TABLE 5.11 Bridged Ring Systems



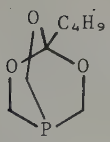
-79[131]
oxide, +38[131]



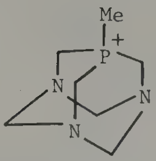
-14[131]
oxide, +26[131]



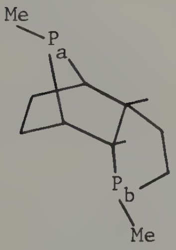
P(III), -58 (C_5H_{12})[132]
oxide, +26 (C_6H_6)[132]
sulfide, +22.1 (C_6H_6)[132]
MeI salt +12 (MeOH)[132]
HSO_3F salt, -13 ($HFSO_3$)[132]



-81(CH_2Cl_2)[133]



I^- -39[134]

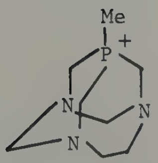


P(III), P_a -18.0, P_b -21.7 (J_{PP}=22.0)[69]

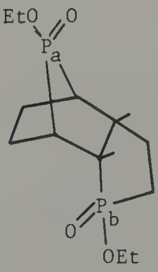
oxide, P_a =+68.8, P_b =+67.1 (J=43.0)[69]

sulfide, P_a =+67.1, P_b =+59.6 (J=49.0)[69]

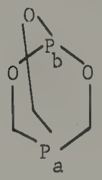
MeI, P_a =+58.3, P_b =+52.5 (J=46.0)[69]



I^- -32.1[135]



P_a +77, P_b +70
($CHCl_3$)[51]

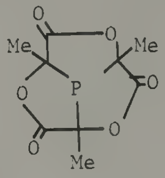


P(III),P_a -70.6,^{136*}

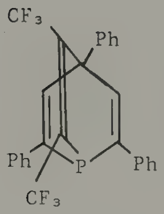
P_b +90(DMSO)

dioxide,P_a +6.4,^{136}

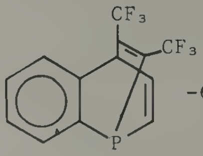
P_b -18.1



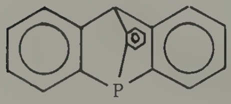
-21^{137}



-65(C_6H_6)^{138}



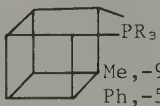
-68^{139}



P(III),-64.8 ($CDCl_3$)^{140}

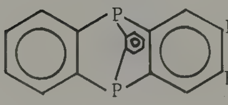
MeI salt, -2.4 (TFA)^{140}

$HFSO_3$ salt, -23.3($HFSO_3$)^{141}



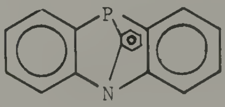
Me,-90(C_6D_6)^{142}

Ph,-53(C_6D_6)^{142}

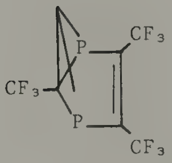


P(III), -43.1^{141}

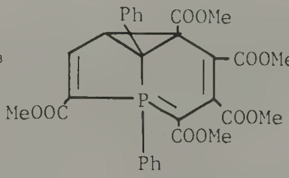
$HFSO_3$ salt, -20.1 ($HFSO_3$)^{141}



-80^{140}

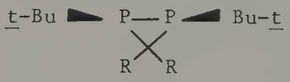


-18.0^{143}



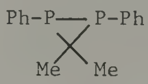
-35^{64}

TABLE 5.12 Systems with Two or More Phosphorus Atoms

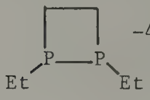


R=H,-168.8(C_6H_6)^{144}

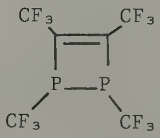
R=Me,-91.7(C_6H_6)^{144}



-122(C_6H_6)^{145}

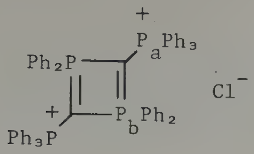


-42.8^{146}

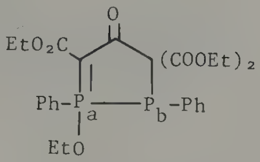


-40^{147}

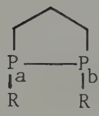
TABLE 5.12 continued



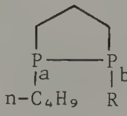
$+14.4$ and $+33.6^{148}$
$({}^{2}J_{ab}=7.4)$



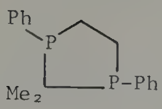
$P_a +80,^{149}$ $P_b -34$
$(J_{ab}=207)$



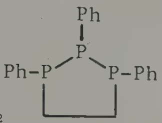
H $-9.7(J_{ab}=167)$
(neat)^{150*}
n-Bu -27(neat)



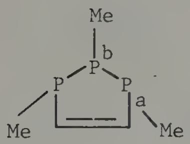
R=H,P_a -39,P_b -86
$(J_{ab}=194)$(neat)^{150}
R=Li,$P_a$$-25$,$P_b$$-117$
$(J_{ab}=315)$(THF)^{150}



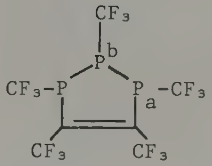
cis $+22.2$
(tetralin)^{151,152}
trans $+17.7$



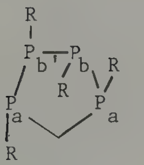
$-17.2,+14.7^{153}$
$({}^{1}J=273)$



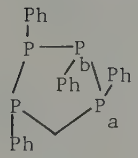
P_a $+11.3^{154}$
P_b -68.0
$(J_{ab}=236.2)$



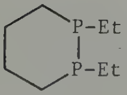
P_a $+55^{155}$
P_b -41
$(J_{ab}=220)$



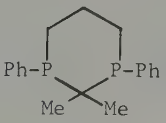
R=Me,P_a $+34.6$,P_b $-9.3(C_6D_6)^{146*}$
$({}^{1}J_{ab}=236.8,{}^{2}J_{ab'}=2.5,{}^{3}J_{aa}=23.2,$
${}^{1}J_{bb'}=264.2)$
R=Et,P_a $+38.2$,P_b -2.7(neat)^{146}
R=t-Bu,P_a $+56.8$,P_b $+20.5(C_6H_6)^{146}$



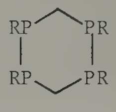
P(III), P_a -48.1,P_b $-21.0(CS_2)^{156*}$
sulfide, P_a -39.9,P_b $+15.6$



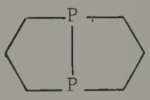
P(III),-46.0^{157}
sulfide,
$+39.4^{157}$



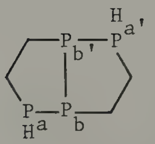
cis -2.0(tetralin)^{151,152*}
trans -4.0



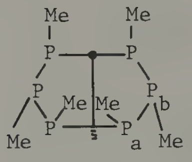
R=Ph, -26.3^{155}
R=t-Bu, -26.2^{144}



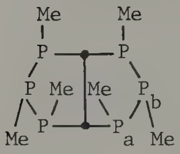
P(III), -27^{150*}
monosulfide, +90, −50 (^1J=238) (C_6H_6)
disulfide, +46 (DMF)
monomethiodide, +38, +6 (^1J=503) (H_2O)



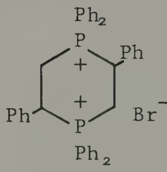
P_a −23.3, P_b -65.4^{158}
$^1J_{ab}$=224.2
$^2J_{ab'}$=20.0
$^3J_{aa'}$=2.3
$^1J_{bb'}$=237.7



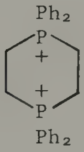
P_a −20,
P_b +20
$(C_6H_6)^{154}$



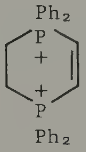
P_a +5, P_b −45
$(C_6H_6)^{154}$



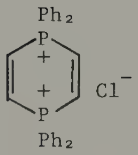
+20.4
$(MeOH)^{159}$



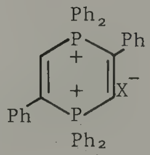
+14.4
$(MeOH)^{160}$



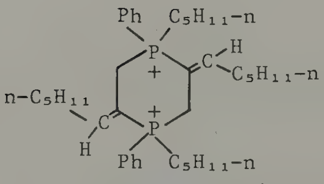
+2.8
$(MeOH)^{160}$



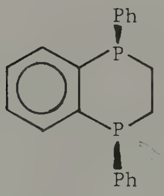
−16.0
$(MeOH)^{161}$



−3.5
$(MeOH)^{162*}$

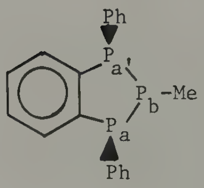


+17.0$(MeOH)^{162*}$



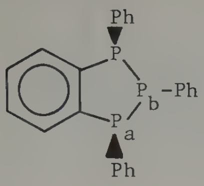
P(III)
+22.2
$(CHCl_3)^{163}$

disulfide
+33.6
$(CHCl_3)$

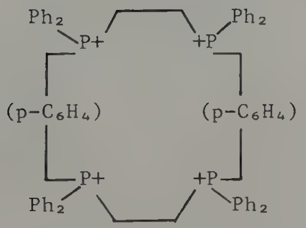


P(III), P_a +32.8, P_b $-67.5(CHCl_3)^{163}$
(J_{ab}=252Hz)
disulfide (a,a')
P_a +60.6, P_b −77.5
(J_{ab}=250Hz)

TABLE 5.12 continued

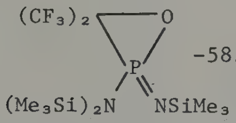


P_a +32.5,P_b −39.4(CHCl$_3$)[164*]
(J_{ab}=265Hz)

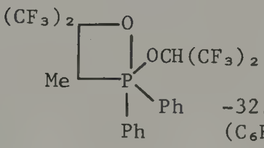


+27.4(TFA)[165]

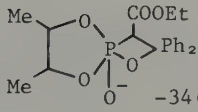
TABLE 5.13 Rings with O, N, or S[a]



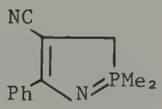
−58.9[166]



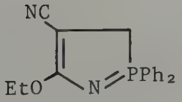
−32.1
(C$_6$H$_6$)[167]



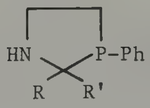
−34(THF)[168]



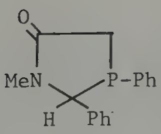
+71.4[169*]



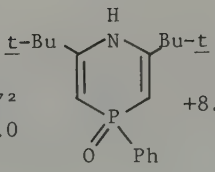
+57.9
(CH$_2$Cl$_2$)[170]



R=H,R'=Ph
−2.9[171*]
R=R'=Et 0.0

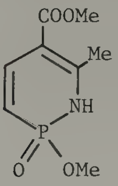


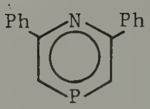
cis,−29.0
(CDCl$_3$)[172]
trans,−25.0

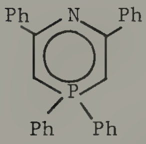


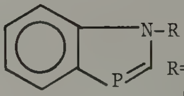
+8.5[173]

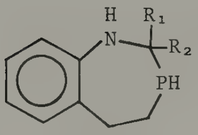
TABLE 5.13 continued

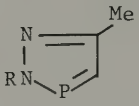

-14.5^{174b}

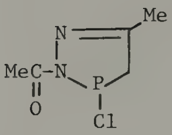

$+245.4^{175}$

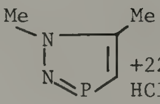

$+1.5^{176}$

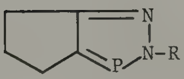

R=H, $+77.2$ (MeOH)^{177}
R=Me, $+69.8$ (MeOH)^{177}
R=Ph, $+72.1$ (MeOH)^{177}

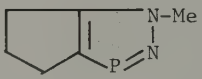

H,H, -72.4^{178*}
Me,Et, -21.7 and -31.4^{178}
$(CH_2)_5$, -29.2^{178}

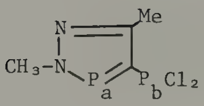

R=MeCO, $+238.4^{179}$
R=Me, $+228.9$ (neat)^{180}
R=Me, HCl salt, $+230.7$ ($CDCl_3$)^{180}

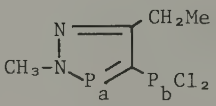

$+110.9^{179}$

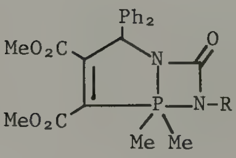

$+223.0$ ($CDCl_3$)^{181*}
HCl salt $+211.0^{181}$


Me, $+204.4$ ($CDCl_3$)^{180}
HCl salt $+209.3$ ($CDCl_3$)^{180}
C_6H_{11}, $+211^{182}$


N-Me $+204.1$ ($CDCl_3$)^{181}
HCl salt $+195.2$ ($CDCl_3$)^{181}


P_a $+247$, P_b $+158^{183}$ ($^2J=70.7$)


P_a $+248$, P_b $+157^{183}$ ($^2J=60.5$)


-67.3 ($CDCl_3$)^{184*}

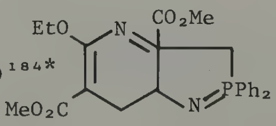
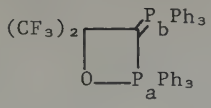
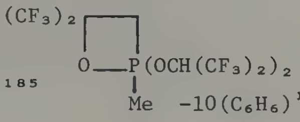

$+59.7$ (CH_2Cl_2)^{170}

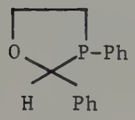
TABLE 5.13 continued



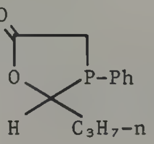
P_a -54.0, P_b +7.3 (CH_2Cl_2)[185] (^2J=47)



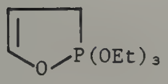
-10(C_6H_6)[186]*



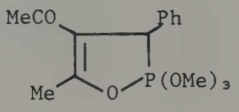
cis -7.5 $(CDCl_3)$[182]* trans -4.0



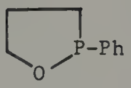
cis -23.5[172] trans -27.0



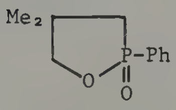
-30.1[187]



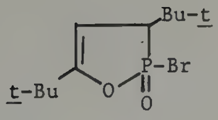
-27.9[188]



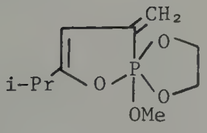
P(III), +110.2[189]* oxide, +58.4[189] sulfide, +102.4[189]



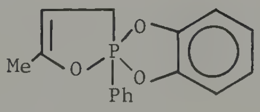
+58.6 $(CDCl_3)$[190]



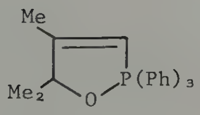
+53.0[191]



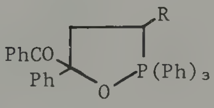
-26[192]*



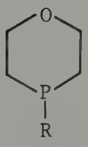
+8.0 (CCl_4)[193]*



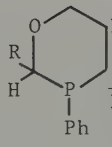
-59.7$(CDCl_3)$[194]



R=Me,-48.5 $(CDCl_3)$[195]* R=H,-49.5 (CH_2Cl_2)[196]

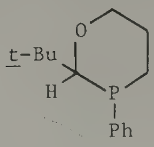


R=H,-79[197]
R=n-C_8H_{17} -52[197]
R=n-$C_{12}H_{25}$ -52[197]

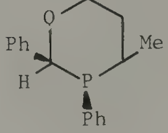


R=Ph,cis,-22.6 (C_6D_6)[198]*
trans,-33.7
R=Bu-t,cis,-9.1 (C_6D_6)
trans,-22.4

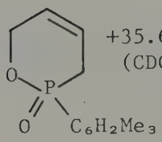
TABLE 5.13 continued



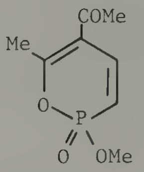
cis,-9.1 $(CDCl_3)^{198}$ trans,-22.4



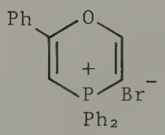
cis Me,-11.8 $(CDCl_3)^{198}$ trans Me,-11.7



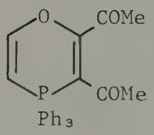
+35.6 $(CDCl_3)^{199}$



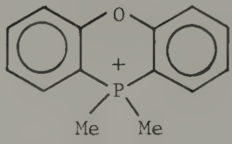
+9 ^{174*b}



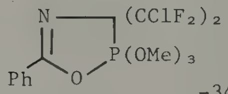
-17.2 $(DMSO)^{200*}$



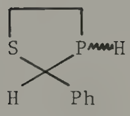
+17 $(dioxane)^{201}$



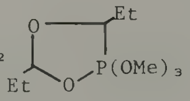
I^-, -7.5 $(TFA)^{72}$



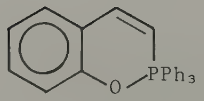
-34.1 $(C_6D_6)^{202*}$



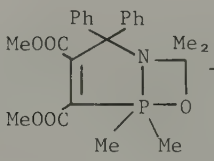
cis -5.6 $(C_6D_6)^{172}$ trans -15.6



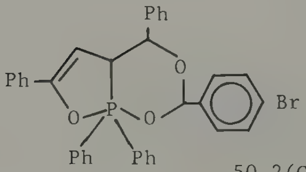
-34.2, -32.8^{192}



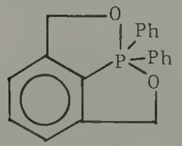
$-50.9(CDCl_3)^{203}$



-55.4 $(CDCl_3)^{204*,205}$

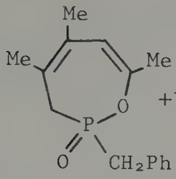
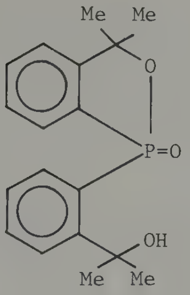
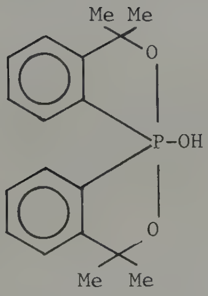
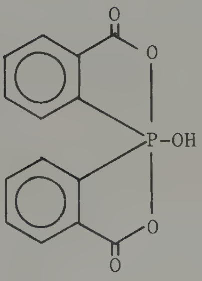


$-50.2(C_6H_6)^{206}$



$+22.9(CDCl_3)^{207*}$

TABLE 5.13 continued

	+71 ($CDCl_3$)^{105}		ca. +52 (MeOD, −50°)^{208}
	ca. −27 (MeOD, −50°)^{208}		−38.5 ($CDCl_3$)^{209*}

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[a] References bearing asterisks have data on related compounds.

[b] Standard not reported; presumed to be H_3PO_4.

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chapter six

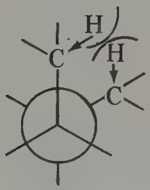
^{13}C NMR Spectra of Heterocyclic Phosphorus Compounds

Phosphorus chemistry has shared in the benefits for structural elucidation made possible by the introduction in about 1970 of practical ^{13}C NMR spectroscopy. New instruments capable of signal enhancement by the pulsed Fourier transform technique, with broadband ^{1}H decoupling, were responsible for this event. As elsewhere in organic chemistry, little use was made of the technique for phosphorus compounds prior to this date, and a review[1a] published in 1972 has entries for only about 20 substances with C-P bonds. Only one of these is heterocyclic (1H-phospholane, for which, alas, the assignments[2] of δ 31.6 to C-1 and 21.2 to C-2 seem to require reversal). The tables of selected ^{13}C NMR data in the present chapter (Tables 6.5-6.7) show that quite a diversity of heterocycles has been studied in the past decade, and the stream of publications is flowing unabated. The ^{13}C NMR technique is especially useful for phosphorus compounds, for both chemical shift and ^{31}P-^{13}C coupling information is provided by the spectrum. The coupling, to be sure, does add complexity to the spectrum, and occasionally serious peak overlap can occur. However, the magnitude of the coupling constants can be an aid in assigning signals, as well as in detecting stereochemical features, and is playing an important role in making ^{13}C NMR almost the first choice among the various modern structure-elucidating techniques. The discussion of ^{13}C NMR will center primarily on practical aspects such as useful correlations of shift or coupling phenomena, effects of conformations of ring systems on these parameters, and influences of conjugation. A more sophisticated treatment of NMR theory is left in the original literature.

6.1 A BACKGROUND FROM RESULTS WITH NONCYCLIC P COMPOUNDS

As of this writing, there is no review in the literature of the general ^{13}C NMR properties of phosphorus compounds. To appreciate effects in cyclic compounds, such a background is essential.

Each phosphorus functional group has its own influence on the ^{13}C NMR shift of attached carbon chains or rings, and each has its own array of coupling constants (for one- , two- , or three-bond coupling; small coupling through four or more bonds is possible,[3] though frequently observed only in unsaturated systems). The chemical shift effects on chains are controlled, of course, by the same factors operating for nonphosphorus functions. It has proved to be generally useful in interpretive ^{13}C NMR to assign increments to a particular function to express its net influence on the α, β, γ, and δ carbons of a chain. The increments are additive, and serve remarkably well to predict chemical shifts. α-Effects are usually deshielding, as they are dominated by electron induction; effects from atoms of electronegativity less than that of carbon can be shielding, however. β-Effects are almost always deshielding, but of uncertain origin, whereas γ-effects are always shielding, in part arising from the operation of steric compression that induces bond polarization. This effect, most clearly understood in alkanes, can be expressed with the notion of nonbonded interactions between C-H bonds of the γ-related atoms in the gauche conformation:



Both of the involved C atoms undergo upfield shifting as the result of the increased electron density. With heteroatoms in the γ-position, another effect seems to contribute to the upfield γ-shift, as some rather small groups have remarkably large γ-constants (cf. -2.4 ppm for CH_3 to -5.8 for OH). δ-Effects, also of uncertain origin, are frequently of negligible size, but deshielding in direction. When these ideas are applied to phosphorus functions,[4] a typical set of $\alpha, \beta, \gamma, \delta$-constants can be developed that are additive with constants[1b, 5a] for carbons or other substituents, and can be used to predict ^{13}C shifts. The data available for a few typical P functions are summarized in Table 6.1. Of equal importance is an understanding of how structural differences in the P functional group can influence these constants, for this understanding will be of great help with heterocyclic systems where no constants can be developed. As for other functions, the α-effect of a phosphorus group is determined to a large degree by the net electronegativity of the group, but the atoms attached directly to P in the function stand as β-substituents

TABLE 6.1 Substituent Constants for P Functions on Carbon Chains

Function	α	β	γ	δ
$-PH_2$[a]	-2.3			
$-PHCH_3$[a]	+9.2			
$-P(CH_3)_2$[b]	+19.4	+3.3	-0.5	+0.7
$-\overset{+}{P}(CH_3)_3$[a]	+13.4			
$-PCl_2$[b]	+29.7	+0.1	-1.6	+0.5
$-P(OCH_3)_2$[b]	+20.4	-0.2	-0.3	+0.8
$-PS(CH_3)_2$[b]	+21.4	-0.2	-1.1	+0.4
$-PO(C_4H_9\text{-}n)_2$[b]	+14.6	-1.0	-0.6	+0.4
$-PO(C_6H_5)_2$[c]	+16.8	-0.1		
$-\overset{+}{P}(C_6H_5)_3$[d]	+9.3	-0.5	-1.4	+0.5
$-PO(OC_2H_5)_2$[e]	+12.1	-0.06	-1.4	-0.2

[a] Taken from chemical shifts of -4.4 for CH_3PH_2, 7.1 for $(CH_3)_2PH$, 11.3 for $(CH_3)_4\overset{+}{P}$, with δ $CH_4 = -2.1$; Ref. 1, p. 158.

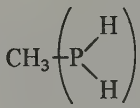
[b] Ref. 4.

[c] Ref. 6; taken from shifts for P-C_2H_5 derivative, with C_2H_6 having δ 5.9.

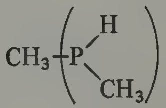
[d] Ref. 7; taken from shifts for P-C_4H_9-*n* derivative, with C_4H_{10} having δ C-1 = 13.2, C-2 = 25.0.

[e] Ref. 3.

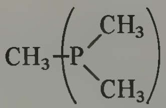
with regard to the α-carbon of a chain and hence can act *through* P to exert the usual β-deshielding effect on the α-carbon. These concepts are amply demonstrated by the effects on the methyl carbon of the series[1a] of related P(III) substituents below.



δ -4.4



+7.1



+17.3

P is less electronegative (2.1) than C (2.5); the PH_2 group is therefore relatively electron-releasing and shielding. A CH_3 replacing H, however, provides a deshielding β-effect (11.5 ppm), and a second CH_3 provides a similar effect (10.2 ppm). These β-effects are similar in size to the β-effect of CH_3 when installed directly on a carbon chain (9.5 ppm). The large α-constant (Table 6.1) for PCl_2 must be understood as a combination of the deshielding by the greater electronegativity of this polar group relative to carbon, and by the β-effects of each Cl (+10.5 in alkanes). P(IV) functions, such as $R_2P(S)$ or $R_2P(O)$, are also polarized with phosphorus positive, and in addition have three atoms to act as β-substituents to the α-carbon of an attached chain; acting together, a large α-effect can develop for such groups [e.g., +21 for $(CH_3)_2P(S)$]. Of course γ-effects can be transmitted through P, so that β-carbons of the chain might experience a compensating shielding effect. An apparent anomaly exists for functions containing a unit positive charge; it might be expected that a large deshielding α-effect would be exhibited by such ionic groups, but the value is surprisingly small and the unusual observation is made that quaternization of a tertiary phosphine leads to net *shielding* by several ppm [cf. δ $(n\text{-}C_4H_9)_3P$, 25.2 to $(n\text{-}C_4H_9)_3\overset{+}{P}CH_3$, 20.6]. This is not a problem unique to P substituents, however, and has been widely studied and discussed for positive nitrogen functions, especially as created by protonation of amines.[5b] For present purposes, it is the empirical observation that is important, and the theoretical explanation (based on shielding by local electric fields) will not be further developed.

β-Effects from P functions similarly have to be viewed as a combination of the inherently deshielding effect of the β-located P atom, and the *shielding* effect of atoms attached directly to P, as they are γ-oriented to the β-carbon of a chain. Frequently the effects nearly cancel each other, and surprisingly small β-constants (either positive or negative) can result (Table 6.1). Effects at γ-chain carbons are similarly composed of small shielding influences by the steric compression in gauche conformations, plus the "other" contribution to γ-shielding seen for polar groups, as well as a small deshielding provided by atoms on P that serve as δ-substituents to a γ-chain carbon. The net γ-constants of Table 6.1 are rather small compared to γ-constants of other common organic substituents; the compensating δ-effect provides a partial explanation, but it is likely that the differing geometry (especially the longer C-P bonds, about 1.85 Å) acts to diminish the steric compression in the gauche conformation. (An important manifestation of this diminished interaction is felt in heterocyclic derivatives, where the conformational biasing by a substituent on P in the ring will be seen to be remarkably small.) It was recognized some time after general acceptance of the shielding effect in γ_{gauche} conformations that even in the antiperiplanar position, where steric compression cannot operate, small upfield shifts could occur at γ-carbons.[8] This effect is weaker (< 2 ppm) for groups based on second-row elements; for phosphorus functions, it can be seen by studying the effect of axial *versus* equatorial substitution on C-3,5 of the cyclohexane ring,[9] where it is found that most, but not all, ^{13}C functions have the expected small shielding in the equatorial position. The effect is absent at the 6-position of 2-norbornyl phosphorus compounds.[10] It is an effect that is not likely to be of importance in cyclic compounds.

The concepts of additive constants for a substituent are equally applicable when attached to an alicyclic system; many constants are available[5] for cyclohexane, and a recent study[9] has provided constants for P substituents as well. Here it should be remembered that constants will differ if the substituent occupies the axial or the equatorial position, or is in a system equilibrating between the extremes. Table 6.2 provides data for some P substituents when equatorial on 4-alkyl cyclohexanes. The data are easily understood from the discussion already presented. Included here are β- and γ-constants for $-PH_2$, missing from Table 6.1; the β-constant is seen to be quite large (+8.3), as there are no atoms on P to act as γ-substituents. Table 6.2 also reveals that the δ-constants are consistently shielding in the cyclic compounds, whereas deshielding is the rule in chain structures. This is, however, a general situation and not peculiar to P substituents.

Axial substituents on cyclohexanes have quite different values than equatorial, a consequence of the increased γ-interaction between the substituent and the gauche 3,5-carbons. This causes all four carbons in the gauche array to be shifted upfield, with the effect largest at C-3,5 (cf. δ 28.5 and 21.8 for trans and cis 4-*t*-butylcyclohexylphosphines[9]).

TABLE 6.2 Substituent Constants for Equatorial P Functions on Cyclohexanes[a]

Function	α	β	γ	δ
$-PH_2$	−0.5	+8.3	−0.3	−1.8
$-P(CH_3)_2$	+11.6	+1.2	−0.7	−1.7
$-PCl_2$	+20.8	−2.1	−1.7	−1.9
$P(OCH_3)_2$	+13.6	−2.1	−1.0	−0.8
$PS(CH_3)_2$	+13.4	−2.1	−1.5	−2.0
$\overset{+}{P}(CH_3)_3$	+4.3	−2.6	−2.2	−2.6

[a] Ref. 9

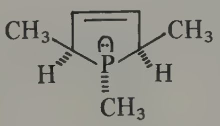
This is an extremely important property that provides ready assignment of cis, trans geometry to a pair of isomers. The effect also causes the carbon of an exocyclic P-substituent to be shifted several ppm upfield in the axial conformer. These steric effects are of special value in studies of heterocyclic systems.

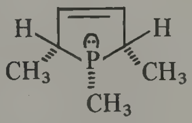
Coupling phenomena between ^{13}C and ^{31}P have been extensively studied, both theoretically (as in Ref. 11 and papers cited therein) and experimentally (as in Ref. 3, also providing leading references). For some compounds, determination of the relative sign of coupling has been made. Although this information is occasionally quite useful, as will be seen in consideration of ^{3}J especially, sign determination is not routinely made and very few data are available for heterocyclic compounds. The use of absolute values, as in practical ^{1}H NMR spectroscopy, is quite satisfactory. For simplicity, sign information is not provided in the tables of heterocyclic compounds even when known. However, certain generalities do exist, as are indicated below:

	P(III)	P(IV)
$^1J_{PC}$	−	+
$^2J_{PC}$	+	+
$^3J_{PC}$	+	

Important exceptions can occur in cyclic phosphines,[12,13] and have been discussed in detail.[13]

Table 6.3 summarizes the coupling constants that have been observed for a variety of alkyl and cycloalkyl P compounds. The ranges of values will be helpful in studies of compounds with P incorporated in rings because, within limits, similar values will be found for comparably composed P functions, with the important exception of the strongly sterically dependent ^3J values. Thus, the large ^1J and small ^2J values for the $-PS(CH_3)_2$ substituent will apply to cyclic P-methyl sulfides, etc. Some important generalities emerge from the data compiled in Table 6.3. All P(IV) functions have very large ^1J values (50-150 Hz, but mostly 50-70), a fact related[11] to the large amount of s-character, but have very small ^2J values (0-5 Hz); ^3J rises again depending on the dihedral angle (ϕ) relating P to the vicinal carbon and is quite high (vide infra) (15-17 Hz, $\phi \sim 180°$) in the alkyl models. The P(III) functions have much smaller ^1J values (7-23 Hz, except 40-46 for PCl_2) but larger ^2J values (11-28 Hz) than the P(IV) series. The ^1J value for a given phosphorus function can vary with the substitution pattern on the α-carbon; for example, ^1J in dimethyl cyclohexylphosphonate is 143.2 Hz, whereas in the α-hydroxy derivative it is 165.5 Hz. ^1J is also dependent in certain functionalities to some extent on steric environment,[15,16b,16c,17] but no predictable relation applicable to all P functions seems present. For example, in rigid cyclohexylphosphonates[16c] the isomer with axial P has a slightly smaller ^1J value ($\Delta\,^1J = 5$Hz) than the equatorial; in the phosphonite[9] the opposite is true ($\Delta\,^1J = 4$ Hz), and for other functions the difference is insignificant (1-2 Hz). Cyclic compounds offer other opportunities to explore the effect of stereochemistry on ^1J, and the point will arise in subsequent discussions. Both ^2J and ^3J can exceed ^1J in the P(III) series, and several cases are known where $^3J_{\phi=180°}$ is larger than both ^1J and ^2J. Although not obvious from the data for noncyclic P compounds, there has been discovered a steric control of two-bond coupling in P(III) cases that should also be presented at this time. Thus, the magnitude of ^2J in cyclic phosphines seems to be strongly controlled by the dihedral angle associating the lone pair orbital (assuming substantial s-character in the hybridization about P(III)) and the β-carbon of a group attached to P. Thus, in the phospholenes below, coupling to the $C\text{-}CH_3$ group is quite different in the cis (small ϕ) and trans (large ϕ) forms[18]; several other examples are known (e.g., Ref. 19) among cyclic compounds, as is discussed in Section 6.2.





trans $^2J_{PCCH_3} = 28.1$ cis, $^2J_{PCCH_3} = 0$

Closer examination of the nonheterocyclic compounds leading to the data in Table 6.3, however, then reveals that this effect could be operating in special cases where steric congestion tends to favor a particular rotamer. Thus, the endo isomer of

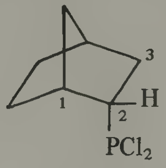
TABLE 6.3 Summary of ^{31}P-^{13}C Coupling Ranges

	PH_2	PCl_2	$P(CH_3)_2$	$P(OCH_3)_2$	$PO(CH_3)_2$	$PS(CH_3)_2$	$PO(OCH_3)_2$	$\overset{+}{P}(CH_3)_3$	$PO(C_6H_5)_2$	$PO(C_4H_9\text{-}n)_2$	$\overset{+}{P}(C_6H_5)_3$
<u>$^1J_{PC}$</u>											
Alkyls[a]		43-45	12	17-23	66	54			73[e]	65[e]	50-57[f]
Cyclohexyls[b]	6-7	45	7-9	14-15		53-54		51-52			
7-Norbornyl[c]		46	11								
Anti-7-nor-bornenyl[c]		48	12			45		41			
Syn-7-nor-bornenyl[c]		40	6								
Exo-2-nor-bornyl[d]		46	8	20	71	53	143	51			
Endo-2-nor-bornyl[d]		43-44	6	17	70-75	56					

$^2J_{PC}$											
Alkyls[a]		14	14	16-18	5	4			4.7^e	3.9^e	$4\text{-}5^f$
Cyclohexyls[b]	7-8	16	14	17		2-3		2-3			
7-Norbornyl[c]		13	12-13								
Anti-7-nor-bornenyl[c]		15	11			0		0			
Exo-2-nor-bornyl[d]		15-18	11-15		1-4	0-4	0-5	0-5			
Endo-2-nor-bornyl[d]		12-28	9-19		0-1	0-2	0-2	0			
$^3J_{PC}$ ($\phi \sim 180^\circ$ only)											
Alkyls[a]	8-9	11	10-11	9-11		13-15		14-15		13.9^e	$16\text{-}17^f$
Equatorial-1-cyclohexyl[b]		11-12	11	11-12	13	16					

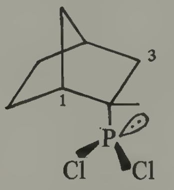
[a] Ref. 3.
[b] Ref. 9.
[c] Ref. 14.
[d] Ref. 10.
[e] Ref. 6.
[f] Ref. 7.

2-norbornylphosphonous dichloride[10] has quite different ^2J values for coupling to β-oriented C-1 and C-3.



endo, $^2J_{PC\text{-}1} = 12$ Hz
$^2J_{PC\text{-}3} = 25$ Hz

The difference is also present for the corresponding $P(CH_3)_2$ derivative (endo, $^2J_{PC\text{-}1}$ and $^3J_{PC\text{-}3}$ = 11 and 19 Hz). From the 3-phospholene models, it can be suggested that the larger ^2J values will be found for the rotamer that places the lone pair orbital at a small dihedral angle relative to the β-carbon. Thus, the data indicate that the *endo*-2-norbornyl compounds have the favored conformation below, a proposal quite consistent with the intuition that this structure is the least crowded.



C-1: ϕ large, J small
C-3: ϕ small, J large

The two-bond coupling to the methyl of an ethyl group on phosphorinane is also larger[20] when in the axial than in the equatorial position, implying a similar conformational preference that minimizes steric congestion and increases proximity of the lone pair to the methyl.

It is more common for three-bond coupling to be under dihedral angle control (as in the well-known Karplus relations for H-C-C-H), and considerable data are now being gathered that unequivocally support this concept in P(IV) derivatives such as phosphine oxides[21] and sulfides,[10,14] phosphonates,[16,22] and phosphonium salts.[10,14] For the particular functions $(CH_3)_2PO$, $(CH_3)_2PS$, $(CH_3O)_2PO$, and $(CH_3)_3\overset{+}{P}$, regular Karplus plots can be produced[10] from data for several different carbon skeletons (as in Table 6.3) that show similar coupling at $\phi = 0°$ or $180°$, with minima near 90°. Figure 6.1 is an example of such a plot for the $(CH_3)_2PS$ group. It is reasonable to expect that parameters for other types of phosphine sulfides will be predictable (within limits) from such a curve. However, ^3J does seem to depend on the substitution pattern of the α-carbon,[16c] and caution is required in the use of the relation for diverse structures. The P(III) derivatives, while showing even stronger dependence on the dihedral angle, give a unique Karplus plot, with ^3J for $\phi = 0°$ about 2-3 times that for $\phi = 180°$, and with the minimum at $\phi = 105°\text{-}110°$. Figure 6.2 is an example of such a plot for the $(CH_3)_2P$

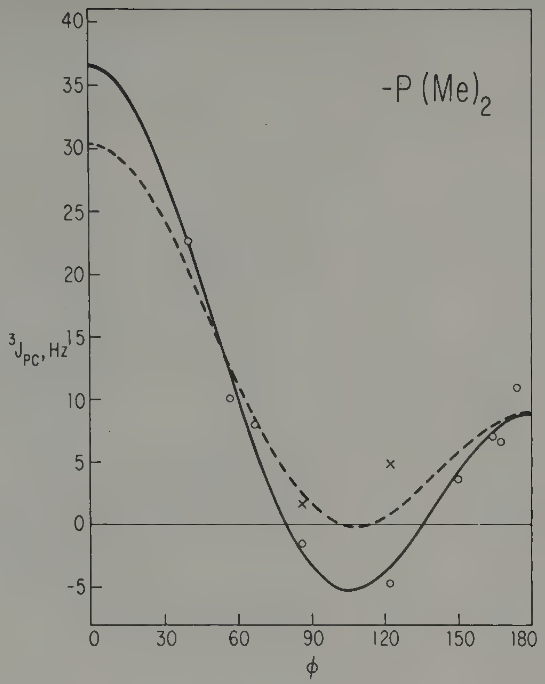


Figure 6.1 Dependence of vicinal P-C coupling on dihedral angle for the $-PS(CH_3)_2$ group. [Reprinted from *Journal of the American Chemical Society*, **102**, 3136 (1980). Copyright 1980 American Chemical Society.]

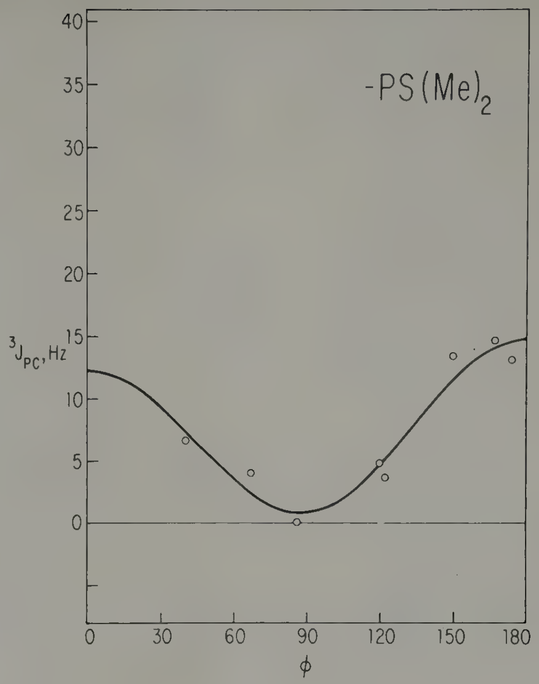


Figure 6.2 Dependence of vicinal P-C coupling on dihedral angle for the $-P(CH_3)_2$ group. [Reprinted from *Journal of the American Chemical Society*, **102**, 3136 (1980). Copyright 1980 American Chemical Society.]

group.[18] A theoretical explanation is lacking at present for this striking difference between the P(III) and P(IV) cases.

One-bond ^{31}P-^{13}C coupling can also be influenced by steric properties of noncyclic compounds. It has been deduced that, as in other systems, the percent of s-character in the carbon hybrid involved in bonding to phosphorus has a definite effect on ^1J, with a decrease in s-character causing a decrease in ^1J. This is quite evident from the following trend in ^1J for a series of alkyltriphenylphosphonium salts[23]:

$$^1J_{CH_3} > {}^1J_{C_2H_5} > {}^1J_{i\text{-}C_3H_7} > {}^1J_{t\text{-}C_4H_9}$$

This is derived from the increased branching at the C attached to P, causing greater s-character in the C-C bonds to minimize steric congestion, at the expense of s-character in the C-P bond.

New situations develop when these P functions are bonded to sp^2 carbons, and an especially extensive study has recently been published on aryl derivatives.[24] Some of these shift and coupling data are reproduced in Table 6.4, in order to indicate the trends. It is immediately obvious that the α-effect at the ipso carbon is greatly reduced for both P(III) and P(IV) functions relative to their values for sp^3 attachment [e.g., PCl_2 + 12.6 *versus* +29.7; $PS(CH_3)_2$ +6.7 *versus* +21.4], a characteristic of non-P functions as well [e.g., $N(CH_3)_2$ + 22.6 *versus* +49.6]. All values for the ortho carbons show deshielding, whereas most aromatic substituents cause shielding at this position. Effects at the meta and para positions are more associated with the inductive and resonance characteristics of the substituents. Using this "dual substituent parameter" approach, Modro has separated the electronic effects of the various P substituents into inductive constants (σ_I) and resonance constants (σ_R), using the expressions

$$^{13}\text{C}\ \delta_{\text{para}} - {}^{13}\text{C}\ \delta_{\text{H}} = 3.986\ \sigma_I + 19.79\ \sigma_R$$
$$^{13}\text{C}\ \delta_{\text{meta}} - {}^{13}\text{C}\ \delta_{\text{H}} = 1.54\ \sigma_I - 1.61\ \sigma_R$$

In brief, the findings are that $P(CH_3)_2$ has constants of almost negligible size (quite consistent with other data for its interactions with the aromatic system) whereas more polar P(III) functions (especially PCl_2) have both inductive and resonance effects that act to cause substantial electron withdrawal. Little is known about the interaction of P(III) with olefinic groups. Data for phenyldivinylphosphine[25] simply show that the C_6H_5P grouping has a deshielding α-effect on the ethylene sp^2 C (δ 137.0, from 122.8) whereas the β-carbon (δ 128.1) is more weakly deshielded. These data reveal nothing about any conjugative effect. As a substituent on the benzene ring, $(CH_2{=}CH)_2P$– differs negligibly from $(CH_3)_2P$ in its effect on the ring carbons. Vinylphosphonous dichloride[26] has similar carbon shifts, with α-C more downfield (δ 142.7) due to the stronger deshielding effect of attached –PCl_2 (Table 6.2) and β-C at δ 130.3.

TABLE 6.4 Chemical Shift Effects and ^{31}P-^{13}C Coupling Constants for Aryl P Derivatives[a]

Function	ipso (α)	ortho (β)	meta (γ)	para (δ)
Me_2P		+2.5 (18.4)	+0.07 (5.8)	−0.33 (≃0)
Cl_2P	+12.6 (51.8)	+2.0 (31.2)	+0.57 (8.0)	+4.2 (≃0)
$(EtO)_2P$	+13.9 (23.2)	+1.6 (18.4)	−0.39 (5.0)	+1.0 (≃0)
$(Et_2N)_2P$		+2.9 (16.6)	−0.31 (2.8)	−1.2 (≃0)
Me_2PO		+1.7 (8.8)	+0.10 (11.8)	+2.7 (2.2)
Me_2PS	+6.7 (82.0)	+2.0 (10.6)	+0.19 (11.8)	+2.9 (3.0)
Ph_2PO	+5.8 (102.8)	+3.9 (9.6)	−0.10 (11.6)	+3.0 (1.8)
$(EtO)_2PO$	+1.6 (187.4)	+3.6 (10.0)	−0.17 (14.8)	+3.4 (3.0)
$(CH_2{=}CH)_2P$[26]	+8.6 (9.2)	+3.6 (18.7)	−0.2 (6.7)	−0.1 (0.5)

[a] Data taken from Ref. 24 except as noted.

The P(IV) groups, as would be expected, have substantial electron-withdrawing effects at the para position, and most of them have inductive effects acting in the same direction. These results are compelling in indicating that polarization occurs through resonance where a d-orbital on P accepts electrons.

The σ_R value of PCl_2 suggests that even this P(III) group is involved in such delocalization, a property enhanced by the more electronegative chlorine substituents compared to the phosphines.

The ^{31}P-^{13}C coupling constants are noticeably different for the aryl derivatives relative to saturated derivatives. ^1J is definitely larger, perhaps a consequence of the greater s-character in the orbital of carbon. To a smaller extent, ^2J values are also larger for the sp^2 cases for all functions; ^3J values for the P(III) cases are, however, reduced to about half the size seen for sp^3 carbons, whereas for P(IV) the values remain essentially the same. The control of ^3J by dihedral angles is obviously less important for P(III) than some other factor that operates in the aromatic system. The aromatic derivatives also provide good examples of the rare four-bond coupling; from Table 6.4 it can be seen that the π-system allows effective transmission (2-4 Hz) from a P(IV) function to the para carbon.

Olefinic P(IV) compounds have received less study, but here as well it is clear that some interaction between the P atom and the unsaturated center must occur. This is confirmed by studies[27] on vinyl triphenylphosphonium salts, where the β-carbon is strongly deshielded just as in α,β-unsaturated carbonyl compounds.

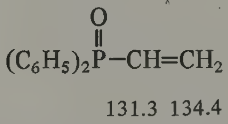
$CH_2{=}CH_2$ $(C_6H_5)_3\overset{+}{P}{-}CH{=}CH_2$

δ 127.8 119.2 145.2

Again the proposal has been made that a d-orbital acts to accept electron density and positively polarizes the β-carbon.

$$(C_6H_5)_3P{=}CH{-}\overset{+}{C}H_2$$

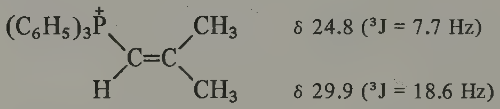
Vinyl phosphine oxides[6] show a similar but smaller polarization of the β-carbon relative to ethylene. The larger α-effect of phosphoryl *versus* positive P accounts for the considerable difference at the α-carbons in the two systems.



$$(C_6H_5)_2\overset{O}{\overset{\|}{P}}{-}CH{=}CH_2$$

131.3 134.4

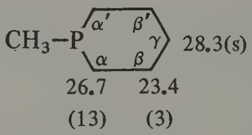
Carbons cis or trans to a P-substituent show the expected differences due to steric compression in the former.



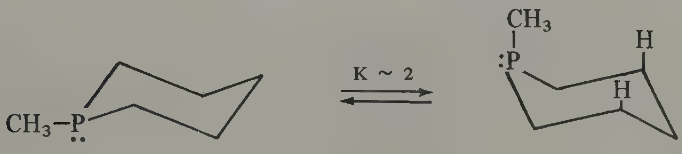
The three-bond coupling constants to the CH_3 groups are quite different, following the trend of $^3J_{HH}$, where trans coupling is larger than cis coupling.

6.2 CYCLIC PHOSPHINES

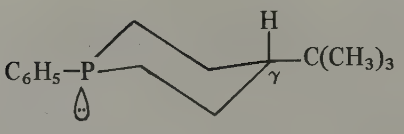
From the background provided by the noncyclic phosphorus compounds, it is possible to appreciate some of the spectral features of cyclic systems. Of great importance in the assigning of signals will be influences on chemical shifts associated with the conformations adopted by the rings, especially as manifested by differences in the relation of γ-related atoms, both endocyclic and exocyclic. Coupling constants, both ^{2}J and ^{3}J, will also be influenced by conformations. The 6-membered ring provides an easy starting point for such considerations. The assignments to a typical 1-alkylphosphorinane[28] are given below.

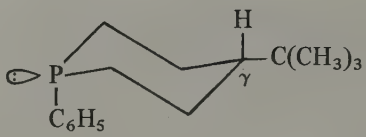


The C-α chemical shift is consistent with the value reported[3] for the α-carbons of $CH_3P(CH_2CH_2CH_2CH_3)_2$ (δ 30.3), but with some upfield shifting due to the γ-gauche relations of C-α and C-β′, and of C-α′ and C-β. The CH_3 group has considerable axial character,[29] and this also is known to cause upfield shifting at α-ring carbons. This point will be established in a consideration of rigid rings to follow. The ^1J value for the acyclic compound (15 Hz) does not differ from that for the phosphorinane. The effect of any crowding due to axial disposition of the P-substituent will be felt at C-β,β′, and this provides a ready explanation for these carbons being the most upfield of the ring carbons.

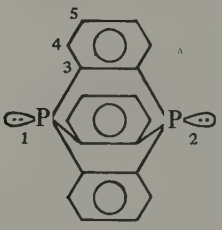


As the P-substituent gets larger, the equilibrium shifts to favor the equatorial form, and this should result in a more downfield position for C-β,β′. In fact, the shift is 25.0 for the t-C_4H_9 substituent. The ^2J value should also vary, as the preferred orientation of the lone pair orbital relative to C-β,β′ changes from a dihedral angle of about 180° (small coupling) to about 60° (larger coupling) in the equatorial form. This is just what is observed for the t-C_4H_9 derivative with a maximum of $^2J = 7$ Hz, compared to a minimum of 3 Hz for the CH_3 derivative. The maximum of 7 Hz should be compared to the larger value for freely rotating phosphines (11-15 Hz, Table 6.3), when the rotation necessarily allows the opportunity for conformations to be passed where ϕ becomes 0°. In the restricted cyclic system, the dihedral angle can never become less than 55°-60°. At C-γ, a chemical shift not unlike that of cyclohexane (27.8[1c]) is observed. Of greater interest is the coupling of the γ-C to ^{31}P, for such a three-bond relation is known to be under strong steric control. However, the magnitude of $^3J_{PC\text{-}\gamma}$ in the phosphorinanes is consistently quite small (0-3 Hz). If the Karplus plot for the $(CH_3)_2P$- group (Figure 6.2) is considered, such a range would arise from a dihedral angle of 70°-150°; yet the ϕ value imposed by the cyclic structure cannot exceed 55°-60°, for which ^3J is 10 Hz. Does this imply that another effect operates also on ^3J, possibly one that is present when free bond-rotation is not allowed? Or is it that a Karplus curve for one type of structural organization in a phosphine is simply not applicable to another? Too few data are presently available to clarify this matter. One point does seem certain, however—the orientation of the lone pair orbital relative to the coupled carbon has no pertinence to this particular situation, for neither of the rigid cis, trans isomers[30] below have a measurable value for coupling to the γ-carbon.



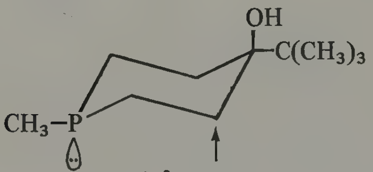


That lone pair orientation *can* influence ^3J has been suggested for the observation of two entirely different values for ^3J in a diphosphatriptycene,[31] where necessarily ϕ is 180° in each case. The lone pair orbital is obviously oriented differently relative to the coupled carbons.

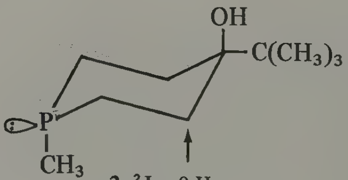


$^3J_{P\text{-}1,\,C\text{-}5} = 13.8$ Hz
$^3J_{P\text{-}2,\,C\text{-}4} = 1.4$ Hz

Where there are present on the γ-carbon substituents that prevent ring-inversion, the effects at C-α,α' and C-β,β' are more clearly seen. Thus, in the 4-*t*-butyl derivatives[20] 1 and 2, the ^2J values are 0 Hz for an equatorial lone pair (2, P-substituent axial) and 7.5 Hz for an axial lone pair (1, P-substituent equatorial). The value of 3 Hz seen for 1-methylphosphorinane is quite consistent with the notion that its conformational equilibrium has a slight dominance by the axial CH_3 conformer.

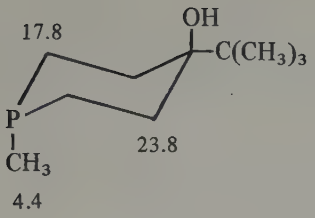


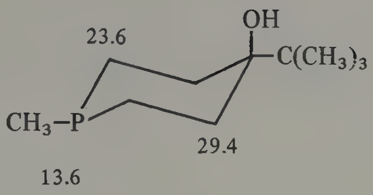
1, $^2J = 7.5$ Hz

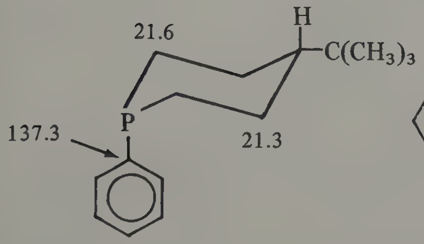


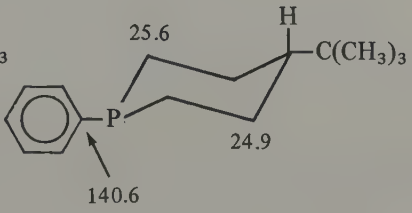
2, $^2J = 0$ Hz

Similar values for ^2J are found for other cis, trans isomers (Table 6.6). The shielding at C-β,β' by the axial P-substituent is magnified, and consistently amounts to 3-5 ppm relative to the equatorial isomer. A particularly useful effect is found at the exocyclic carbon on phosphorus as a reciprocal of crowding with C-β,β'; as is well known also in cyclohexanes, the carbon of an axial substituent always occurs well upfield of that for an equatorial carbon. The effect of greater steric compression in the axial isomer also shows up in the relatively greater shielding at C-α,α'. These various shielding effects are amply demonstrated by the isomer pairs below[20,30]:



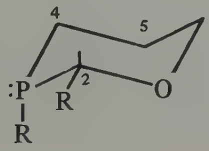




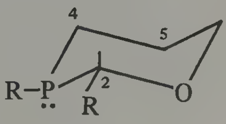


The effects of steric compression on ring carbons are less pronounced in 3-substituted phosphorinanes,[32] as suggested by the data in Table 6.6 for the 1,3-dimethyl derivatives. However, the P-CH_3 group is, as usual, markedly upfield (δ 6.8) when the axial form is compared to the equatorial (δ 14.3). The unsubstituted β-ring carbon responds in the expected way to this compression ($\Delta\,\delta$ 4.1 ppm), but the CH_3 substituent on the other β-carbon tends to moderate the effect ($\Delta\delta$ 0.9 ppm). The C-methyl presents an interesting test of the importance of dihedral angle effects on ^3J. This methyl is related to ^{31}P by a dihedral angle of about 180°; the coupling observed for both the cis and trans isomers (10-12 Hz) is remarkably close to the value predicted for this angle from Figure 6.2 (14 Hz) and tends to validate the use of this curve for other phosphines. However, the ring carbon again has no observable coupling, whereas for its dihedral angle (55°-60°) Figure 6.2 would suggest a value of about 4-5 Hz. Again there is implied a constraint on vicinal coupling where the involved atoms cannot rotate freely.

That the concepts developed for the phosphorinane ring can be extended to other 6-membered phosphorus-containing rings is amply demonstrated by the data[33] for isomer pairs in the 1,3-oxaphosphorinane systems. Reasoning that a C-substituent has a greater demand for the equatorial position than does a P-substituent, a 2,3-disubstituted derivative would have the preferred conformations below.



3, cis



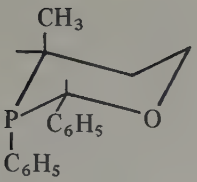
4, trans

The axial P-substituent would then exert its usual shielding effects at the γ-related

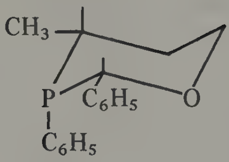
5-position and at the β-related 2- and 4-positions. The ^2J values (to C-4) should also differ, being larger in the trans form than in the cis. Data for isomer pairs do indeed show that most of these effects are present, as evidenced by the 2,3-diphenyl derivative:

	cis (3, R=C_6H_5)	trans (4, R=C_6H_5)
C-2	80.9 (24.5 Hz)	86.2 (7.3)
C-4	22.0 (15.6)	23.8 (16.1)
C-5	20.2 (1.6)	25.4 (3.4)

Thus, the axial P-phenyl of the cis isomer does indeed produce the expected shielding, and at C-5 the smaller ^2J value is observed. A remarkable new effect is observed here, however—^1J at C-2 is totally different for the two isomers, with the more crowded cis form (3) having the larger value. A difference in ^1J to ring carbons is apparent also in the phosphorinanes of Table 6.6, with the larger ^1J again being associated with the more crowded (axial P-substituent) form. The magnitude of the difference is not great, however. It is more pronounced (12 *versus* 2 Hz) in isomers of 3-keto-8-phenyl-8-phosphabicyclo[3.2.1]octane (Table 6.5). The exocyclic carbon attached to P can also have the larger coupling when in the axial position. This apparent relation of crowding with increased ^1J (absolute) is also found in 2-norbornyl phosphorus compounds[10] [e.g., for $P(CH_3)_2$, PCl_2, $P(OCH_3)_2$: exo 7.8, 45.8, and 19.5, endo 6.0, 43.2, and 16.5], but there is no consistency in ^1J values for the same groups on the 4-*t*-butylcyclohexyl ring[9] (equatorial 9, 45, and 14; axial 10, 44, and 18). In P(IV) phosphorinanes (Table 6.6), there is a similar lack of consistency, whereas in some other systems (1,3,2-dioxaphosphorinane[34,35] and 1,2-oxaphosphorinane[22]) and in cyclohexyl derivatives,[22,36] a consistent and useful relation exists that $^1J_{\text{equatorial}}$ is greater than $^1J_{\text{axial}}$. With further study of the influence of stereochemistry on ^1J, a useful new device for structure assignment may result. It does seem clear that large differences will exist only for P(III) forms, and then only when crowding by nearby substituents is present. Returning to the 1,3-oxaphosphorinane system,[33] further application of these conformational relations was made for 4-methyl and for the quite crowded (and distorted) 4,4,6-trimethyl derivatives. Considering only the former, ^2J values to ring carbon 5 and the 4-CH_3 play a very important role. For the 5-position, ^2J is equal and quite small for both cis, cis and cis, trans isomers, implying an equatorial lone pair orbital for both. The CH_3 coupling is large (24.9 Hz) for cis-cis and small for cis-trans (∿ 10 Hz), so the CH_3 orientation differs in the isomers. These results lead to the proposal of structures 5 and 6 as preferred conformations, both with equatorial 2-phenyl.



5, cis-trans

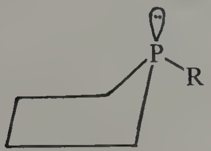


6, cis-cis

The axial CH_3 of **5** can then be expected to cause greater shielding at all ring carbons, which indeed it does. The complete spectrum is given in Table 6.5. A new effect operates on the 4-CH_3 group itself; in the equatorial position (**6**) it is more crowded (by P-phenyl) than in the axial (**5**), so that the equatorial CH_3 has the most upfield shift (δ 18.0 *versus* 19.2).

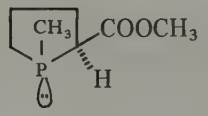
It should be mentioned that the very important class of P(III) 1,3,2-dioxaphosphorinanes shows the same effects on chemical shifts and coupling constants associated with ring conformations[35]; ^{13}C NMR is playing a vital role in current studies on this and related heterocycles.

Fewer data are available for saturated 5-membered cyclic phosphines, but some familiar features are visible. The α-carbon is easily recognized from its typically larger (14-23) ^1J value, whereas ^2J is quite small and within the extremes seen for the 6-membered ring (0-7.5 Hz; commonly 5-6 Hz) as a result of the restricted motion of the ring. If the dihedral angle to the lone pair orbital is truly in control of ^2J, then the observed coupling might suggest a preference of the 5-membered ring for a conformation such as **7** (small angle) over **8**, where the dihedral angle should approach 180° and *no* coupling might be expected. However, other supporting criteria should be sought for a prediction of this type, especially in view of the considerable difference in the conformational properties of 5- and 6-membered rings. Of more importance is the ^2J value to exocyclic carbons attached to the α-positions; as already noted these values are drastically different in cis, trans isomers, as is displayed by the carbonyl of ester derivatives[37] **9** and **10**, and the effect is highly useful for assigning structures.

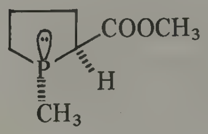


7

8



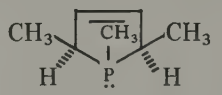
9, cis, δ 173.8, $^2J_{PC=O}$ <1.5 Hz



10, trans, δ 177.3, $^2J_{PC=O}$= 17 Hz

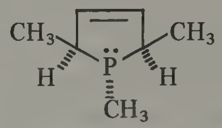
These derivatives also serve to show that the usual effects of steric compression apply, for in **9** both CH_3 and C=O are upfield by several ppm relative to **10**. Other examples of the ^2J and steric compression effects are present among the 2,5-dimethyl derivatives of 3-phospholenes[38] and 5-methyl-2-phospholenes.[39]

δ 13.9
(0 Hz)



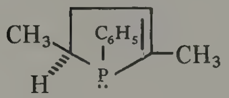
11, δ PCH_3 = 0.5 (24.4 Hz)

δ 21.0
(28.1 Hz)

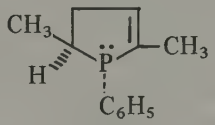


12, δ PCH_3 = 12.8 (18.6 Hz)

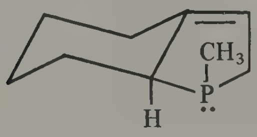
δ 15.1
(2 Hz)

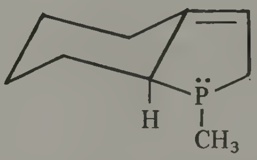


δ 20.2
(25 Hz)



Of great value is the persistence of these relations in bicyclic compounds,[40] which allows ready solution of a cis, trans assignment problem that could be quite troublesome. The P-substituent is the most obvious indicator of geometry through the steric compression when cis-oriented to a fused ring.



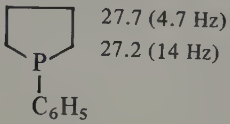


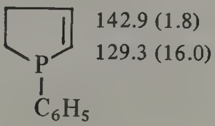
Although not so readily understandable, another piece of useful information is the ^1J value to the exocyclic carbon; it is larger in the crowded forms of isomer pairs **9** and **10**, **11** and **12**, and **13** and **14**, just as has been noted for other P(III) forms.

^1J cis PCH_3 (Hz)		^1J trans PCH_3 (Hz)	
9	27	**10**	20
11	24	**12**	19
13	23	**14**	18

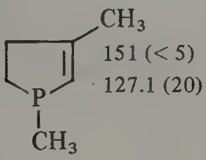
The oxides and sulfides of **11**, **12** and **13**, **14** show no such effect, and the isomers have virtually identical ^1J values.

Unsaturated (phospholene) derivatives are, of course, far more common in 5- than in 6-membered rings. At the 3,4-position, no unusual ^{13}C effects are seen, and a value that seems normal for ^2J is observed for the sp^2 carbon (it is conceivable in a 5-membered ring that the coupling occurs via the other pathway, and is then ^3J). In one 2-phospholene,[30] the sp^2 carbons have slightly larger ^1J and smaller ^2J values than in the saturated counterpart.[14]

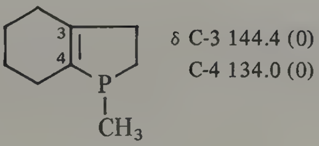




Few additional data are available; one structure[41] (**15**) supports the larger value for ^1J whereas a bicyclic compound[42] (**16**) has *no* coupling to either of the sp^2 carbons. This peculiar result certainly needs further exploration with other related compounds.



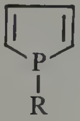
15



16

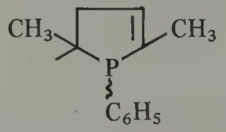
The 2-phospholenes in general seem to exhibit greater shielding at the α-sp^2 carbon than at β-, although in the open chain counterpart $C_6H_5P(CH{=}CH_2)_2$ the opposite is true. The usual multiple effects are present at both α and β carbons and attaching any special electronic significance to this relation is hazardous. Were p_π-p_π conjugation of special importance, a shift in the opposite direction (as in enamines) would have been contributed to the milieu, whereas p_π-d_π conjugation would have increased the positive character on the β-carbon and added to the deshielding. Arguments for both types of interaction are found in the literature, but it is not yet clear if the ^{13}C NMR data are adding much new information. In the related phospholes (see below), the difference between α and β carbons nearly vanishes.

Other unusual effects are present in phospholes.[25,41] ^1J becomes quite small (5-7 Hz) and ^2J increases to the same range (4-8 Hz), making peak assignments tenuous.

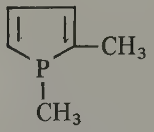


R	α	β
C_6H_5	135.1 (5.2)	136.7 (8.2)
CH_3	134.8 (7)	135.8 (8)

In symmetrical C-methyl derivatives, assignments are firmer, as the α-effect of CH_3 pinpoints the substituted carbon. Other carbons remain difficult to assign. An attempt has been made[25] to relate the increased ^2J value of phospholes to the well-established property that in this system the barrier to pyramidal inversion is greatly decreased. It is said that the increase in ^2J probably corresponds to a decrease in the average dihedral angle relating the P-substituent to β-C (and increased lone pair dihedral angle), which results from the lowering of the inversion barrier. However, if the geometric change at P is solely responsible for this coupling effect, it should also be observed for ^2J at a 2-CH_3 group. Few data are available; comparing 2-phospholene[39] 17 to phosphole[41] 18 does show that the effect, if present at all, is not of large size.

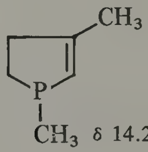


17, cis $^2J_{PCH_3\text{-}2} = 19$
trans, $^2J_{PCH_3\text{-}2} = 18$

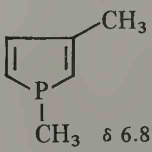


18, $^2J_{PCH_3} = 22$

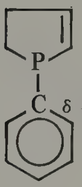
Another remarkable effect occurs at the exocyclic carbon on phosphorus; there is pronounced shielding of this carbon in both P-CH_3 and P-phenyl phospholes relative to the 2-phospholenes, and in the latter ^1J is sharply reduced.



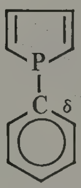
δ 14.2 (25 Hz)



δ 6.8 (20)



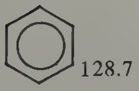
δ 140.6 (25.9)

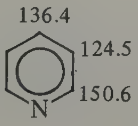


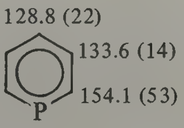
δ 129.6 (8.6)

As always, there is more of a change in geometry than just the introduction of another double bond and the institution of delocalization or "aromaticity" in the system, and it is difficult to explain this observation with confidence. The electron delocalization effect lowers the inversion barrier, causing motion about phosphorus in phospholes at room temperature that is otherwise absent in 2-phospholenes. In addition, one ring α-C changes its character from sp^3 to sp^2, with resulting differences in geometry and steric interactions; ring conformations differ as well. Nevertheless, the effects on the exocyclic carbon are consistent features of phosphole character.

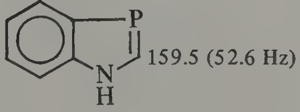
Unsaturation directly at P, creating the P(II) state, produces yet other unusual results. The phosphorins represent such a class of compounds. Especially noticeable in all derivatives[43, 67, 68] is the very large ^1J value (50-53 Hz); ^2J is also quite large to a ring carbon (12-16 Hz), whereas ^2J to an exocyclic carbon reaches an extraordinary size of 37 Hz (in 2-methylphosphorin). In addition, there is consistently present in phosphorins (and for other Group 5 atoms) a strong deshielding of the α-carbon, beyond that seen for pyridine, where the electronegativity of N provides a ready explanation for its own deshielding relative to benzene.







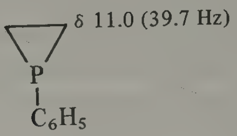
An explanation[43] for the α-deshielding based on the special importance of diamagnetic currents operating on the heteroatom in these aromatic systems, which would also account for strong deshielding of the proton on the α-C (δ 8.61), has been advanced tentatively, with the reservation that current chemical shift theory does not predict an effect of the size observed to arise from anisotropic magnetic susceptibility. The P-C coupling phenomena have been the subject of a theoretical study by SCF-INDO-FPT calculations[44]; it was found that all of the three coupling mechanisms (Fermi contact, orbital-dipole, spin-dipole) make a contribution to the coupling at each carbon, but with the first being the least important. The calculations reproduced the experimental values reasonably well and have taken out of them some of the strangeness felt in comparing these to P(III) values, where arguments based on dihedral angle relations to β- and γ-carbons are so helpful. Recognizing the large ^1J value as a P(II) characteristic has proved helpful in confirming the presence of a C-P double bond in the 5-membered ring of the novel compound **(19)**.[45]



19

Future research is likely to lead to many more heterocyclic systems based on C-P double bonds where ^{13}C NMR will play a major role in structural proof.

Phosphines based on rings of smaller size introduce new situations for consideration. Thus, the 3-membered phosphirane[13] **(20)** has its ring carbons at quite high field (δ 11.0) compared to a phospholane (δ 27.2 for 1-phenyl). The unique bonding required in the construction of this ring must be responsible for the effect, as it appears also in simple alicyclic compounds (cf. C_3H_6, δ −2.6, to C_5H_{10}, 26.5). The ^{1}J value becomes very large, as it does also in diphosphiranes (e.g., 21[46]).



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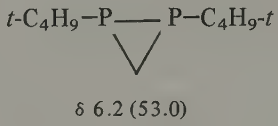
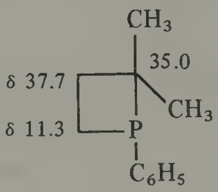


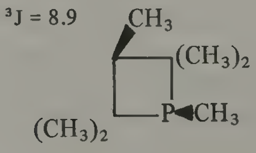
21

On the other hand, in the 4-membered phosphetane ring,[13,47] ^{1}J is very small (0.6-8 Hz), much below that seen in phospholanes (1-phenyl, 14.2 Hz). Little can be said about chemical shifts in phosphetanes, because all derivatives studied so far have 2-5 C-methyl groups that introduce the usual α, β, γ shifts at the ring carbons. The least-substituted phosphetane examined as yet is **22**, where the α-CH_2 is found at δ 11.3. The two α-effects of CH_3 on the other carbon bring its shift far downfield. The two β-effects from the methyls similarly deshield ring position 3.

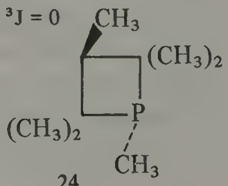


22

These α and β effects are unusually large. Coupling (^{2}J) to two methyls on the α-carbon exhibits the usual stereospecificity throughout a variety of derivatives, and in fact it was with these phosphetanes that the first observation of the relation of the lone pair orbital to two-bond coupling was made. For the CH_3 cis to the P-substituent (large dihedral angle to the lone pair), typical values are 2-5 Hz, whereas the trans relation (small dihedral angle) leads to values of 25-25 Hz. The cis, trans methyls are also easily distinguished, of course, by the upfield shifting in the cis isomer that arises from steric compression. The ring 3-position has the usual small value for ^{2}J (1-6 Hz), but a methyl attached to this carbon can be coupled by a larger value. Here the position of the P-substituent makes a difference; a cis orientation is associated with large coupling, whereas trans can be of negligible size (as in **23** *versus* **24**).



23



24

The recently acquired knowledge of the dependence of ^3J on dihedral angles may well be helpful in explaining this situation; the puckered shape of the 4-membered ring, and the preference for a particular conformation that minimizes nonbonded interactions at the P-substituent,[13] can lead to a difference in dihedral angles for an isomer pair. Thus, a cis isomer might prefer conformation **23b** (large dihedral angle) over **23a** in order to minimize 1,3-interactions. A trans isomer must have an appreciable contribution from conformation **24a** (small dihedral angle) to account for the absence of observable coupling.

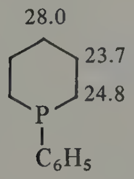
23a **23b**

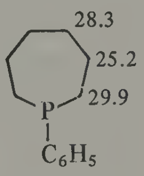
cis

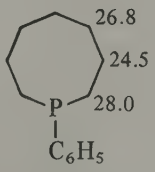
24a **24b**

trans

When the ring is expanded to 7 or 8 members, a greatly increased number of conformations become possible, and the steric relations between ring members and between carbon and the phosphorus substituent can make changes in the chemical shifts of the α,β,γ-carbons from those seen in 6-membered rings. Such changes are small, however, for when a given carbon is examined in a series of compounds[13] all values fall within about a 3 ppm range.





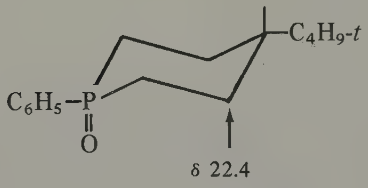


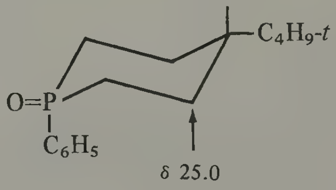
More important is a coupling effect at β-C; the value increases with ring size (^2J: 2.4 → 10.6 → 12.3 Hz). The known sensitivity of ^2J to the lone pair orientation suggests that this angle becomes much smaller in the larger rings. This could come about from a P-substituent exerting a greater demand for an equatorial-like position in the larger rings, whereas the important contribution of axial forms in the 6-membered ring insures a large averaged dihedral angle character to the lone pair orbital. Alternatively, ring puckering may be so different that considerable variation in the β-C to lone pair orbital is present in the series. When more information becomes available on the conformational preferences of the larger rings, the pertinence of these suggestions can be evaluated. ^3J is also sterically controlled, but as has been noted the constraint of ring structure on the γ-carbon seems to interfere with this effect, or to lead to a compensating effect that reduces the coupling expected for the imposed angle. The 6- , 7- , and 8-membered rings all have very similar ^3J values to the γ-carbon in spite of the fact that the shapes of the rings could differ enough to cause wide variation in ϕ.

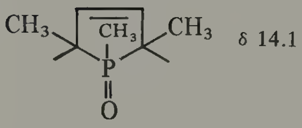
6.3 PHOSPHINE OXIDES

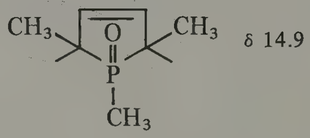
The comparison of acyclic phosphine oxides to phosphines given in Section 6.1 makes it possible to anticipate general changes in chemical shifts and coupling constants, but several effects are noted that are the consequence of cyclic structure.

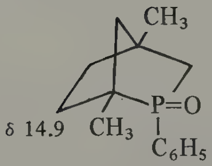
First, upfield shifts at a γ-carbon of phosphorinanes from an axial P-oxygen can be as large as or larger than for an axial P-alkyl group, and the value of the γ-effect as a criterion of cis, trans structure is destroyed. The same is true in other ring systems. Because oxygen is a significantly smaller substituent than alkyl or phenyl, the implication is that more is involved in the γ-effect of a polar group than just steric compression. This is also true in carbocyclic systems.[48]

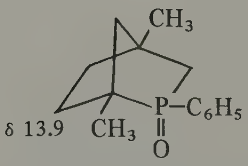




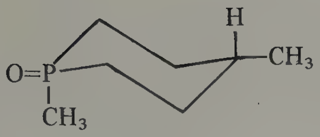






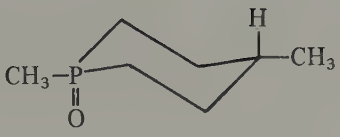


The reciprocal γ-effect on a P-CH$_3$ group remains, however, and the crowded form always gives signals that are upfield by several ppm. This is an extremely useful structural test in a variety of systems, as the selection below shows.

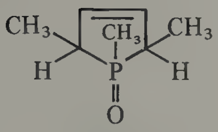


δ PCH_3 = 12.0

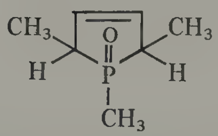
to



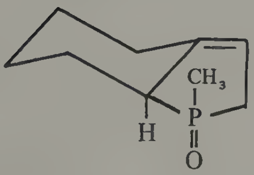
δ PCH_3 = 15.6



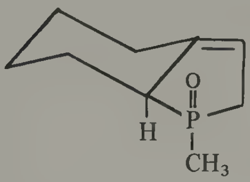
δ PCH_3 = 7.6



δ PCH_3 = 16.0

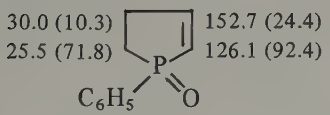


cis, δ PCH_3 = 9.6

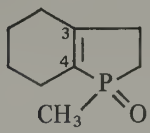


trans, δ PCH_3 = 13.6

Polarization of an α,β double bond is pronounced, with the direction expected for overlap of the π electrons with a d orbital of phosphorus. Thus, the β-carbon is strongly deshielded as a result of the acquisition of positive character.

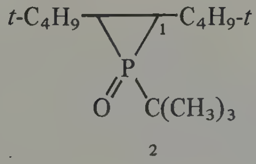


25[49]



δ C-3 = 144.1 (30)[40]
C-4 = 130.3 (85)

As noted for 25 (and true also for rings of 6-9 members) ^1J values to sp^3 carbon are much larger than for phosphines and fall in the range expected from the acyclic systems. This makes detection of α-carbon signals on spectra a relatively simple matter. An additional and striking enhancement of ^1J consistently occurs for sp^2 carbon, reaching values of 90-100 Hz in 2-phospholene oxides. In a 3-membered ring,[50] ^1J is drastically reduced for endocyclic carbons (12.5 Hz in 26) but

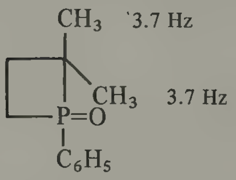


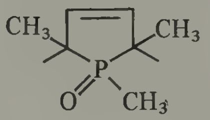
δ C-1 = 37.0 (12.5)
C-2 = 32.7 (64.0)

26

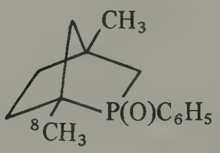
exocyclic carbons have normal values. Shifts for 4-membered rings (50-60 Hz) are only slightly below the range for 5- and 6-membered rings.

Two-bond coupling is small and frequently independent of stereochemistry, and is of little value in structure assignment. Some examples from the tables that indicate the absence of a relation (and emphasize the relevance of the lone pair in the case of phosphines) are given below.



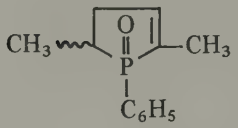


cis CH_3, $^2J = 3.7$ Hz
trans CH_3, $^2J = 4.0$ Hz

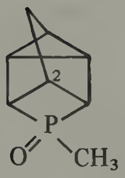


$^2J_{PC\text{-}8} = 0$
in syn and
anti

However, some ^2J values do differ for an isomer pair, and for the few cases known it appears that the more crowded form has the smaller value for ^2J.



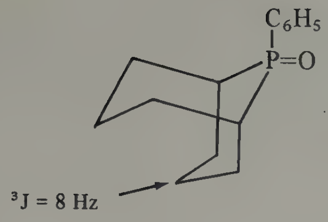
cis CH_3, C_6H_5, $^2J = 0$ Hz
trans CH_3, C_6H_5, $^2J = 4$ Hz



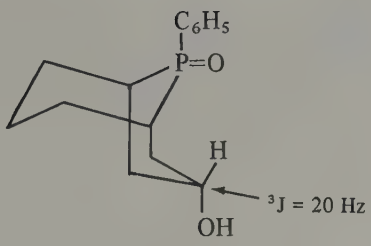
syn-CH_3, C_2 $^2J = 7.1$ Hz[51]
anti-CH_3, C_2 $^2J = 20.1$ Hz

More examples are needed before this can be accepted as a generality, however.

The steric control of ^3J in a regular Karplus relation such as that of Figure 6.2 for $PS(CH_3)_2$ can lead to useful effects in cyclic structures, but some special influences are introduced. A pair of compounds[52] where ^3J seems compatible with the dihedral angle are 27 ($\phi \sim 60°$) and 28 ($\phi \sim 0°$).

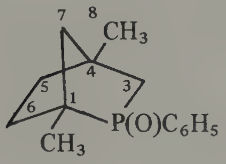


27



28

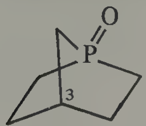
Also in the 2-phosphabicyclo[2.2.1]heptane system (29)[53] the three three-bond couplings present all seem consistent with the dihedral angle relations although the bicyclic structure introduces the complication of two different P-C-C-C pathways to C-5, and of a combination with a two-bond pathway to C-7.



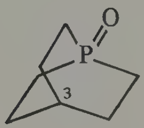
29

^3J	ϕ	endo C_6H_5	exo C_6H_5
PC-7	~ 40°	6	7
PC-5	~ 90°	0 or 6	0
PC-8	~180°	11	13

Multiple coupling pathways appear in other systems and are of yet undefined importance. For example, in the rigid systems[54] **30** and **31**, ^3J has remarkably large values, quite beyond the values expected simply for a situation where the dihedral angle is fixed at 0°.



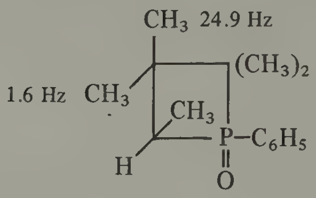
30, $^3J_{PC\text{-}3}$ = 35 Hz



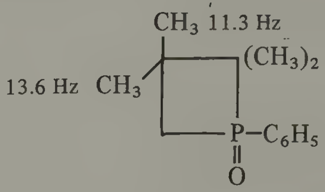
31, $^3J_{PC\text{-}3}$ = 47 Hz

The presence of two three-bond and one two-bond paths in **30** and of three three-bond paths in **31** has been pointed out,[48] but the relevance of this observation to the measured constants is not yet clear. The presence of two three-bond pathways to the γ-carbon of phosphorinane oxides does not lead to any special exaltation, and a typical value (5-7 Hz, Table 6.6) compatible with the dihedral angle of 55°-60° is observed. Incidentally, ^3J to an exocyclic 3-CH_3 (16-17 Hz) in phosphorinane oxides,[32] which would have $\phi \sim 180°$, is quite in line with expectation. In the bridged compounds **30** and **31**, there is present another property that makes them differ from the phosphorinanes: there is considerable rigidity in the systems, and no bond rotation or flexibility due to chair-chair inversion takes place. But again the relevance of this observation to the unusually large coupling for $\phi = 0°$ is unknown.

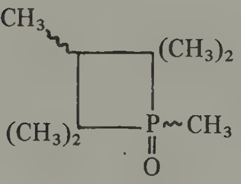
Phosphetane oxides[55] present other cases where the nature of effects controlling ^3J are not certain.



32

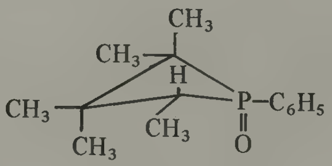


33



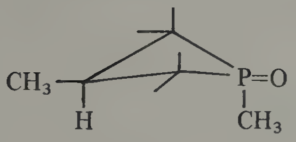
34 cis-1,3 $^3J = 12.6$ Hz
trans-1,3 $^3J = 23.0$ Hz

Thus 3-CH_3 groups can have nearly identical ^3J values (**33**) or differ widely in the same molecule (**32**) or in cis, trans isomers (**34**). The shape adopted by the folding possible in a 4-membered ring seems to be involved[55] in these couplings, as marked deviation from $\phi = 120°$ for a planar ring can occur. In 32 the values suggest that folding creates $\phi > 120°$ for the CH_3 cis to C_6H_5 (140° has been proposed[54]) where ^3J is large and $\phi < 120°$ for trans CH_3 [90° (Ref. 54)] with small ^3J. This results in a conformation such as **32a**. This argument requires that the ring be rigid to maintain the difference between the two methyls relative to P.

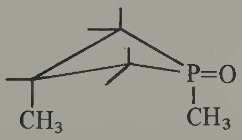


32a

In other phosphetanes, the structure is less clearcut. If it is accepted that the dihedral angle is still the major factor controlling ^3J (which may be incorrect), then it is necessary to assume for some molecules that the 4-membered ring is flexible[55] but that there are definite conformational preferences that lead to excess population of a particular form. An example is **34**, where trans has a ^3J value almost twice the size of cis. To use only the dihedral angle explanation would require trans to have a preference for conformation **35** to give an average of $\phi > 120^\circ$, whereas cis would prefer conformation **36** with averaged $\phi < 120^\circ$. An alternative explanation, that the orientation of substituents on P influences ^3J at a constant ϕ, is no more satisfactory.



35

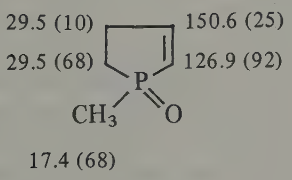


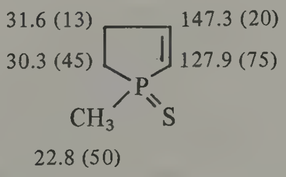
36

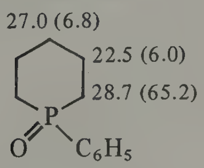
In the larger (7-9) rings, ^3J is routinely small (< 2 Hz) or even negligible, as in the β,β′ diketo derivatives (Table 6.7). Again, if the dihedral angle alone is in control, the implication is that the conformation in solution has ϕ around the Karplus minimum of 90°. No information yet bears on this point, although it is known that for the solid state ϕ varies from a low of 75.6° in the 7-membered ring to 120° in the 9-membered ring.[56]

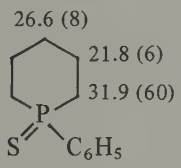
6.4 OTHER PHOSPHORUS FUNCTIONS

Much less information is available on compounds based on other types of phosphorus functions. Phosphine sulfides would be expected to resemble the oxides rather closely, with modification of chemical shifts and coupling constants in the way predicted from the acyclic models. Some examples show the relationship between cyclic sulfides and oxides.

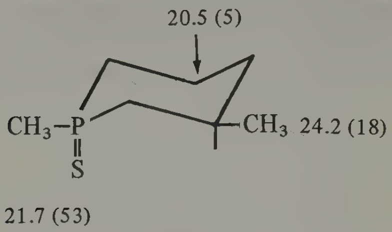




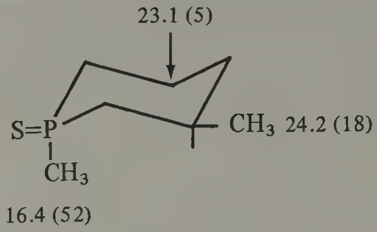




The most obvious difference occurs at the α-carbons, which are always more deshielded in sulfides than oxides and with a smaller ^1J value. Assignments of steric structure to sulfides can be made as easily as with oxides, the 1,3-dimethylphosphorinane sulfides[32] serving as examples.



37a cis

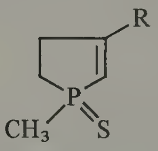


37b trans

Because the C-CH_3 groups have the same chemical shift in the isomers, they are both either axial or equatorial in a heavily favored conformation. But their $^3J_{PC}$ values are only consistent with an equatorial assignment (^3J = 18 Hz requires $\phi \sim 180°$). The configurational difference must occur at P, and this is amply demonstrated from the P-CH_3 signals. That which is the more upfield (δ 16.4 *versus* 21.7) is obviously the sterically crowded axial CH_3 and is present in the trans isomer. Structures such as these and the 1,4-dimethyl isomers show that the γ-effect of axial sulfur on ring carbons exceeds that of axial methyl, a result explainable only on the basis of an effect being active other than steric compression due to group size. This effect is true also for the P-oxides of phosphorinanes.[32] Thus, in **37a**, with axial sulfur, ring position 5 is upfield of **37b** with axial CH_3 by 2.6 ppm. It has already been pointed out that polar substituents on cyclohexane have exalted γ_{gauche} effects,[48] possibly for a reason, yet to be identified, in common with the polar P-substituents.

Cyclic phosphonium salts present no new shift or coupling features, and have modifications in these parameters in accord with trends seen in the acyclic models. The characteristic shielding that occurs on the α-carbon by quaternization is quite noticeable, and in a given series one generally finds α-C shifts decreasing in the order sulfide, oxide, phosphonium ion. The steric control of ^3J is present in salts and useful as always in proving structures. Phosphetanium salts have been especially well studied in this regard.[55]

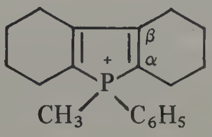
A series of α,β-unsaturated phosphine sulfides[57] shows a definite dependence of one-bond coupling on the electron density of the α-carbon. In the structure 38, values for ^1J were the following: R=H, 75 Hz; R=CH_3O, 92 Hz; R=$(CH_2CH_2)_2N$, 100 Hz. A similar trend has been noted in acyclic β-substituted vinylphosphonium salts[58] and has been attributed to sharing of the electron density with d orbitals.



38

The ^2J value to the β-carbon also is influenced by the substituent: values varied from 20 Hz (R=H) to 47 Hz (R = $(CH_2CH_2)_2N$). Such values as the latter are extremely large for ^2J.

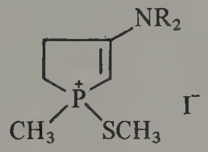
Positive phosphorus without any occupation of d-orbitals by back bonding from heteroatoms has the potential for acting as the strongest acceptor of π-electrons from a C-C double bond, but a series of comparative cyclic structures testing this possibility is not yet available. Certainly the strong deshielding at the β-carbon of phospholium ion **39**[59] attests to the operation of the anticipated strong electronic effect.



δ β-C = 157.1 (22)
δ α-C = 122.9 (79.2)

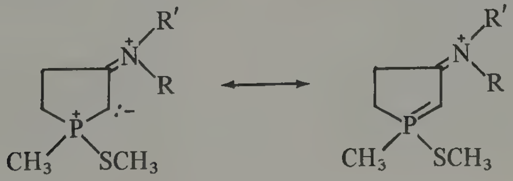
39

Strongly increased polarization of the C-C double bond occurs when an electron releasing group is simultaneously present on the β-carbon. A series of compounds with positive phosphorus containing a methylthio group conjugated with an enamine group (**40**) shows some striking effects because of this electron interaction.[57]



40

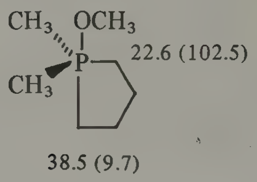
Using data for the 3-pyrrolidino derivative reported in Table 6.5, it is seen that the α-sp^2 carbon absorbs at the remarkable upfield value of 62.3 ppm due to electron release from N, with the β-carbon at 166.5 ppm from the electron withdrawal effect of both N and the phosphorus function. The net effect is to spread the sp^2 carbons out by the extraordinary value of 104 ppm! In addition, the C-N double bonding that develops is of such a magnitude as to restrict free rotation at room temperature, causing the α-carbons of the pyrrolidine ring to become nonequivalent. A coalescence temperature of about 97° with $\Delta G^{\neq}$ = 18.7 kcal/mole was observed for these carbons. To adequately express the degree of resonance interaction involved, forms **40a** and **40b** have been proposed to make important contributions.



40a **40b**

These methylthiophosphonium salts have the same very large ^{2}J value (42 Hz) for the β-sp^2 carbon as seen in the corresponding phosphine sulfides.

Only recently have ^{13}C data been published[60] for cyclic P(V) functions, of form R_4POR. Phospholane derivative **41** was assigned a trigonal bipyramidal structure at −50° with axial oxygen and the ring carbons axial-equatorial, in accord with the observation of nonequivalence of the two α- carbons of the ring.

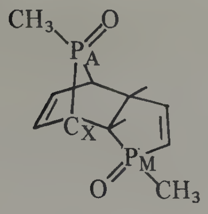


41

This system has an incredibly large difference in $^1J_{PC}$ to the ring α-carbons, which of course are attached to P by orbitals with different degrees of s-character. This phenomenon for ^{13}C has been observed for a number of acyclic P(V) compounds containing CF_3 groups in apical or equatorial positions.[63] The α-carbon in the equatorial position of **41** has $^1J_{PC}$ nearly the same as for the two equatorial CH_3 groups ($^1J_{PC}$ = 107.4 Hz). On raising the temperature, the spectrum changes as molecular motion (pseudorotation) sets in to cause equilibration of the two α-carbons. At +60°, only one signal (δ 31.9, with an averaged $^1J_{PC}$ of 56.1 Hz) is observed. Similar observations were made for the corresponding phosphorinane derivatives. These experiments demonstrate clearly the value of dynamic ^{13}C NMR in phosphorus chemistry, a capability that surely can be extended to other cyclic systems involved in mobile conformational equilibria.

6.5 DIPHOSPHORUS COMPOUNDS; SECOND-ORDER ^{13}C SPECTRA

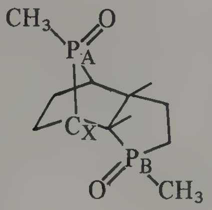
When two (or more) phosphorus functions are present in a molecule both may couple to the same carbon if each is within 3-4 bonds of the carbon. Three situations arise: (1) The phosphorus functions are chemically nonequivalent and have substantially different ^{31}P shifts; the spin system is then AMX, where A and M are ^{31}P and X is ^{13}C. The ^{13}C spectrum is a doublet of doublets. There is no visible effect of the coupling on the ^{31}P signal because of the low abundance of ^{13}C nuclei. This situation is present in all of the dimers of P(IV) phospholes,[62] as in the selected example 42.



42

$\delta\ ^{31}P_A = +9.14$
$\delta\ ^{31}P_M = +61.8$
$\delta\ ^{13}C_X = 42.4$
$^3J_{AM} = 35.0$ Hz
$^1J_{AX} = 60.3$ Hz
$^2J_{MX} = 2.6$ Hz

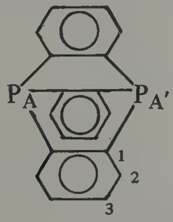
(2) The phosphorus nuclei are chemically nonequivalent but have a small difference in ^{31}P chemical shifts ($\Delta\delta$ less than 5-10 times the size of J). The ^{31}P spectrum will become second order (AB, as discussed in Section 5.9), and the coupling to ^{13}C produces an ABX spectrum. In this case the ^{13}C spectrum could theoretically consist of six lines arranged symmetrically, the outer two being quite weak and not always observable. The coupling constants cannot be derived from simple inspection but can be calculated from the data, or obtained from a computer simulation approach. An example[62] of such a spectrum is provided by the hydrogenation products of the phosphole dimers; here the ^{31}P shifts lose the large $\Delta\delta$ so characteristic of the directly formed dimer system and give second-order ^{31}P and ^{13}C spectra unless run at high field. The ^{13}C signal of C_X of **43**, for example, at 15 MHz is a pair of doublets with the outer lines being of greater intensity; the *apparent* J_{BX} is 10.2. At 75 MHz, the spectrum is nearly first order and provided the coupling data below.



43

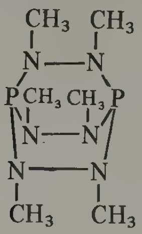
$\delta\ ^{31}P_A = +68.8$
$\delta\ ^{31}P_B = +67.1$
$\delta\ ^{13}C_X = 38.2$
$^3J_{AB} = 43.0$ Hz
$^1J_{AX} = 64.4$ Hz
$^2J_{BX} = 1.5$ Hz

(3) The ^{31}P nuclei are chemically equivalent but magnetically nonequivalent through mutual coupling to a given ^{13}C by different magnitudes. Several examples are known, a particularly informative one being provided by the diphosphatriptycene system.[31] The observed spectrum consists of 11 lines.

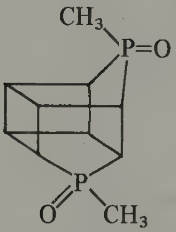


C-1: pseudotriplet, $^1J_{P_{A'}C} = -7.6 \pm 2.0$, $^2J_{P_AC}$ = not assigned
C-2: five lines, $^2J_{P_{A'}C} = +44.1 \pm 0.6$, $^3J_{P_AC} = +1.8 \pm 0.6$.
C-3: pseudotriplet, $^3J_{P_{A'}C} = +12.5 \pm 2.0$, $^4J_{P_AC} = -0.1 \pm 2.0$

Other examples are



(Ref. 63) The N-CH_3 signals are pseudotriplets in an AA′X spectrum.



(Ref. 64) The phosphorus groups are chemically equivalent, but the P-CH_3 signal is a pseudotriplet in an AA′X spectrum. The unusual feature of 4-bond coupling to CH_3 in the unit P-C-C-P-CH_3 must be present to produce this result.

6.6 EXPERIMENTAL TECHNIQUES AND TABLES OF ^{13}C NMR DATA

In the foregoing sections, assignments of signals as proposed by numerous authors have been accepted largely without development of the thinking behind them. It should be obvious, however, that sound knowledge of chemical shift effects and coupling phenomena will provide an excellent basis for approaching the interpretation of a spectrum. Depending on the presence of P(III) or P(IV) character, definite ranges for each parameter can be expected, with the usual influences of any substitution by other functionalities. They are, however, some special aids to interpretation that are sometimes necessary for complex spectra.

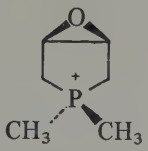
1 The usual device of running the spectrum with full or partial proton-coupling will aid in recognizing the number of protons on a carbon. Each component of a doublet from P-C coupling will acquire the extra splitting.

2 Frequently it is not clear if two lines constitute a doublet or arise from different carbons, and peak merger, complete or partial, can occur from the added complexity of signal splitting. In these cases, running the spectrum at a different magnetic field on another instrument can be of great help. The usual rule that coupled signals remain separated by the same frequency applies, of course, and doublets became more recognizable, especially at high field, where resolution is improved.

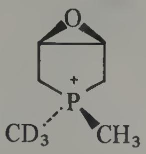
3 Selective replacement of a proton by deuterium will cause the ^{13}C signal to change appearance. As C-D coupling will remain when C-H coupling is elimi-

nated, the ^{13}C signal is split (I = 1 for D) and loses intensity because the nuclear Overhauser effect provided by H decoupling is lost. The net result can be the virtual elimination of the signal for the spectrum. A CD_3 group is a case in point; quaternization of a phosphine with CD_3I gives a salt whose FT spectrum prepared with normal accumulations shows no signal for the added group. This effect has been used to advantage to differentiate between two CH_3 groups on positive phosphorus that differ because of rigid molecular geometry; when phosphine **42** was obtained by deoxygenation of the phosphine oxide,[65] it was not known if epoxy oxygen was syn or anti to the CH_3 group, but it was known that quaternization gave a salt (**43**), with two different CH_3 signals (δ 10.4 and 13.7). By quaternizing with CD_3I, a salt (**44**) with δ P-CH_3 = 13.9 was obtained, implying that the original CH_3 group gave the downfield signal in the salt and that it must be syn to O, because δ-deshielding by *syn*-epoxides is a known phenomenon.

42



43



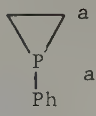
44

4 ^{13}C Spin-lattice relaxation times can be quite different for carbons in the ring or as methyl ring-substituents, as was pointed out clearly in a study of phosphetanes.[66] In this system, ring carbons with protons had relatively short T_1 values (0.6-4.0 sec) whereas fully methylated carbons had longer values (8-18 sec). Restrictions to internal rotations of C-methyl groups can lead to different T_1 values; in this system, a crowded methyl had a longer T_1 than an uncrowded, pseudoequatorial methyl. Such effects, when more fully studied and conducted with model systems of known geometry, could prove extremely useful in the stereochemical examination of other phosphorus heterocyclic systems.

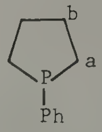
5 Carbon signals in congested areas of a spectrum may be spread out with the use of pseudocontact complexation with the lanthanide shift reagents. Phosphoryl groups respond better to this technique than phosphines. Little use has been made of it so far in ^{13}C NMR of phosphorus compounds, but the potential for resolving complex spectra is certainly high.

Tables 6.5-6.7 provide representative data on a wide selection of cyclic phosphorus compounds. For consistency, all data are based on the use of tetramethylsilane as reference. Solvents are not specified; effects are generally small, but not necessarily negligible, and for precise comparisons of the data the original literature should be examined for the medium used.

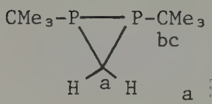
TABLE 6.5 ^{13}C NMR of Selected Heterocycles with Five or Fewer Members



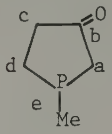
a	11.0(39.7)[13]



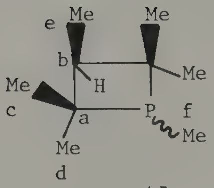
a	27.2(14)[13]
b	27.7(4.7)



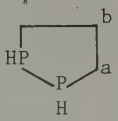
a	6.2(53.0)[46]
b	25.9(s)
c	29.7(s)



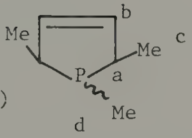
a	39.0(17.7)[69]
b	210.2(6.3)
c	34.5(4.2)
d	19.6(10.4)
e	9.6(20.8)



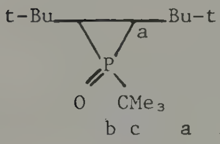
	cis[47]	trans
a	28.6(6.5)	26.4(7.7)
b	51.1(2.9)	51.4(3.3)
c	19.2(4.3)	25.1(30.5)
d	32.5(26.9)	25.0(2.1)
e	8.7(8.9)	9.3(s)
f	5.2(37.9)	6.7(33.7)



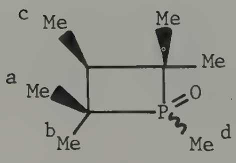
a	24.0(20.9)*
b	34.7(6.6)[70]



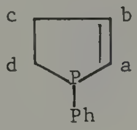
	cis[38]	trans
a	38.2(12.2)	43.4(9.8)
b	134.5(4.9)	134.1(3.7)
c	13.9(s)	21.0(28.1)
d	0.5(24.4)	12.8(18.6)



a	37.0(12.5)[50]
b	32.7(64.0)
c	25.6(1.5)

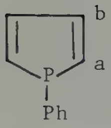


	cis[47]	trans
a	19.8(10.0)	17.3(6.3)
b	24.7(4.4)	24.7(4.6)
c	9.7(12.6)	7.3(23.0)
d	11.5(36.9)	9.8(40.9)

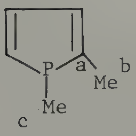


a	129.3(16)[25]
b	142.9(1.8)
c	34.2(5.4)
d	25.9(10.2)

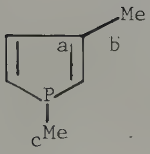
TABLE 6.5 continued



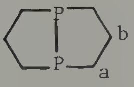
a**	135.1(5.2)[25]
b**	136.7(8.2)



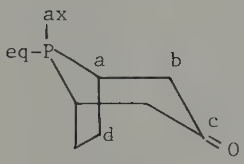
a	151.5(5)[41]
b	15.4(22)
c	6.8(19)



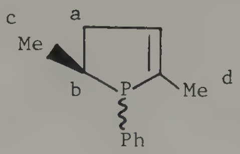
a	146.8(4)[41]
b	18.6(5)
c	6.8(20)



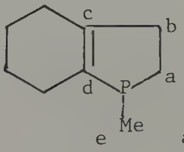
a	30.3(31.5)[70]
b	29.9(9.3)



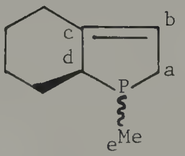
	eq. Ph[71]	ax. Ph
a	36.2(12)	33.2(s)
b	49.1(16)	46.2(s)
c	210.0(s)	210.4(s)
c	29.6(6)	28.2(24)



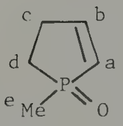
	cis[39]	trans
a	41.8(6)	42.3(s)
b	33.5(6)	38.5(4)
c	15.1(s)	20.2(25)
d	17.4(19)	16.8(18)



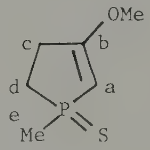
a	25.0(21)[42]
b	37.6(4)
c	144.4(s)
d	134.0(2)
e	12.7(18)



	cis[40]	trans
a	33.2(13)	33.8(10)
b	120.7(3)	119.2(3)
c	144.0(3)	146.7(3)
d	44.0(15)	51.5(10)
e	9.2(23)	14.6(18)

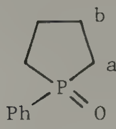


a	126.9(92)[73]
b	150.6(25)
c	29.5(10)
d	24.5(68)
e	17.4(68)

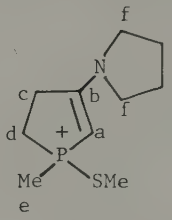


a	91.2(92)[73]
b	171.6(40)
c	30.4(s)
d	29.9(60)
e	25.0(50)

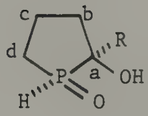
TABLE 6.5 continued



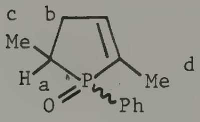
a 30.3(66.8)[47]
b 25.7(7.9)



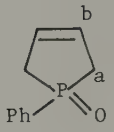
a 62.3(107)[57]
b 166.5(42)
c 30.6(s)
d 22.3(55)
e 16.8(59)
f 48.2,49.3



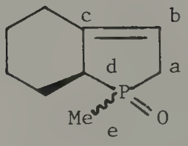
a 69.4(72.1)[74]
b 33.8(16.2)
c 20.3(7.4)
d 26.6(64.7)



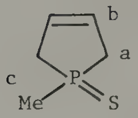
	cis[39]	trans
a	32.1(72)	29.8(72)
b	36.3(13)	36.2(11)
c	11.7(s)	12.4(4)
d	12.0(10)	11.5(11)



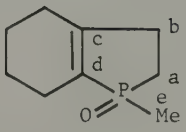
a 33.5(67.4)[49]
b 128.1(11.7)



	cis[40]	trans
a	30.1(65)	31.4(60)
b	113.8(12)	112.9(11)
c	143.5(14)	144.6(13)
d	40.8(70)	39.9(68)
e	9.6(63)	13.6(63)

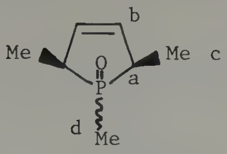


a 38.9(55)[73]
b 127.6(10)
c 20.6(50)

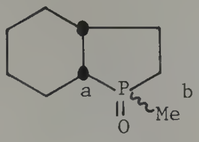


a 24.8(65)[39]
b 28.5(10)
c 144.1(30)
d 130.3(85)
e 15.9(70)

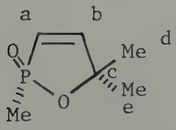
TABLE 6.5 continued



	cis[47]	trans
a	39.0(64.9)	36.9(65.4)
b	133.5(14.3)	133.8(13.4)
c	14.1(3.7)	14.9(4.0)
d	7.6(58.8)	16.0(59.7)



	α-Me[40]	β-Me
a	39.8(70)	38.1(70)
b	13.7(60)	17.3(60)

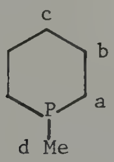


a	114.5(159)[75]
b	156.8(15)
c	85.3(10)
d	27.4(0)
e	26.6(0)

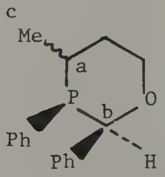
*(^1J + ^2J), AA'X.

**May be reversed.

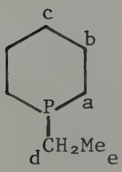
TABLE 6.6 ^{13}C NMR of Selected Heteorcycles with Six Ring Members



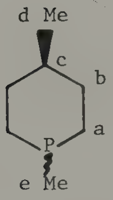
a	26.7(13)[28]
b	23.4(3)
c	28.3(2)
d	10.9(19)



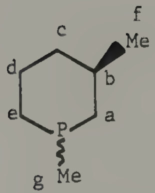
	cis,cis[33]	cis,trans
a	28.8(12.7)	25.9(13.2)
b	81.2(23.5)	76.8(28.0)
c	18.0(24.9)	19.2(∿10)



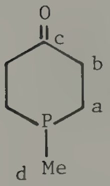
a	24.9(14)[28]
b	23.7(4)
c	28.4(3)
d	20.1(14)
e	9.7(16)



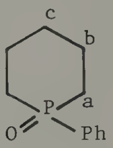
	cis[32]	trans
a	22.7(14)	28.5(11)
b	28.5(s)	33.3(6)
c	34.1(s)	34.2(s)
d	23.5(s)	22.9(s)
e	5.7(20)	13.8(18)



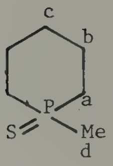
	cis[32]	trans
a	32.0(8)	31.4(10)
b	37.1(3)	36.2(2)
c	37.8(s)	38.3(s)
d	25.5(8)	20.4(2)
e	28.5(10)	26.2(12)
f	25.2(5)	26.2(2)
g	14.3(16)	6.8(18)



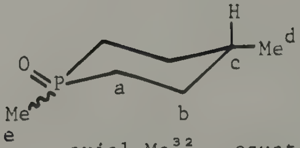
a	23.8(14)[72]
b	36.3(<2)
c	20.9(<2)
d	7.9(18)



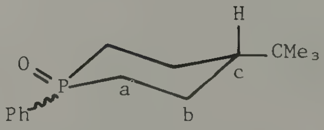
a	28.7(65.2)[47]
b	22.5(6.0)
c	27.0(6.8)



a	32.7(49)[28]
b	22.4(6)
c	26.2(8)
d	18.5(53)

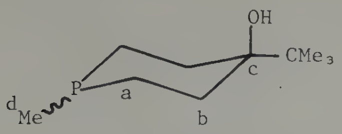


	axial Me[32]	equat.
a	28.5(63)	27.6(62)
b	32.1(6)	29.0(7)
c	32.5(5)	32.3(5)
d	21.7(0)	21.7(0)
e	12.0(65)	15.6(66)

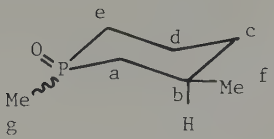


	axial Ph[30]	equat.
a	27.6(64.8)	28.7(64.2)
b	25.0(3.8)	22.4(5.8)
c	48.1(s)	49.0(s)
d	130.1 (75.0)**	133.3 (94.9)**

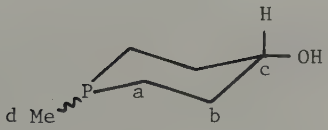
TABLE 6.6 continued



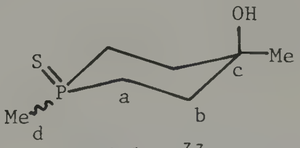
	equat.[20]	axial
a	23.6(10)	17.8(12)
b	29.4(7.5)	23.8(s)
c	76.6(1-2)	74.6(1-2)
d	13.6(12)	4.4(16)



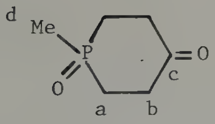
	axial[30]	equat.
a	37.3(63)	36.6(62)
b	31.5(4)	28.1(6)
c	34.5(6)	35.3(6)
d	22.9(4)	20.6(7)
e	28.1(65)	27.4(66)
f	24.3(17)	24.6(16)
f	12.3(66)	16.2(68)



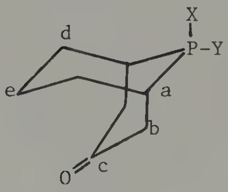
	equat.[20]	axial
a	24.2(10)	21.7(10)
b	32.3(4)	29.4(s)
c	70.2(s)*	69.6(s)*
d	11.3(14)	6.7(14)



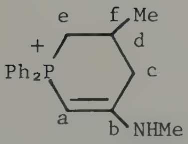
	axial Me[77]	equat.
a	30.2(50)	28.9(52)
b	37.0(4)	35.1(6)
c	69.8(6)	70.3(8)
d	17.1(50)	21.3(54)



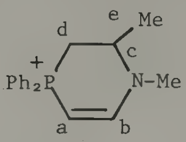
a	23.3(65)[72]
b	32.8(7)
c	204.9(7)
d	11.5(68)



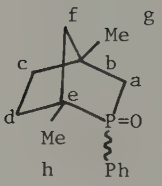
	Y=O[52] X=Ph	Y=Ph X=O
a	30.8(62)	29.3(62)
b	42.8***	44.9***
c	208.3(7)	207.0(7)
d	29.1***	27.0***
e	17.1***	18.2***



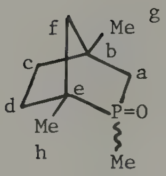
a	51.1(114.7)[78]
b	165.7(13.2)
c	25.6(2.9)
d	37.2(4.4)
e	27.5(54.4)
f	22.5(14.7)



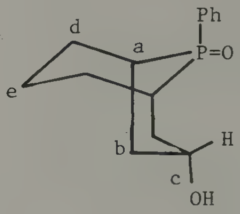
a	55.5(98.2)[78]
b	155.6(0)
c	50.2(5.9)
d	23.6(54.4)
e	16.7(5.9)



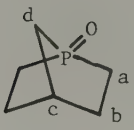
	endo[53]	exo
a	40.0(59)	41.5(59)
b	43.8(0)	43.2(0)
c	37.5(0)	36.9(0)*
d	31.5(4.5)*	31.1(0)*
e	43.4(68)	45.2(68)
f	50.1(12)	50.4(8)
g	24.1(12)	23.5(12)
h	14.9(0)	13.9(0)



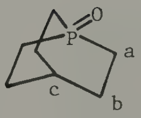
	endo[53]	exo
a	41.1(60)	44.7(56)
b	43.6(0)	43.5(0)
c	37.4(0)*	36.8(0)*
d	30.4(6)*	32.3(0)*
e	44.4(68)	44.4(68)
f	50.6(6)	49.4(7)
g	24.3(11)	23.8(13)
h	14.0(0)	14.2(0)



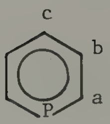
a	27.6(63)[52]
b	34.5***
c	61.4(20)
d	30.8***
e	15.6



a	18.8(63)[54]
b	28.6(4)
c	27.4(35)
d	28.5(64)

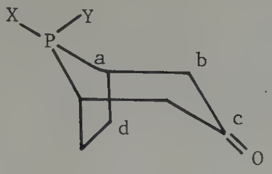


a	20.9(63)[54]
b	27.4(5)
c	22.3(47)

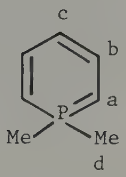


a	154.1(53)[43]
b	133.6(14)
c	128.8(22)

TABLE 6.6 continued



	X=Ph[71] Y=O	X=O Y=Ph
a	30.2(65)	31.8(66)
b	44.9(5)	47.3(3)
c	207.7(6)	206.9(6)
d	23.5(15)	25.9(7)



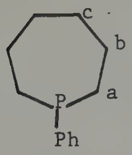
a	67.5(94)[79]
b	139.2(s)
c	94.0(22)
d	24.7(57)

*Assignment uncertain.

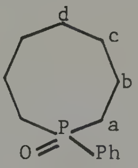
**Ipso carbon.

***Coupling not reported.

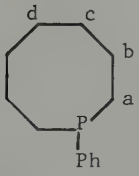
TABLE 6.7 ^{13}C NMR of Selected Large-Ring Heterocycles



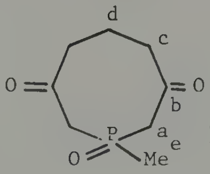
a	29.9(15.0)[13]
b	25.2(10.6)
c	28.3(4.6)



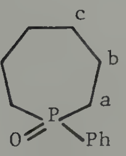
a	29.3(65.5)[13]
b	20.2(4.6)
c	27.2(1.9)
d	23.4(0.5)



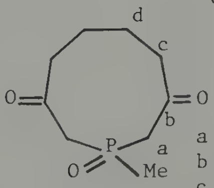
a	28.0(17.0)[13]
b	24.8(12.3)
c	26.8(5.3)
d	25.5(2.1)



a	45.3(48.8)[80]
b	204.5(4.9)
c	45.6(0)
d	19.0(0)
e	14.7(70.8)

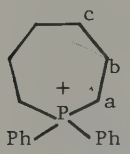


a	31.8(65.0)[13]
b	21.7(4.5)
c	29.6(1.2)

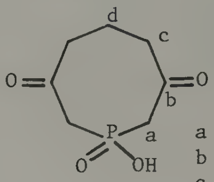


a	46.1(54.7)[80]
b	206.0(4.9)
c	44.5(0)
d	23.4(0)
e	19.2(72.3)

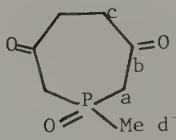
TABLE 6.7 continued



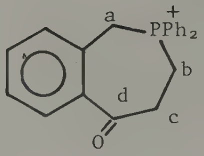
a 22.9(49.9)[13]
b 22.1(1.5)
c 27.7(1.4)



a 47.4(77.2)[78]
b 205.8(2.9)
c 42.5(s)
d 23.0(s)



a 49.2(50.1)[80]
b 202.8(4.9)
c 38.5(0)
d 16.2(70.8)



a 24.6(47.6)[81]
b 13.8(56.0)
c 34.8*
d 200.0*

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*Coupling not reported.

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chapter seven

Proton NMR Spectroscopy of Cyclic Phosphorus Compounds

Structural analysis of phosphorus compounds by proton NMR spectroscopy commenced in the 1950s immediately upon the introduction of commercially available instrumentation, and a vast number of compounds have now been examined. The correlation of structural features with chemical shifts, the recognition of influences on coupling parameters, and the development of methods for dynamic and conformational studies have progressed much more rapidly in this area of NMR than in ^{31}P or ^{13}C NMR. Excellent reviews[1,2] exist on the subject and extensive tables of references to data have been published.[2] Heterocyclic compounds are abundant in these tables, and discussion of their spectra is included in this review. Consequently, the treatment of the subject given in this chapter need not start with a background but can proceed immediately to the consideration of cyclic compounds. Emphasis is placed on the special effects that result from the presence of ring structure, especially those due to conformational and stereoisomerism properties and to electron delocalization phenomena. Only selected examples are taken from the huge literature, and unlike the treatment of ^{31}P and ^{13}C NMR no extensive tabulation of data is provided.

Most of the published chemical shift data use the delta scale, referenced to tetramethylsilane as 0 ppm. Published data based on the tau scale have been recalculated in this chapter for consistency. Unless required for a particular reason, relative signs of coupling are not mentioned even when known, and only absolute values are quoted. Generalities do exist for ^{31}P-^{1}H coupling signs, however, and may be applied with reasonable certainty to the absolute values for particular atomic pathways and phosphorus functionalities. These are gathered in Table 7.1. For expediency, the solvent is not specified in the NMR data quoted in this chapter; the majority of spectra were run in $CDCl_3$, and in general solvent effects are not common. However, it is known that benzene and aromatic solvents sometimes form collision complexes with polar functional groups that can cause pronounced changes in chemical shifts. Examples of this are noted in the discussions to follow. Also, strongly hydrogen-bonding solvents, especially water and alcohols, can influence phosphoryl functions and modify their shift effects. Finally, a pronounced difference (downfield) in shifts can accompany the use of an external TMS standard (in a capillary tube) rather than the more common internal standard. Shift differences of 0.5-1.0 ppm can be caused by this change in technique.

Dynamic NMR measurements are generally not included in this discussion. To do so would have extended its length, and the decision was made to keep the discussion focused on the interpretation of spectra and their application in establishing molecular structure. Some examples, however, are provided in Chapter 8.

In the following presentation of examples of NMR data for particular structural features, it is to be understood that the δ value is given simply as the number, and J_{PH} is indicated by enclosure in parentheses. Additional ^1H-^1H coupling is specified where it is present.

TABLE 7.1 Signs of ^1H-^{31}P Coupling[a]

Compound	$^1J_{PH}$	$^2J_{PH}$	$^3J_{PH}$
R_2PH	+	+	+
R_3P		+	+
$R_3P(O)$		–	+
$R_3P(S)$		–	
$R_2P(O)OR$			+
$R_2P(O)H$	+	–	
$R_3\overset{+}{P}H$	+	–	+
R_4P^+		–	

[a] Taken from the information of Ref. 2.

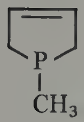
7.1 CHEMICAL SHIFTS AND COUPLING CONSTANTS FOR PROTONS OF P-ALKYL SUBSTITUENTS

The majority of P heterocycles have exocyclic alkyl or aryl groups on phosphorus; rarely is a P-H bond encountered. Aryl groups have received little attention because of the bunching and complexity of the signals, and in routine NMR spectroscopy they are usually ignored and reported as a "complex multiplet." P-Alkyl signals, however, are generally easily recognized on spectra, and this study starts with them.

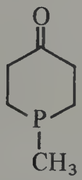
7.1.1 P(III) Compounds

Methyls on P(III) are generally the most upfield signals on a spectrum (δ 0.7-1.0) and stand out clearly as doublets with the usual[2] small two-bond coupling constant

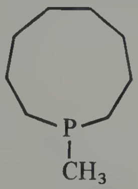
(2-4 Hz) characteristic of noncyclic phosphines [e.g., $(CH_3)_3P$ has $^2J = 2.7$ Hz]. These characteristics are not influenced by ring-size, ring substituents, or unsaturation (unless α-β, vide infra).



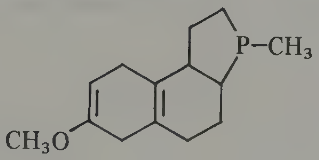
0.82 (3.5)[3]



0.76 (3.2)[4]

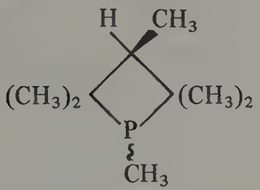


0.96 (3.5)[5]

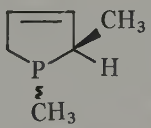


0.99 (3)[6]

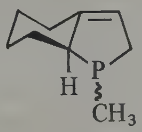
Small differences do exist in a pair of cis, trans isomers:



cis, 0.93(3)[7]
trans, 1.09(3)



cis, 0.73(4)[8]
trans, 0.83(4)



cis, 0.73(3.5)[9]
trans, 0.88(3.5)

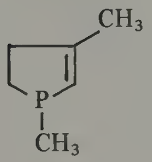
1

axial 0.89(4) in benzene[10]
equatorial 0.95(2.1)

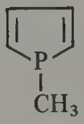
In the 4- and 5-membered rings, the effect seems to be consistent that the more crowded isomer gives the upfield P-CH_3 signal. The data given above for a phosphorinanol (1) may suggest the same relation, but as the signals are not distinguishable unless an aromatic solvent is used, it appears that more is involved (solvent collision complex with the axial OH group) than simply the disposition of the P-CH_3. In fact, when the conformers of 1-methylphosphorinane are frozen out at 154°K it is found that the axial P-CH_3 is downfield of the equatorial by 0.09 ppm.[11] In any case, the effect is small and ^{13}C NMR of P-CH_3 groups is far more useful for cis, trans assignments than is ^1H NMR. Of greater interest is the variation of $^2J_{PH}$ for P-CH_3 groups of phosphorinanes, where it is consistently found[4,10,11] that the axial CH_3 has the larger value. As will be discussed in Section 7.2, $^2J_{PH}$ in phosphines is under strong steric control; the orientation of the lone pair to the proton is important, and it may be that conformational differences in the

6-membered ring can cause slight modification of this orientation by inducing different populations of rotameric forms.

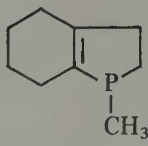
A definite interaction takes place between P(III) and an α,β-double bond in cyclic compounds,[12] and a downfield shift of P-CH_3 relative to the range seen for saturated systems is a consequence.



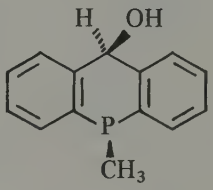
2, 1.23 (2.8)[13]



3, 1.38 (~0)[14]



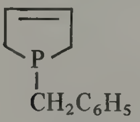
1.09[15] (~0)



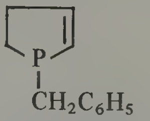
4, 1.75 (2.5)[16]

An explanation has been advanced[13] for this deshielding in 2-phospholenes on the basis that phosphorus can develop some positive character from p_π-p_π interaction with the double bond, a notion finding general acceptance in the phosphole system (Chapter 8). Other effects must also be considered, especially the diamagnetic consequence in the phosphole system (3) of a ring current, and of the benzene ring currents in 4. In the latter, extra deshielding may also be contributed by the *cis*-OH group, held in close proximity in a boat conformation (see Section 7.5). The diminished $^2J_{PH}$ value in the phospholes seems to be quite characteristic of this system, and a number of such compounds show values in the 0-2 Hz range.[17]

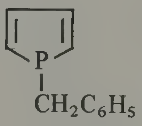
P-Benzyl groups also give clearly recognizable doublets in P(III) compounds. On the 5-membered ring, the coupling is weak or not noticeable:



2.60 (s)[17]

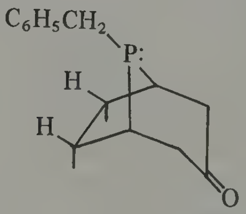


2.76 (broad s)[17]



3.01 (s)[17]

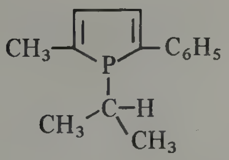
The downfield shift of α,β-unsaturation is evident in these compounds, as it was for the P-CH_3 series. In a quite different type of heterocycle (5), a very large $^2J_{PH}$



5

value (14 Hz) is reported[18] for the benzylic protons. Such a large value is common at ring protons, as will be discussed, due to a conformational influence. Although such an effect may operate here, it would be desirable to insure the prevalence of such large ^2J values in related compounds where restricted rotation may be present.

The α-CH signals for longer alkyl chains are not always distinguishable from ring C-H signals, unless unsaturation is present to create a different environment. The same is true of CH signals on more distant chain positions, and little practical use has been made of their spectral properties. A prominent exception is the phosphole system, where no saturated ring carbons are present. This has allowed a detailed variable temperature study[19] of the diastereotopic methyls of P-isopropyl groups in unsymmetrically substituted phospholes, such as **6**, where loss of nonequivalence of the CH_3 groups is attributed to the inversion of the pyramidal phosphorus. This led to $\Delta G^{\neq}$ value for phospholes that were remarkably small relative to phosphines. The significance of this experiment in phosphole chemistry is discussed in Chapter 8.

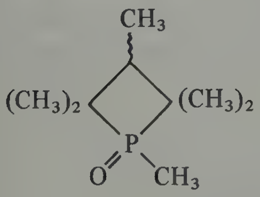


6

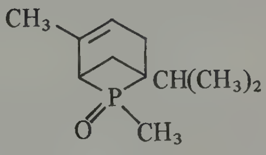
at 42°: both CH_3 δ 1.12 ($^3J_{PH}$ = 13.5, $^3J_{HH}$ = 7.0)
at 0.8°: δ CH_3 = 1.02 ($^3J_{PH}$ = 13.9) and 0.85 ($^3J_{PH}$ = 12.2)

7.1.2 P(IV) Compounds

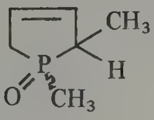
When P(IV) groups are present, α-CH signals are shifted downfield from those of the P(III) counterparts, and the magnitude of $^2J_{PH}$ is greatly increased. The latter value is remarkably constant (12-15 Hz) for CH_3 exocyclic on P=O, P=S, and phosphonium groups. Some typical heterocycles below illustrate these parameters. Steric effects on P-CH_3 are generally small or nil, and these signals are not very reliable for cis, trans assignment purposes. P-Methyl signals are generally very sharp doublets that stand out clearly on spectra.



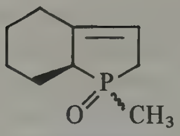
1.56 (11.5)[20]



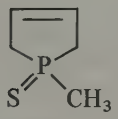
1.63 (12)[21]



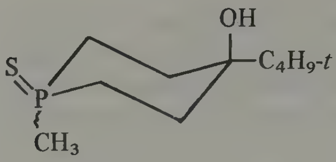
cis 1.33 (12.5)[8]
trans 1.34 (12.5)



cis 1.46 (13)[9]
trans 1.58 (13)

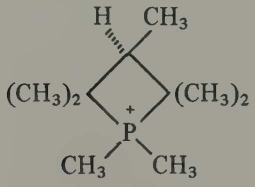


1.82 (13)[22]

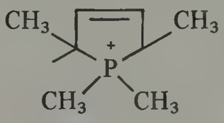


7, axial CH$_3$ 1.75 (13.5)[23]
equatorial 1.79 (14.0)

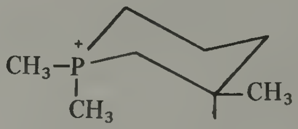
In quaternary salts with two P-CH$_3$ groups, steric differences can cause the CH$_3$ doublets to appear at different field (as in **8** and **9**) but this is not always the case (as in **10**).



8, 2.09 (14.0) and
1.99 (14.0)[20]

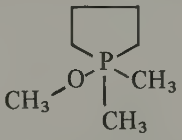


9, 1.98 (14.7) and
1.94 (14.3)[24]



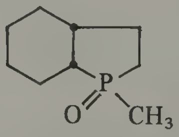
10, both 1.95 (13)[25]

Few cases of P-CH$_3$ groups on P(V) are known, but from the data[26] for **11**, it is apparent that values very similar to P(IV) can be expected.

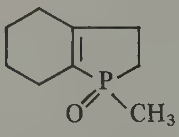


11, 1.80 (13.5)

α,β-Unsaturation seems to release electron density to P(IV) via p_π-d_π overlap, and consequently diminished deshielding of α-CH on chains should be experienced from this effect. On the other hand, a magnetic effect (deshielding) should be felt on P from the field of the π-electrons, and of course conformational changes are experienced as well. The net result on P-alkyl groups is not easily predicted, and few experimental data are available for saturated *versus* α,β-unsaturated counterparts to assess the true effect. Upfield shifting by unsaturation is exhibited in phosphine oxides **12** and **13**.

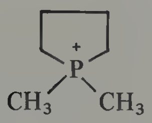


12, cis, 1.57 (13)[9]
trans, 1.62 (13)

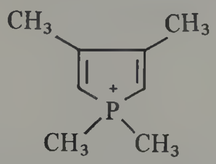


13, 1.48 (13)[9]

On the other hand, downfield shifting is apparent on comparing salts **14** and **15**.



14, 2.57 (15)[27]
in D_2O,
external TMS



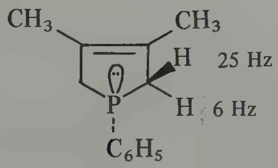
15, 3.05 (15)[28]
in $CDCl_3$,
external TMS

It is not yet possible to draw any conclusions on the generality of the result on P-CH_3 from conjugation of P(IV) groups.

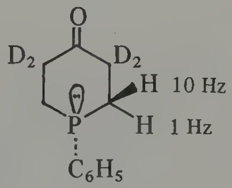
7.2 PROTONS ON SATURATED RING CARBONS AND C-ALKYL SUBSTITUENTS

7.2.1 P(III) Compounds

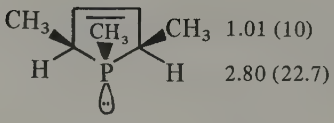
Here the most important property to consider is that of coupling, for the chemical shifts generally are in the range expected from noncyclic structures. Indeed, signal overlap can be quite severe for ring CH signals, and they are often not analyzed in practical NMR spectroscopy. In special cases, where unsaturation or other functionality is present to bring certain signals downfield, or when specific deuteration has been performed, it becomes possible to locate protons on α-carbons, and a unique effect is then revealed: the $^2J_{PH}$ value is strongly dependent on the geometrical relation of the proton to the pyramidal P function. The generality has emerged[29] that $^2J_{PH}$ is much larger when the coupled proton lies close to the orbital of the lone pair, and is quite small when remote. The lone pair orbital on P is treated as directional and lying along the line connecting the midpoint of the basal plane of the pyramid and the P nucleus; this orbital then has a dihedral angle dependence from the vicinal CH bond. The heterocyclic structures **16** and **17**, among others, were instrumental in the recognition of this coupling effect, another example of which is found in the isomer pair **18a**, **18b**.[30]



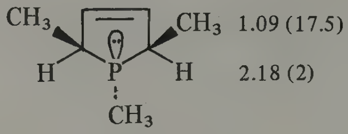
16



17

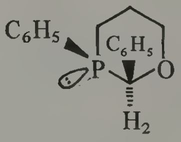


18a

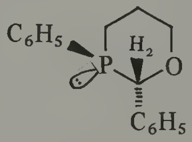


18b

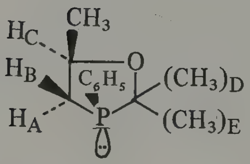
Much approximation is involved in arriving at the lone-pair-α-CH dihedral angle in these and other structures, and some assumptions that were made about molecular geometry are no longer satisfactory (e.g., that the phospholene ring is planar, that phenyl in 1-phenyl-4-phosphorinanone is primarily equatorial in a regular chair; see Chapter 8). Nevertheless, it was evident that the dependence had a regular geometric variation, and the data were plotted to give a smooth curve, with a positive ^2J at $\phi = 0°$ (27 Hz), a minimum at 120° (−6 Hz), and an increase to 0 Hz at 180°. The curve is in need of revision, and placing too much significance on numbers derived from it is unwise. It does seem safe to say that absolute ^2J values in excess of about 6 Hz are to be associated with small dihedral angles (<60°) with the maximum coupling (at 0°) exceeding 25 Hz. Absolute values in the range 0-6 Hz could have ϕ anywhere in the range 60°-180°, but a sign determination would narrow the possibilities considerably. Even in this form the general relation is enormously useful for assigning structure to an isomer pair where $^2J_{PH}$ can be measured for each member, as well as in interpreting complex spectra. The following examples are typical of structural assignments that resulted from the publication of the plot (another example, compound **47**, is found in Section 7.3).



19a, δ H_2 = 5.11,
$^2J_{PH}$ = 18.0[31]
cis, ϕ small



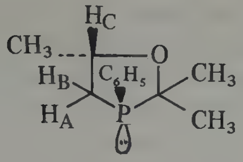
19b, δ H_2 = 4.45,
$^2J_{PH}$ = 5.7
trans, ϕ large



20a

δ H_A = 1.91, $^2J_{PH}$ = 19.5 (ϕ small)[32]
δ H_B = 2.43, $^2J_{PH}$ = 2.7 (ϕ large)
δ H_C = 4.45, $^3J_{H_AH_C}$ = 9.6
δ $(CH_3)_D$ = 1.02, $^3J_{PH}$ = 6.4
δ $(CH_3)_E$ = 1.53, $^3J_{PH}$ = 18.2

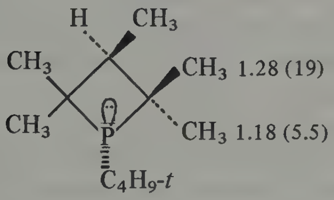
In compound **20a**, it is found that the proton cis to the lone pair (large $^2J_{PH}$) is coupled to the vicinal H_C by 9.6 Hz; this magnitude is known from the normal Karplus relation for vicinal proton-proton coupling to require a cis relation of H_A and H_C, which then defines the position of the CH_3 group as being cis to P-C_6H_5. The isomer **20b** has a smaller value for $^3J_{HH}$; hence it has the trans relation for these protons and CH_3 must be placed trans to P-C_6H_5.[32]



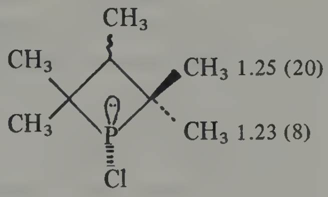
20b

$\delta\ H_A = 2.50,\ {}^2J_{PH} = 24.4$
$\delta\ H_B = 1.89,\ {}^2J_{PH} = 6.2$
$\delta\ H_C = 4.10,\ {}^3J_{HH} = 6.9$

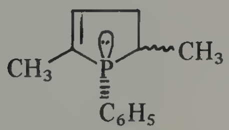
Not only is ${}^2J_{PH}$ controlled by the orientation of the lone pair but it has become obvious that ${}^3J_{PH}$ has a very similar dependence. Vicinal ${}^{31}P$-${}^1H$ coupling will first be under the normal control of the dihedral angle in the Karplus relation, as has been clearly defined for ${}^3J_{PH}$ in phosphonates.[33] However, given a similar dihedral angle in an isomer pair where P(III) is present, quite different values for ${}^3J_{PH}$ will still result if the lone pair orientation is different. The relation once again is that greater coupling occurs when the lone pair is closer to the CH bond vicinal to CP. Many examples of this highly useful effect have been encountered; structures **18a** and **18b** should now be reexamined, where the C-CH_3 remote from the lone pair (**18a**) has small three-bond coupling (10 Hz) and that close to the lone pair (**18b**) has large coupling (17.5 Hz). Nearly the same values are reported for the C-CH_3 groups in the isomers of the 1-methyl and 1-phenyl derivatives of the 2-methyl-3-phospholene system.[8] Other rings display the effect; it is present in oxaphospholene **20a**,[32] where the 2-CH_3 groups have different coupling constants, very nearly the same as in the phospholenes. The generality of the effect persists throughout a change in ring size (21), in the nature of the P-substituent (22), and in modification of the electronic environment at P (23).



21[34]



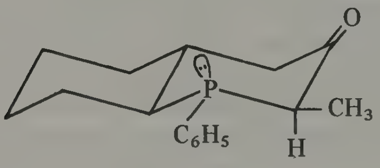
22[35]



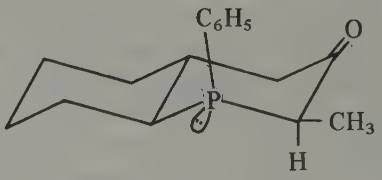
23[36], cis CH_3, 1.12 (11.5)
trans CH_3, 1.60 (19.7)

In the 6-membered ring, important conformational properties have to be considered, and the situation is less clearcut. Thus, a CH_3 group at the α-carbon of a phosphorinane, if placed in the equatorial position, will not differ greatly in its orientation to the lone pair in either the cis or trans isomers. In the cis isomers, the

P-substituent will be axial and the lone pair equatorial (ϕ to $CH_3 \sim 60°$), whereas in the trans isomer the P-substituent will be equatorial and the lone pair axial (ϕ again 60°). Deviations will occur from these angle predictions, which strictly apply to the ideal shape of cyclohexane, but they do serve to show that no great difference can be expected in $^3J_{PH}$ values in this situation, and without more knowledge of the shape of the ring it would not even be possible to predict with confidence which orientation will produce the larger ^3J value. The uncertainty is quite clearly demonstrated in the trans-fused bicyclic phosphorinane derivative **24**, for which both isomers are known.[37] If the CH_3 group is assumed to occupy the equatorial position in each, the configurational difference will occur at phosphorus, which is quite permissible based on studies that have revealed P-substituents to exert far less demand for the equatorial position than might be expected.[11]



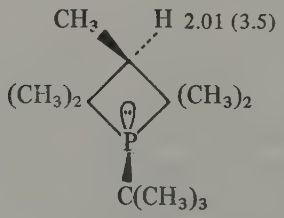
24a



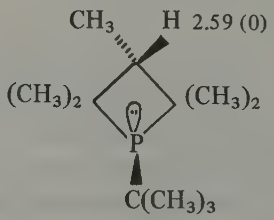
24b

The methyl signals appear at δ 0.93 ($^3J_{PH}$ = 16.5) and 1.27 ($^3J_{PH}$ = 13). The difference in ^3J is thus seen to be much smaller than usual, just as predicted from the dihedral angle considerations. The chemical shift difference is undoubtedly due to preferential shielding by phenyl (see Section 7.5) but again it is difficult to predict which isomer will provide phenyl with the greater opportunity to influence $2\text{-}CH_3$ with its shielding cone. Such molecular structures can be more easily elucidated with ^{13}C NMR, but once a collection of data with 6-membered rings of known structure becomes available it is likely that the $^3J_{PH}$ effect will be more useful.

$^3J_{PH}$ can also be different for ring protons if the conformation of a ring is such as to lead to different dihedral angle relations to the lone pair. It is usually quite difficult to locate the signals for ring protons, but the heavily substituted phosphetanes do allow this opportunity, and in **25**[34] the single ring CH signal is actually used to analyze the cis, trans ratio of an isomer mixture because it is downfield of all CH_3 signals.

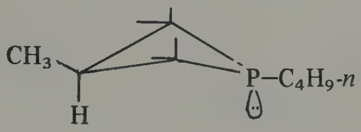


25a (cis)

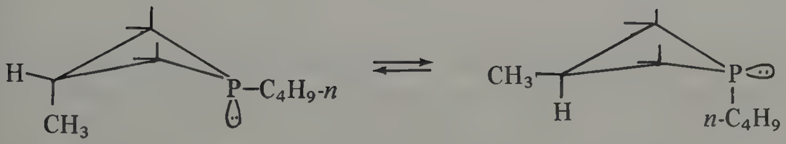


25b trans

Puckering of the 4-membered ring in cis isomer **25a**, with methyl and *t*-butyl both preferring pseudoequatorial positions to avoid interactions, leads to conformation **25a′**. The trans isomer is less likely to be involved in a biased equilibrium.



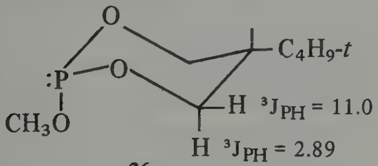
25a′



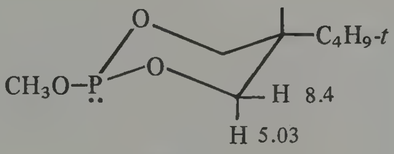
25b′ **25b″**

In **25a′** the H-CC-P dihedral angle and lone-pair orientation effect compete with each other, the former causing small coupling because of an angle somewhere around 90°, the latter increasing the coupling because of the proximity of the lone pair. The net result is a small but definite $^3J_{PH}$ (3.5 Hz). In the trans isomer, there is probably less of a preference for one of the two possible conformations; in neither does the lone pair approach the proton to enhance the coupling, and the diminished H-CC-P dihedral angle of **25b″** apparently disallows any coupling. This result may suggest a greater contribution of **25b″** than **25b′**, which would not be too surprising as P-substituents in general seem to require less space than C-substituents. The effect is probably general for phosphetanes since the isomers of 1,2,2,3,4,4-hexamethyl phosphetane also show a similar difference for 3-H (cis δ 2.5, $^3J_{PH}$ = 2.5; trans 2.54, $^3J_{PH}$ = 0)[7]. The consistency of these conformational conclusions with those derived from ^{13}C NMR should be noted (Section 6.2).

The dihedral angle control and lone-pair orientation control of $^3J_{PH}$ operate through heteroatoms and have found use in, for example, the 1,3,2-dioxaphosphorinane system (**26**).[38]

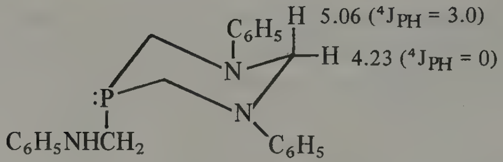


26a



26b

The weak four-bond coupling in phosphorus heterocycles is also known to be subject to control by steric factors. For example, the 1,2,5-trimethyl-3-phospholene isomers[30] show quite different values for $^4J_{HCPCH}$ (**18a**, 3.2 Hz; **18b**, < 1 Hz), and in the 1,3,5-diazaphosphorinane[39] **27**, where the methylene protons of the 2-position are coupled differently to ^{31}P ($^4J_{PCNCH}$).

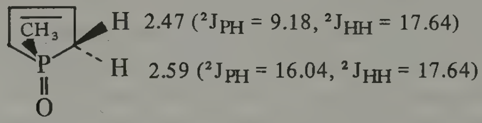


27

Both examples have the larger coupling when the involved atoms are in the "W" relation, familiar from carbocyclic chemistry.

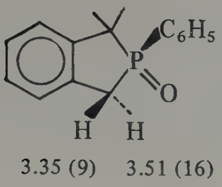
7.2.2 P(IV) and P(V) Compounds

The α-CH signals of the 3-phospholene system present an excellent opportunity to consider the NMR properties of P(IV) functions on ring carbons. Their signals are generally easily recognized on spectra and are useful, along with the olefinic proton signals, in insuring the 3-position for the double bond in this rearrangeable system. An α-CH_2-group should in principle exhibit an AA′BB′X spectrum (X = ^{31}P), and under special conditions this can be observed[40] (for 1-methyl-3-phospholene oxide, a 50% solution in $CDCl_3$ at 270 MHz). The spectrum is markedly dependent on concentration and temperature, and a 9% solution at 270 MHz gave an ABX spectrum with the parameters below.

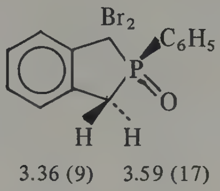


A similar spectrum was observed for the 1-phenyl compound at 270 MHz.[41] In each case, the proton cis to oxygen is assumed to be the more deshielded (see Section 7.5). Of special interest is the presence of different coupling constants for ^{31}P to the two protons, and the relation is suggested that coupling is greater for that proton cis to oxygen. At the more common frequencies of 60-100 MHz, and in solutions of greater concentration, the spectra are simplified even further and give the simple doublet of an A_2X system. This was the type of spectrum reported early,[3,42] and still routinely observed, in the study of 3-phospholene derivatives; 1-methyl-3-phospholene oxide, for example, was first reported[3] to have a doublet ($^2J_{PH}$ = 11 Hz) at δ 2.43 when measured at 60 MHz in a strong $CDCl_3$ solution. The remarkable simplification of the spectrum must be derived from medium effects, which remain to be defined.

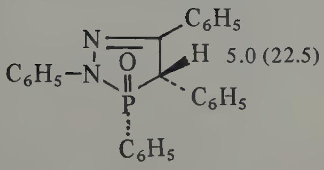
The steric dependence of $^2J_{PH}$ in phosphoryl compounds is revealed in other compounds without special experimental conditions, as in the isophosphindoline derivatives[43] 28 and 29, the pair of 1,2,3-diazaphospholene isomers[44] **30a** and **30b**, and the 1,3-oxaphospholane **25**.[32]



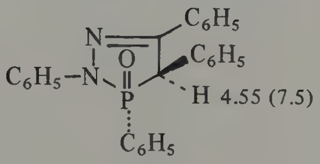
28



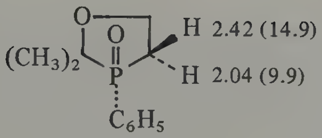
29



30a



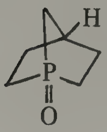
30b



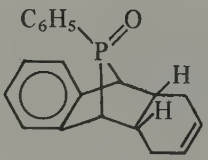
31

It seems to be a well-established generality that proximity to oxygen is associated with extra coupling, just as was noted for the lone pair. There are not sufficient data available at present to determine if the generality also holds for phosphine sulfides.

Protons on carbons β- to P(IV) functions have coupling that is controlled by the dihedral angle to ^{31}P. Although there are not sufficient data available to provide Karplus plots for the common functions of heterocyclic chemistry, as has been done for the phosphonate group,[33] there seems to be little reason to believe that the minimum coupling will deviate much from 90°, and that maxima will occur at 0° and 180°. A particularly good example[45] of the augmented coupling resulting from the presence of a 180° angle in a rigid skeleton is provided by 32, where the bridgehead proton has $^3J_{PH} = 28$ [cf. to 16.3 for the open chain model $(CH_3CH_2)_3PO$]. Equally informative is the case[43] of 33, where $^3J_{PH} = 0$ as a consequence of a dihedral angle of about 90°. This property was instrumental in assigning the endo structure to this compound; had the exo structure been correct, the dihedral angle would have approached 180° and coupling such as seen in 32 would have resulted.

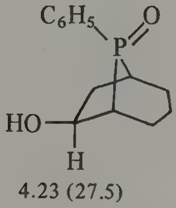


32

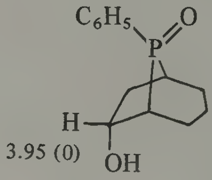


33

Another example[46] of structure assignment aided by $^3J_{PH}$ is provided by the isomers **34a** and **34b**; in the former the dihedral angle is large (about 150°) and coupling is strong, whereas in **34b** the angle is close to 90° and no coupling is observed.

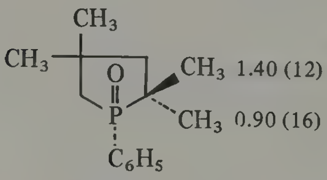


34a

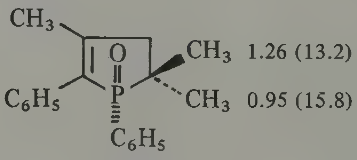


34b

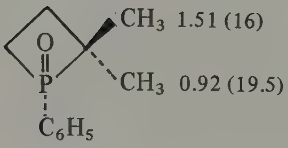
Methyls attached to α-carbons are three-bond coupled to ^{31}P but necessarily the protons have the same dihedral angle. Here the orientation of oxygen, unlike the orientation of a lone pair in phosphines, has a small influence on $^3J_{PH}$, and as is suggested from examples **35-37** it appears that cis oxygen is to be associated with the weaker coupling. The effect is probably too small to be useful for structural analysis, which is more reliably accomplished by the obvious shielding differences.



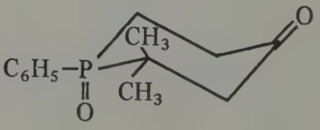
35[47]



36[48]

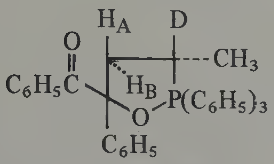


37[49]

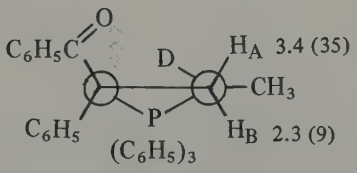


38[50] 0.98 (15.0) and 1.13 (13.0)

Dihedral angle control of coupling can exist for the P(V) state as well. This accounts for the widely different ^3J values for the protons at C-4 in **39**,[51] which thereby demonstrates a preference for a nonplanar conformation that places one H at a large dihedral angle (giving J = 35 Hz) and one at a small angle (J = 9 Hz). This is accommodated by conformation **39a**.



39

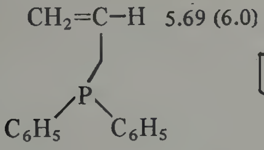


39a

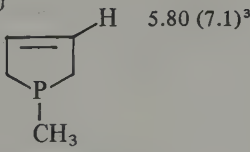
7.3 PROTONS IN NONCONJUGATED UNSATURATED SYSTEMS

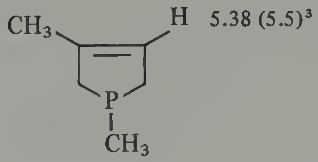
7.3.1 P(III) Compounds

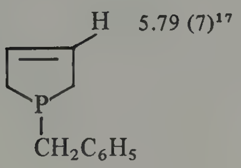
Neither the chemical shifts resulting from closure of a ring around an allylic P(III) system (e.g., **40**[52]), nor the coupling constants, seem exceptional at first glance. Examples of both parameters in simple ring systems may be illustrated by the 3-phospholenes.

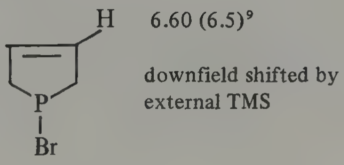


40



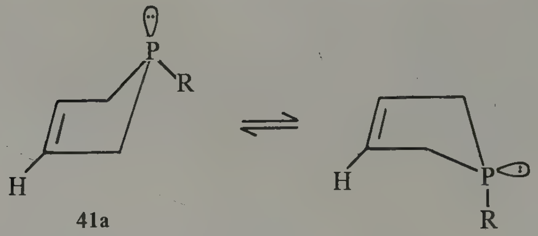






In these cases, the signal is a sharp doublet, and generally no coupling is observed with the protons of the 2-position, which are themselves an ABX system.

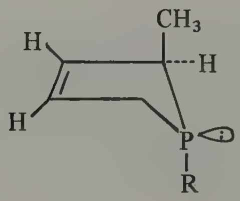
The $^3J_{PH}$ values in phosphines have already been noted to be controlled by the two properties of the P-CC-H dihedral angle and the proximity of the lone pair. In the 3-phospholenes, the former will be averaged at 180° if the ring is undergoing the ususal flipping in an unbiased equilibrium.



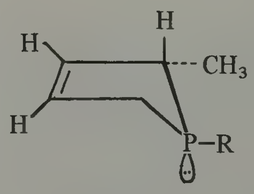
41a **41b**

If the conformational equilibrium is biased in either direction, then the averaged angle is reduced and coupling will be diminished. If the biasing is towards **41a**, the latter effect arises, as greater proximity of the lone pair to the olefinic proton creates the possibility of enhanced coupling. Biasing toward **41b** would minimize the coupling, which can in fact be negligible in noncyclic tertiary phosphines. No X-ray data are yet available for a 3-phospholene (except in a $NiCl_2$ complex[53]) to reveal any preference for a pseudoequatorial (as in **41a**) or pseudoaxial (**41b**) position, but the fact that the large dihedral angle did not increase the coupling value over that for noncyclic systems suggests a moderation of the coupling by the disposition of the lone pair. In other words, the equilibrium may be biased toward **41b**.

A possible test of this proposal of a conformational influence on $^3J_{PH}$ might develop from a change in the steric demands about P, as by the introduction of a 2-substituent. The equilibrium position may be modified, with an influence being shown on the olefinic proton. In fact, this is precisely the result of introduction of CH_3 at the 2-position; although the trans isomers show no departure from the simple doublet (J ∿ 6) seen above, even though the two olefinic protons are in principle nonequivalent, the cis isomers present a much more complicated spectrum. Unfortunately, no example of these spectra has yet been fully analyzed, and no value for $^3J_{PH}$ is known. It is obvious, however, that the spectral complexity results from a biasing of the conformational equilibrium towards that form where nonbonded interactions between the 1,2-substituents are alleviated. This must imply that the equilibrium position for the trans form is similar to that of the unsubstituted, a fact that seems better accommodated by dominance of conformer **42a** (1,2-anti) than **42b** (1,2-gauche).

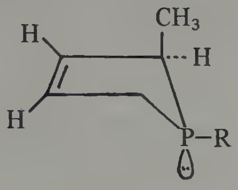


42a

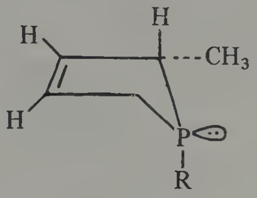


42b

The cis form then has conformations **43a** and **43b** to populate, and models suggest that the 1,2-interactions are not greatly different in them, both resembling gauche interactions.

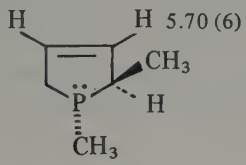


43a

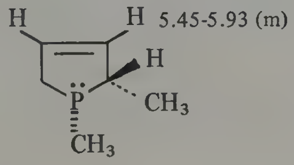


43b

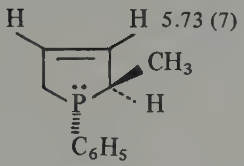
Therefore, to the extent that conformational differences do influence $^3J_{PH}$ in allylic systems, it is not at all surprising to find the pronounced coupling differences between cis and trans isomers of the types below.[8] The absence of a detailed analysis makes it impossible at this time to explain the origin of the greater complexity of the cis isomers, whose spectra at 60 MHz consist of many close-lying lines of no obvious pattern.



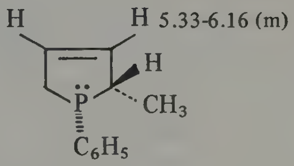
44a



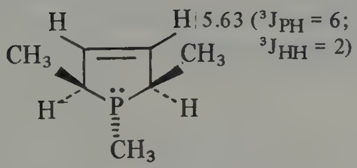
44b



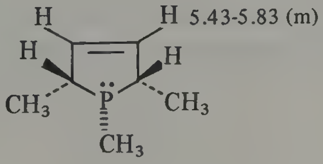
45a



45b



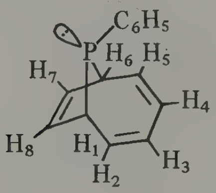
46a



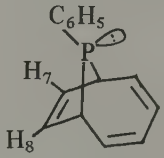
46b

Compound **46a** displays the only recognizable coupling of a 2-proton to the olefinic proton, and a definite doublet of doublets is observed. This is also observed[36] in the 1-phenyl derivative (δ 6.09, $^3J_{PH} = 7.5$, $^3J_{HH} = 1.0$).

That the orientation of the lone pair on phosphorus can control $^3J_{PH}$ to olefinic protons is made quite clear from consideration of a bridged system where a single conformation, with fixed dihedral angle, is allowed. Such a system is 9-phosphabicyclo[4.2.1]nonatriene, for which both isomers (**47a**, **47b**) of the 9-phenyl derivative are known.[54]



47a

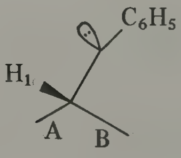


47b

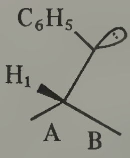
The structures of the isomers were first assigned[54] from the shielding effect of the phenyl, on H_2-H_5 in **47a** and on H_7-H_8 in **47b**. It was later pointed out[29] that the pronounced difference in $^2J_{PH}$ to $H_{1,6}$ in the two isomers (18.3 Hz in **47a**, 2.2 in **47b**) is exactly what should be expected for these structures, as the lone-pair orbital makes a dihedral angle of only about 20° in **47a** (large $^2J_{PH}$) but obviously a much larger angle in **47b** (small $^2J_{PH}$). A point that seems not to have been articulated previously is that there are also striking differences in the three-bond coupling, both to the olefinic protons $H_{7,8}$ of the 3-phospholene moiety as well as to $H_{2,5}$ of the 8-membered ring:

	47a	**47b**
$H_{7,8}$	5.43 (11.9)	6.16 ($\geqslant$5)
$H_{2,5}$	5.38 (3.4)	6.20 (13.1)

The reason for these differences is immediately obvious by extending the knowledge of lone pair influence on $^3J_{PH}$ on saturated CH to olefinic CH. Models clearly show that the lone pair is much closer to $H_{7,8}$ in **47a** than in **47b**, and coupling is therefore larger. In **47b**, the lone pair is directed more to $H_{2,5}$ than in **47a**, and coupling is stronger in the former. These steric relations, as well as those for $H_{1,6}$, are quite obvious from a silhouette of the model for each isomer.



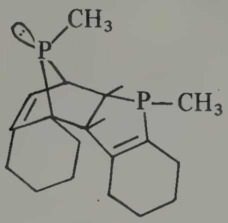
47a′



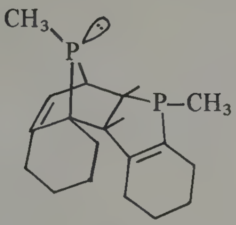
47b′

Segment A refers to the 2-atom bridge and B to the 4-atom bridge, which is assumed to have planarity.

Recognition of steric control of $^3J_{PH}$ in rigid, unsaturated phosphines constitutes a useful new device for structural analysis. Not only can isomers be differentiated, but the absolute value of $^3J_{PH}$ for a single isomer can be meaningful. Thus, it is noticed that $^3J_{PH}$ can be considerably greater (12-13 Hz) or smaller (3-5) in **47a,b** than in the monocyclic 3-phospholenes (7 Hz). A value for a new phosphine significantly greater than 7 Hz implies that there is present a geometry that positions the lone pair close to the olefinic proton, and vice versa. The structure at the 3-phospholene unit of the recently prepared diphosphines from the deoxygenation of phosphole oxide dimers can be proved with this device. Because the $^3J_{PH}$ value to the olefinic protons is a broadened singlet (at 100 MHz), only structure **48b** is allowed; **48a** will necessarily have a small dihedral angle and a much larger value (> 7 Hz) is expected.

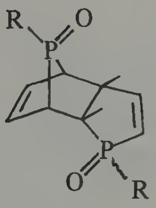


48a



48b

From the configuration established for a P(III) compound, it is then possible to determine the same feature in phosphine oxides, sulfides, or salts, because they can be interrelated by stereospecific reactions. Therefore, the phosphole oxide dimer system, for which no configuration has heretofore been established, must be expressed by structure **49**, as oxygen was removed from it with retention by trichlorosilane.

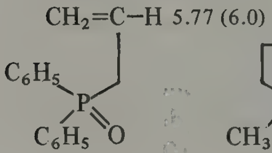


49

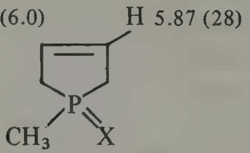
7.3.2 P(IV) Compounds

Again the 3-phospholenes present the best model system for establishing NMR effects in cyclic allylic system. One is immediately struck by the very large size of

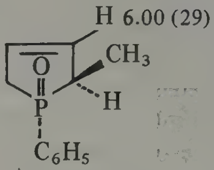
$^3J_{PH}$ in simple compounds of this type relative to noncyclic models (e.g., **50**). The olefinic proton is normally an easily detected doublet, rarely showing any further splitting from adjacent methylene or methine protons. Phosphine oxides and sulfides have nearly identical parameters (**51** and **52**) and the configuration at P is seen to have no influence on $^3J_{PH}$ (cf. **53a** to **53b**, or the identity of signals for the isomers of **54** and **55**).



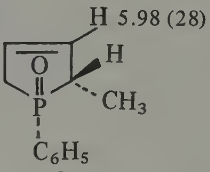
50[52]



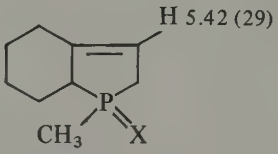
51 X = O[3]
52 X = S[22]



53a[8]

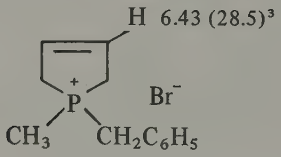


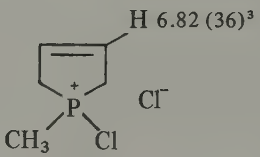
53b[8]



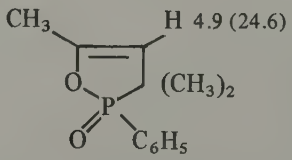
54, cis-trans mixture, X = O[9]
55, cis-trans mixture, X = S[22]

With positive phosphorus, chemical shifts are more downfield; the same large $^3J_{PH}$ values are found:



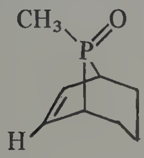


Replacement of an α-carbon by a heteroatom does not change the magnitude of the coupling constant between ^{31}P and the olefinic protons, but electron release from a heteroatom with a lone pair can cause a substantial upfield shift of the β-oriented proton. Both effects are illustrated by **56**.[55]



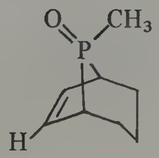
56

The magnitude of $^3J_{PH}$ (28-30 Hz) in P(IV) compounds, which is much greater than that seen for noncyclic (6.0 Hz in **50**) or saturated compounds [16.3 in $(CH_3CH_2)_3PO$], is similar to that observed for the rigid 1-phosphabicyclo[2.2.1]-heptane system **32** (27.5 Hz). This strongly suggests that the cause of the large coupling is simply the imposed dihedral angle of about 180° relating ^{31}P to the olefinic proton. In support of this statement can be offered the fact that when the P atom is displaced toward the olefinic proton in rigid ring systems, thus reducing the dihedral angle, the $^3J_{PH}$ values are greatly reduced. This condition is met in a number of systems (**57**,[46] **58**,[56,57] and **59**[58]) and in all $^3J_{PH}$ is greatly reduced over that known for conformationally unrestrained 3-phospholene oxides ($^3J_{PH} \sim$ 28-30 Hz).



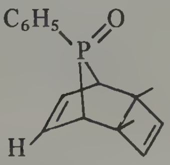
6.01 (18)

57a



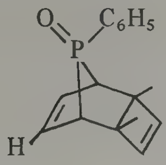
6.25 (18.5)

57b



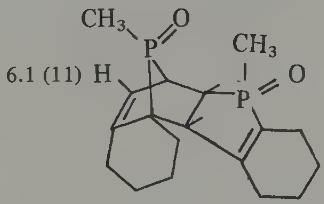
6.27 (11.0)

58a



6.0 (12.5)

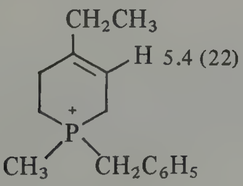
58b



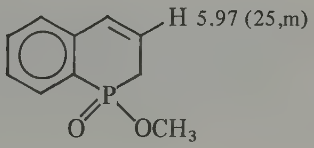
59

The failure of the configuration at P to influence ^3J is apparent in the isomers of **57** and **58** and is of course not unexpected.

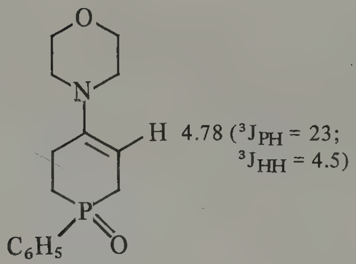
Allylic systems are also encountered in 6-membered rings. Here the nonplanarity of the ring needs to be considered, as well as the tendency for the conformational equilibrium to be strongly biased in such a way that it effectively creates a dihedral angle relating P to H of less than 180°. This may account for the somewhat smaller values for $^3J_{PH}$ than are seen for 3-phospholenes; the doublets are sometimes further split by the α-CH group, and a doublet of triplets is reported for **62**.



60[59]



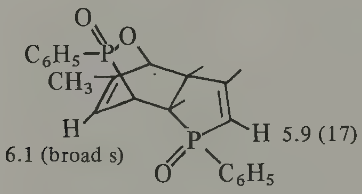
61[60]



62[61]

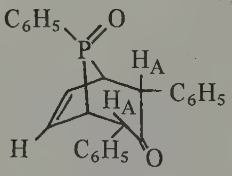
63[62]

The $^3J_{PH}$ value is especially small in **63** and can be related to the substantial puckering and rigidity imposed by the two double bonds. The reality of such an effect is again seen in a bridged system (**64**[58]) where the dihedral angle to P is sharply reduced and at 60 MHz no distinct coupling is observed.



64

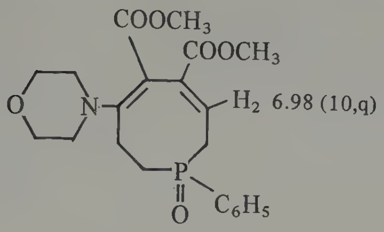
An excellent example of the occurrence of the stereospecificity of $^3J_{PH}$ in a 6-membered ring is found in the rigid system of **65**. Coupling to H_A is only 7.5 Hz,



65[63]

which is consistent with these protons occupying the axial ($\phi \sim 60°$) rather than equatorial ($\phi \sim 170°$) position of a chair moiety.

In the 8-membered ring of **66**,[61] the $^3J_{PH}$ value is only 10 Hz, and this is a strong indication that there is preferred a conformation that produces a dihedral value not unlike that of **58** (about 120°, $^3J_{PH}$ = 11.0).



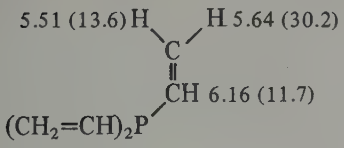
66

It will be of great interest in the future of large-ring compounds to determine if ^{1}H NMR can be as valuable in conformational analysis as it has in other systems.

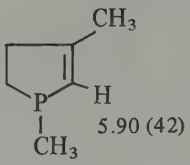
7.4 PROTONS IN CONJUGATED UNSATURATED SYSTEMS

7.4.1 P(III) Compounds

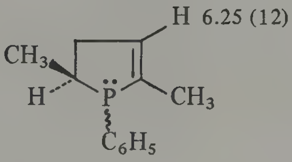
Although attachment of ^{31}P to an olefinic group causes no pronounced chemical shift differences from a noncyclic model (**67**), some striking coupling phenomena result. $^2J_{PH}$ at the α-carbon reaches the extraordinary size of 35-45 Hz in several 2-phospholene derivatives.



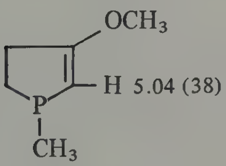
67[64], $(CH_3)_6Si_2$ ref.



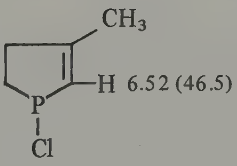
68[12]



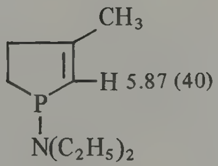
69[65]



70[66]

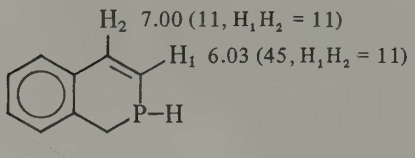


71[13]

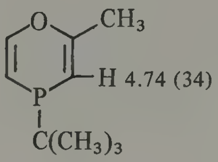


72[13]

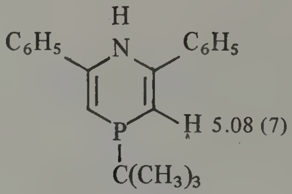
Insufficient data are available to explore the effect in 6-membered rings; one secondary phosphine (**74**) does have the large $^2J_{PH}$, however. Heterorings are represented by **75** and **76**, and it is seen that although the effect is present in 4-oxa it is absent in 4-aza.



73[67]

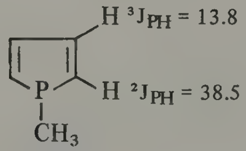


74[68]

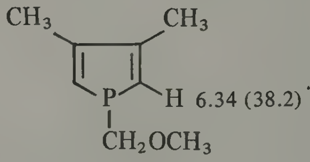


75[69]

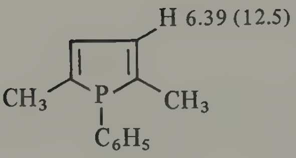
The presence of additional conjugation does not alter this fundamental property of $^2J_{PH}$; phospholes (**76-79**) and P(II) azaphospholes (**80-81**) display values in the same range, as do even phosphorins (**82**). An azaphosphorin (**83**) shows exaltation over the dihydro form (**75**) but still has a much lower value than the phosphorin.



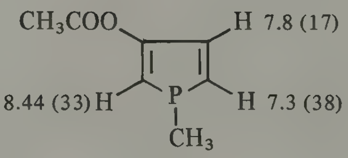
76[14]



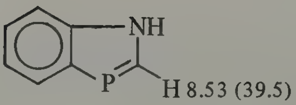
77[70]



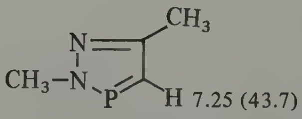
78[71]



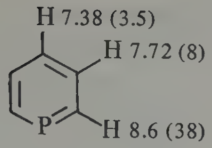
79[17]



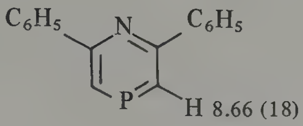
80[72]



81[73]



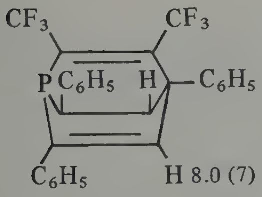
82[74]



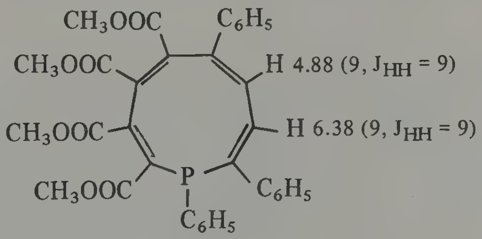
83[69]

The common feature in all of these structures is the coplanarity of the coupled atoms imposed by the double bond; the second common feature is the fixed location of the lone pair orbital relative to the proton. The importance of the latter point in accounting for the large coupling seems obvious from comparing the $^{2}J_{PH}$ value to that of noncyclic, freely rotating vinyl phosphines, which, as for **67** (11.7 Hz), are much smaller. However, the bond order varies in the types of compounds exhibiting the phenomenon, and so does the dihedral angle relating the lone pair to the proton; it is possible that there is present another coupling effect that receives partial compensation, with the fortuitous occurrence that all $^{2}J_{PH}$ values fall in the range of 35-45 Hz.

$^{3}J_{PH}$ in the α,β-unsaturated P(III) compounds is, as always, controlled by both the H-CC-P dihedral angle, which is close to 180° due to the double-bond geometry and the proximity of the lone pair. The dihedral angle is the same as that found from P to the trans proton of trivinylphosphine ($^{3}J_{PH} = 30.2$); the reduced value in the 2-phospholene **69** (12 Hz) and the dihydrophosphorin **73** (11 Hz, albeit a secondary phosphine) is then the result of the differing disposition of the lone pair, with closer proximity in the noncyclic case (90° has been proposed[75]). This point has been raised[75] to account for the small $^{3}J_{PH}$ in some other unsaturated ring systems where geometry may influence the orientation of the lone pair. Thus, in a phosphabarrelene **84**,[76] the value is only 7 Hz, and in a phosphonin **85**[75] it is 9 Hz. For the latter, a puckered ring is proposed to place the lone pair away from the double bond. With adequate data, it is quite possible that in the future conformational analysis of large α,β-unsaturated rings may be aided by the size of $^{3}J_{PH}$.



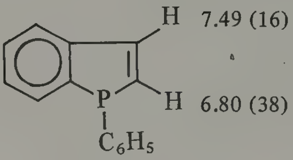
84



85

It may also be noted that $^{3}J_{PH}$ to the β-proton of phosphorin **82** is only 8 Hz but here the coupling passes through a C-P double bond and it probably is not safe to treat this case in the same way as the others.

The chemical shifts of the olefinic protons of phospholes fall distinctly downfield of the values for vinylphosphines (e.g., **69** and **70**); indeed the shifts for 1-methylphosphole (δ 6.5-7.5 in an AA′BB′X spectrum[14]) are nearly the same as those seen for thiophene. It is commonly believed for the latter that this is the result of extra deshielding of peripheral protons by a ring current, associated with the cyclic delocalization ("aromaticity") in this 6π-electron system. This NMR evidence continues to be cited as supporting the presence of similar delocalization in phospholes (see Chapter 8 for further discussion). The notion has been extended[77] to phosphindoles as well, where the same downfield shifting is present.

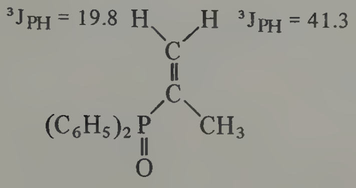


86[77]

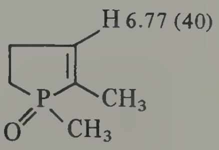
Chemical shifts in λ^3-phosphorins are more difficult to interpret, especially those at the α-position. The deshielding (to δ 8.6) in the parent (**81**[74]) exceeds that in pyridine (8.29), where a strong electron-attracting inductive effect acts along with the ring current. Other heavy atoms have similarly large α-proton deshielding, and at present the view[74] is that this requires explanation as a diamagnetic anisotropic effect arising from electron circulation on the heteroatom. Why it is so pronounced in phosphorin is, however, not clear. The γ-position (δ 7.38) in phosphorin is slightly upfield of that of pyridine (δ 7.75), whereas the β-position (δ 7.72) is downfield (δ 7.38). In any case, the deshielding expected from the operation of a ring current of an aromatic system seems present. In 1,1-dimethyl-λ^5-phosphorin,[78] the ylide character (discussed in Chapter 8) causes substantial upfield shifts: H-2, δ 3.98 (17); H-3, δ 6.70; H-4 δ 4.62.

7.4.2 P(IV) Compounds

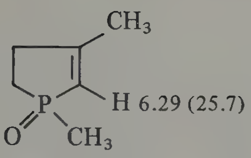
α,β-Unsaturation in P(IV) compounds is associated with pronounced chemical shift as well as coupling effects. The former is to be associated with polarization of the double bond by interaction with the P-atom, presumably offering its d orbitals as has been discussed in Chapters 5 and 6. The consequence is the development of considerable positive character at the β-carbon (as seen in ^{13}C NMR), which is transmitted to the attached proton. This causes the β-proton to resonate at substantially lower field than the α-proton, just as is true for α,β-unsaturated carbonyl compounds. The magnitude of ^{31}P coupling is best revealed by examination of compounds with only one olefinic proton (e.g., **88** and **89**). These give simple spectra, frequently appearing as doublets but occasionally showing further splitting from other ring protons. $^2J_{PH}$ is then shown to have a magnitude not inconsistent with that to saturated CH, but $^3J_{PH}$ assumes a very large size, frequently 40 Hz or more. This is undoubtedly the consequence of the trans relation of the β-proton to ^{31}P, for in noncyclic vinyl phosphine oxides (e.g., **87**) trans coupling is of similar large magnitude whereas cis coupling is much smaller. The spectra of P=O and P=S compounds are very similar, and the generalities also apply when another heteroatom is present. Many examples are known, a few of which are collected below.



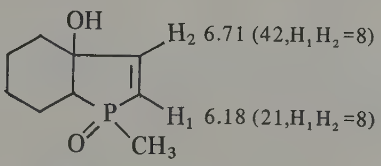
87[79]



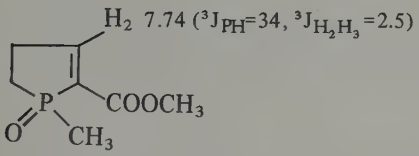
88[3]



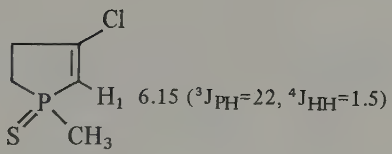
89[3]



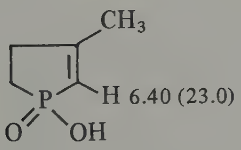
90[80]



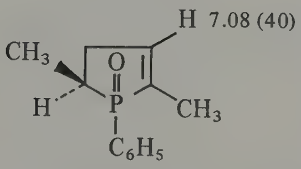
91[81]



92[22]

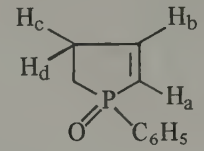


93[13]



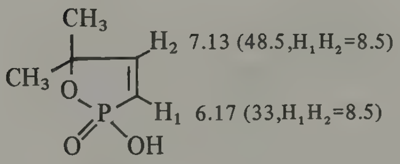
94[36]

Coupling occurs when both olefinic protons are present. Compound **90** provides a particularly good example of the AMX spectrum (100 MHz) resulting. The complication of further coupling to the γ-protons is avoided in this structure. However, in simple 2-phospholenes having no substituents on the α,β,γ-carbons, this extra coupling can cause the spectrum to become quite complex.[42] A particularly detailed analysis[41] of such a spectrum (for **95**) resulted from operation at 270 MHz, where 8 triplets for an ABM_2N_2X spectrum were observed over the region δ 6.21-7.23. With the aid of a decoupled 90 MHz spectrum, it was possible to assign coupling constants as follows: $^2J_{PH_a} = 25.4$, $^3J_{PH_b} = 43.2$, $^3J_{H_aH_b} = 8.4$, $^4J_{H_a\text{-}H_cH_d} = 2.0$, $^3J_{H_b\text{-}H_cH_d} = 2.7$.

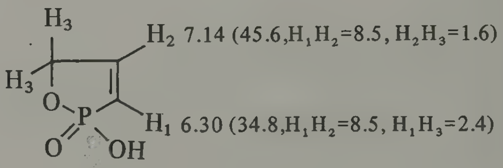


95

Several 1,2-oxaphospholene derivatives are known that show similar spectra to the phospholenes.

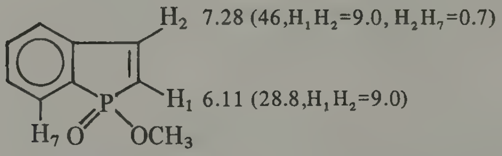


96[82]

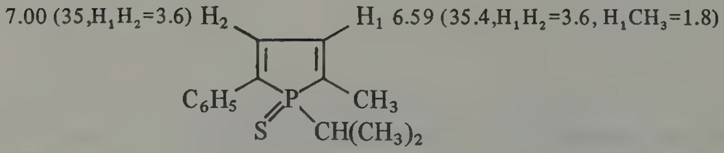


97[83]

Other modifications, such as benzo fusion (as in **98**) or introduction of another double bond to create the phosphole system (**99**), do not alter the picture.

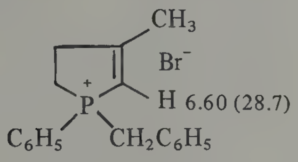


98[84]

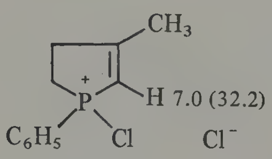


99[19]

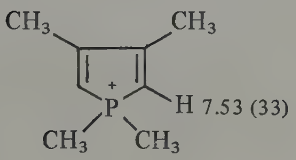
Endowing phosphorus with full positive charge increases the deshielding and coupling at the α-proton (as it does in noncyclic compounds[85]), although **103** shows that electron release from a β-substituent (an enamine) reverses the deshielding effect.



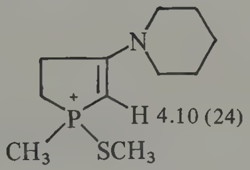
100[3]



101[3]

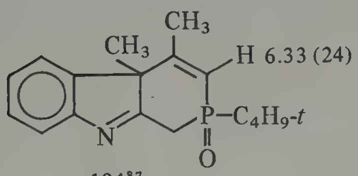


102[28]

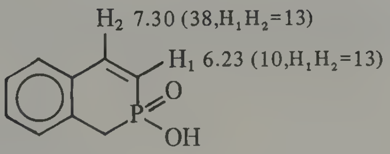


103[86]

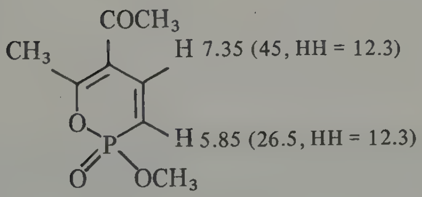
α,β-Unsaturation in 6-membered cyclic compounds leads to similar spectral effects:



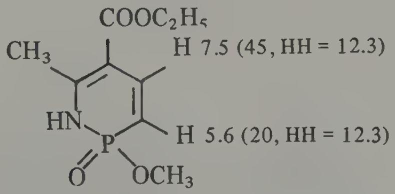
104[87]



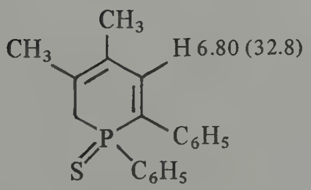
105[68]



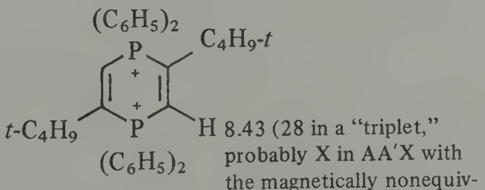
106[88]



107[88]



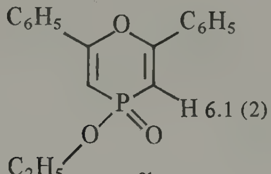
108[89]



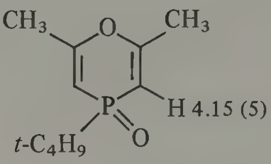
109[90]

probably X in AA′X with the magnetically nonequivalent ^{31}P nuclei)

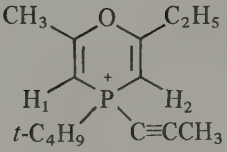
However, 1,4-oxaphosphorin derivatives, which are being encountered more frequently in the literature, have coupling constants to the α-proton that are surprisingly small compared to the examples above.



110^{91}

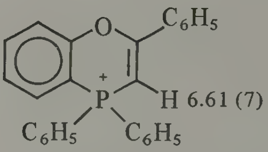


111^{92}



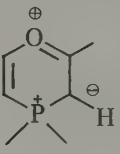
H_1 or H_2, 5.93 (9, $^4J_{H_1H_2} = 4$) or 6.23 (9, $^4J_{H_1H_2} = 4$)

112^{93}



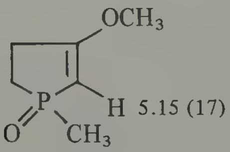
113^{94}

The enol ether character of these compounds must be responsible for this effect, operating through resonance form **114**.



114

The negative charge can be shared with phosphorus d-orbitals. It is not clear, however, why electron release in 2-phospholene derivatives such as **103** or **115** does not produce the same reduction in $^2J_{PH}$, since this electronic interaction is evident from the upfield shifting of the α-proton.



115^{95}

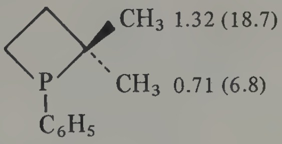
Nor is it obvious why the enol ether character in a phosphine of the 1,4-oxaphosphorin system (**74**) shows the perfectly normal $^2J_{PH}$ value (34 Hz) for a cyclic vinyl phosphine, unperturbed by the electron release. Searching for the effect in a comparable 5-membered ring (a 1,3-oxaphospholene) would be of interest.

7.5 THROUGH-SPACE SHIELDING EFFECTS INVOLVING PHOSPHORUS FUNCTIONS

In the preceding sections, several instances were noted where the steric disposition of groups or atoms caused specific, through-space modification of shielding. The P-phenyl group is very often found acting in this regard, casting a shielding influence on protons cis related to it. These effects can be enormously useful in recognizing the presence of, and in distinguishing, cis, trans isomers. A summary of some typical and useful anisotropic effects in phosphorus heterocycles is given below.

7.5.1 Shielding by P-Phenyl Groups

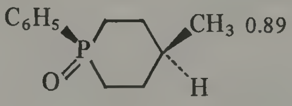
This well-known property of phenyl, which results from conformations placing a proton in the area above or below the plane of the ring, can be found in many examples of P(III) compounds. It acts to send a *cis*-2-methyl group in a phosphetane[49] (**116**) upfield of *trans*-2-methyl by 0.51 ppm; a similar effect separates the methyls in oxaphospholane **20a**[32] by 0.51 ppm.



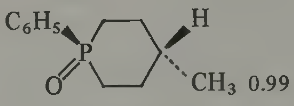
116

It permits ready distinction[8] of the 2-methyl isomers of 1-phenyl-3-phospholene (**45a**, *trans*-2-CH_3, δ 1.17; *cis*-2-CH_3, δ 0.71). Protons at the α-position of the ring are differentiated in the same way, as seen, for example, in **20a**[32] ($\Delta\delta$ 0.52 ppm), and in 1,3-oxaphosphorinane isomers[31] **19a** and **19b** (0.66 ppm). (The opposite assignment[96] of α-CH_2 signals in 1-phenyl-4,4-dimethyl-1-2-oxaphospholone oxide may need reconsideration; if reversed, the $^2J_{PH}$ values will conform with the generality already noted of cis H and O having the larger value.) Olefinic protons likewise feel the effect, which was used to distinguish the 9-phenyl-9-phospha[4.2.1]nonatriene isomers[54] (**47a**, **47b**; $\Delta\delta$ $H_{7,8}$ = 0.73 ppm; $\Delta\delta$ $H_{2,5}$ = 0.82 ppm). The effect abounds in P(IV) derivatives as well; here oxygen is the most common fourth group on P, and as is seen in the next section it is possible for this atom to exert a deshielding influence. Nevertheless, in most cases, the shielding by

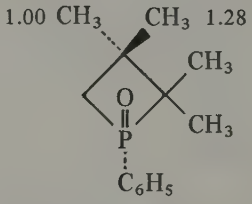
P-phenyl is clearly the dominant force over deshielding by oxygen in causing the differentiation of protons. Thus, in the isomers of **53**, shielding by phenyl causes the cis 2-CH_3 to go upfield (to δ 0.93) whereas the trans 2-CH_3 (cis to 0) is at δ 1.38. Further defining the role of phenyl is the failure of any significant difference to develop when methyl replaces phenyl in this system (Δδ 0.11 ppm, order reversed). Similarly, in the P-phenyl phosphetane **37**, one methyl is obviously moved upfield (δ 0.92) relative to the other (δ 1.51), whereas in 1,2,2,3,4,4-hexamethylphosphetane oxide[20] the methyls appear at δ 1.27 and 1.18. Other examples of the strong distinction of protons by phenylphosphoryl groups may be found in the methyl signals of P-oxide of **20a**[32] (δ CH_3 1.02 and 1.57), in the ring protons of phosphindolines[43] **28** (Δδ 0.16 ppm) and **29** (Δδ 0.23 ppm), and of diazaphospholenes[44] **30a** and **30b** (Δδ 0.45), of the 2,2-dimethyls of 1-phenyl-4-phosphorinanone oxide **38**,[50] and of the 3,3-dimethyls of 1,2-oxaphospholene **56**[55]; longer-range effects are observed on the 4-methyl group in cis and trans forms of the oxide of 1-phenyl-4-methylphosphorinane (**117**[97]) as well as the benzo[b] derivative (Δδ 0.10 ppm)[98] of the oxide and the dibenzo [b, e] derivative of the methiodide of the phosphine,[99] of the 3,3-dimethyl group in the phosphetane oxide **118**,[20] of the carbinol proton of the bicyclic alcohols **34b**, etc.



117a, cis



117b, trans

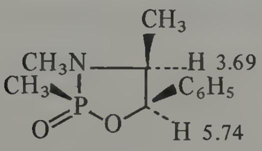


118

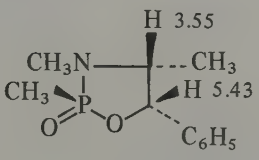
The benzene ring of a P-phenyl group of a phosphonium salt can also exert long-range shielding effects on ring protons, if structural features allow the proper conformation to be adopted. Thus, the olefinic protons of benzyl bromide salts of 3-phospholenes are more shielded in *trans*-1-benzyl-2-methyl derivatives, where free rotation is possible, than in *cis*-1-benzyl-2-methyl derivatives, where hindrance prevents the movement of phenyl close to these protons. The effect can achieve Δδ of 0.4 ppm.[8]

7.5.2 Deshielding by Phosphoryl Oxygen

In the preceding section, it was noted that methyl groups on α-ring carbons of phosphetanes and 3-phospholenes failed to be influenced in a noticeable or even consistent way by phosphoryl oxygen. This is true also in 2-phospholenes.[48] Protons directly on this ring carbon are similarly influenced only to a small extent ($\Delta\delta$ 0.12 in 1-methyl-3-phospholene oxide[40]). Nevertheless, the literature makes frequent reference to phosphoryl deshielding, and the concept is in use even if on shaky ground. Part of the confusion comes from cases where P-phenyl is present, and signal differentiation that is attributed to phosphoryl deshielding is more likely the result of phenyl shielding. Examples of useful $\Delta\delta$ differences do appear in such nonphenyl compounds as 1,3-dimethylphospholane oxides[100] (cis, 0.90; trans, 0.71 in benzene) and 1,3,2-oxazaphospholanes,[101] **119a** and **119b**.

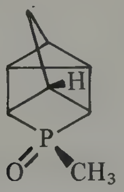


119a

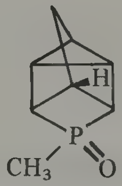


119b

The reality of a phosphoryl deshielding effect becomes more obvious and useful in rigid bridged systems, where the atoms involved are held in a definite relation to each other. Thus, it is reported[102] that the bridgehead proton in the isomers of **120** differ in chemical shift by 1.40 ppm; this is clearly the result of phosphoryl deshielding, since the upfield signal is in the region expected for a methine in the phosphetane system.[20]

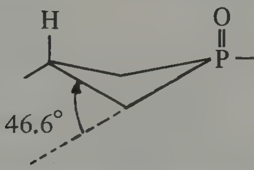


120a, δ 1.90

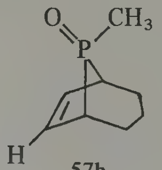


120b, δ 3.3

An X-ray analysis[103] of a salt of this ring system has shown the phosphetane moiety to be extraordinarily puckered (dihedral angle of 46.6°), and a model shows that the bridgehead C-H and P=O bonds would almost be parallel.

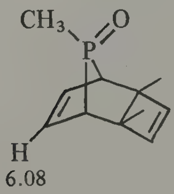


The implication is that the phosphoryl deshielding may be maximal in this geometric arrangement, and weakens as the C-H group is forced from this parallel alignment in other structures. Thus, in the rigid system **57**[46], there is a weak influence of P=O on the olefinic protons, as **57b** has these signals 0.24 ppm downfield of the anti arrangement.

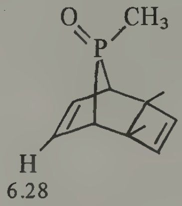


57b

Similarly, the olefinic protons in **121**[57] are differentiated by 0.20 ppm.

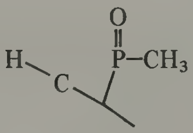


121a



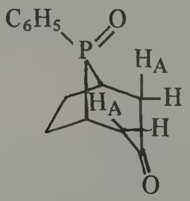
121b

In these structures, the C-H and P=O bonds are far out of the parallel alignment, as the silhouette below illustrates, accounting for the weakening of the effect.



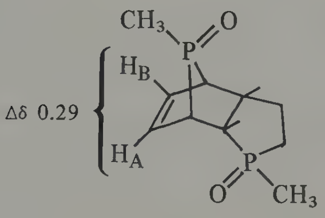
Other examples that seem to authenticate a deshielding role for phosphoryl are the following:

1 Selective deshielding on H_A occurs in the conversion of phosphine **5** to its oxide[18] (**122**). Two of the protons on C-2 and C-4 are strongly deshielded (0.7 ppm) whereas the others, presumably equatorial on a chair shape for the 6-membered ring, are unchanged.



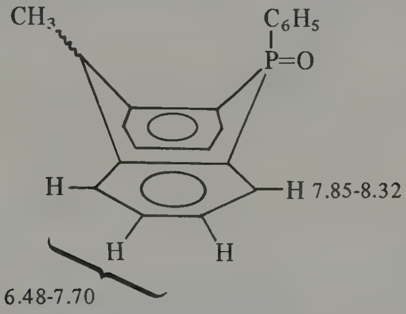
122

2 In the framework of the dimers of phosphole oxides, it is possible for selective deshielding of olefinic proton H_A relative to H_B in the 5-membered ring to occur from the endo-phosphoryl group, and this seems to be realized in the dihydro derivative **123**.[58]



123

3 Aromatic protons ortho to a rigidly held P=O group show pronounced deshielding, as in the dibenzophosphorinane derivative **124**, where they are well separated from the other aromatic protons.[104]



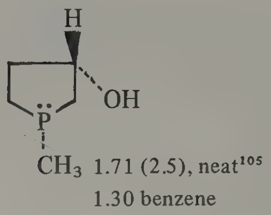
124

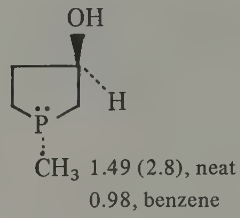
In spite of these and other examples that could be cited, there is in fact no detailed theoretical analysis of the origin of the deshielding action by a phosphoryl group, and it would be most helpful if other structures with rigid geometry could be studied in order to define the direction of the effect experimentally. It seems just as possible that the effect arises from the electric field of P=O as from magnetic anisotropy resulting from the circulating electrons.

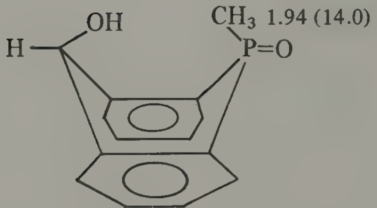
7.5.3 Shielding Influences on P-Substituents

Several cases are known where C-substituents exert long-range influences on P-methyl groups. Frequently these can be useful in assigning cis, trans structure.

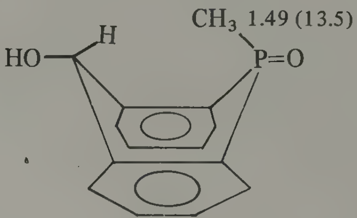
1 OH groups are well known in cyclohexane and cyclopentane chemistry to exert small deshielding effects on cis-oriented CH_3 groups, and examples of this can be found in phosphorus heterocycles as well:





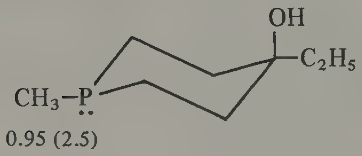


125a[16]

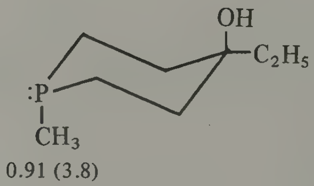


125b[16]

A weak effect can also be detected in the 4-phosphorinanols[4,10] (e.g., **126**) when examined in benzene solution, where the P-methyl signals are cleanly separated doublets.



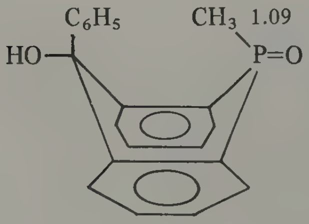
126a



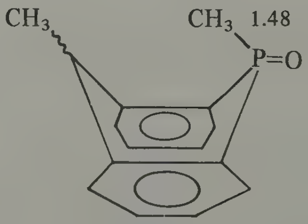
126b

That the presence of an aromatic solvent is necessary for the signals to be differentiated suggests the transmission of an effect through a solvent collision complex[11] with the OH group, rather than a direct deshielding mechanism.

2 Shielding of P-CH_3 by double bonds is possible when molecular geometry places a methyl over the shielding cone, as in **57a**[46] (δ CH_3 = 1.48) relative to **57b** (1.78). Shielding by the cone of a benzene ring is also possible, as may account for the relatively upfield position (δ 1.09) for a phosphine oxide seen in **127** relative to **128**.[104]



127

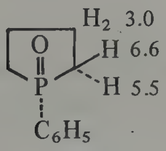


128

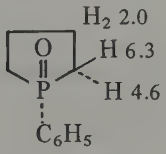
7.6 LANTHANIDE SHIFT REAGENTS IN PHOSPHORUS CHEMISTRY

Phosphoryl oxygen was early[106] in the lanthanide-induced shift (LIS) era found to form pseudocontact complexes that resulted in substantial spreading out of signals, in relation to the proximity of the proton to oxygen. The LIS effect is especially useful in resolving the troublesome bunching of signals associated with protons on sp^3 ring carbons. Applications in the elucidation of configuration at P, and the assignment of structure to isomers, are numerous. With signal resolution improved, it also becomes possible to measure coupling constants and apply correlations of $^2J_{PH}$ and $^3J_{PH}$ in the determination of stereochemistry. The technique can be enormously useful in heterocyclic phosphorus chemistry. A number of the compounds already discussed in this chapter have been studied with the aid of LIS; a few cases are singled out below to illustrate the power of the technique, but others may be found in Refs. 43, 84, and 102.

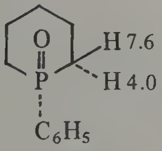
In simple monocyclic compounds, α-protons are more downfield shifted than β-protons, and within an α-CH_2 group, that proton cis to oxygen is more affected. The same cis effect is true, but to a smaller extent, on ring CH_3 groups. In the structures below, LIS values are Δδ at 1:1 reagent ratio; the complexing reagent used was tris(dipivalomethano)europium(III), Eu(DPM)$_3$, unless otherwise noted.



Ref. 107

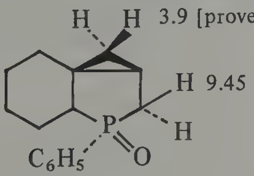


Ref. 45

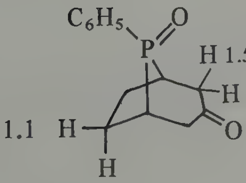


Ref. 45

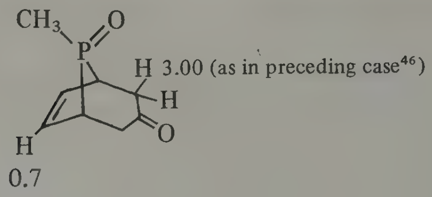
Similar values at α-CH_2 in benzo derivatives of these rings have been reported.[108] The protons of bridged systems with phosphorus at a bridgehead are cleanly separated; for 1-phosphabicyclo[2.2.1]heptane 1-oxide (32) the signals are clustered at δ 1.7-2.5, but with LIS are spread out by Δδ values of 4.5(C-2), 3.7(C-7), 1.9(C-3), and 2.0(C-4).[45] Stereochemical assignments by shift effects are illustrated by the cases below.



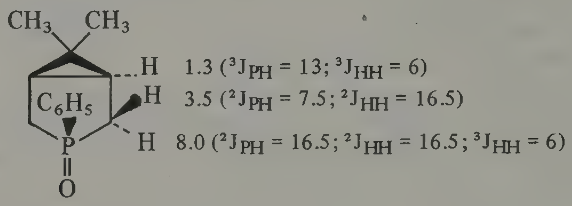
3.9 [proves CH_2 and O are syn[109]; Eu(fod)$_3$]



H 1.51 (proves O is above 3-C bridge, not 2-C bridge[46]; complexation at P=O, not C=O)



A particularly good illustration of the use of the shift effect to separate signals so that the stereospecificity of coupling constants can be utilized is found in compound **129**[110] [with Eu(fod)$_3$].



129

By spreading out the α-methylene protons, their $^2J_{PH}$ values become obvious, and once again it is seen that they differ considerably. That proton with the greatest LIS value is cis to O, and it is this proton that is also coupled to the proton on the β-carbon. The magnitude of this vicinal coupling (6 Hz) is consistent with the small dihedral angle (∿ 30°) allowed by a cis arrangement of these protons, for if they were trans the angle would be ∿90° and no coupling would be expected. This defines the position of the cyclopropane ring as being anti to oxygen; the relative size of $^2J_{PH}$ is also in accord with this assignment, in that the α-H identified as cis by its LIS value has the expected large coupling constant.

Phosphines do not respond well to the lanthanide reagents, and no useful examples of shift effects involving this oxidation state seem to have been reported. In the 1,3-azaphospholane or 1,3-oxaphospholane system,[111] complexation with Eu(DPM)$_3$ occurred preferentially at O or N (or at a carbonyl O) rather than P, but nevertheless induced shifts at ring positions that were useful in assigning the structures of diastereoisomers.

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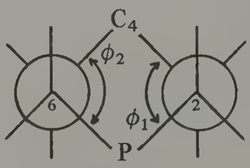
chapter eight

Special Properties of Phosphorus Heterocycles: Conformation and Cyclic Electron Delocalization

8.1 THE SHAPES OF PHOSPHORUS HETEROCYCLES IN THE SOLID STATE

In the last decade or so, over 80 detailed molecular structure analyses by single-crystal X-ray diffraction techniques have been performed on phosphorus heterocycles. In addition, electron diffraction in the gaseous state has been used to determine a few structures. From these studies has emerged a considerable mass of data on the shapes adopted by the various types of heterocycles, as well as details of bond length and angle. The shape adopted is the consequence of the system's attempt to minimize nonbonded interactions; the shape is expressed quantitatively by dihedral angles (or torsion angles, numerically identical but given plus or minus signs). The Newman projection for the phosphorinane ring looking down the C_2-C_3 and C_6-C_5 bonds illustrates the use of this concept.



The angle ϕ_1 is formally the angle of intersection of the plane P-C_2-C_3 with the plane C_4-C_3-C_2, and is equal to ϕ_2. In an ideally staggered cyclohexane ring, the dihedral angle would be 60°; some reduction of this angle is common as a system attempts to alleviate nonbonded interactions. It must always be kept in mind, however, that the conformation observed in the solid state may in part be determined by crystal packing forces and may not be truly representative of the situation in solution. Indeed a crystalline form of a compound capable of participating in a conformational equilibrium between two energy-minimized structures generally consists of only one of the possible forms (an important exception, compound 22, to this will be noted, however), and thus an X-ray measurement fails to provide any indication of the vigor of the competitive situation in solution. Nevertheless it seems safe to state that *usually* whatever conformation is measured for a solid will be reproduced by a major species in solution, and that the various molecular parameters recorded for the solid will apply to that species. This is especially true for bond lengths and bond angles. From a prediction of the shape of a ring, it is then possible to propose a location for ring substituents and, hence, to apply the various generalities of NMR spectroscopy that depend on stereo relationships.

From the mass of knowledge available to date, is it possible to make a prediction of ring shape and dimensions for a new derivative of a heterocyclic system, or for that matter for an entirely new system? The rest of this section is organized in a manner that will attempt to show that the answer is, for the most part, positive. Most of the heterocycles for which structural data have been reported are woven into the discussion to follow, so that another purpose being served is the provision of an extensive bibliography of the structural aspect of heterocyclic phosphorus chemistry. To facilitate the discussion, little additional mention will be made of the specific values for bond angles and lengths beyond those ranges that are gathered in Table 8.1, unless an exceptional situation is present. Substitution of a heteroatom at the β- or γ-position to P generally does not change these parameters, so that many systems can be studied with the aid of these ranges. Two useful generalities

TABLE 8.1 Ranges of Bond Angle and Length (in Å) of Selected P-C Heterocycles

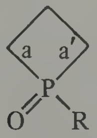
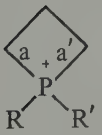
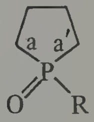
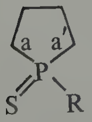
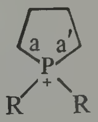
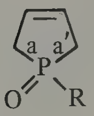
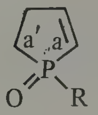
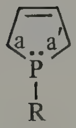
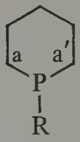
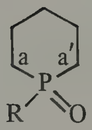
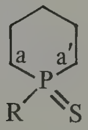
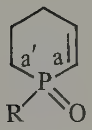
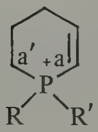
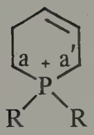
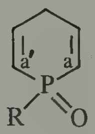
	a = 1.867 (microwave) $\angle aa' = 47.4^\circ$ Ref. 1		a = 1.79-1.91[a] $\angle aa' = 79.4^\circ$-82.5° Refs. 2-5
	a = 1.92 $\angle aa' = 83^\circ$ Ref. 6		a = 1.79 $\angle aa' = 94.8^\circ$ Ref. 7
	a = 1.82 $\angle aa' = 96.6^\circ$ Ref. 8		a = 1.77-1.82 $\angle aa' = 94.8^\circ$-96.0° Refs. 9-11

TABLE 8.1 continued

	$a = 1.84$ $\angle aa' = 98.5^\circ$ Ref. 12		$a = 1.78\text{-}1.79$ $a' = 1.82\text{-}1.83$ $\angle aa' = 94.2^\circ$ Refs. 13-15
	$a = 1.85^b$ $\angle aa' = 94.0^\circ$ Ref. 16		$a = 1.84\text{-}1.85$ $\angle aa' = 97.7^\circ\text{-}98.2^\circ$ Refs. 17-20
	$a = 1.793$ $\angle aa' = 99.8^\circ$ Ref. 21		$a = 1.81$ $\angle aa' = 101.3^\circ\text{-}104.0^\circ$ Refs. 22 and 23
	$a = 1.79^c$ $a' = 1.76$ $\angle aa' = 104.3^\circ$ Ref. 24		$a = 1.79^c$ $a' = 1.78\text{-}1.80$ $\angle aa' = 105.7^\circ\text{-}106.0^\circ$ Refs. 25 and 26
	$a = 1.79^d$ $a' = 1.77$ $\angle aa' = 102.5^\circ$ Ref. 27		$a = 1.79^{c,e}$ $\angle aa' = 103.7^\circ$ Ref. 28

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[a] The C-P range is unusually large in this system, and is a function of the degree of methyl-substitution at the α-carbons. A value of 1.87 Å is calculated for any C-P from van der Waals radii. The smaller values here are found for α-CH_2 and α-$CHCH_3$, the larger values for α-$C(CH_3)_2$, especially with P-C_6H_5.

[b] No data are available for a free phosphine; these values are for a $NiCl_2$ complex of 1-benzyl-3-phospholene, but it is probable that they closely resemble values for the free ligand. This is borne out by comparing data for the ligand 1-phenyl-4,4-dimethoxyphosphorinane[18] ($a = 1.83$, $\angle aa' = 99.6^\circ$) to those for its $NiCl_2$ complex[20] ($a = 1.83$, $\angle aa' = 99.6^\circ$).

[c] Benzo derivative.

[d] Pyrimido derivative.

[e] Data also available for P(III)[29] and its methiodide.[30]

that are obvious from Table 8.1 are (1) bond lengths are generally shorter (by about 0.05 Å) for P(III) than P(IV) forms, and (2) bond angles about P(III) are several degrees smaller than about P(IV), the latter approaching the tetrahedral value.

A survey of the structural data reveals that almost all of the phosphorus-containing rings, including those with other heteroatoms present, adopt regular shapes familiar from studies of carbocyclic rings. Distortions do occur, of course, because the C-P bond is considerably longer than a C-C bond (1.54 Å) and for P(III) forms because bond angles at P are considerably smaller than tetrahedral. These generalized shapes are presented in Table 8.2. The type of compound utilizing each shape is discussed below.

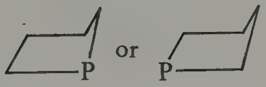
TABLE 8.2 Shapes Adopted by Phosphorus Heterocycles

4-Membered Ring

A (folded)

5-Membered Ring

B (envelope-
P flap



C (envelope-C flap)

D (half-chair)

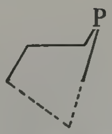
E (planar or
nearly planar)

6-Membered Ring

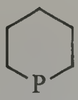
F (chair)

G (twist-boat)

H (boat)

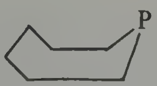


I (half-chair)



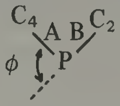
J (planar)

7-Membered Ring



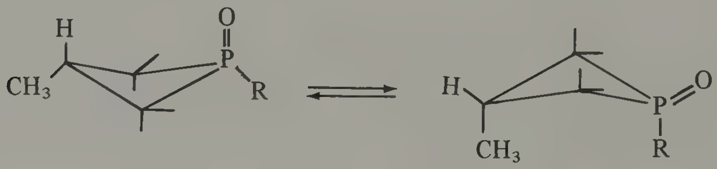
K (boat)

8.1.1 Shape A All phosphetanes are puckered, with the puckering angle (ϕ) defined as the angle for the intersection of the planes P-C_4-C_3 (**1**, line A) and P-C_2-C_3 (**1**, line B). In structure **1**, C_3 is positioned behind P.



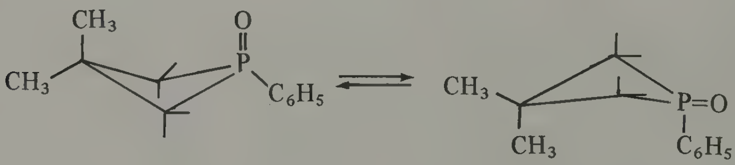
1

The puckering angle as found in seven different phosphetanes varies from 16.7° to 29.8°. The puckering is the result[5] of the nonbonded interactions between substituents on adjacent carbons of the ring; the largest value is found for 1-phenyl-2,2-3,3,4-pentamethylphosphetane oxide, where there are three cases of C-CH_3 groups being cis to each other, and the smallest value is found for 1-phenyl-2,2,3-trimethylphosphetane oxide, where only one such cis interaction occurs. On this basis, it has been predicted[5] that an unsubstituted phosphetane would have a folding angle smaller than any observed so far. When a single methyl is present at C-3 (as in **2**), it is found in the pseudoequatorial (**2a**), rather than pseudoaxial (**2b**), position, as a result of the system adjusting to minimize the cross-ring interaction of this methyl with a P-substituent.



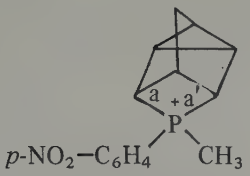
2a **2b**

When there are two methyls at C-3, as in **3**, the folding occurs in the direction that places the largest substituent on P in the pseudoequatorial position (**3a** favored over **3b**).

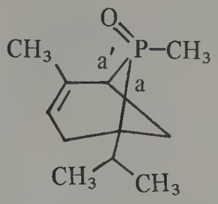


3a **3b**

No quantitative data are available on the energy differences between phosphetane conformations, however, and it must be remembered that in solution the clearcut preference for a single conformation found in the solid will not be present (this aspect of phosphetane chemistry has been discussed in Chapter 6). Two phosphetanes are known where bridging by other rings occurs, and in each the folding is greatly accentuated. The internal C-P-C angles are also the smallest recorded.

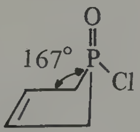


$\angle aa' = 74.8^\circ$ (Ref. 31)
$\phi = 46.6^\circ$



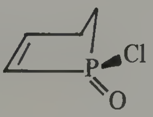
$\angle aa' = 76.9^\circ$ (Ref. 32)
$\phi = 41^\circ$

Shape B. Placement of a double bond in the 3,4-position (as in 3-phospholenes) insures that phosphorus will occupy the flap position of an envelope.[12,16] The folding angle, defined here as the angle between the planes C_2-C_3-C_4-C_5 and C_1-P-C_5, is 167° in the vapor of 1-chloro-3-phospholene oxide (electron diffraction).[12] Oxygen occupies the pseudo-axial position (4).

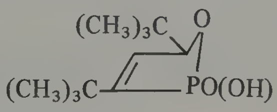


4

Shape C. A 2,3-double bond also insures an envelope shape, but necessarily phosphorus lies in the plane of the double bond and a carbon occupies the flap position.[13,14] In 1-chloro-2-phospholene oxides (vapor, electron diffraction[13]), the flap is directed to the side of the P-Cl bond (5).

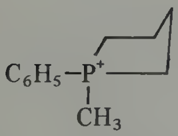


5

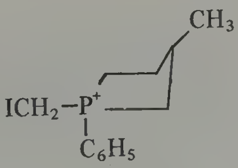


6

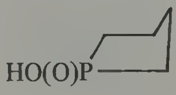
The envelope shape is less pronounced, but still observable, in oxaphospholene 6.[33] In the absence of a double bond, the C-flap envelope can still be discerned:



Ref. 9

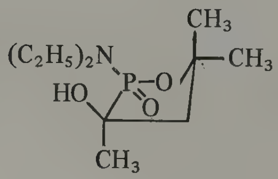


Ref. 11



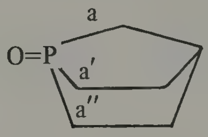
Ref. 7

Ref. 34

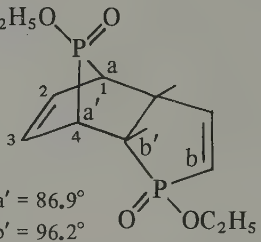


Ref. 35

There thus seems to be emerging the notion that phospholanes consistently adopt an envelope shape with a β-C at the flap. Two bridged-ring derivatives (7^{36} and 8^{15}) are known; **7** has a normal C-P-C angle in the 5-membered ring but a reduced value (from 100°-104°) in the 6-membered ring.



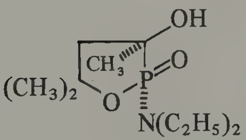
7 ∠aa′ = 99.4°
∠a′a″ = 99.8°



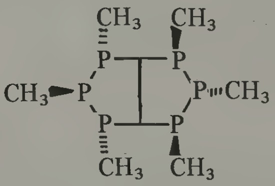
8 ∠aa′ = 86.9°
∠bb′ = 96.2°

In **8**, the bridging of a 6-membered ring by P requires considerable contraction of the C-P-C angle, resulting in the smallest value (86.9°) for any P(IV) derivative except for rings with 3 or 4 members.

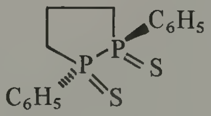
Shape D. Distortions of the envelope are well known and result in the half-chair conformation, wherein three connected atoms lie in a plane, with a fourth atom above, and a fifth below, this plane. Apparently, this shape allows further minimization of nonbonded interactions due to substituents on adjacent atoms, as for the most part it is this type of crowded molecule (**9-12**) that adopts this shape. An exception may be **13**.



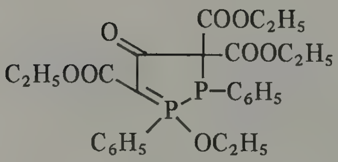
9^{35}



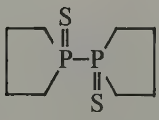
10^{37}



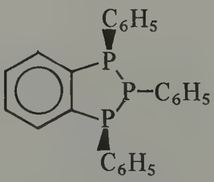
11^{38}



12^{39}



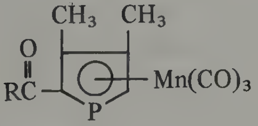
13^{8}



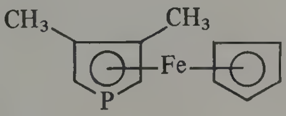
14^{40}

The puckered 1,2,3-triphospha arrangement of **10** is not reproduced in **14**, where the 5 atoms of the ring are essentially coplanar. The differing geometry of a cis, trans pair can cause the adoption of different shapes; the trans isomer of **9** has the envelope shape.[35]

Shape E. Planarity is to some extent a matter of definition; how far can an atom deviate from a plane comprising four members before a system is designated "envelope"? That point is especially important in the phospholes, where just such a small deviation does occur. The first X-ray analysis of a phosphole (1-benzyl[41]) clearly established that the P atom was removed from the plane of the four carbons by 0.21 Å, and that the planarity found in such related systems as pyrrole, thiophene, etc. was absent. The pyramidal character of P(III) was retained. A deviation from ring planarity of similar magnitude was later found for 1,2,5-triphenylphosphole[42]; a smaller deviation has been reported for 1,2,3,4,5-pentaphenylphosphole oxide[43] (P 0.08 Å above the plane), 5-hydroxydibenzophosphole 5-oxide[44] (0.064 Å), and 1,2-diphenyl-3-[2-(phenylethinyl)phenyl] phosphindole (0.1 Å).[45] Phosphole character imposes sharply reduced bond angles on both P(III) (90.7° in 1-benzyl[41]; 88.1° in the phosphindole[45]) and P(IV) (93.3° in pentaphenylphosphole 1-oxide[43]). The manganese complex **15**[46] (a phosphacymantrene; see Section 8.4) also has a very small C-P-C angle (88.5°). Both **15** and the iron derivative **16** (phosphaferrocene[47]) have rings with P slightly out of the plane.

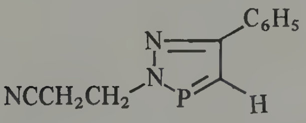


15

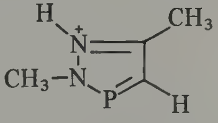


16

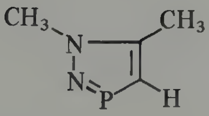
Bond lengths in phospholes are important in considerations of delocalization (see Section 8.4). The 1,2,3-diazaphosphole system, on the other hand, is clearly definable as planar, as measurements on three different derivatives (**17**-**19**) show.



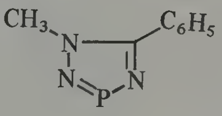
17[48]



18[49]

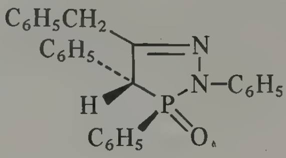


19[50]



20[51]

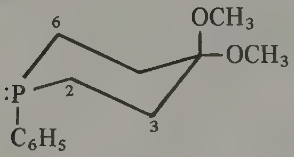
In the first two, the unique P-C double bond is present; delocalization reduces its bond order, however, and the length (1.70-1.75 Å) is not unlike that (vide infra) for phosphorins (bond order 1.5, 1.74 Å). In **19**, the P-N bond is of intermediate length (1.654 Å; normal P-N 1.77 Å, P=N 1.54 Å). In 1,2,4,3-triazaphosphole (**20**) planarity is also present, and again an intermediate length is seen for the nearly equivalent P-N bonds (1.63 for 2,3; 1.65 for 3,4). "Almost planar" is also the description given[52] to a dihydro derivative of the 1,2,3-diazaphosphole system (**21**).



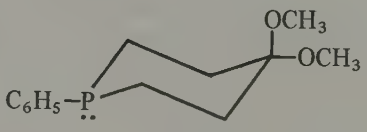
21

A feature of this molecule is the planarity about the tertiary N, causing it to have the highly unusual sp^2 hybridization. The suspicion is strong, here as elsewhere, that overlap of the lone pair with a d-orbital on P is involved.

Shape F. Without exception, phosphorinanes assume the chair conformation, which is modified only slightly relative to that of cyclohexane by some flattening at the phosphorus end. The positioning of the substituent on P is important in causing this flattening; an equatorial substituent in a P(III) phosphorinane allows dihedral angles (ϕ) to develop at the C_6-P-C_2-C_3 site that are much like that of cyclohexane (54.5°), but an axial substituent is more crowded (with the axial proton on $C_{3,5}$) and some of this strain is relieved by flattening of the ring. This is best seen in the ligand 22 when complexed to $NiCl_2$, for it happens that the complex is formed from a molecule of each of the two conformers, **22a** and **22b**, and data become available for each from a single X-ray analysis.[20]

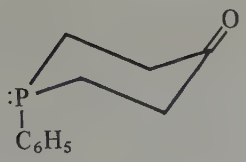


22a

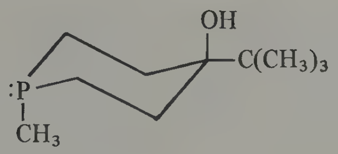


22b

In **22a**, ϕ for C_6-P-C_2-C_3 is 46.5° (cf. to 45.2° for the free ligand[18]), whereas for **22b**, ϕ is 54.0°. The metal will have some influence on the parameters, but these influences are considered to be small.[18] Both isomers of 1-methyl-4-*t*-butyl-4-phosphorinanol have been studied, and the same effect is present (axial CH_3, ϕ = 46°; equatorial CH_3, ϕ = 57°). Two other phosphorinanes (**23** and **24**) with axial P-substituents have been found to have nearly the same ϕ values (45.3° and 43.5°, respectively).

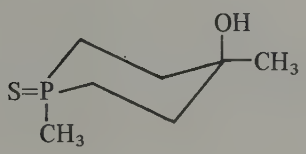


23[17]

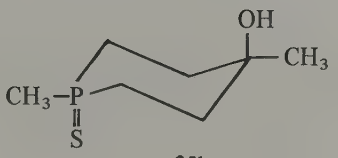


24[18]

Another unique property revealed by these studies is the preference for the crystal of free 22 and 23 to form with the axial and not the equatorial conformer. As is discussed in Section 8.2, this is the consequence of unusual conformational tendencies in phosphorinanes in solution that tend to minimize energy differences between axial and equatorial conformers and even to create a situation where the axial form predominates. The $NiCl_2$ complex comprised of a molecule each of the axial and equatorial form of 22 is a result of the equalizing of the concentrations of the two forms. Less is known about P(IV) forms, but some flattening at P also occurs in those forms with the larger group in the axial position. Thus **25a** has $\phi = 45°$ whereas its isomer **25b** has $\phi = 52°$ as a result of the size of CH_3 exceeding that of S as P-substituents.[23]

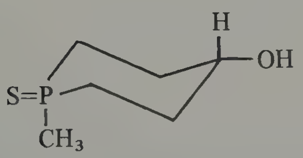


25a

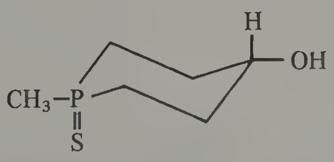


25b

Similar values are found for the isomers **26a** and **26b** ($\phi = 45°$ and $50°$, respectively).

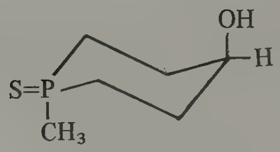


26a



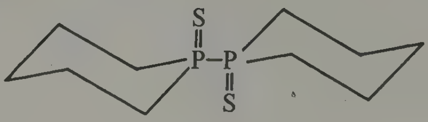
26b

It is remarkable that nonbonded interactions at P can be relieved so readily that the conformer with axial P-CH_3 is more stable than that with axial C-OH, even though the size of CH_3 is far greater than that of OH. This is another manifestation of the greatly reduced tendency towards bias in the conformational equilibrium of phosphorinanes. Indeed, the crystal formed from a solution of the trans isomer of 1-methyl-4-phosphorinanol sulfide was comprised of *both* possible conformations, **26b** and **26c** (2:1). This result is without precedent in carbocyclic chemistry.



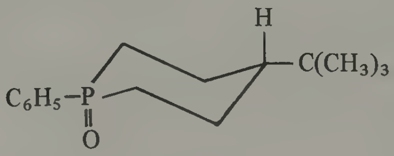
26c

One other phosphorinane sulfide that has been subjected to X-ray analysis is the diphosphine disulfide 27,[22] which had exclusively equatorial attachment between rings in chair shapes.



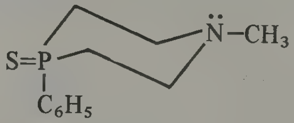
27

One phosphorinane oxide (28[21]) has been examined and found to have torsion angles (54.7°) at the P-C bonds much like those of the equatorially substituted sulfides, and an overall similar shape.



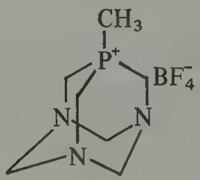
28

A 4-heterosubstituted phosphorinane (29) also has the chair conformation.[53]



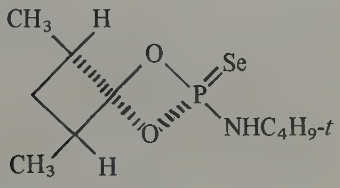
29

The alternative conformation would have an axial N-CH_3 group, and the nonbonded interactions resulting from this orientation once again must be larger than those for an axial P-phenyl group. The chair shape is of necessity found in the adamantane-like structure 30.[54]

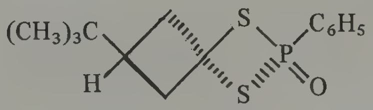


30

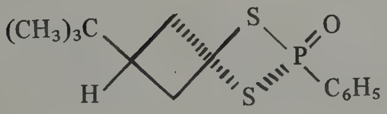
Shape G. The twist-boat is a possible conformation for phosphorinanes when, for example, very large substituents would be forced into the axial position in a chair. To date, there is no structural evidence that phosphorinanes have utilized this possibility. However, its reality in phosphorus chemistry has been recently demonstrated by X-ray analysis of the 1,3-diheteraphosphorinanes **31**,[55] **32a**,[56] **32b**,[56] and **33**,[57] and the diminished nonbonded interaction that comes from replacement of ring CH_2 by an atom with one or no protons, or of greater bond length, may cause similar preferences in other heterocyclic systems. Solution NMR studies have led to proposals of a twist-boat for a derivative (**34**) of the 1,3,2-oxazaphosphorinane system[58] and a boat for *cis*-2,5-di-*t*-butyl-2-oxo-1,3,2-dioxaphosphorinane.[59]



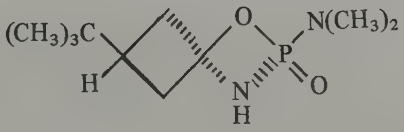
31



32a



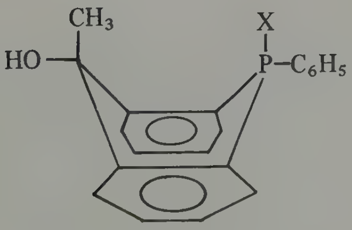
32b



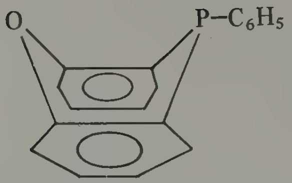
33

34

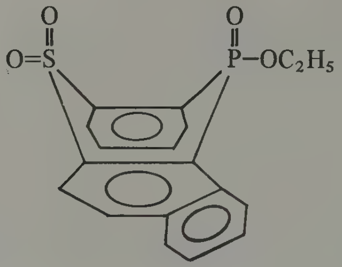
Shape H. The boat conformation has been found in three different systems. *Dibenzo Derivatives of Phosphorinanes* (**35-37**) *and Certain 4-Heteraphosphorinanes* (**38-39**).



35, X = O[28] $\phi = 18.4°$
36, X = lone pair[29] $\phi = 42.6°$
37, X = $CH_3(I^-)$[30] $\phi = 9.9°$

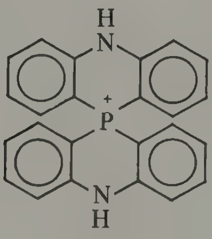


38^{60} $\phi = 15°$



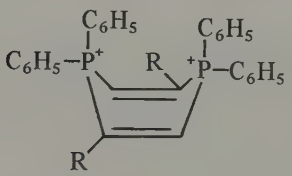
39^{61} ϕ 46.2°

The dihedral angle (ϕ) relating the intersecting planes passing through the benzene rings is quite variable, and a consistent trend has not yet emerged. If there is the capability for resonance interaction between a 4-heteroatom with a lone pair and a P(IV) group, then the system may flatten out to near planarity. This has been demonstrated in only one case (40^{62}), but as will be noted below the counterpart situation holds for certain monocyclic systems and the postulate does not seem unreasonable. The spiro structure of **40** should have no bearing on the fact that the central ring becomes planar.



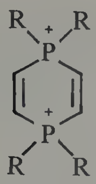
40

1,4-Diphosphacyclohexadiene Derivatives (**41-42**).



$41,^{63}$ R = C_6H_5, $\phi = 29°$
$42,^{64}$ R = t-C_4H_9, $\phi = 23°$

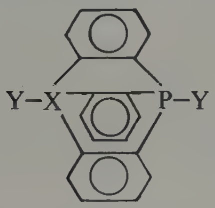
The dihedral angles (ϕ) formed by intersection of the P-C=C-P planes are consistent with those observed for the dibenzo cases. When there are no C-substituents, the ring has been observed to flatten to planarity (**43**) and even to adopt the chair shape (**44**).



43, R = C_2H_5[65]
44, R = C_6H_5[66]

Prediction of the shapes for other 4-heteraphosphacyclohexadienes is hazardous at this point, but it does seem likely that the parent rings seen to be folded in the dibenzo series may retain their folding in a monocyclic setting.

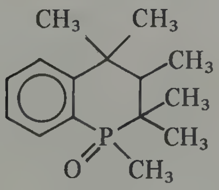
Phosphatriptycenes (**45-47**).



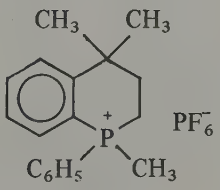
45, X = P, Y = lone pair[67]
46, X = N, Y = lone pair[68]
47, X = P, Y = 0[67]

Of interest are the bond angles at P in these derivatives. The diphosphine **45** has an angle of 97.0°, hardly different from that of a simple phosphorinane (Table 8.1). The diphosphine dioxide (100.5°) has a value only slightly reduced from that (103.7°) for dibenzo-phosphorinane oxide **35** and larger than that for a phosphorinane oxide (**28**, 99.8°) and it does not seem that the caged structure for the diphospha compounds suffers any great bond angle strain in its formation. However, there is a marked contraction of the C-P-C angles in the azaphosphatriptycene (93.3°), presumably the result of the introduction of the relatively short C-N bond.

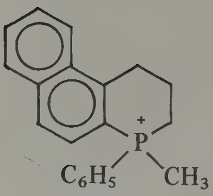
Shape I. Installation of a double bond in the phosphorinane ring always distorts the regular chair to a half-chair shape. This shape can be defined as the case where the double bond and the two attached ring carbons are coplanar, with a fifth carbon above this plane, the sixth below. In the benzo[b] derivatives **48-50**, puckering occurs at the two-carbon unit attached to P, whereas in the pyrimido[c] derivative **51** it is P and (to a less extent) C-3 that are forced out of the plane.



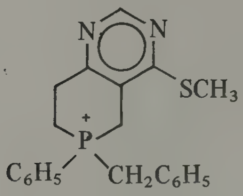
48[24]



49[25]

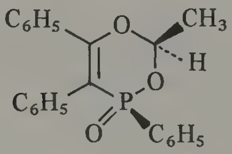


50[26]

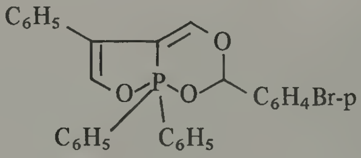


51[27]

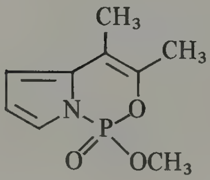
Bond length and angle data for all of these compounds are summarized in Table 8.1. In the benzo[b] derivatives, the expected shortening of the aromatic to P bond due to the sp^2 character of this C is evident. However, there is a significant shortening of the other C-P bond, apparently a result of the ring trying to accommodate the strain imposed by placement of larger bond angles at the two sp^2 carbons. This bond shortening is absent in saturated phosphorinanes (1.81 Å in sulfides[22,23]) where strain is more readily relieved by adjustments of dihedral angles. The C-P-C angle does not seem to change in the strain accommodation. The half-chair is also recognizable, even if distorted, in some heterosubstituted unsaturated phosphorinanes (**52-54**), and in a dibenzo[b,d] phosphorinane **55**.



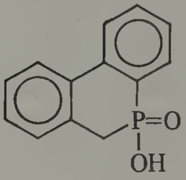
52[69]
(CH_3 and O pseudo-equatorial)



53[70]
(P—O bonds apical in trigonal bipyramid)

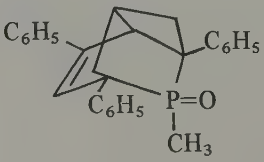


54[71]



55[72]

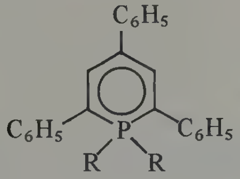
The unsaturated phosphorinane ring is also present, but in obscured form, in the bridged compound **56**.[73]



56

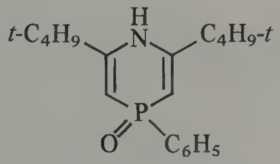
This molecule represents a case where the C-P-C bond angle adjusts to the steric strain (98.2°) while bond lengths retain their normal value (1.84-1.86 Å).

Shape J. λ^3-Phosphorins are planar[74,75] and have two identical C-P bond lengths as called for by the aromatic delocalization. These lengths (e.g., 1.74 Å in 2,6-dimethyl-4-phenylphosphorin[74]) fall between those expected for pure C=P or C-P, consistent with the bond order of 1.5. The ring is spread farther apart around P to accommodate to the length of the C-P bond. The C-P-C angle is in the usual range (103°), but the C-C-C angles are increased to 122°-126° to maintain planarity. A benzo[b]phosphorin (2-phenyl[76]) has similar parameters. λ^5-Phosphorins (**57-59**) have also been found to be almost planar, and have the important characteristic of two identical C-P bonds, with length (1.72-1.75 Å) between a double and a single bond. The significance of this is discussed in Section 8.8. The C-P-C angle is slightly increased (105°-107°) over that in λ^3-forms.

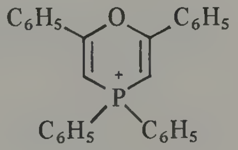


57[77] R = CH_3O
58[78] R = CH_3
59[79] R = $(CH_3)_2N$

Electron delocalization must account for another type of ring that is planar, or nearly so, that where an electron-releasing atom (O or NH) is in the 4-position of a P(IV) phosphacyclohexadiene. Two examples (**60**, **61**) are known, but it is quite likely that many similar structures will be found to have this shape. Without the resonance capability, 4-heteraphosphacyclohexadienes fold, as already noted, into the boat shape.

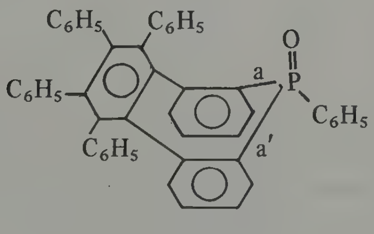


60[80]

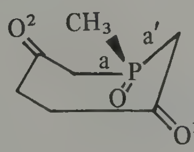


61[81]

Shape K. Two quite different P compounds, **62**[82] and **63**[83], adopt the boat shape of the 7-membered ring.

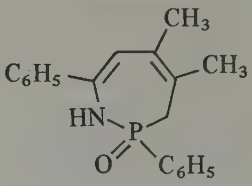


62, $\angle aa' = 99^\circ$



63, $\angle aa' = 105.0^\circ$

The asymmetrical conformation of 63 places one carbonyl oxygen (O^1) syn to P = O, the other (O^2) anti. It will be of great interest to determine if this shape, which is not common in cycloheptanes, is retained in the parent ring. The structure of an azaphosphepin (**64**) has also been reported.[84,85]



64

Only a few rings of 8 or more members have been studied; their rather specialized structures do not allow useful generalizations at this time, and the results are summarized briefly below.

8-Membered Rings Two dibenzo[b,g] phosphocanes[86,87] and a 3,7-diketophosphocane,[83] the latter in the boat-chair shape as defined by Hendrickson have been studied.[88] The structure of a diazaphosphocane[89] has also been reported.

9-Membered Rings Several 3,8-diketophosphonanes[83] have adopted the twist-chair-chair[88] shape. Best seen in perspective, the P-CH_3 oxide has the unusual feature of a positioning of the three oxygens on the same face, and the P atom does not fall on the C_2 axis of symmetry. The C-P-C angle (106.3°) is only slightly larger than found in smaller-sized rings (Table 8.1).

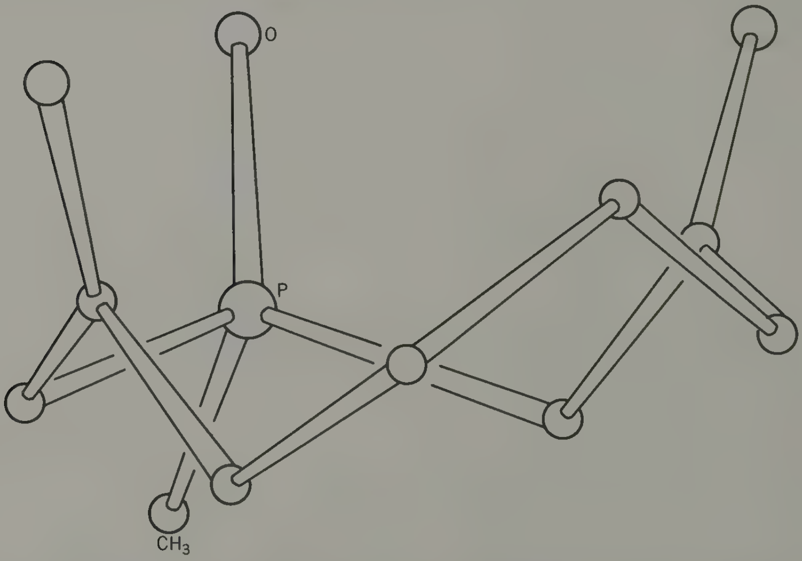
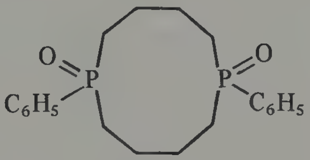


Figure 8.1 Structure of 1-Methyl-3,8-diketophosphonane 1-Oxide (courtesy of Andrew T. McPhail).

10-Membered Rings The only representative so far reported is the diphospha compound **65**,[90] which is said to have the normal conformation of cyclodecane. Although the average C-P length is a typical 1.804 Å, the internal C-P-C is increased to 110.8°, which is the largest angle yet recorded for a phosphorus heterocycle. The two P-phenyls are in the pseudoaxial positions, the oxygen pseudoequatorial.



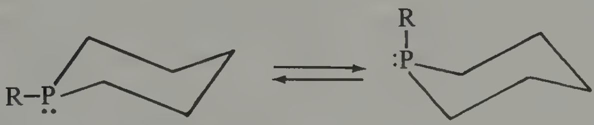
65

8.2 CONFORMATIONAL PROPERTIES OF PHOSPHORUS HETEROCYCLES IN SOLUTION

As is true in carbocyclic chemistry, more is known about conformational behavior of the 6-membered phosphorus-containing system than of other ring sizes, and the subject has earned an important part of a recent review on the family of pentamethylene heterocycles.[91] Much less is known about conformational aspects of 4- and 5-membered rings. The emphasis in this section is on the dynamics of the conformational equilibrium; steric differences in phosphorinanes that influence NMR properties and are useful for configurational studies were discussed in Chapters 5-7.

8.2.1 Phosphorinanes

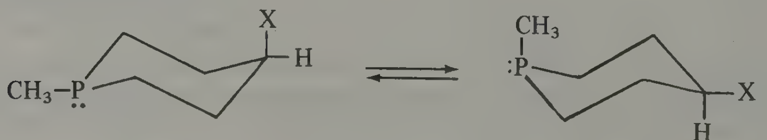
The P(III) phosphorinanes undergo a rapid (on the NMR time scale) equilibration between the two possible chair conformations:



The energy of activation ($\Delta G^{\neq}$) for this process has been determined experimentally[92] by the conventional technique of line-shape analysis; the temperature is lowered progressively, whereupon separate ^{31}P NMR signals for the two conformers appear. For $R = C_2H_5$, the peak coalescence temperature is 177°K, at which $\Delta G^{\neq}$ is 8.3 kcal/mole. The more approximate method of visual estimation of T_c and utilization of $\Delta \nu$ at the low temperature limit gave a similar value (8.4 kcal/mole) as well as values in the range 8.7-9.3 when the P-substituent was methyl, *i*-propyl, or phenyl. These values are slightly less than that of cyclohexane (10-11 kcal/mole), but predictable theoretically[93] from force-field calculations as a consequence of the smaller torsional energies in the required rotation of the ring C-P bonds. The equilibrium has some remarkable features[92]: (1) At low temperatures (130°-150°K), the equilibration is halted and concentrations of the individual conformers can be measured directly by their different ^{31}P signals (for PCH_3, also by its ^1H signal). It is then found that the equatorial conformers are in predominance, but by surprisingly small amounts [$K_{e/a}$ = 2.03 (CH_3), 2.10 (C_2H_5), 2.33 (C_6H_5)]. This clearly indicates that the axial form is destabilized by the usual nonbonded interaction with the axial 3,5-protons, but that the ring has a way of adjusting itself to make this interaction minimal. As noted in Section 8.1, this energy minimization is accomplished by a flattening of the ring about the P-C bonds, whose torsion angles are reduced to about 45° from the usual 55°. (2) For simple P-substituted derivatives, the entropy change is significant and cannot be ignored as is done in cyclohexanes ($\Delta S°$ P-CH_3, -3.4 ± 0.7 eu; P-C_2H_5, -3.2 ± 1.6; P-C_6H_5, -2.6 ± 0.9). (3) As a consequence of these $\Delta S°$ values, and because the enthalpies ($\Delta H°$) calculated from the equilibrium constants are very small, an increase in temperature to 27°C causes the position of equilibrium to change so that the *axial* form is in slight predominance (roughly 2:1; $\Delta G°_{27°C} = +0.35 \pm 0.07$ for CH_3, $+0.26 \pm 0.12$ for C_2H_5, $+0.19 \pm 0.10$ for C_6H_5). This result for P-C_6H_5 is, of course, in accord with the crystallization phenomena for both 1-phenyl-4-phosphorinanone[17] and 1-phenyl-4,4-dimethoxyphosphorinane,[18] which crystallize exclusively in the axial conformation. NMR properties (e.g., $^2J_{PC}$ values; Chapter Six) also are explainable on the basis of an equilibrium biased to the axial side. Again, recent force-field calculations[93] have been able to reproduce these experimental results, at least for P-CH_3 and P-C_2H_5. (4) Increasing the bulk of the P-substituent to $(CH_3)_2CH$- and $(CH_3)_3C$ produced the anticipated shift to the equatorial side, although the experimental methods were not adequate for determining quantitative values.

Phosphorinane itself, bearing a hydrogen rather than alkyl, has an even higher preference for the axial conformation at room temperature (at least 9:1).[94] The ^1H NMR spectrum shows the expected splitting from an axial α-H (12 Hz) and an equatorial α-H (2.5 Hz) coupled to an axial PH; signals for the equatorial PH conformer were not detected. In this case, an attractive interaction between the P-H and axial protons on C-3,5 has been proposed to explain the large preference for the axial conformer.

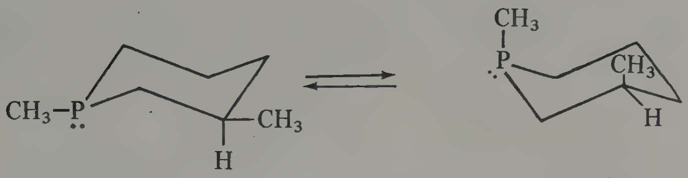
With this understanding of the conformational equilibria, it then becomes possible to interpret some other effects in phosphorinane stereochemistry: (1) Given the positive $\Delta G°$ values, the placement of almost any common substituent on the 4-carbon will bias the equilibrium so that conformation **66b** will predominate over **66a**, as most substituents on cyclohexane have $\Delta G°$ values that are *negative* by substantial amounts.



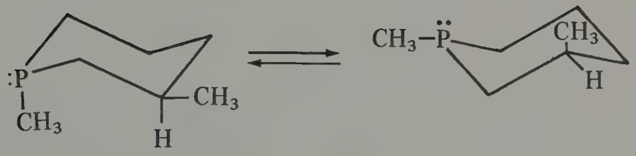
66a **66b**

This is clearly seen in the case where X = CH_3 ($\Delta G^\circ = -1.7$, ax → eq); NMR properties of the trans isomer are easily interpreted by assuming that the contribution from the P-equatorial form **64a** is negligible.[95] It is even true for a small group such as OH ($\Delta G^\circ = -0.89$ in benzene); 4-OH forces P-CH_3 largely into the axial position, a fact that was learned from chemical and NMR properties[96,97] before the quantitative understanding was developed, and which is just the opposite of the case for CH_3 pitted against 4-OH on cyclohexane. The effect holds also for P-phenyl; even though this group is considerably "larger" in terms of ΔG° values from cyclohexane studies (−2.6 to −3.1), it is no greater in effective size than CH_3 when on phosphorus, a result understandable from the X-ray analyses that show the benzene ring aligning itself in the mirror plane passing through P and C_4. The benzene ring may also readily relieve the compression by displacement from the P-atom, as there is no fourth group on P to interfere with (buttress) this phenyl displacement. Consequently, 4-OH forces even P-phenyl predominantly into the axial position in the cis isomer!

Substituents at other ring positions will cause displacements in the position of equilibrium predictable on the basis of the above considerations. Thus, a 3-methyl group can form the cis, trans isomers **67a** and **67b**, each of which can theoretically exist in another conformation (**67a′** and **67b′**).



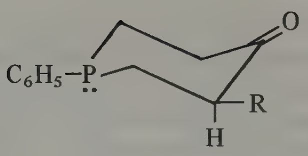
67a **67a′**



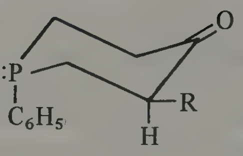
67b **67b′**

However, there exists strong ^{13}C NMR evidence indicating, as predicted, that only the former conformations are important[95] (i.e., δ C-CH_3 identical in both; Δδ P-CH_3 consistent with conformationally rigid models).

This approach to predicting conformational biasing should apply to other systems as well. Thus, a 3-substituent on a 4-phosphorinanone should demand the equatorial position in both cis (**68a**) and trans (**68b**) forms, making them differ by the disposition of the P-substituent.

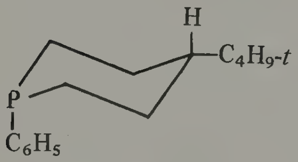


68a

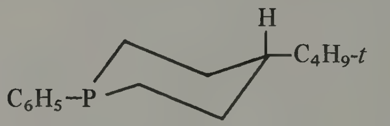


68b

This has been demonstrated in the case of the 3-CN and 3-$COOC_2H_5$ derivatives[98] by the presence of two ^{31}P signals and a ^1H signal for 3-H that has axial coupling characteristics. These compounds also have a high concentration of the enol form, and thus equilibration of cis and trans isomers occurs with ease. ^{31}P NMR analysis of solutions in certain solvents (e.g., dioxane) shows that all three forms are present and the mixtures are readily analyzed. On the basis that the more downfield ^{31}P signal of the keto forms was derived from equatorial P-C_6H_5 (**68a**), and the upfield from axial, as was found for 1-phenylphosphorinane in the low-temperature studies,[92] it was concluded that the P-equatorial form predominated slightly over P-axial (for R = CN, by 3:1 in dioxane). However, there was later introduced[21] a word of caution in the use of ^{31}P signals for assignments of axial-equatorial character that may make it desirable to confirm the assignments with other techniques. Thus, it was found that, as expected, *cis* (**69a**) and *trans* (**69b**) 1-phenyl-4-*t*-butylphosphorinane had different ^{31}P chemical shifts but that the axial form in this case was at *lower* field than the equatorial. The structures were firmly established by ^{13}C NMR and by relation to the oxide of **69b**, whose X-ray analysis was performed.



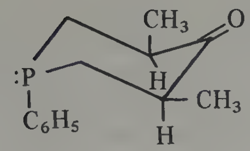
69a, δ $^{31}P = -32.9$

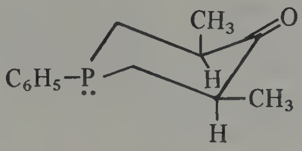


69b, δ $^{31}P = -38.6$

It was proposed[21] that, in this case where two large groups are present, there occurs some distortion of the chair to a twist conformation; this seems to be a reasonable explanation for the reversal of the ^{31}P shifts, which are of course highly sensitive to the steric environment. Although this may be an effect unique to system **69**, it does suggest that additional criteria (especially ^{13}C NMR) should always be used in addition to ^{31}P NMR in conformational studies of P-phenyl phosphorinanes.

The conformations of the isomers of 3,5-dimethyl-4-phosphorinanone agree with the conclusion of only a small positional demand by P-phenyl relative to C-substituents.[99] As synthesized by the addition of $C_6H_5PH_2$ to methyl methacrylate, two major isomers (42:58) were obtained that had the cis arrangement of the C-CH_3 groups (a single ^1H signal for CH_3 was observed for each). The isomers therefore had to differ in configuration at P.

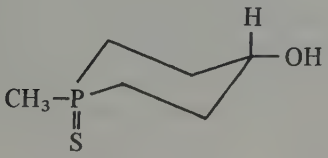




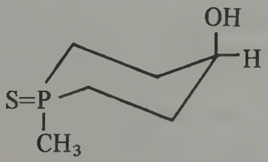
These compounds, incidentally, would be useful models to probe the ^{31}P NMR anomaly, as the isomer structures could be conclusively proved from ^{13}C shift effects (γ-shielding at C-3,5 by axial phenyl).

The conclusions of low steric demand by such common P-substituents as CH_3, C_2H_5, and C_6H_5 should apply to other 6-membered rings, such as 3- or 4-hetero-substituted phosphorinanones. (The effect is already known for 1,3,2-diheteraphosphorinanes.[100]) Bicyclic phosphorinanes may well have similar tendencies. These interesting areas remain unexplored at this time.

For P(IV) phosphorinanes, no direct determination of the position of any conformational equilibria in solution has yet been made, and hence no thermodynamic parameters are available. However, an important generality has emerged from studies of 3- or 4-methylated phosphorinanes[95]: a C-methyl controls the conformation adopted, as it always occupies the equatorial position. This means that a pair of cis, trans isomers will have the same configuration at C-3 or C-4, but different configurations at P. There is an obvious implication that the longer C-P bonds have minimized the nonbonded interactions that accompany placement of a group in the axial position. This generality is valid for both P-oxides and P-sulfides.[95] Even with 4-hydroxy, there is appreciable (but not commanding) occupation of the equatorial position. A consequence of the lack of strong configurational preference at either end of such molecules is that both conformations must have appreciable concentrations in solution. A vivid demonstration of this property is seen[101] in the crystallization phenomena for *trans*-1-methyl-4-phosphorinanol sulfide; the crystal lattice is formed with *both* of the possible conformations (**70a** and **70b**, 2:1) present.



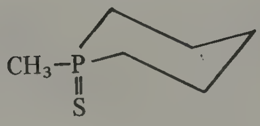
70a



70b

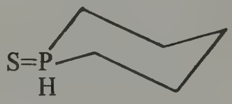
Although it would be incorrect to infer that the same ratio would be present in solution, it certainly can be inferred that both conformations, even the one with two axial groups (**70b**), are significantly populated.

An X-ray analysis of 1-methyl-phosphorinane sulfide is reported to indicate[95] that the crystal has formed from the conformer with equatorial methyl (**71**).



71

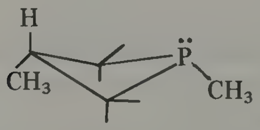
This can be taken to show that there may be a preference of P-alkyl over P = S (and presumably P = O) for the equatorial position, a reasonable assumption on the basis of group size. There seems to be no reason to state this result in the opposite way: that polar groups prefer the axial position. With this view of the importance of group size of P substituents, it is not surprising that sulfur in phosphorinane sulfide (72) takes the equatorial position in preference to hydrogen,[94] and again an explanation based on attractive forces at axial hydrogen may not be necessary.



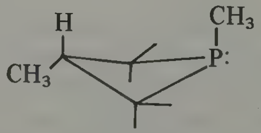
72

8.2.2 Phosphetanes and Phospholanes

Only indirect evidence bears on the behavior of these systems in solution. From X-ray analyses, each is known to adopt nonplanar conformations, but it cannot be assumed that this conformation will remain the exclusive, or even the major, one in solution. In the corresponding cycloalkanes, barriers to ring interchange processes are quite small, but even here little is known about preferred conformations. However, some NMR evidence for phosphetanes does indicate that the direction of folding found in the solid prevails also in solution. This evidence is derived from ^{13}C NMR, where it can be convincingly demonstrated that a 3-CH_3 group takes up the pseudoequatorial position. As discussed in Chapter 6, *cis*- and *trans*-1,2,2,3,4,4-hexamethylphosphetane have quite different values for ^{31}P coupling to the 3-CH_3, which implies a major difference in their preferred conformations.[102] From the Karplus relation for $^3J_{PC}$, it can be deduced that cis has a preference for structure **73a** and trans for **73b**.



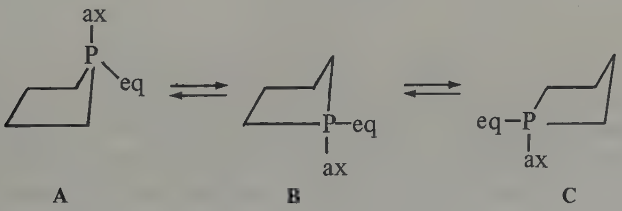
73a



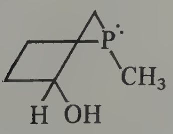
73b

In each, the 3-methyl occupies the pseudoequatorial position; steric demand by P-methyl is therefore of smaller magnitude. This is precisely the situation seen in phosphorinanes and, again, the longer C-P bonds, and the ability of phosphorus to adapt to steric compression, must be involved. It is not yet known if the ring is in a state of rapid interconversion with a small concentration of the other possible conformer. The situation is less clearcut for oxides of phosphetane; the arguments based on ^{13}C NMR for and against the adoption of preferred conformations in solution were discussed in detail in Section 6.3 and are not repeated.

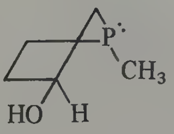
With phospholanes, conventional ring pseudorotation can place P at the flap of an envelope or at two different positions in the 4-atom plane.



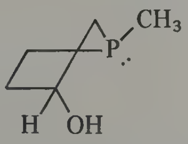
At any position, a substituent on P(III) can occupy a pseudoaxial or pseudoequatorial site. Although P(IV) derivatives from X-ray data seem to prefer form C in the solid, and no doubt to some extent in solution as well, no structural data are available yet for a P(III) derivative. However, in Section 6.2 it was suggested that a pseudoequatorial substituent would better accommodate the size of $^2J_{PC}$ than a pseudoaxial substituent, based on the known stereocontrol of this coupling. Placement of a substituent on a ring carbon could introduce the possibility of a bias to a conformation accommodating the spatial demands of both substituents. The only structural study in solution that bears on this point is based on the 1-methyl-3-phospholanol system[103] and particularly on the relatively large difference between the δ-deshielding of OH on P-CH_3. The cis isomer has the more downfield CH_3 doublet, 13 Hz from that for trans. To accommodate this fact requires placing the two interacting groups closer together in cis than in trans, leading to proposed conformations **74a** for cis, and **74b** or **74c** for trans.



74a



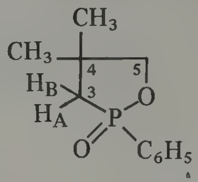
74b



74c

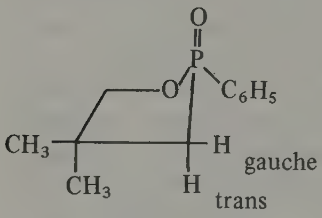
In 74a, P-CH_3 occupies the pseudoaxial position which no longer seems a novelty. Indeed, in cyclopentanol, the hydroxy group is thought also to occupy the pseudoaxial position, attesting to the diminished importance of nonbonded interactions in controlling 5-membered ring conformations. The phospholane system requires more intensive study to place these concepts on sound ground, however.

Conformations of some heterosubstituted phospholanes have been considered from NMR studies. On the basis of no change occurring in the ^1H spectrum after reducing the temperature to −80°, a single conformation was believed[104] to prevail for oxaphospholane **75**.

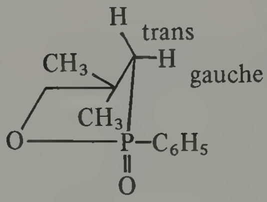


75

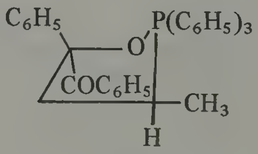
Because H_A and H_B showed different coupling of ^{31}P ($^2J_{PH}$ 12.8 and 7.7 Hz), there was proposed a conformation (**76a**) that placed these protons in trans and gauche positions with respect to P = O (in conformity with a generality discussed in Section 7.2). This conformation is that of an envelope with P at the flap. This is not the only conformation that will give this trans, gauche arrangement, however (e.g., consider **76b**). Based on ^1H NMR properties it is believed[105] that a P(V) 1,2-oxaphospholane (**77**) also exists in a P-flap envelope (see Section 7.2).



76a

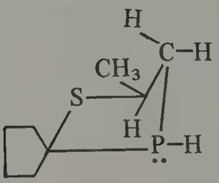


76b



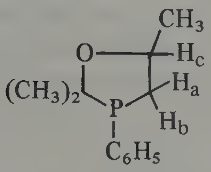
77

A similar envelope (**78**) was deduced[106] for a 1,3-thiaphospholane, on the basis of ^1H-^1H coupling in the fragment HP-CH_2.



78

For the cis and trans forms of the 1,3-oxaphospholane **79**, different and probably rigid shapes have been proposed.[107] This suggestion arises from the observation of a reversal of relative size of $^3J_{H_aH_c}$ or $^3J_{H_bH_c}$ in the isomers. The data were taken to suggest envelope shapes with P at the flap in the cis isomers and O at the flap of the trans isomer, but confirmation by other techniques is clearly called for. Similar coupling effects were found for the oxide.

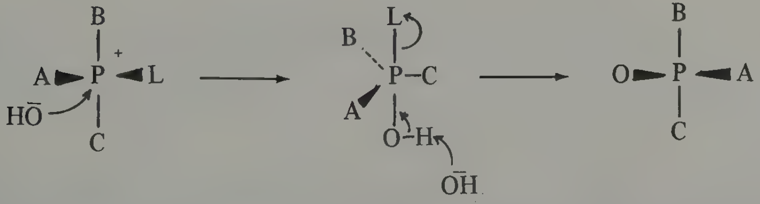


79

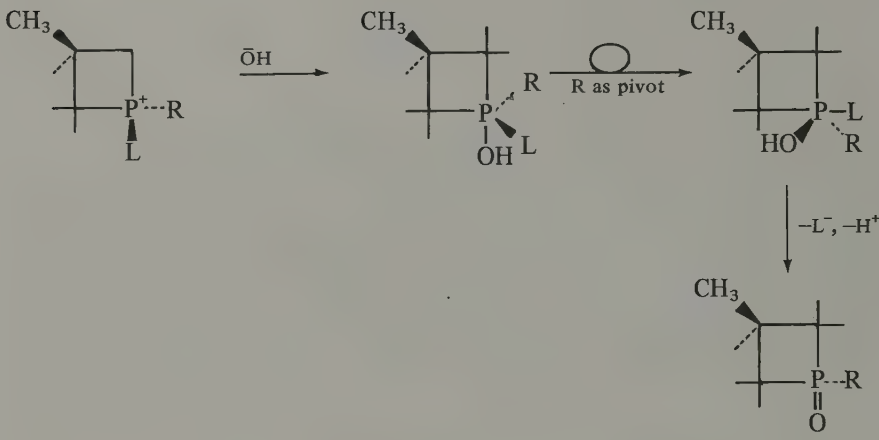
$^3J_{H_aH_c}$ = 6.9 (trans), 9.6 (cis)
$^3J_{H_bH_c}$ = 8.3 (trans), 5.6 (cis)

8.3 INFLUENCE OF RING SIZE ON REACTIONS AT PHOSPHORUS

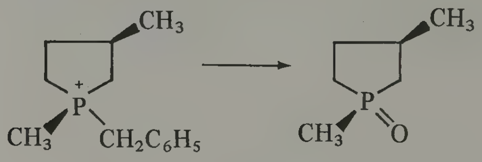
A highly active area of research in recent years has been that concerned with the stereochemical and rate differences that prevail when a family of related compounds differing in ring size is subjected to a common reaction. An excellent review has appeared on this subject.[108] The topic is injected into the present chapter, in very brief form, primarily to highlight the great influence of ring structure on the course of simple reactions. Much remains to be done with other reactions and substrates, and the area will continue to be explored in years to come. The importance of ring size on the steric outcome of a simple reaction is best illustrated in the formation of phosphine oxides by displacement with OH^- of a P-benzyl group from a series of related quaternary phosphonium salts. For noncyclic compounds, the process occurs with inversion of configuration and is kinetically of third order (first in salt, second in OH^-). The well-known McEwen mechanism, outlined below, indicates that the stereochemistry is determined in the first step, in which OH^- attacks to form a pentacovalent, trigonal bipyramidal species, which breaks down on attack of a second OH^- to establish the phosphine oxide.



The initial attack of OH^- places it at an apical position of the trigonal bipyramid, and the leaving group (L) then departs from the other apical position. The net result is inversion of the configuration at phosphorus. Ring size presents a complication in this mechanism in that the ring must span either apical-equatorial (90°) or equatorial-equatorial (120°) positions in the intermediate, and a given ring will take whichever choice best matches its own internal bond angle. This point has already been made in Section 4.1, in the discussion of phosphetane transformations, where it was seen that the 4-membered ring (C-P-C about 80°) generally demands the apical-equatorial position. The consequence of this is that the leaving group cannot depart directly from the trigonal bipyramid as formed, but must await a pseudorotation (polytopal rearrangement) to place it in the requisite apical position. It then departs, but with the consequence that phosphorus *retains* its configuration in the oxide product.



For phospholanium salts, whose internal C-P-C angle is about 95°-96°, the outcome is also clearcut; the ring takes up an apical-equatorial site, and *retention* of configuration is again found in the oxide. For example, from salt **80**, the only product was oxide **81**.[109] The trans salt similarly gave the trans oxide.

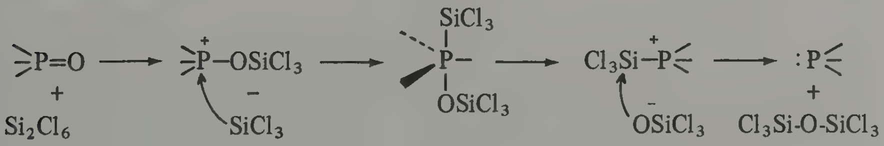


80 81

For a phosphorinanium ion, the situation is more ambiguous; the internal angle is probably best typified by that in P=O and P=S derivatives, which have values in the 100°-105° range (Table 8.1), and this gives the ring the choice of being equally uncomfortable with either a 90° or 120° fit in the trigonal bipyramid. This is precisely what is observed in the OH^- reaction; some oxide product is formed with retention, and some with inversion, the latter resulting from the 120° fit being taken up, which places the leaving group in the apical position.[110] The retention/inversion ratio varies in subtle ways with the nature of the substituents on the 6-membered ring,[110c] but the dual stereochemical pathway is clearly established. With a 7-membered ring, the reaction proceeds entirely with inversion,[111] a clear indication that this ring cannot span the 90° site of the trigonal bipyramid. The same is essentially true for the 8-membered ring.[112] However, the trend observed above for benzyl phosphonium salts is not to be taken as absolute, for there can enter other factors that modify the preference seen for a given ring size. Thus, if phenyl (a poorer leaving group) is to be displaced from a 5-membered ring salt, it is generally found that some inversion (causing stereomutation) will also occur,[113] and if a highly electronegative group ($-OCH_3$,[114] $-OSiCl_3$[115]) is to be displaced, its demand for the apical position is so strong as to deny this position to a small ring, thus forcing it equatorial-equatorial and leading to predominant inversion of configuration. In the 6-membered ring, *complete* inversion can occur in the displacement of CH_3O^-. This competition of stereoelectronic and ring strain effects must always be kept in mind when attempting to predict the outcome of some new process with a ring system.

Such considerations of the steric demand of rings for certain sites on the trigonal bipyramid should be made before conducting a reaction that is known, or is likely, to proceed via the pentacovalent state, as either retention or inversion can occur. On the other hand, if a reaction follows a mechanism that does not involve this state, then a consistent stereochemical result can be expected regardless of ring size. The well-known process of deoxygenation of phosphine oxides by silicon compounds should be considered in this context, for there are reagents known to fit into both categories. The subject has been extensively reviewed.[116,117]

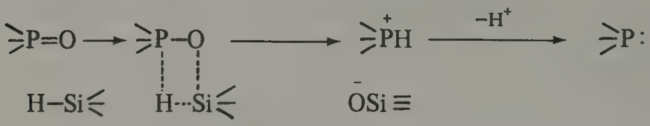
1 Deoxygenation via P(V) forms. This mechanism has been well established[115] for reductions with Si_2Cl_6 or $HSiCl_3$-$(C_2H_5)_3N$. Consistent with this mechanism,[118] acyclic, optically active phosphine oxides are reduced with inversion. An intermediate 82 has been proposed as common to both processes, as illustrated below for the case of Si_2Cl_6.



82

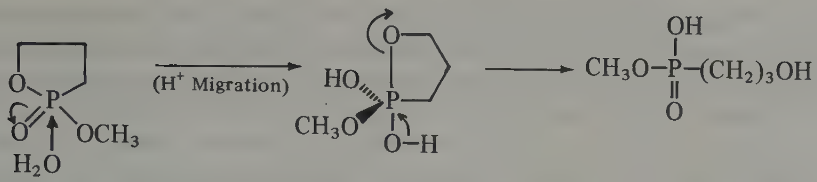
It is obvious that the constraint of a 4-membered ring will prevent ready formation of an intermediate when two equatorial positions of 82 are occupied; as in phosphonium salt hydrolysis, the nucleophile $^-SiCl_3$ attacks at an apical site and the $OSiCl_3$ fragment is forced into an equatorial position. Pseudorotation then occurs to place this group apical for departure, and the net result is retention of configuration at phosphorus.[119,120] Inversion is experienced with phospholanes[115] (and presumably larger rings[116]), as the ring strain is not as severe in the diequatorial form and in this case is less important than the stereoelectronic demands. With highly strained phospholane oxides as in the bridged structures from dimers of phosphole oxides (Section 2.7) retention might well be experienced.

2 Deoxygenation with retention. When the reducing agent is $C_6H_5SiH_3$ or Cl_3SiH (also when complexed with the weak bases pyridine or dimethylaniline), retention is the result for acyclic, optically active phosphine oxides[121] and for cyclic compounds regardless of ring size (examples of 4- through 8-membered rings are known[111,112,122]). A general mechanism[121,122] that accounts for this result is shown below, where hydride transfer to P is believed to occur from the same face as O, synchronously with its removal by silicon.

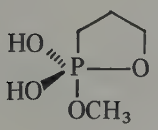


Some complexation on O with the more electrophilic trichlorosilyl reagents may also be involved, but this would not influence the steric result. Some racemization[123a] with the use of $HSiCl_3$ is not uncommon [possibly via a P(V) form] but, except in the case of certain phosphetanes,[123b] phenylsilane was stereospecific in the numerous reactions so far reported. One case[124] of inversion in the use of $HSiCl_3$ on a bridged phosphetane oxide has been attributed to stereomutation by HCl.

Another aspect of ring strain effects is that of influence on reaction rates. Effects can be felt in various types of processes, summarized[108] as occurring at (1) electrophilic phosphoryl and phosphonium centers, where attack by nucleophiles leads to the already familiar pentacovalent intermediates, (2) nucleophilic P(III), where addition of electrophiles creates tetrahedral intermediates with expansion of the C-P-C angle of the original heterocycle (98-100°), and (3) electrophilic P(III), where addition of nucleophiles creates a $P(IV)^-$ species of presently uncertain geometry (an example of which was seen in Section 4.1 in the displacement, with inversion, of Cl from a chlorophosphetane). The best known case is the first of these, typified by the extraordinary rate increase (relative k of 10^6) seen in the acid hydrolysis of cyclic versus noncyclic counterparts. Encountered early with 5-membered cyclic phosphates[125] and oxyphosphoranes[126] (both being 1,3,2-dioxaphospholanes), the effect also prevails for cyclic phosphonates[127] (1,2-oxaphospholanes, 10^5), which exclusively undergo ring-opening. Both the rate effect and the direction of the displacement are readily explained[128] by the following mechanism.



The initial attack of nucleophilic H_2O creates a P(V) form that increases the strain in the 5-membered ring, as it must assume the apical-equatorial position with a reduction in angle from about 105° to 90° (becoming diequatorial would produce a similar strain in the opposite direction). It is the relief of this strain, which easily occurs by the displacement of the ring oxygen from the favored apical position, that accounts for most (an increase in entropy in the transition state approaching the P(V) form may also be important[108]) of the enormous rate increase relative to a noncyclic model. Furthermore, this view explains beautifully why *only* the oxygen in the ring, and not the OCH_3 group, is displaced; for the latter to achieve the requisite apical position for departure, a pseudorotation to 83 must occur, thus creating a higher-energy situation of a carbon occupying an apical position and yet another O going equatorial. (In cyclic phosphates, this problem does not exist and some exocyclic displacement does occur.) How then can it be explained that a cyclic phosphinate (a phospholane) hydrolyzes at much the same rate (faster by 2) as a noncyclic model?[128] The pentacovalent form will have high-energy features however it is formed, for example, in 84 through ring strain, in 85 through unfavorable stereoelectronic dispositions.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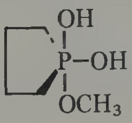
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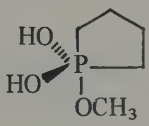
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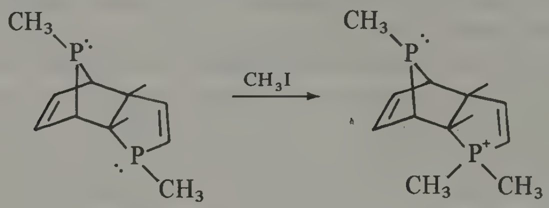
The pitting of the favorable against the unfavorable aspects of each possibility in the case of the phosphinate results in a standoff, and the rate is virtually the same as in the noncyclic model. The balance need not be so close, however, in every case. The displacement of benzyl from phosphonium salts, considered already from the stereochemical standpoint, proceeds at quite different rates for 5- as opposed to 6-membered rings, being 10^3 times faster for the former.[129] This is clearly due to the greater ring strain in the trigonal bipyramid incorporating a 5-membered ring; its relief is responsible for the faster displacement of benzyl.

The behavior of the new diphosphine 86 towards reaction with 1 mole of methyl iodide illustrates the importance of strain considerations in reactions of electrophiles with P(III) centers. The product (87) is largely that from attack at the 2-phospholene phosphorus.[130] The contraction of the angle at the bridging phosphine (probably < 90°) would persist in the quaternary salt, which ideally would have tetrahedral angles. A salt formed at this P would therefore be constructed with the high-energy feature of ring strain. No such exalted strain difficulty is present at the 2-phospholene P, and reaction occurs here selectively. This reasoning is similar to that developed[108] to account for the generally reduced reactivity of cyclic versus noncyclic P(III) compounds toward electrophiles.



86 87

In the basic hydrolysis of phosphinates bearing the same carbon framework, it is the bridging P that reacts the faster (much faster also than monocyclic models), as the strain in the ring is partly relieved by the creation of the trigonal bipyramid intermediate.[131] Strain considerations therefore account nicely for the different sites of attack by electrophilic and nucleophilic reagents on this system.

The detailed review of stereochemistry of heterocyclic phosphorus compounds by Gallagher (see Ref. 100) contains considerable elaboration on points made in this chapter, and provides other examples of great interest.

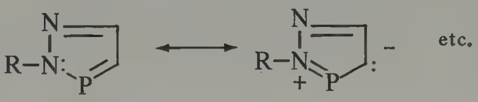
8.4 PARTICIPATION OF P IN CYCLIC ELECTRON DELOCALIZATION; AROMATIC P COMPOUNDS

One of the fastest growing areas of cyclic phosphorus chemistry is that concerned with the incorporation of P functions in structures where they can make a contribution to a 6π-electron delocalized system. Phosphorus may be involved in such phenomena in several different ways, and each monocyclic system then can have benzo- or hetero-aromatic rings present, so that a very large field is at hand. It is convenient for discussion purposes to classify the various ways in which phosphorus can participate in delocalized systems:

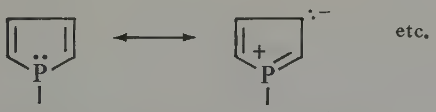
Type 1 A C-P double bond based on P(II) can add two π-electrons to the four of a diene unit to create the aromatic sextet, as in the λ^3-phosphorins.

Variations include the replacement of one or more carbons by N or even P. The double bond based on P(IV), as in the λ^5-phosphorins, can be included here even though the bond is formed from a d-orbital on P that must give it different character, as is discussed.

Type 2 The C-P double bond (λ^3 or λ^5) in a 5-membered ring, along with another double bond and an atom contributing a lone pair, constitute a 6π-electron system, as in the diazaphospholes.

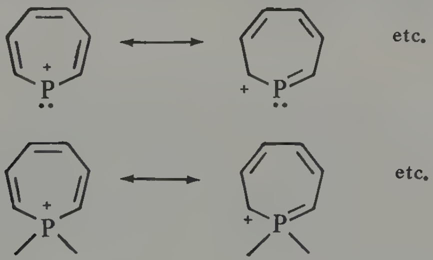


Type 3 The lone pair of P(III) and the four π-electrons of a diene unit in a 5-membered ring can constitute a cyclically delocalized system, as in the phospholes.



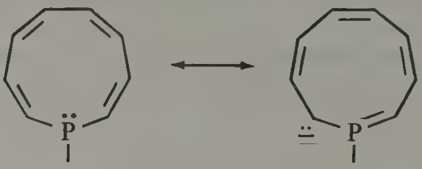
Carbon, in principle, may be replaced by N in this system.

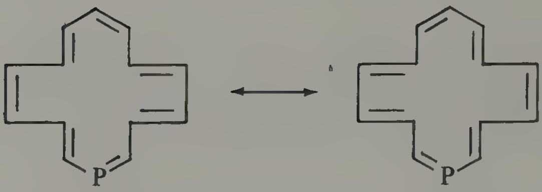
Type 4 Phosphorus may use an unoccupied orbital (p- from $>\mathrm{P}^+$, d- from $>\overset{+}{\mathrm{P}}<$) to form an aromatic system in a 7-membered ring with a triene unit, in the same way that a carbonium ion establishes the tropylium ion.



Type 5 As in type 4, positive phosphorus may act as does a carbonium ion in establishing the pyrylium ion.

Type 6 By any of the above types, phosphorus may participate in creating other Hückel $4n+2$ systems, where $n = 2,3$ etc.; phosphonin and phospha[14]-annulene (unknown) are illustrative of these heteroannulenes.

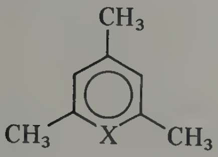




What are the chemical and physical consequences of placing P in such systems? Is there an "aromatic chemistry" possible for this element? This section will view the considerable body of literature on the subject from this standpoint, but will make no attempt to present a complete survey of the properties of each type of system. Such surveys are available on the phospholes,[132-134] the phosphorins,[135-138] and some of the aza derivatives based on P(II).[138] Synthetic methods leading to the phosphole ring were discussed in Chapter 2, the phosphorin ring in Chapter 3, and the larger rings in Chapter 4. As necessary, synthetic methods leading to the other systems will be introduced.

8.4.1 Type 1

THE λ^3-PHOSPHORINS. Of all the various types of systems, the phosphorins are clearly the easiest to classify as aromatic and alone can provide the answer that there is indeed an aromatic chemistry for phosphorus. The remarkable stability of the system has allowed many derivatives to be prepared, both mono- and multicyclic. The system can take on functional groupings of aromatic chemistry and impart to them the expected chemistry. Thus, a hydroxy group replacing a ring proton remains in this form (i.e., is phenolic) and does not ketonize. Already discussed in preceding chapters are the compelling properties of molecular structure by X-ray analysis (Section 8.1), which shows the ring to be planar and the two C-P bonds to be of equal length, intermediate between single and double; the C-C bonds are similarly modified. Also discussed was a ring current augmenting the deshielding of ^1H nuclei, especially significant being the influence at the β- and γ-positions where the local magnetic anisotropic effect of the P-atom is minimized (Section 7.4); when corrected for the anisotropic effect, these values are only slightly upfield of benzene[137]. Other physical properties that directly indicate the presence of aromaticity are ultraviolet spectra, which resemble closely the spectra for the corresponding benzene or pyridine, as in the systems below.[135]



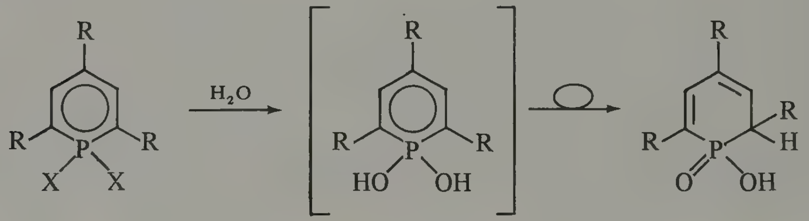
	λ_{max} (ϵ)
X = CH	213 (8200) and 263 (219)
N	212 (8800) and 265 (6630)
P	227 (27,200), 261 (7390) and 312 (246)

The long wavelength absorption in the phosphorin appears to be an n→π* transition, while the others are π→π*. Photoelectron spectra (UV), first taken on 2,4,6-tri-*t*-butylphosphorin[139] and more recently on phosphorin itself[140] and benzo derivatives,[141] provide a measure of the energies of the filled molecular orbitals of the ground state and reveal great similarity for phosphorin to the spectrum of pyridine (and other heterobenzenes). One unusual feature was that the HOMO in phosphorin is a π-molecular orbital, whereas in pyridine it is the n-orbital. Theoretical studies of the bonding in phosphorins (e.g., Ref. 142) support this picture of similarity to aromatic systems, as well as the use of a phosphorus p-orbital in the π-bonding. Other properties of phosphorins that have been determined are ^{31}P NMR spectra (Chapter 5), which show strong deshielding (δ +211 in the parent), ^{13}C NMR spectra (Chapter 6), and mass spectra, in which the molecular ion is generally the most intense peak,[135] as it is in phosphorin itself.[143] Fragmentation of the latter produces $C_2H_2^+$ as a major ion, with some production of HCP^+, and the dipole moment of phosphorin, which, as expected from the diminished electronegativity, is considerably smaller (1.54 D) than that of pyridine (2.215 D) and with the same direction of the dipole[144] (P negative).

Phosphorins have some unique chemical properties. P(II) is a state scarcely known (but attracting increasing attention) outside aromatic heterocycles, and to some extent the peculiar chemistry of phosphorins is dictated by this state. However, the double-bond system is intimately involved in many of the reactions. Most of the chemistry known so far has been developed with 2,4,6-trisubstituted derivatives, both stabler and more easily obtained than simpler derivatives. Many of the same properties are found for the benzo derivatives and are not separately cited in the following summary of general properties.

Reactions at P. The lone pair on phosphorus is not available for protonation or quaternization, even under forcing conditions. This is a striking departure from the chemistry of pyridine, and more notably from that of other phosphorus functions with a lone pair. The low basicity has been attributed both to an electronic effect on the lone pair[145] (which calculations indicate to have some "delocalized" character[146]) as well as to resistance of the system to the necessary geometric deformation to form the protonated species with its widened C-P-C angle.[147] A report[148] that H-bonding studies on 4-cyclohexylphosphorin indicate its basicity to be greater than triphenylphosphine suggests that salts could be made in this particular case, as this is a common property of triphenylphosphine. This has not yet been achieved, however, and the possibility remains that the H-bonding involves the π-system and not the lone pair. With "softer" Lewis acids, σ-bonding can occur at P, as happens with metal ions.[149] π-Complexes can also be prepared from phosphorins, one example being the $Cr(CO)_3$ complex of 2,4,6-triphenylphosphorin.[150]

1,1-Dihalo adducts may be formed[151], in a typical phosphine property, from bromine or chlorine. Light facilitates the process. The adducts appear to be covalent (λ^5) and the halogen can be displaced with nucleophiles to give a variety of other λ^5-derivatives in a highly useful process. Hydrolysis might be expected to create a phosphoryl group, but this process is accompanied by proton migration from the intermediate dihydroxy form 88 to the 2-position, forming nonaromatic phosphinic acids (89) instead. This may be a reflection of the carbanionic (ylide) character at C-2 in the λ^5-phosphorins (vide infra). Only recently, and in the benzophosphorin system, has a stable λ^5-structure with P-OH been produced (90).[152]



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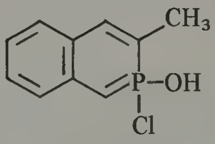
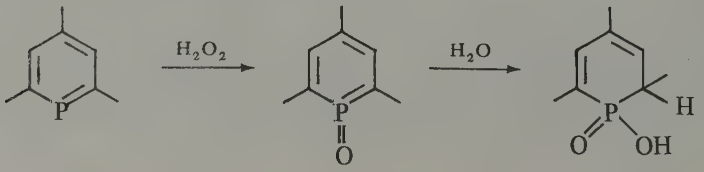
89



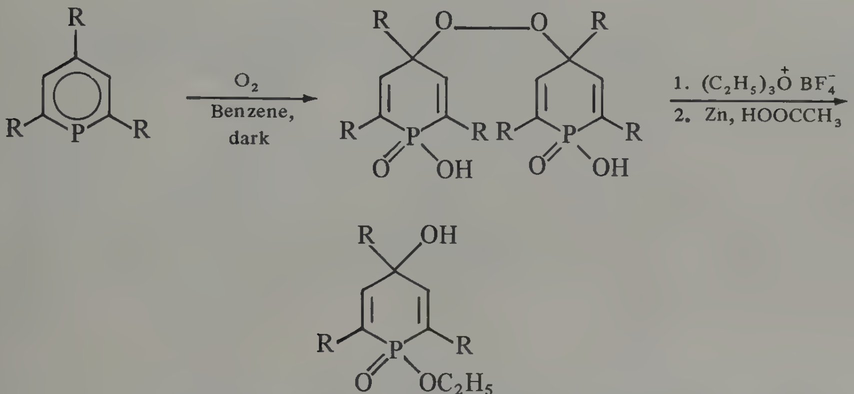
90

Oxidation on phosphorus takes place with a number of reagents, but in no case has a simple phosphine oxide been isolated. Such normally useful reagents as H_2O_2[135] give the phosphinic acid 89. It is not known if this process passes through the 1,1-dihydroxy form (88), which rearranges to 89, or if the phosphoryl group is the initial product in the usual way of phosphine oxidation, and then undergoes very rapid hydration of the C-P double bond.



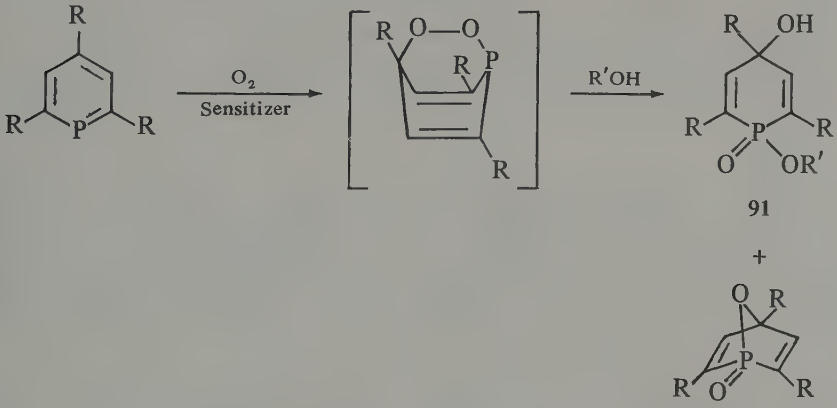
The high sensitivity of the C=P=O group to nucleophiles is a known property,[153] and this may account for the failure so far to achieve the phosphorin oxide as a discrete substance.

Oxidation with some other agents occur both at P and C-4, as in the reaction with oxygen.[135]

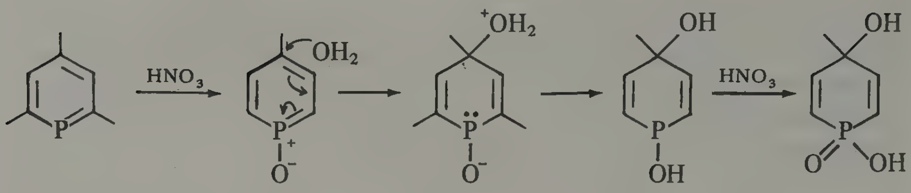


(cis, trans isomers)

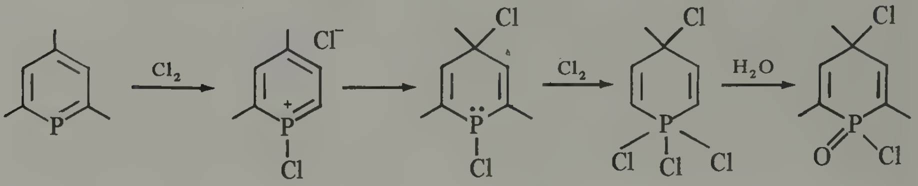
The final products (nonplanar and chiral) of the above sequence have been made in great variety. With singlet oxygen, a nonisolatable endo peroxide is presumed to be formed, as judged by the nature of the products actually isolated:



Oxidation with nitric acid also yields the 4-hydroxy phosphinic acid (91, R′ = H).[135] No mechanism has yet been established for this process but again it seems possible that the initial step is the formation of the powerfully electrophilic P-oxide, which then directs hydration at the 4-position (alternative to 2-). A final step of oxidation then occurs on P.

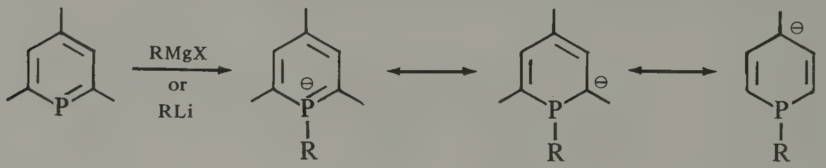


Sensitization of the 4-position to nucleophiles is seen in other reactions, such as in the addition of excess chlorine. After hydrolysis, a 4-chlorophosphinic chloride is obtained.[135] This can be interpreted as follows:

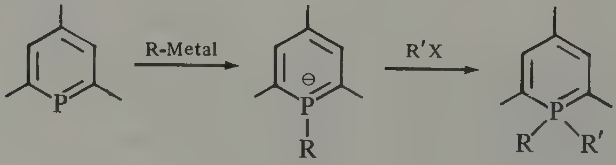


The chemistry of pyridine N-oxides has some resemblance, in that the 4- (and 2-) position is made remarkably sensitive to nucleophiles. Final products are quite different, of course.

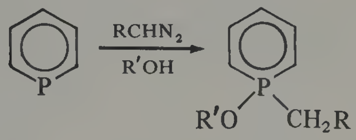
In keeping with the very low nucleophilicity of phosphorins is their increased electrophilicity, made apparent by the smooth addition of carbanionic species.[154]



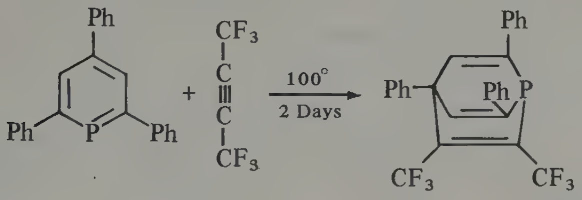
Distribution of the negative charge throughout the system no doubt contributes to the stability of these anions (red). Attack of electrophiles can then occur at either the 2- or 4-positions, as well as at P (forming λ^5-phosphorins). These reactions are extremely useful in preparing phosphorin derivatives, especially in crossing from λ^3 to λ^5.



Carbenes also add to phosphorins, but subsequent changes result in loss of the phosphorus and formation of a benzene derivative.[155] More useful are additions of diazoalkanes, which when conducted in alcohols lead to λ^5-phosphorins.[156]

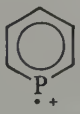


Cycloaddition Involving P and C-4. Diels-Alder reactions occur with phosphorins at the C-P bond, and some unusual barrelene-like structures can be formed.[157] Potent dienophiles (hexafluorobutyne, dicyanoacetylene, arynes) are required to bring out this character in phosphorins, however.

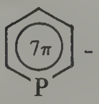


Phosphorin itself also reacts with this reagent under the same conditions.[158] Benzophosphorins (e.g., 10-methyl-9-phosphaanthracene[159]) are much more reactive, forming adducts even with maleic anhydride.

Formation of Radical Cations and Anions. Particularly characteristic of the phosphorin system is the great ease with which either stable radical cations (92) or anions (93) are formed.

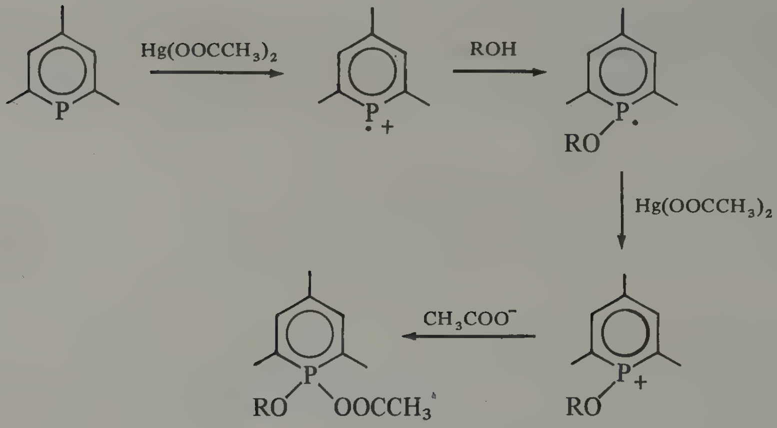


92

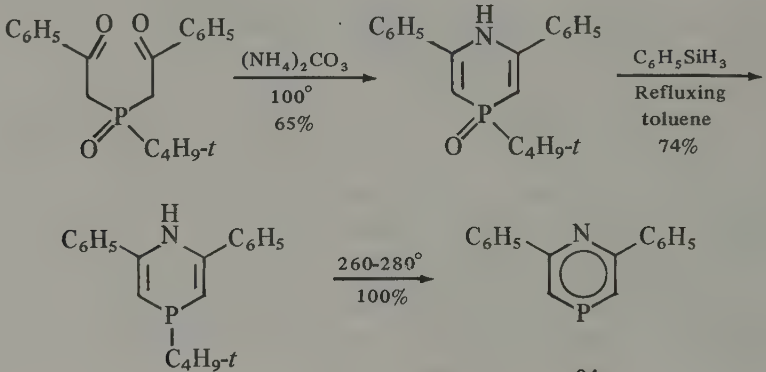


93

The former species result[135] from electron-removal with such reagents as organic free radicals (2,4,6-triphenoxyl), metal ions, or even oxygen. The anions are formed from alkali metals under carefully controlled conditions. Di- and even tri-anions have been detected from these reactions. The radical cations have some synthetic value,[160] as they can serve as relays from λ^3 to λ^5 phosphorins:

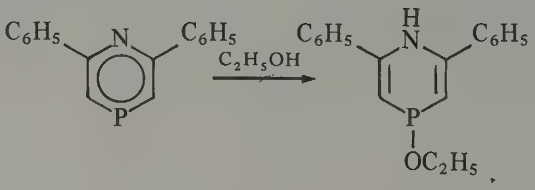


HETEROSUBSTITUTED λ^3*-PHOSPHORINS.* The best characterized compound of this type is the 4-aza derivative (**94**). It is a stable, distillable oil, prepared[161] in excellent yield by the simple sequence below.

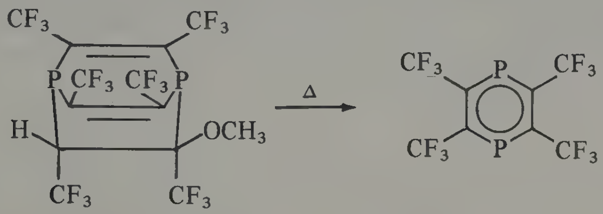


94

The final step is analogous to the thermolysis used to create phosphorins (Section 3.8). The azaphosphorin showed the expected strong deshielding of the ring protons (δ 8.66, but with unusually small $^2J_{PH}$ of 18 Hz; see Section 7.4); the deshielding of ^{31}P (δ +245.4) is exceptionally large, a result of the added strong electron attraction by divalent N. This effect also increases the electrophilic character at P; not only does the expected nucleophilic addition of organometallics to the P=C bond occur, but also less nucleophilic species, such as ROH, ArOH, RSH, and amines, are easily added.

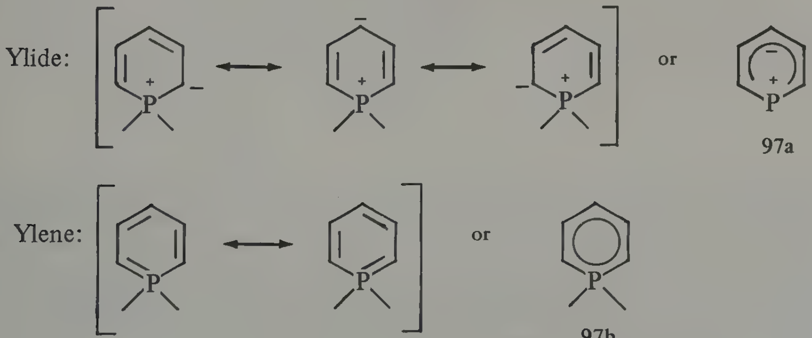


The only other heterophosphorin known to date is the 1,4-diphosphorin **96** prepared[162] by refluxing diphosphabarrelene **95** in hexane. The diphosphorin was too unstable to isolate as a pure substance; it was characterized in the hexane solution by UV spectroscopy (λ_{max} 282 nm, $\epsilon > 4000$-5000) and mass spectrometry (giving a weak molecular ion). Cycloaddition with acetylene derivatives occurred readily at the two P atoms to reform diphosphabarrelenes.



95 **96**

λ^5-*PHOSPHORINS AND HETEROSUBSTITUTED SYSTEMS.* The λ^5-phosphorins, although numerous, stable, and well studied,[135] present something of a paradox. In many respects, they display properties that could be used to characterize them as aromatic, and yet to achieve cyclic delocalization P must use a different orbital (d) than is used in the λ^3-system (p). There has been considerable debate regarding the nature of the bonding in the λ^5-system (and in the phosphazenes as well, where a similar problem exists), and indeed as to whether or not they are "aromatic." To begin with, the system is describable as a delocalized ylide, with a contribution of ylene character from the utilization of a d-orbital.

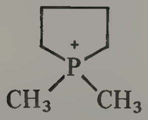


97a

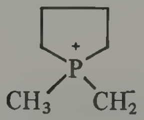
97b

In the most recent theoretical discussion of the bonding,[163] these contributing forms are examined in detail, and photoelectron spectra are interpreted. The conclusion, in simplified terms, is that there is indeed a superposition of bonding types, which the authors represent by **97a** and **97b**. Form **97a** can be viewed as an internal salt, in which the positive P atom is quite separate from the delocalized pentadienide unit, but provides electrostatic stabilization; the PES spectra are primarily interpreted as resulting from this delocalized unit. Form **97b** includes the feature of

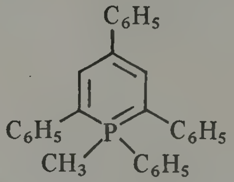
π-bonding involving P; where the d_{yz}-orbital is used, the system gains in stability and can be considered to be of Hückel character (i.e., "aromatic"). The shortening of the C-P bond, as determined by X-ray analysis, to a value (1.72-1.75 Å, Section 8.1) less than that of a regular single bond is explainable by the contribution made from this form. The ^{31}P shifts are upfield of the region expected for phosphonium ions and are closer to values for simple, nondelocalized ylides. Exact models are not available, but the data below (from Chapter 5) suggest these relations. Allowance needs to be made for the deshielding always seen in 5- versus 6-membered rings; compounds **98** and **99** then have comparable influences from the ylide moiety.



+47.8

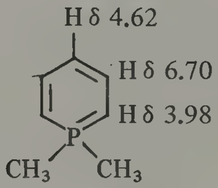


98, +24.9



99, −6.5

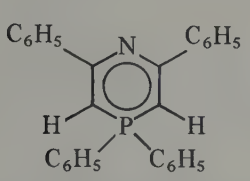
Ylide character also appears to dominate in the ^{1}H NMR spectra, and, taking seriously the criterion for aromaticity[137] that a ring current must be present and substantial deshielding of protons must occur, then the λ^5-phosphorins fail the test, as the values[164] below indicate.



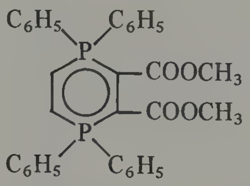
100

Similar upfield shifts are reported for a series of 1-alkoxy-1-phenyl-4-substituted phosphorins.[165] The ^{13}C NMR spectrum of **100** also points to high electron density on carbon[164]; for example, signals for C-2,6 appear at δ 67.5 (94 Hz), more than 60 ppm upfield of the usual position for olefinic or aromatic carbons, and quite in keeping with ylide character. Regardless of these ambiguities, a considerable chemistry has been developed around the λ^5-phosphorins, and they are intriguing substances. This chemistry is reviewed in detail by Dimroth[135] and is not summarized here. Suffice it to say that in keeping with their ylide character they are basic substances, easily protonated (reversibly) at C-2; some are alkylatable as well, but none show the well-defined ylide character required to participate in the Wittig olefin synthesis. This was taken as an early chemical indication of their "aromatic" character, later supported by the observation that certain compounds can experience displacement of a ring 4-substituent by an electrophile.[166]

With this background of uncertainty regarding λ^5-derivatives, only brief mention will be made of heterosubstituted derivatives. The 4-aza (**101**)[167] and 4-phospha (**102**)[168] systems are both known. Both have the relatively high field signal for the α-proton; the former has as well a shielded ^{31}P nucleus.

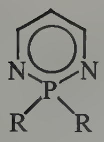


101 $\delta\ ^{1}H\ 5.10\ (^{2}J = 12)$
$\delta\ ^{31}P + 1.5$

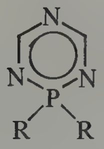


102 $\delta\ ^{1}H\ 5.0\text{-}5.6$ (m)

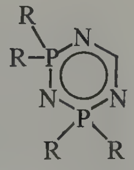
Some di- and tri-aza-λ^5-phosphorins for which λ^3-forms have not been synthesized are also known; although they lack C-P bonds, the parent systems are shown below for completeness.



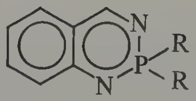
Ref. 169



Ref. 170



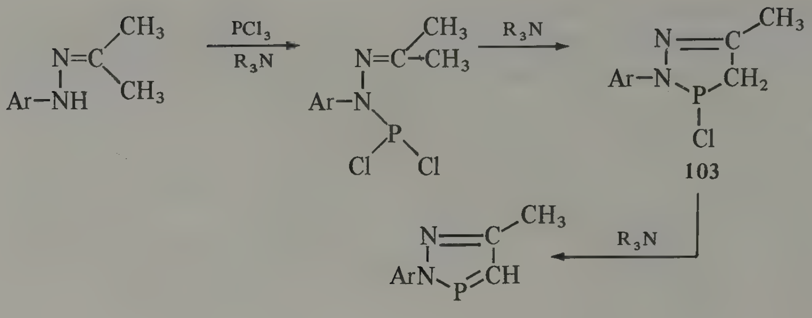
Ref. 171



Ref. 172

8.4.2 Type 2

DIAZAPHOSPHOLES. The 1,2,3-diazaphosphole system was first constructed in 1967 by a Russian group,[173] who continued the study of these substances in following years (e.g., see Ref. 174). The synthesis is remarkably simple. The organic starting material is an aryl- or acyl-hydrazone of a simple carbonyl compound; this is allowed to react with an excess (3 moles) of PCl_3 and triethylamine (3 moles) in a solvent such as ether or CH_2Cl_2 for several hours. The products are generally recovered by vacuum distillation. Yields are quite variable but some as high as 60-80% have been reported. The following explanation of the course of the reaction seems reasonable, although variations are possible.



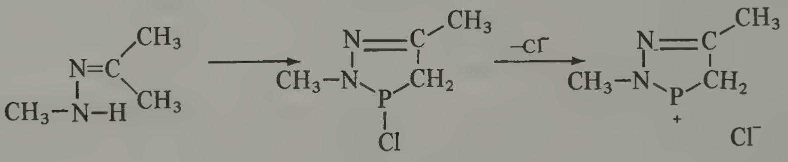
103

104

That the final step is the dehydrohalogenation of a cyclic monochloro intermediate was shown by the actual isolation of species such as **103** in certain cases[174] and the demonstration that 1 mole of triethylamine did indeed accomplish dehydrohalogenation to form the P=C bond. This step is reminiscent of procedures discussed in Section 3.8 for establishing C=P in phosphorins, where allylic phosphinous halides are dehydrohalogenated.

$$-\underset{\text{Cl}}{\underset{|}{\text{P}}}-\text{CH}=\text{CH}-\text{CH}_2- \xrightarrow{\text{DBU}} -\text{P}=\text{CHCH}=\text{CH}-$$

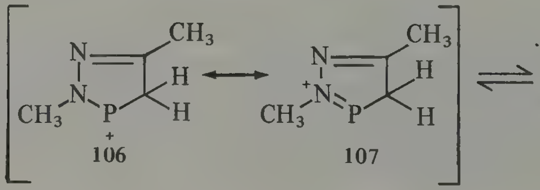
In later work, Schmidpeter showed[175] that methylhydrazones also could be used in the process, thereby preparing a series of 2-alkyl 1,3,2-diazaphospholes. In this case, there was isolated a crystalline intermediate that had ionic character and that was characterized as the dissociation product of the cyclic P-chloride (**105**).

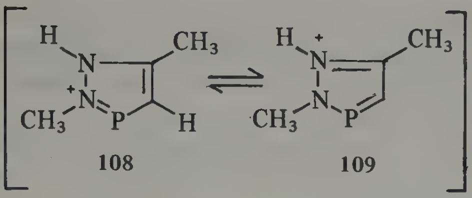


105

106

The initially formed cation **106** is stabilized by delocalization (**107**) as well as by tautomerism to other delocalized forms (**108**, **109**).

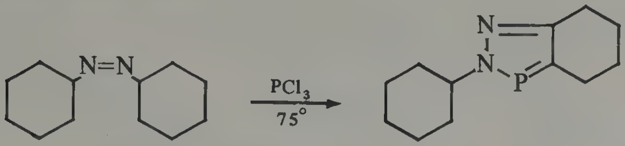




108 **109**

In the tautomeric forms (**108**, **109**) special stabilization is present from the 6π-electron aromatic system, and this is considered to be the major factor in the ready formation of the cationic species. Further treatment with triethylamine gives the free 1,2,3-diazaphospholes.

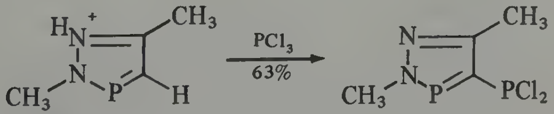
A second approach[176] to the diazaphospholes is based on the use of azo compounds in reaction with PCl_3. Simply heating the mixture at 75° for 1-3 hr produces the phosphole (**110**).



110

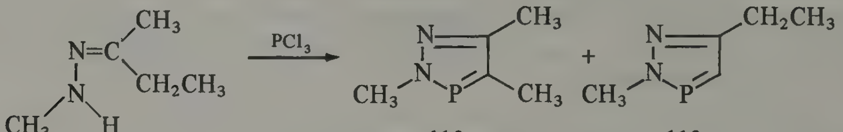
The azo compound rearranges to the hydrazone, which then participates in the cyclization process as in the preceding synthesis.

The spectral properties clearly support the presence of the C-P double bond in these compounds; δ ^{31}P values are in the far downfield region (+200 to +250) characteristic of P(II) in the phosphorins, and the olefinic proton at C-4 is strongly deshielded (δ 7.2-7.8) with the characteristic large $^2J_{PH}$ value (43-45 Hz) of the phosphorins. Two structures have been studied by X-ray analysis[48,49] and, as noted in Section 8.1, the ring is planar and the C-P bond length is like that of phosphorins. This is a strong indication that the double bonds are not localized. This is also suggested by the UV spectra, which have maxima in the region 250-280 nm [e.g., **100**, λ_{max} (hexane) 258 (log ϵ 3.89)]. One instance of an apparent electrophilic substitution at C-4 of a diazaphosphole has been noted[177]; when the preparation of a diazaphosphole from a methylhydrazone purposely employs excess PCl_3 in a longer reaction time than usual, another product is obtained as a distillable liquid. Its ^{31}P NMR spectrum shows the presence of two coupled nuclei, one in the usual diazaphosphole range and the other indicative of $-PCl_2$. This allowed the assignment of structure **111**.



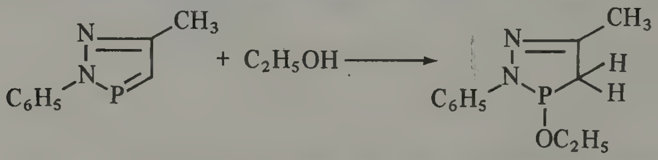
111

No other case of substitution has yet been reported, but this reaction certainly suggests that such processes could be very facile. The reaction has been used to advantage to separate the mixture of isomers that results when a hydrazone of an unsymmetrical ketone is used; two diazaphospholes can be formed (e.g., **112, 113**) by cyclization at the two different α-carbons but only one (**113**) will have an open 4-position for attack by PCl_3. This product is separated from the unchanged diazaphosphole (**112**).



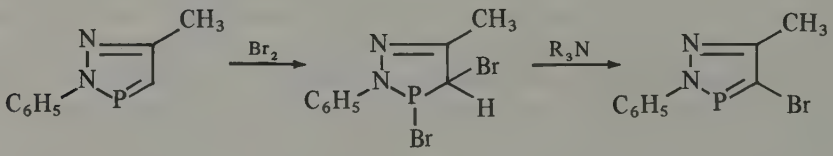
112 **113**

The C-P bond is electrophilic, and nucleophiles readily attach themselves (reversibly) to phosphorus to form diazaphospholene derivatives (e.g., **114**).[178]



114

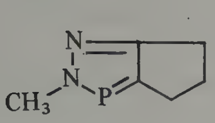
In phosphorins, only nucleophiles of the reactivity of carbanions can bring about a comparable reaction; the attached nitrogen apparently increases the positive character of P. Bromine also adds to the C-P bond[178] and the adduct can be dehydrohalogenated to a 4-bromo derivative of the diazaphosphole.



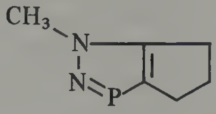
The parent 1,2,3-diazaphosphole system can exist in two tautomeric forms, as do pyrazoles.

115 **116**

The compounds discussed so far have all been derivatives of the 2H-tautomer (**115**). When acetone methylhydrazone was reacted with PCl_3, a small amount of a derivative of the 1H-form was obtained[50]; with cyclopentanone methylhydrazone, equal amounts of the two isomers (**117**, **118**) were obtained.

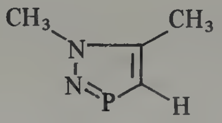


117



118

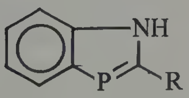
The two were separated by fractional sublimation; 1H-derivatives are the more volatile, and also have higher boiling points. The NMR properties of the 1H isomers are quite in keeping with their structure; the ^{31}P shift of **118**, for example, is +223, and the ring proton is well downfield (δ 7.22) and strongly coupled to ^{31}P (32 Hz). The PCl_3 substitution reaction also occurs at C-4 of **119**.



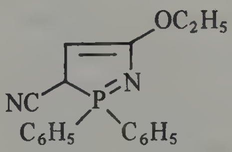
119

The X-ray analysis of **119** (Section 8.1) shows the expected shortening of the P-N bond and lengthening of C-P relative to the 2H-isomer, and all in all there is no reason to believe that substantial differences exist in the delocalization, which clearly depends on use of the π-electrons of the C=P bond.

No example of a benzo derivative of a 1,2,3-diazaphosphole has yet been reported, but benzo derivatives of 1,3-azaphospholes **120** were recently described.[179] A λ^5-derivative of the 1,2-system (**121**) is also known.[180]



120

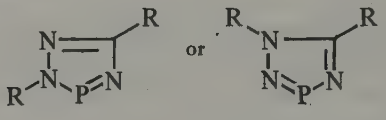


121

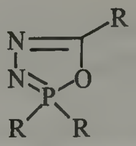
System **120**, prepared easily from condensation of 2-phosphinoaniline with imidoesters, was quite stable. For R=H, the expected low field ^{31}P shift (+ 77.2), and large $^2J_{PH}$ value (39.5 Hz) that convincingly confirm the presence of a C=P bond were both present. Unless the benzo group is a firm requirement for stabilizing the system (which seems doubtful, since phosphorin is more stable then benzo[b]phosphorin), there seems to be little doubt that in time the monocyclic λ^3-parent will be synthesized.

The exciting events of the last few years in this aspect of heterocyclic phosphorus chemistry should stimulate even greater activity, for it is obvious now that phosphorus can be installed in many ring systems, with anticipation of good stability.

Two cases of replacement of C-4 in 1,2,3-diazaphospholes by a heteroatom have been reported. Lacking a C-P bond, they are outside the scope of this book, but are certainly not without interest, and attention is drawn to them with their representations below.



Ref. 181



Ref. 182

The λ^5-system of the oxadiazaphosphole is only of fleeting existence, but it can be trapped in [2+2] cycloaddition reactions. The triazaphospholes, on the other hand, have the good stability of the diaza system.

8.4.3 Type 3

PHOSPHOLES. The phosphorus member of the time-honored family of heterocyclopentadiene derivatives only became known about 20 years ago, and serious study of its properties began just a decade ago. It is logical that it should attract interest as a new member of the family of 5-membered delocalized heterocycles, for there is really no reason, on the surface, for the system not to share in this delocalization with the consequent gross modification of the properties of its two constituent parts, the diene and the tertiary phosphine. To label this delocalization in the 5-membered series "aromatic" causes difficulty, however, and much has been written (e.g., Ref. 183) about whether *any* of the family should carry this label. However, few would disagree that cyclic delocalization is present, and in this discussion that is the term that will be used.

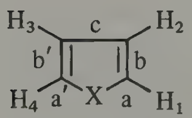
In one sense, thiophene is the best model with which to compare phospholes, for the P and S atoms differ very little in size and both must use 3p-orbitals to overlap with the smaller 2p-orbitals of carbon. Also, both have the potential for involvement of d-orbitals in the bonding, although for thiophene current thinking is tending to deemphasize the role of such interaction.[184] However, the pyrrole system could also be an appropriate model, as it has in common the presence of an exocyclic third grouping, and N and P in tricovalent forms share the property of considerable basicity. In point of fact, neither model is very satisfactory, for phosphorus has its own unique characteristics; one that is highly relevant here is that the phosphines have a high order of pyramidal stability and this places the exocyclic substituent out of the plane of the ring. In pyrroles, the exocyclic substituent lies in the plane, and the hybridization is considered to be sp^2. This set of properties, then, makes the phospholes stand apart in the 5-membered ring series, and only by an experimental examination of their own properties can the importance of delocalization be appreciated. But another feature of phosphole chemistry needs to be considered first: properties related to the electronic characteristics of the system are quite sensitive to substituent effects, and considerable apparent modification of orbital interactions can arise from seemingly minor changes. 3,4-Dimethyl substitution on phospholes especially produces distinct changes in various properties[185] that can be related to diminished delocalization. It has been proposed that distortions of the ring take place to alleviate the crowding of eclipsing methyls, and the efficiency of orbital overlap is diminished. C-Phenyl substitution introduces the possibility of competitive resonance of the ring double bond with the benzene system. 2-Substituents can also be expected to have some degree of steric crowding with the P-substituent. Thus, the worst phosphole to include in any consideration of fundamental properties of the ring is the 1,2,3,4,5-pentaphenyl derivative, followed closely by 1,2,5-triphenyl, the two of these being the first phospholes ever prepared (Section 2.7). Ideally, all studies aimed at elucidating the true nature of the ring should be conducted on monosubstituted derivatives (in the absence, to the present, of a synthesis of the totally unsubstituted parent), but much of the large literature on phospholes is based on the rather readily available 1,2,5-triphenyl derivative. Although this system possesses some fascinating chemistry (discussed in recent reviews[132-134]), the present discussion will focus primarily on the simplest derivatives, with a bias to data that highlight the fundamental characteristics of the ring system. The development of our understanding of the electronic nature of phospholes has been marked by controversy, but there seems to be increasing acceptance of the concept that some degree, even if less than that of furan, of orbital interaction is present. The arguments for and against this position have been evaluated in detail by other authors[132,134] and are not repeated here; in this section, selected aspects of phosphole chemistry are presented from the viewpoint that orbital interaction is important to the system.

First, it must be understood that phospholes represent a stable system. Samples of the monosubstituted derivatives (e.g., 1-benzyl[185]) can be stored for prolonged periods at room temperature if protected from oxidation, and many have been purified by distillation or column chromatography. Some decomposition will occur on prolonged heating (for 1-benzyl, about 50% decomposition after refluxing for 25 hours in xylene[185]), but the nature of the decomposition products is not known. There is no evidence yet that they are Diels-Alder dimers or polymers, although clean dimerization of P(IV) derivatives is a well-known phenomenon (Section 2.7). β-Carboethoxy substitution makes the system quite unstable,[185] but α-carbonyl derivatives are stable.[186]

The molecular structure of 1-benzylphosphole was the first to be determined by X-ray analysis[41] (Section 8.1), and it proved conclusively that the phosphorus retained its pyramidal shape. The heteroatom bond shortening, so characteristic of the other 5-membered rings, was definitely present [1.78 Å; cf. to 1.83 for P(III)-C(sp^2) and to 1.72-1.75 in phosphorins] and suggests the presence of increased bond order from delocalization. The C_3-C_4 bond showed some shortening (to 1.438 Å) but the C_2-C_3 bond did not differ from the double-bond value (1.343 Å). Two difficulties need to be considered, however. The ring is not planar, as in the other 5-membered rings; the P atom lies about 0.2 Å out of the plane of the C atoms. This puckering may in part be a consequence of the conformation adopted by the phenyl group, which lies under the phosphole ring and crowding with ring atoms could be relieved by the displacement of P. Secondly, the pyramidal character of P prevents the lone pair orbital from aligning parallel with the p-orbitals on carbon, which is needed for most effective overlap. This does not mean that *no* overlap can occur, however, as has been pointed out by Dewar[187] and should not be taken to speak against the existence of delocalization.

The interference of heavy substitution with the basic nature of the ring is clearly revealed in a second X-ray analysis,[42] that of 1,2,5-triphenylphosphole. Here the C-P bonds are not contracted (1.822 Å). As noted, this substance has specialized properties, and the structural parameters should not be taken as negating delocalization in the whole family.

Cyclic π-electron delocalization produces a ring current, and there is evidence from ^1H NMR spectroscopy for the presence of this phenomenon in the phospholes. In 1-methyl phosphole,[188] a complex AA′BB′X system results, but the chemical shifts are in the range δ 6.5-7.5, covering the values for thiophene (δ 7.13, 7.35). In 1-benzylphosphole, some of the signals are even entangled with those of the benzene ring.[185] Phosphole shifts are clearly downfield (0.5-1.0 ppm) of any model lacking the possibility for a ring current (e.g., a 2-phospholene; see Section 7.4). The ^1H-^1H couplings are similar to those of other 5-membered heteroaromatics; a comparison with thiophene, which has comparable ring bond angles, is given below.



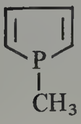
	X = S	X = PR
∠ aa′	92.2°[a]	90.7°[c]
∠ ab	111.5°[a]	110°[c]
∠ bc	112.4°[a]	114.1°[c]
$^3J_{H_1H_2}$	4.92[b]	7.2[d]
$^3J_{H_2H_3}$	2.95[b]	2.0[d]
$^4J_{H_1H_3}$	1.05[b]	1.1[d]
$^4J_{H_1H_4}$	3.45[b]	3.0[d]

[a] Ref. 189
[b] Ref. 190
[c] $R = C_6H_5CH_2$[41]
[d] $R = CH_3$[188]

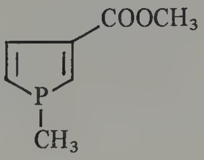
Most other phospholes have related ^1H NMR properties, and respond to substituent effects in ways similar to the other 5-membered rings (e.g., β-COOR causes additional deshielding by its resonance effect[185]; β-CH_3 causes upfield shifts of adjacent H[185]).

Phospholes show very characteristic UV spectra[185,186,188] and consistently have maxima around 280-285 nm, with log ε around 3.3-4.0. Although a theoretical explanation for this absorption has not yet been presented, one point is clear: the maximum is absent in the component units of the phosphole system taken separately (the diene and the phosphine), and can be associated with an interaction between these units that results in stabilization of the excited state. Conjugation of β-COOR causes a pronounced shift to longer wavelength (22 nm for 1-benzyl[185]), and α-carbonyls shift in the same direction [(1-phenyl-2-acetyl-3,4-dimethyl, λ_{max} 311.5 (log ε 4.12)[186]]. One β-methyl substituent has little effect on the maximum (1-benzyl, 286 nm; 3-methyl-1-benzyl 285), but 3,4-dimethyl derivatives are distinctly shifted to shorter wavelength (3,4-dimethyl-1-benzyl, 280 nm). This is an example of the effect tentatively attributed[185] to some distortion of the ring to alleviate the steric congestion.

The ^{31}P NMR spectra of phospholes are also highly characteristic. The shifts are always the most downfield of the family phospholane–2-phospholene–phosphole (e.g., −14.4, 0.0, and +7.9 in 1-benzyl[185]) and indeed fall near the extreme downfield end of the range of phosphine values (except for the highly unusual 7-phosphabicyclo[2.2.1]heptene system; Section 5.5). As also noted in Chapter 5, several factors may be involved in ^{31}P effects, and although the shifts are not inconsistent with the concept of delocalization (causing reduced electron density on P, or increased bond order) they do not *require* this effect for an explanation. With the increasing recognition of steric influences or nonbonded interactions on ^{31}P shifts, it could be argued that the nearly planar phospholes have a minimum of such interactions and as one, and then a second, double bond is saturated new shielding interactions develop. That the ^{31}P shift is sensitive to conjugation effects, however, seems clear from the value for a phosphole carboxylate:

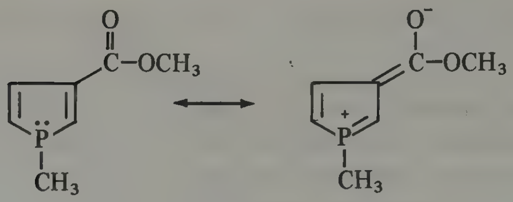


−8.7



+3.0

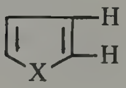
Since a nonconjugating 3-substituent (e.g., CH_3, δ −6.9) has no strong effect, it has been suggested that increased electron removal from P via resonance form **122** is the cause of this pronounced deshielding. The effect is far too large to be attributed to induction[132] (see Chapter 5).



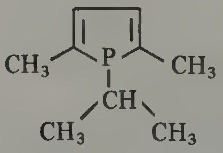
122

α-Substitution by -COR groups also produces a strong shift in the same direction[186] but this could be a result, at least in part, of the familiar β-substituent effect. A parallel between ^{33}S in thiophenes and ^{15}N in pyrroles may be drawn at this point. To a much greater extent, introduction of double bonds causes deshielding of these nuclei, just as seen for the P series. Thus, thiophene has a ^{33}S value 309 ppm downfield of tetrahydrothiophene,[191] whereas pyrrole has a ^{15}N value 137.3 ppm downfield of pyrrolidine.[192] In this sense, then, the ^{31}P NMR properties are quite in line with nuclear properties of related heterocycles.

^{13}C NMR properties of phospholes were considered in Chapter 6; there is some similarity to the spectrum of thiophene,[193] but allowance needs to be made for the effect of the exocyclic P-substituent.

	S[193]	P-C_6H_5[194]	P-CH_3[195]
	127.4	136.7	135.8
	125.6	135.1	134.8

An important discovery in phosphole chemistry was that the barrier to pyramidal inversion is surprisingly small.[196] Tertiary phospholanes have barriers, expressed by the energy of activation $\Delta G^{\neq}_{25°}$, of 36 kcal/mole, whereas phospholes have values of 16. These results were derived from dynamic ^1H NMR measurements of phospholes such as **123**, which has nonequivalent CH_3 groups in the isopropyl substituent at low temperature (0.8°, δ 1.02, and 0.85) where the pyramid is stable, but which loses the nonequivalence when the phosphorus is inverting. The peak coalescence temperature (T_c) is about 42°.



123

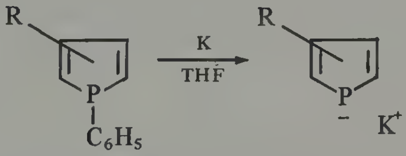
Pyramidal inversion passes through a planar transition state, and in the phosphole system this allows better overlap of the lone pair P-orbital with p-orbitals, thus stabilizing the transition state and lowering the activation energy. This is a telling piece of information about delocalization in phospholes, both in the planar and to a modified extent in the pyramidal state, and is one characteristic of phospholes that is unique in a comparison to thiophenes and pyrroles.

Two important physical properties remain in urgent need of study in phosphole chemistry:

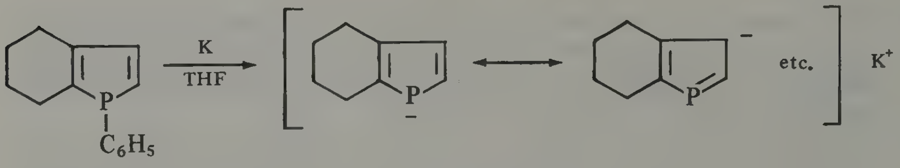
1 Thermochemical parameters. A determination of the energy of stabilization of the system would be of great significance and would allow a much better comparison of the system with the other members of the heterocyclopentadiene family.
2 Dipole moment. Some tentative results have been published,[197] giving, for example, *n*-butylphosphole a value of 1.23 D, but the direction of the dipole has not been unambiguously[132] assigned.

The chemistry of phospholes is less well developed. The basicity at P is greatly reduced (1-methyl, pK_a 0.5[188]) for a phosphine, even when compared to one with comparable, but noncyclic unsaturation (methyldivinyl, pK_a about 5.2). Reduced basicity, of course, is a well-known property of pyrroles, and is strongly suggestive of a common explanation for both based on p_π-p_π conjugation. However, phospholes retain a substantial part of the very strong nucleophilic power of tertiary phosphines; they quaternize readily (but less rapidly than saturated phosphines[188]) and addition of halogen, sulfur, and oxygen (on attack by oxidizing agents) all are known to occur, again at reduced rates. σ-Complexation with metal ions has been well studied[198] and reviewed[132,134]; many phospholes form typical complexes in simple tertiary phosphine manner, but others give different complexes or fail to react. Where molecular features are most favorable for delocalization, complexation is difficult to effect. A case in point is 1-benzylphosphole; it is unreactive to $NiCl_2$, whereas methylated derivatives do form complexes.[186] A Diels-Alder reaction of the diene system of phospholes is known only for the atypical pentaphenyl derivative; monosubstituted phospholes fail to give such adducts, although a reaction at P with dienophiles containing α,β-unsaturated carbonyl units does occur.

A useful property of phospholes is the easy cleavage of a P-aryl bond by alkali metals to form phosphole anions (e.g., 124).[199]



Although valuable as intermediates for attachment of new groups to P with electrophiles, these species have another special feature; the ring is isoelectronic with thiophene, and no longer suffers the complicating problem of an exocyclic substituent enforcing pyramidal character at P. There is, in fact, no reason why this species should not possess delocalization akin to that of thiophene, as a theoretical study has pointed out.[200] So far, only two pieces of experimental information[201] bear on this point: (1) The ^{31}P NMR spectra are shifted far downfield relative to the P-phenyl counterparts, quite in keeping with the expected increase in C-P double bonding represented by resonance form **125**.

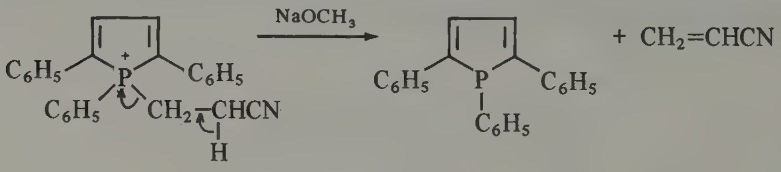


δ ^{31}P +10.5

125, +73.3

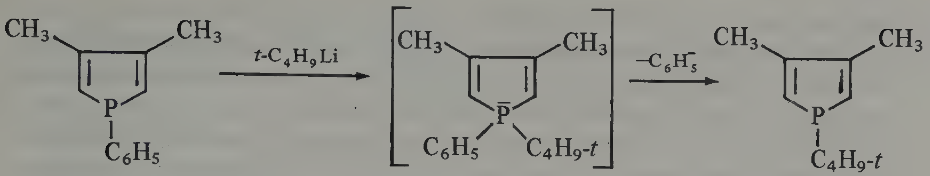
That the downfield shift is significant in revealing an increase in p_π-p_π conjugation, and is not simply due to a change from tricoordinate to dicoordinate P, is clear from considering the nature of this change in other phosphines. Usually, anion formation causes an *upfield* shift, and where downfield, only by small amounts. (2) The stability of the anions, as revealed by their strength as bases, far exceeds that of phosphide ions in general. In a THF solution, anion **125** is not protonated by ethanol, whose pK_a in water is 15.9. The pK_a for the phosphine must greatly exceed that of diphenylphosphine (pK_a 21.7[202]). The phosphole anions, then, readily prepared as they are, may represent the most fruitful area for the future probing of electron-releasing delocalization phenomena of the p_π-p_π type in phosphorus chemistry.

Another P-cleavage reaction in phosphole chemistry bears on the electronic structure of the system. Although developed for the 1,2,5-triphenyl system, the result is of general interest. Retrocyanoethylation[203] of phospholium salt **126** with $NaOCH_3$ occurs at a markedly faster rate compared to other systems (e.g., phospholanium or triphenylphosphonium salts). The result is interpreted to mean that delocalization in the phosphole is substantial and provides the rate-accelerating effect through stabilizing the transition state in the cleavage of the P-C bond.



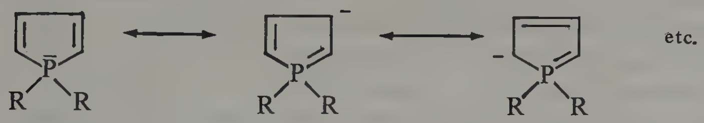
126

A final reaction[204] to be considered (also known for simple acyclic tertiary phosphines[205]) is one explored so far only with 3,4-dimethyl-1-phenylphosphole, but possibly of broader scope:



127

Because the nucleophilic character of P in the phosphole ring is clearly reduced relative to phosphines, it is not inconsistent to find a consequent increase in its electrophilicity (which is implicit in the canonical forms in the resonance hybrid bearing a positive charge). Another view to account for the ease of this reaction is that the intermediate adduct (or transition state) phosphoranyl anion **127**, derives some stability from delocalization of the negative charge:



Such cyclic phosphoranyl anions certainly are deserving of continued attention.

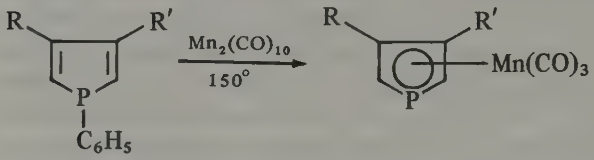
A notable absence in the data on chemical properties developed to date for phospholes is knowledge of their capability to undergo electrophilic substitution. Attempts to employ useful substituting agents from thiophene or pyrrole chemistry[206] (e.g., $HgCl_2$, CH_3CONO_2, ArN_2^+, SO_3, etc.) have been unsuccessful, attack always occurring at the more electron-rich phosphorus atom. An exception is found in a new series of phosphole derivatives, the phosphacymantrenes, which, because of their own unique chemistry, are discussed in the following section.

Relatively little is yet known about the influence of benzannelation on phospholes. By the barrier to pyramidal inversion approach,[196] delocalization is somewhat less important; the values for $\Delta G^{\neq}$ of 24 for a phosphindole versus 35 kcal/mole for a phosphindoline have been recorded. The retrocyanoethylation approach[185] also gives a smaller effect than seen for a phosphole. An X-ray analysis of a 1,2,3-triaryl derivative,[207] again possibly not the best model because of the heavy substitution, did reveal some shortening of the P-C bond in the phosphole ring (0.02-0.05 Å shorter than the P-phenyl bond), which was slightly puckered as in the phospholes. The β-proton of 1-phenylphosphindole shows pronounced deshielding (δ 7.49).[208]

A number of papers have been written on the subject of the bonding in phospholes with fluctuating views on the nature of orbital interaction. They have been concisely reviewed.[132] The most recent view[209] is especially interesting in that it provides an interpretation of photoelectron spectra of phospholes in terms of a substantially delocalized system through p_π-p_π overlap, and develops theory accordingly. An earlier PES study[210] had come, erroneously, to the opposite conclusion (*no* overlap), but was later corrected[211] to agree with this view towards delocalization, adding a component also of p_π-d_π bonding and even electron release from the P-C sigma bond *via* hyperconjugation. Thus, theoretically the concept of delocalization in phospholes is gaining support; certainly many of the properties outlined in this section would be hard to explain on the basis of a model of an isolated diene and a phosphine unit (an attempt by some to do so[212] was countered by strong criticism[132]). The current question, then, involves the *extent* of delocalization rather than the *reality* of delocalization. The extent, as emphasized earlier, is quite sensitive to substitution, and the model must be chosen with care. Even the best case may prove to have the lowest degree of delocalization of the heterocyclopentadiene series.

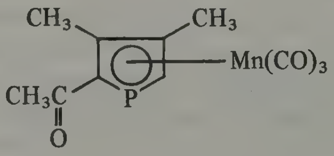
PHOSPHACYMANTRENES AND PHOSPHAFERROCENES. These organometallic derivatives include the feature of π-bonding of the metal atom to a phosphole anion moiety. As such, they are unique substances; they should be treated separately as delocalized species and should not be considered as having character representative of the unperturbed phosphole anion.

Phosphacymantrenes,[46,213] so named because of structural analogy to an older family of compounds called cymantrenes ($C_5H_5Mn(CO)_3$), are prepared in a remarkably simple process of P-phenyl cleavage from a phosphole:



128 R = R′ = H, 50%
129 R = H, R′ = CH_3, 40%
130 R = R′ = CH_3, 80%

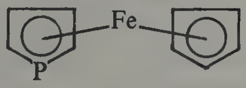
The 2,5-diphenyl derivative was also prepared (30%) in similar fashion.[214] The compounds are yellow solids of high thermal stability. They are immediately seen to differ from free phosphole anions by their ^{31}P NMR (δ −28.7 to −46.6); as already noted, potassium phospholides have values around +80. They have some unique ^{13}C NMR features, namely, strong upfield shifting (20-40 ppm) of both the α- and β-carbons relative to the starting phosphole, with unusually large coupling to α-carbon (62-65 Hz). ^{1}H NMR also shows the effect of negative character in the ring [in **130**; δ 4.38 ($^2J_{PH}$ = 35.5 Hz)]. The most revealing feature about the nature of these substances is their ability to undergo electrophilic substitution. Compound **130** gives an α-acetyl derivative **131** with CH_3COCl-$AlCl_3$ in CH_2Cl_2 at room temperature; other acylations were performed in refluxing CH_2Cl_2, and benzoylation at 110°.



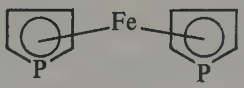
131

The acyl groups are easily reduced to carbinols ($NaBH_4$) or alkyl ($LiAlH_4$ + $AlCl_3$).[214] Since nuclear substitution is a classical test of aromaticity in cyclic delocalized systems, a quality phospholes themselves have not yet been shown to possess, the system has been given the "aromatic" label. The spectral data above do not speak effectively to this point, but some features of the X-ray analysis of the benzoyl derivative support this view. Thus, the C-C bonds in the shallow envelope shape (P out of plane by 0.048 Å) are all of equal length (1.42 Å, similar to values for π-bonded cyclopentadienide). However, the C-P bonds are *not* of equal length, those attached to C_6H_5CO being the longer (1.808 versus 1.743 Å). To place any significance on P-C bond lengths in cymantrenes would require values for a substance without α-substituents.

The phosphaferrocenes can have two formulations, and examples of both are now known.



Ref. 47



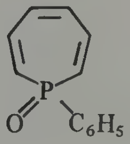
Ref. 215

The first was prepared in the same manner as the phosphacymantrenes, by cleavage of a P-phenyl phosphole with an iron derivative $[(C_5H_5)Fe(CO)_2]_2$. The ^{31}P shift[215] (for 3,4-dimethyl) was in the upfield region (δ −83.5). Acylation effects substitution of a hydrogen in the phospholyl ring, and again the label "aromatic" is considered appropriate. In this system, X-ray analysis of a parent phosphaferrocene (3,4-dimethylphospholyl) was performed, and the feature of C-P bond shortening was indeed present (1.758 and 1.768 Å, for an average only 0.02 Å shorter than the value in 1-benzylphosphole, 1.783). The diphosphaferrocene was prepared in more conventional fashion from the lithium phospholide and $FeCl_2$; ^{31}P values were again in the upfield region (δ −72.1 for 3,4-dimethyl).

New developments in this unique extension of phosphorus heterocyclic chemistry are awaited with interest.

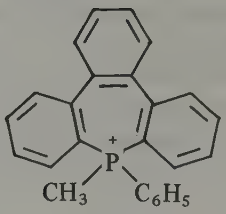
8.4.4 Type 4

PHOSPHEPIN DERIVATIVES. The concept of positive phosphorus acting through its d_{yz} or d_{xz} orbitals in the way that positive carbon does with a p-orbital in the tropylium ion has been tested with two phosphepin derivatives. Märkl prepared phosphepin oxide **132**[216] (Section 4.3), but found no indication from ^1H NMR of delocalization.



132

A salt form with unit positive charge might prove to be a better model for this study, however. A tribenzo derivative of a salt (**133**) was in fact prepared by Winter,[217] but here the benzo groups becloud the issue.

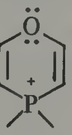


133

The system is nonplanar (boat, Section 8.1) and exists in the form of two isomers with a substantial barrier for interconversion ($\Delta G^{\neq}_{12^{\circ}}$ about 30 kcal/mole). The salt has a smaller barrier by about 2 kcal/mole than the corresponding phosphine or oxide, and while other factors may also be involved this was taken[217] as a possible reflection of some stabilization of the planar transition state by cyclic conjugation in the salt. The phosphepin system clearly deserves continued study.

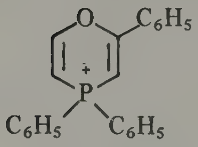
8.4.5 Type 5

PHOSPHONIAPYRANS. There is an analogy between this system and the λ^5-phosphorins, if written in resonance form **134**.

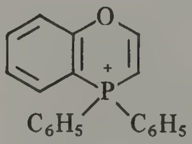


134

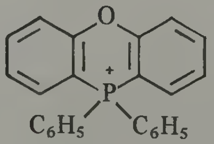
Hence, the same problems of ylide versus p_{π}-d_{π} bonded forms, and of defining the delocalization as "aromatic," will be present. The parent phosphoniapyrans are not entirely planar[81]; benzannelated forms are more likely to achieve planarity.[218] The ^{31}P NMR spectra reveal the expected high degree of phosphonium ion character, and have values not unlike the λ^5-phosphorins. This point implies that much ylide character is present.



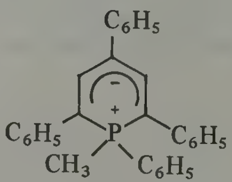
δ ^{31}P −17.2[219]



−12.3[218]

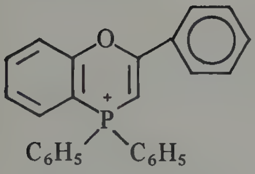


−7.5[220]

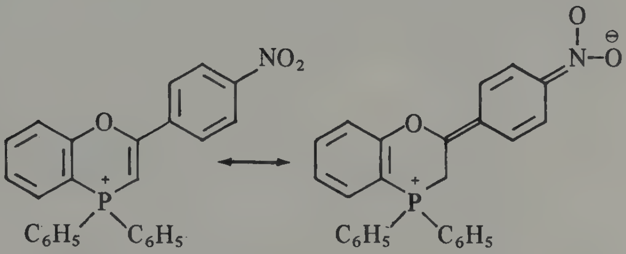


−6.5[221]

The ^{31}P shift can be modified by electron-withdrawing groups at C-2; *p*-nitrophenyl produces strong deshielding relative to phenyl and appears to act by diminishing the electron density on the α-carbon.



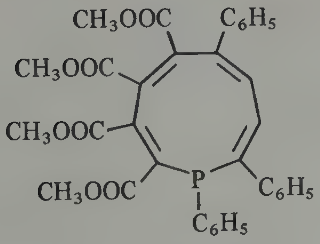
δ ^{31}P −10.3[218]



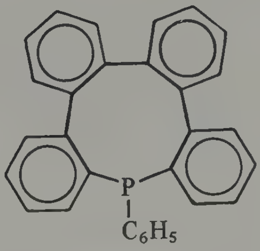
+2.2[218]

8.4.6 Type 6

PHOSPHONINS. It has not yet been possible to test for the presence of delocalization in this potentially Hückel system. In certain azonines, delocalization can be detected from NMR properties; some puckered annelated thionins are known, but monocyclic compounds have not yet been prepared. Simpler systems than the two types (**135**, **136**) that were discussed in Section 4.3 will be requied to probe this intriguing new aspect of phosphorus delocalization phenomena.



135[222]



136[223]

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