Recent Synthetic Developments in Polyquinane Chemistry

By L. A. Paquette

Springer-Verlag
Berlin Heidelberg New York Tokyo
1984

Professor Dr. Leo A. Paquette
Evans Chemical Laboratories
The Ohio State University
Columbus, Ohio 43210, USA

This series presents critical reviews of the present position and future trends in modern chemical research. It is addressed to all research and industrial chemists who wish to keep abreast of advances in their subject.

As a rule, contributions are specially commissioned. The editors and publishers will, however, always be pleased to receive suggestions and supplementary information. Papers are accepted for "Topics in Current Chemistry" in English.

ISBN 3-540-11828-4 Springer-Verlag Berlin Heidelberg NewYork Tokyo
ISBN 0-387-11828-4 Springer-Verlag NewYork Heidelberg Berlin Tokyo

Library of Congress Cataloging in Publication Data.
Paquette, Leo A. Recent synthetic developments in polyquinane chemistry.
(Topics in current chemistry = Fortschritte der chemischen Forschung; 119) Bibliography: p. Includes index.
1. Quinanes. I. Title. II. Series: Topics in current chemistry; 119.
QD1.F58 vol. 119 [QD335] 530s [547'.593] 83-16722

Printed in GDR

2152/3020-543210

Table of Contents

I Introduction

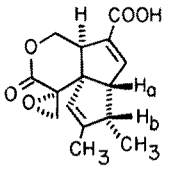
By the mid-1970's it had become clear that the area of polyquinane chemistry was on the verge of an explosive growth period. There were several underlying reasons for this surge of interest in molecules whose frameworks featured mutually fused cyclopentane rings. Perhaps the most evident was the realization that little attention had previously been paid to methodology for annulating one five-membered ring to another. The need for suitably efficient protocols of this type was arising on several fronts. On the one hand, new natural products were being isolated, the di- or triquinane skeletons of which had not heretofore been appreciated as biogenetically derivable from farnesyl pyrophosphate or related precursors. Independently and with equal intensity, a growing fascination for the possibly unusual physical and chemical properties of yet unknown spherical compounds such as dodecahedrane was gaining rapid momentum. In addition, many novel polycyclopentanoid alicyclic systems of theoretical interest were awaiting the implementation of ingenious routes to their acquisition in the laboratory.

In 1979, we authored a review in Topics in Current Chemistry entitled "The Development of Polyquinane Chemistry"[1]. Numerous early experimental investigations in this field were surveyed and compiled therein. In the few, short intervening years, the level of research activity dealing with polyquinanes has literally mushroomed. Accordingly, the writing of an updated, complementary review as a means of keeping oneself abreast of the many new and imaginative developments seemed entirely appropriate and even necessary. As before, the intention has been to gather together all relevant new facets of pertinent synthetic methodology in the polyquinane field with a view to stimulating yet more exciting future scientific ventures.

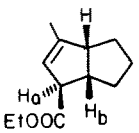
IV Spectral Data on Bicyclo[3.3.0]octanes

^{13}C NMR data for a wide range of bicyclo[3.3.0]octanes, too extensive to compile here, have been reported [44,54,66,187,188]. The influence of a variety of substituents on chemical shifts is now known. Furthermore, the basis for determining regio- and stereochemical features is now at hand. ^{13}C chemical shifts for a much more limited group of linearly fused tricyclopentanoids have also been published [66,189].

Although similar tabulations of ^1H NMR data do not exist per se, it is clear that chemical shifts can be of considerable diagnostic value in structural assignment (see *91*). Coupling constants as illustrated for pentalenolactone (*358*) [190] and *359* [33] can likewise prove most helpful.

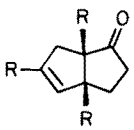


358 (J_{ab} = 9.0 Hz)



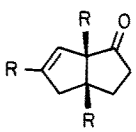
359 (J_{ab} = 3.6 Hz)

Distinction between β,γ- and γ,δ-unsaturated ketones is also feasible by UV spectroscopy. The enhanced absorption of the n → π* transition in the former is clearly apparent when the functional groups reside in different rings [44].



R = H, λ_{max} 293 (ε 25)

R = CH_3, λ_{max} 286 (ε 75)



R = H, λ_{max} 298 (ε 89)

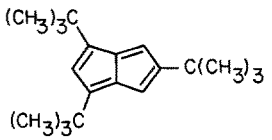
R = CH_3, λ_{max} 298 (ε 254)

In a different context, (+)-*endo-cis*-bicyclo[3.3.0]oct-7-en-2-ol has been shown to be an effective tool for determination of the absolute configurations of chiral acids [191].

V Simpler Molecules of Theoretical Interest

A Pentalene

While theoretical interest in pentalene expectedly persists [192], some progress has been made in unraveling the nature of this electronically unusual alternant cyclic polyolefin. Since 1,3,5-tri-*tert*-butylpentalene (*360*) remains the only alkyl derivative



360

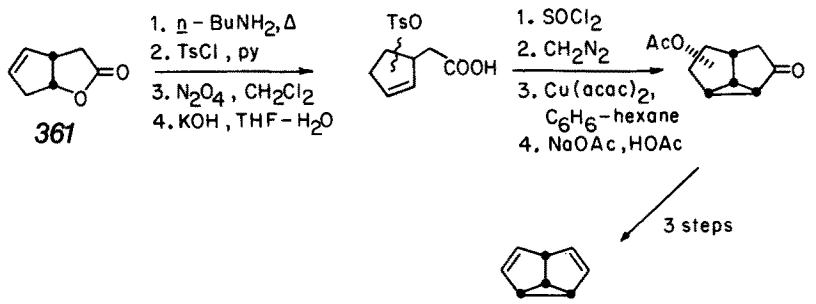
so far which is stable at room temperature, provided that prolonged exposure to air is avoided, it has become a prime target for study. Its photoelectron (PE) and absorption (UV-VIS) spectra have been determined. The first four bands in the PE spectrum have been assigned by comparison with calculated orbital energies. Similar treatment of the absorption data indicates that bond alternance is operative [193].

The ESR spectra of the radical anion and cation of *360* have been reexamined under higher resolution and the coupling constants of all the protons were determined [194]. Since the experimental data agree with values predicted by the simple MO model, the π-spin distributions in $360^{\dot{-}}$ and $360^{\dot{+}}$ appear not to differ significantly from those of the parent species. However, the spectra of 360^{-} taken at low temperatures show no specific line broadening which could arise from bond-shifting between the two Kekulé forms. Proton hyperfine data have also been determined for the radical anions and cations of dibenzo[*b*,*f*]pentalene and its 5,10-dimethyl derivative [195]. The coupling constants approximate closely the values obtained for the radical ions of *360*.

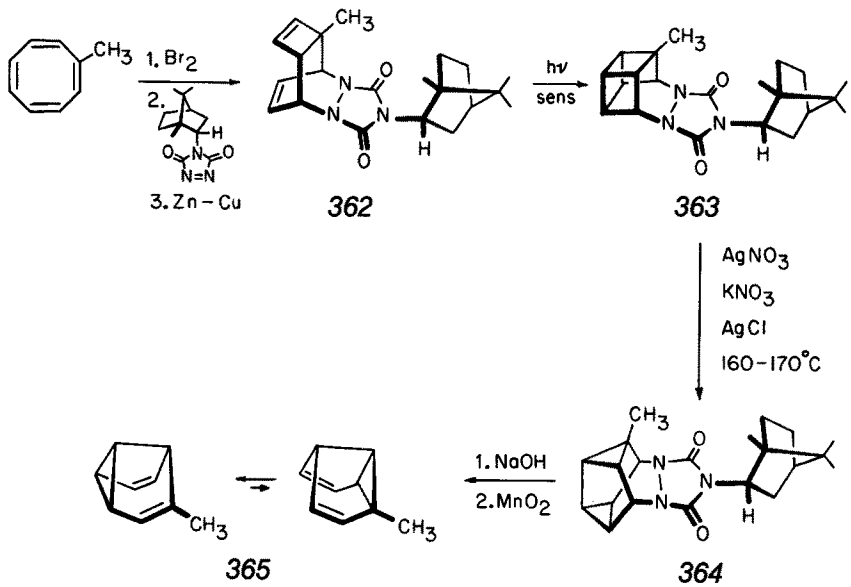
The mechanism of the dehydrogenative transannular ring closure of cyclooctatetraene in the presence of various inorganic reagents to provide complexes of pentalene has been the subject of debate [196,197].

B Semibullvalenes

Serratose, et al., have succeeded in converting readily available lactone *361* to semibullvalene. The scheme, which involves no skeletal rearrangement, is based on diazoketone cyclization chemistry within an oxygenated cyclopentenyl derivative [198].

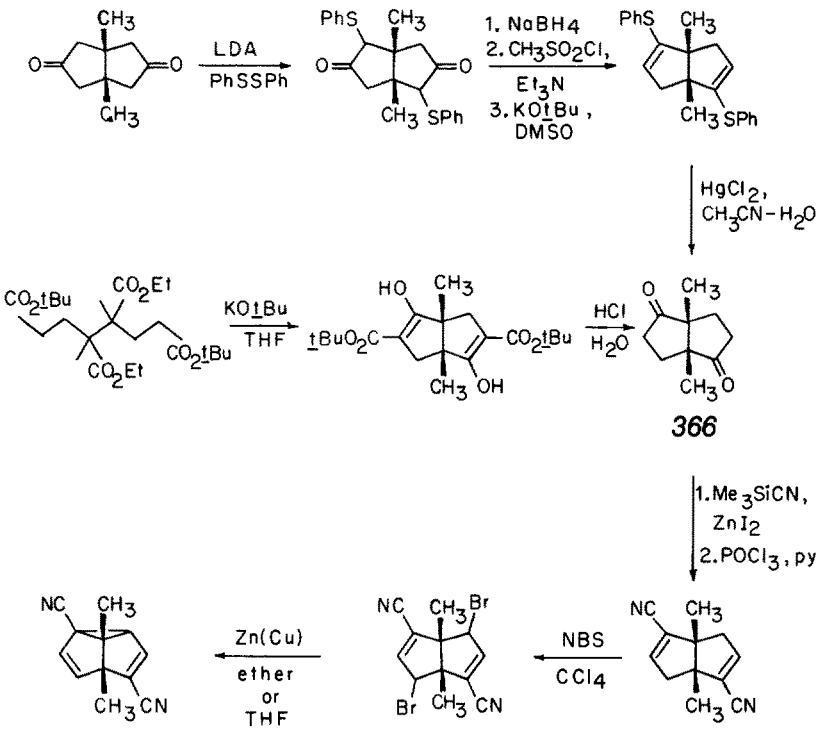


The synthesis of an optically active semibullvalene has been realized for the first time [199]. Sequential reaction of methylcyclooctatetraene with one equivalent each of bromine and (—)-*endo*-bornyltriazolinedione gave a mixture of Diels-Alder adducts which when debrominated afforded *362*. Photocyclization to bishomocubane *363* allowed for chromatographic separation of the two diastereomers. Silver ion-



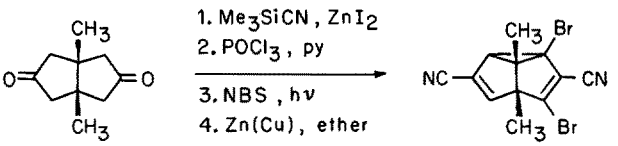
catalyzed rearrangement of the crystalline isomer delivered dextrorotatory *364* whose absolute configuration was elucidated by x-ray analysis. Hydrolysis-oxidation of (—)-*364* gave (+)-*365* whose absolute configuration is as shown.

2,6-Dicyano-1,5-dimethylsemibullvalene (*367*) has been synthesized by two groups and found to exist as a classical ground state molecule which lies 5 kcal/mol below the homoaromatic transition state of the Cope rearrangement [200,201]. Both syntheses proceed ultimately from diketone *366* along identical lines (Scheme XXIX). However, Askani relies on a carbonyl transposition sequence within an existing diquinane while Quast makes use of a cyclization process.



Scheme XXIX

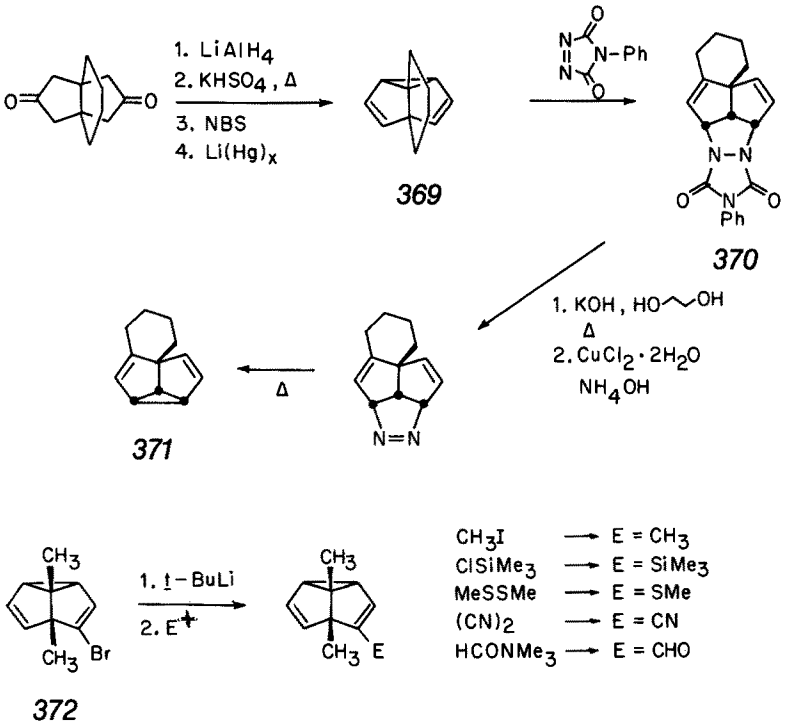
When the dibromo dicyano derivative *368* was later prepared, it was found to exhibit a higher activation barrier to degenerate Cope rearrangement than the parent hydrocarbon [202].



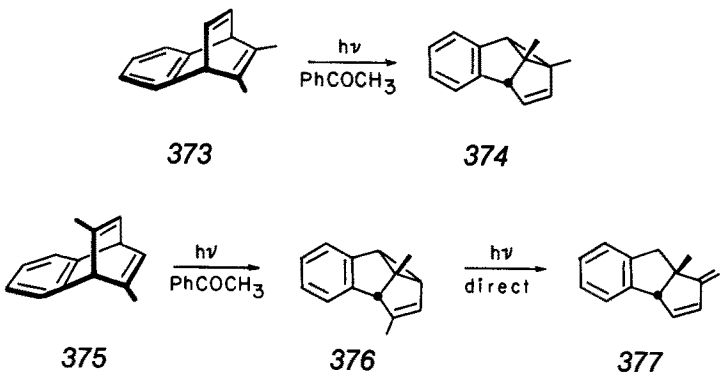
368

Askani has observed that 3- and 7-substituted semibullvalenes, of which *369* is exemplary, undergo cycloaddition to N-phenyltriazolinedione with rearrangement of the carbon skeleton [203]. The products are dihydrodiazatriquinacenes (e.g. *370*) which when converted to their azo counterparts and heated to 80 °C or above are transformed into isomeric semibullvalenes such as *371*.

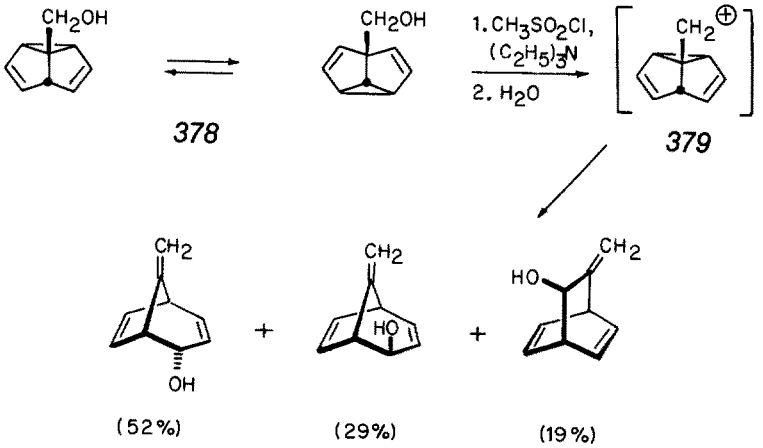
By means of halogen-metal exchange and electrophilic capture, bromosemibullvalene *372* has been functionalized in a variety of ways [204]. 2(4)-Chlorosemibullvalene has been similarly treated [205].



Semibullvalenes *374* and *376* are the major products formed from acetophenone sensitized irradiation of *373* and *375*, respectively. When *376* is in turn subjected to direct or chlorobenzene-sensitized irradiation, conversion to *377* results [206].

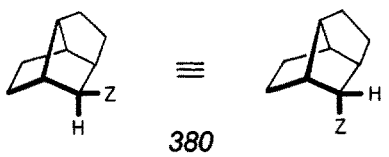


1-Semibullvalenylcarbinol (*378*) undergoes ionization under the conditions of mesylate preparation to generate cation *379* which undergoes cyclopropane ring cleavage to give three alcohols [207].



C Brexanes, Brendanes, and *syn/anti*-Sesquinorbornanes

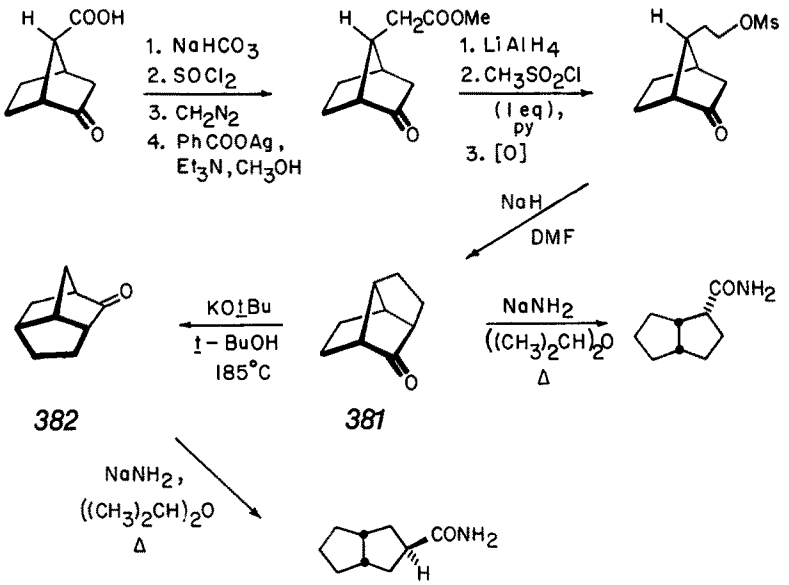
The unique features of the tricyclic C_9 framework *380* called brexane have previously been emphasized [208]. Two norbornyl units can be identified in brexane and these are so arranged that the substituent Z at C_2 is simultaneously exo to one and endo to the other. Thus, interchange of H and Z at C_2 produces neither a diastereomer nor an



380

enantiomer, but a molecule superimposable on the original. The ionization behavior of brex-2-yl systems uniquely reveals the relative importance of anchimeric assistance and steric interference because both of these factors act on Z simultaneously but oppose each other. While the tricyclic cation derived from the departure of Z regenerates its mirror image on Wagner-Meerwein rearrangement, 1,3-hydrogen shifts are detectable because they produce a new ion which can, by a single Wagner-Meerwein shift, give the brendane skeleton. The synthesis of brexan-2-one (*381*) and its isomerization to brendan-2-one (*382*) on heating to 185 °C in the presence of potassium *tert*-butoxide is outlined in Scheme XXX [209].

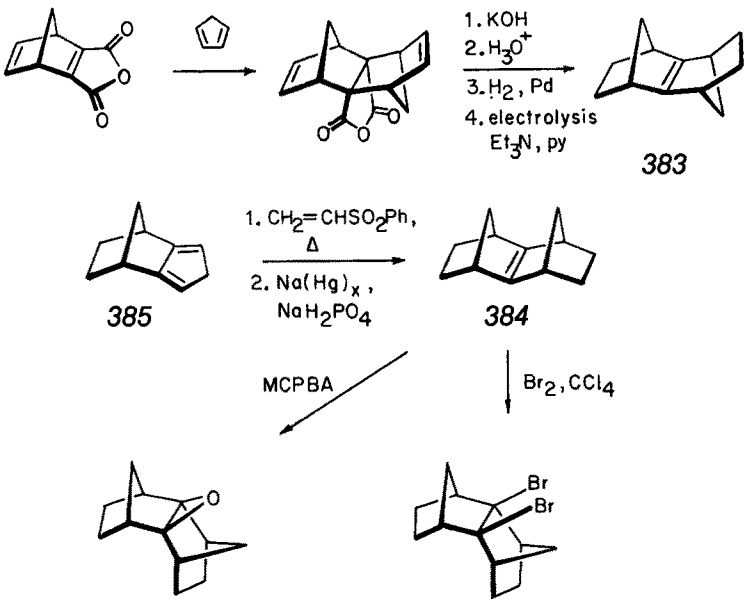
Bartlett [210] and Paquette [211] have recently succeeded in preparing *anti-* (*383*) and *syn*-sesquinorbornene (*384*). Whereas placement of the bridge hydrogen atoms in *383* appear to totally block concerted reaction with the C=C as a whole, attack at one end of the double bond remains possible. Furthermore, the double bond in *383* and its derivatives is essentially planar [212,213]. In contrast, that of *syn*-sesquinorbornenes is bent downwardly rendering the π system highly reactive and prone to ready electrophilic attack from above despite the high steric congestion which develops [212,214–216]. The ready conversion of *384* to its dibromide [217] and epoxide [218] are exemplary. The only exception occurs during acetone-sensitized photochemical



Scheme XXX

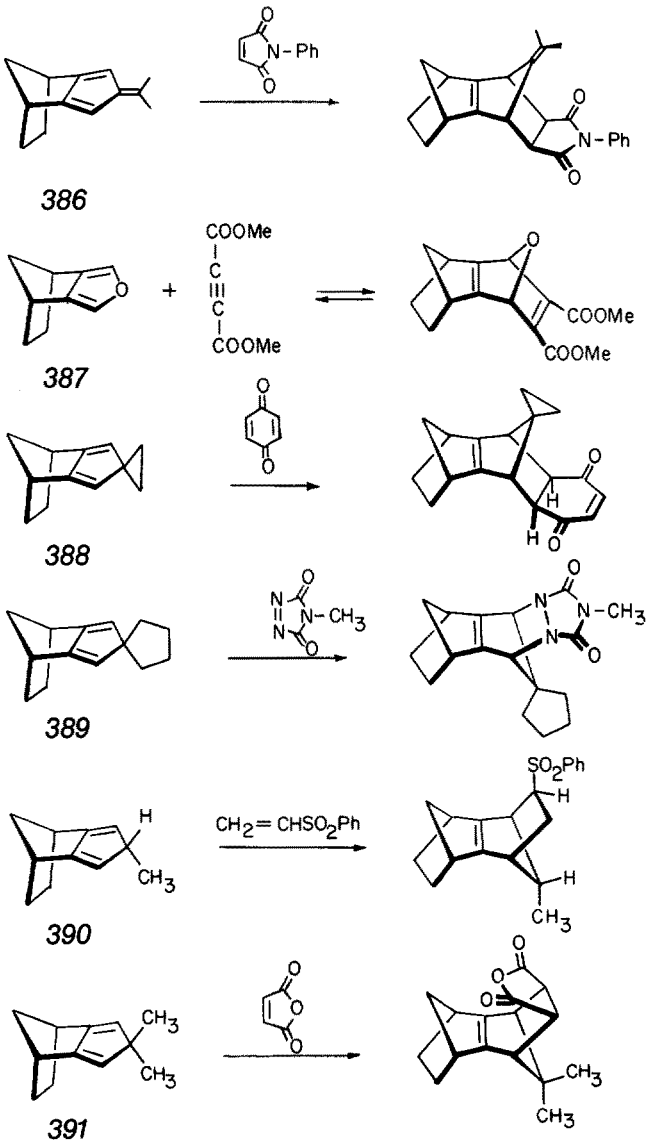
activation, when acetonyl addition and hydrogenation products result. In the latter instance, the hydrogens enter mainly from the endo direction [219].

Isodicyclopentadiene (*385*) adds dienophiles stereoselectively from its endo surface in most cases. While this π-facial behavior is similarly followed by fulvene *386* [220], furan *387* [221], and the spirocyclopropane *388* [214], a reversal of this trend is

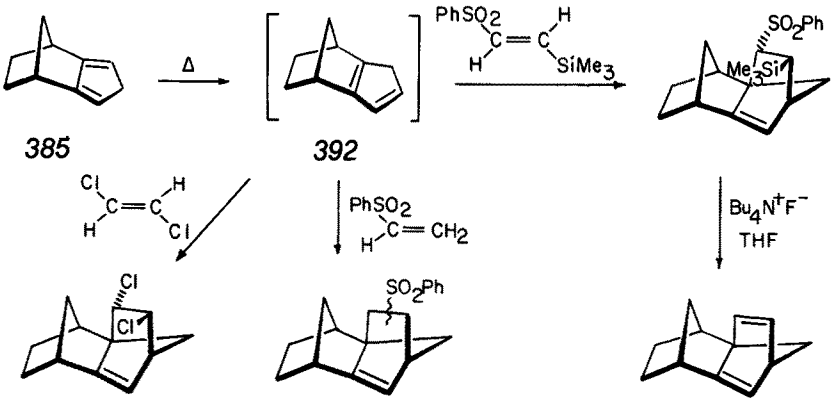


encountered with *389–391* (Scheme XXXI) [213,214]. This phenomenon correlates with ^{13}C NMR shifts of the pendant carbons immediately attached to the cyclopentadiene ring [222] and has been analyzed on theoretical grounds [223,224].

The anion of *385* is captured stereoselectively from its endo face with a host of electrophilic reagents [225]. When *385* is heated, [1,5] hydrogen sigmatropy occurs to give the fleeting isomer *392* which can be trapped if dienophiles of low reactivity are present [226,227]. The higher Diels-Alder reactivity of *392* due to the presence of a norbornene double bond is responsible for this selectivity.

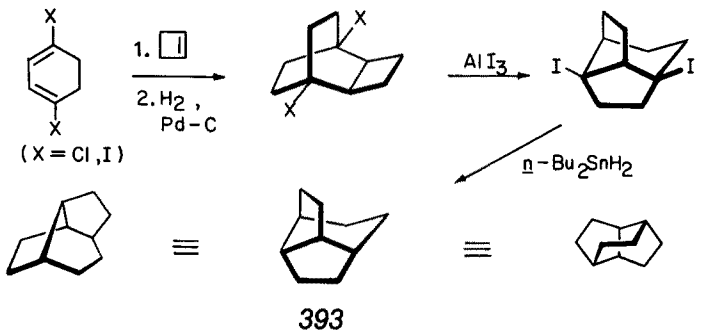


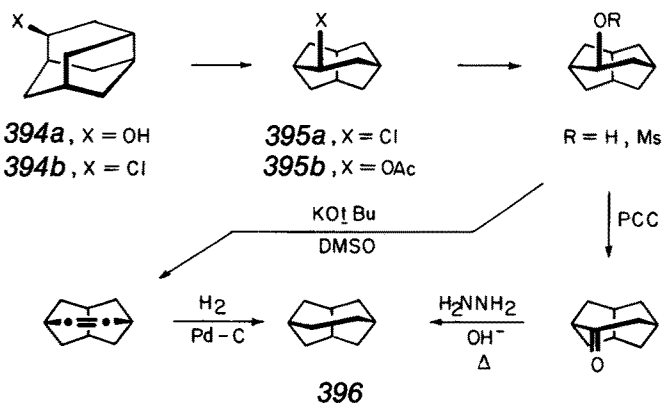
Scheme XXXI

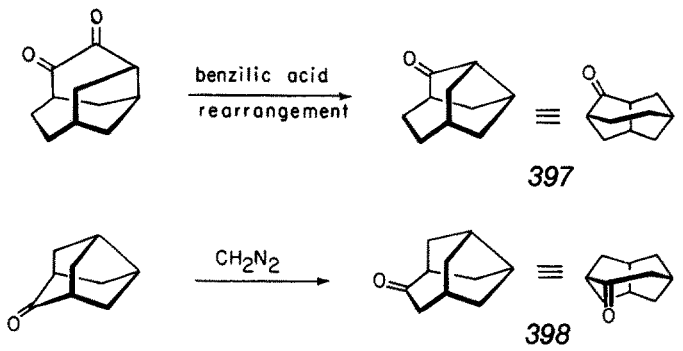


D Adamantane Isomers

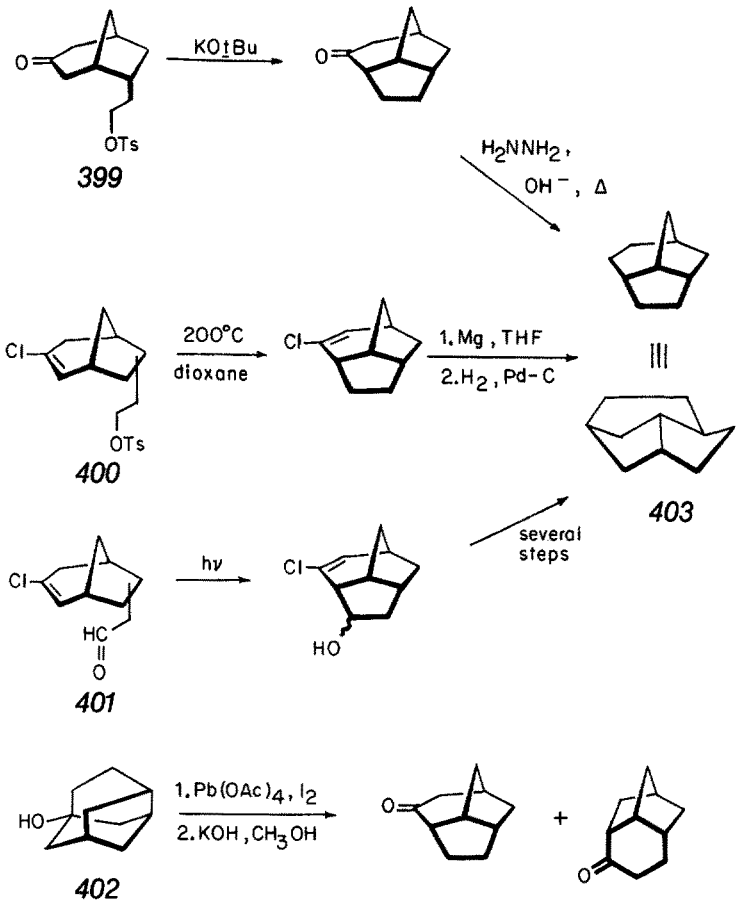
Wiseman and coworkers have succeeded in preparing tricyclo[5.3.0.$0^{4,8}$]decane (*393*), a $C_{10}H_{16}$ hydrocarbon which unlike adamantane is chiral. Their elegantly simple approach entails Diels-Alder addition of cyclobutene to 1,4-dihalocyclohexa-1,3-dienes, catalytic hydrogenation of the adduct, reaction with aluminium triiodide, and ultimately di-*n*-butyltin dihydride reduction.







Scheme XXXII



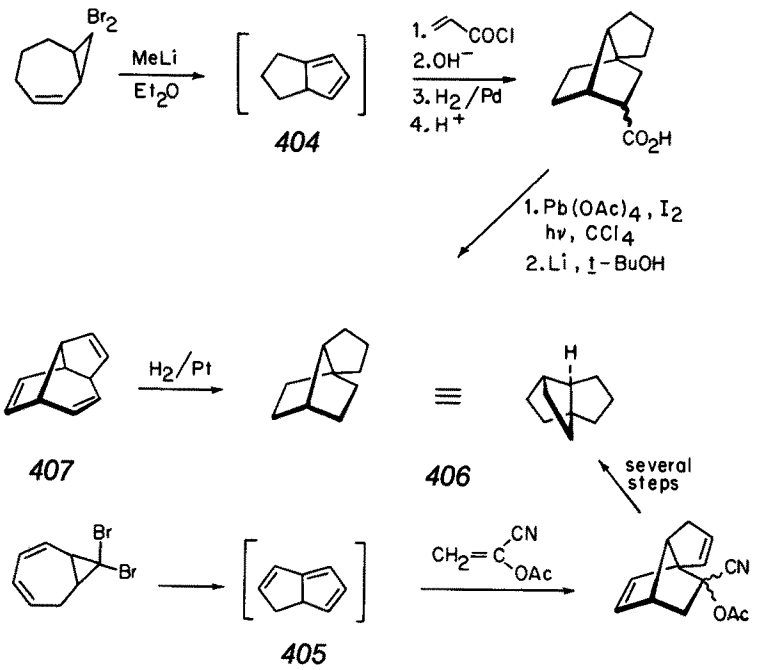
Scheme XXXIII

The isomeric tricyclo[3.3.2.$0^{3,7}$]decane hydrocarbon (*396*) has also recently yielded to synthesis [229]. Thus, reaction of *394a* with either thionyl chloride or phosphorus pentachloride led to rearrangement and formation of chloride *395a*. Alternatively,

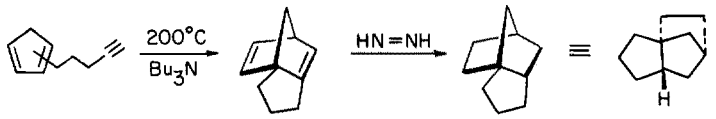
acetolysis of *394b* led to *395b*. Subsequent transformations (Scheme XXXII) gave *396*. Majerski, et al., have arrived at the ketone derivatives *397* and *398* through appropriate ring contraction or expansion processes [230].

Ganter has developed three different approaches to tricyclo[5.2.1.$0^{4,8}$]decane (*403*), yet another of the nineteen isomeric hydrocarbons of "adamantaneland" [231]. As seen in Scheme XXXIII, the routes involve intramolecular cyclization of keto tosylate *399* followed by Wolff-Kishner reduction of the resulting ketone, thermocyclization of *400* and subsequent dechlorination, hydrogenation, and photocyclization of aldehydes *401*. Majerski's approach involved hypoiodite cleavage of alcohol *402* [232].

Only two members of "adamantaneland" contain a *trans*-diquinane ring system as their central structural element and both have recently yielded to synthesis. The first, tricyclo[4.2.2.$0^{1,5}$]decane (*406*), has been independently prepared by Schleyer [233] and Ganter [234]. By making recourse to a carbene rearrangement, *404* could be acquired transiently and trapped with acryloyl chloride. Subsequent functional group manipulation gave *406*. Alternatively, the more highly unsaturated *405* was captured as its α-acetoxyacrylonitrile Diels-Alder adduct, from which point *406* could be easily arrived at. The hydrogenation of *407* [235] served to intercorrelate this chemistry with past experience.



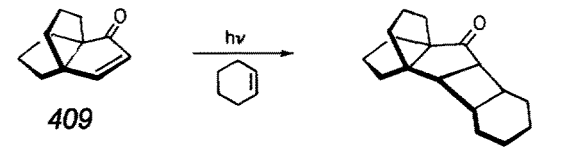
Two very similar and very direct approaches serve to make tricyclo[5.2.1.$0^{1,5}$]-decane (*408*) readily available [236, 237].



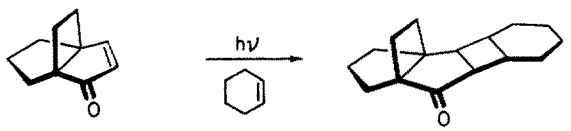
408

E Propellanes

When the propellenones *409* and *410* are irradiated in cyclohexene, the indicated [2+2] adducts are formed as the major products [238].

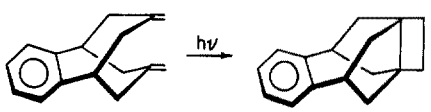


409

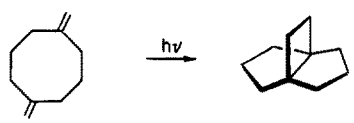


410

When exposed to ultraviolet light, dienes *411* and *412* undergo intramolecular [2+2] cycloaddition. The latter reaction provides a particularly convenient synthetic entry to [3.3.2]propellane from a readily available starting material [239].

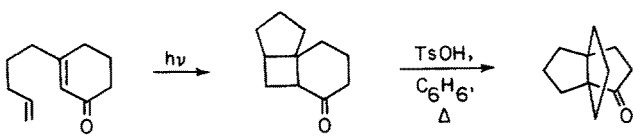


411



412

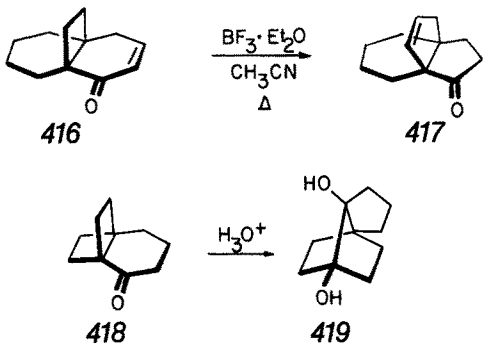
Irradiation of *413* leads in high yield to *414* as the sole product. When heated in benzene solution containing *p*-toluenesulfonic acid, isomerization to triquinane ketone *415* results [240].



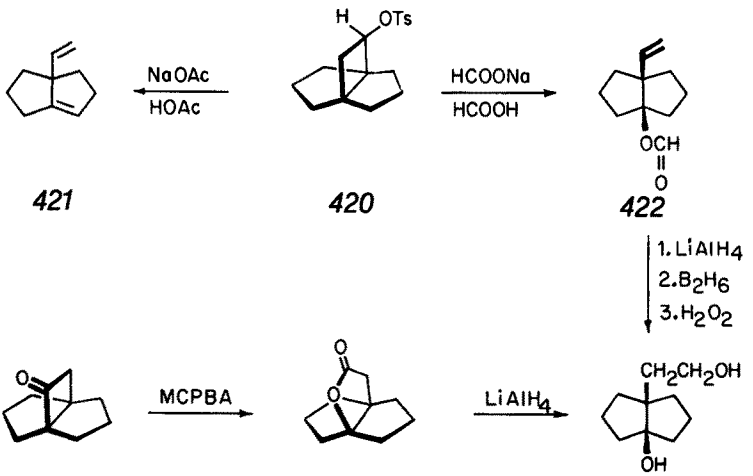
413 *414* *415*

Similarly, boron trifluoride etherate in hot acetonitrile acts on enone *416* to promote its rearrangement to *417* [241].

By comparison, treatment of the [4.2.2]propellanyl ketone *418* with any of a variety of acids leads quickly and efficiently only to *419* [242].

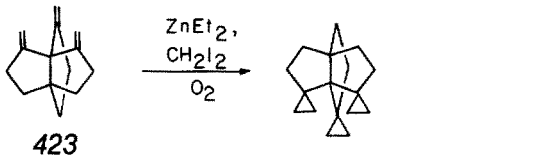


Buffered acetolysis of tosylate *420* gives diene *421* as the major product along with unrearranged acetate. In buffered formolysis, the cis formate *422* evolves as the principal component. The structural assignments were confirmed by the chemical intercorrelations shown [243].

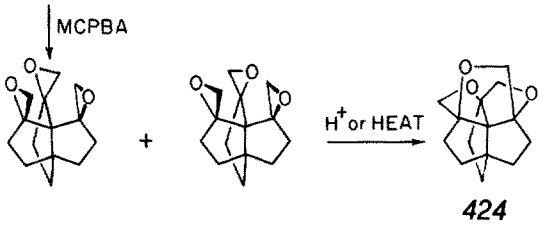


Simmons-Smith cyclopropanation of triene *423* delivers a triscyclopropyl hydrocarbon which exhibits chiral fluxional properties [244]. On epoxidation, a mixture of two triepoxides results; these rearrange rapidly under a variety of conditions to *424*, the first topologically nonplanar molecule [245,246]. The reaction path for this isomerization has been elucidated by means of oxygen isotope effects on ^{13}C chemical shifts [247].

The capped propellane *425* has been proposed as a precursor of a carbocation which might exhibit pure pp-σ bonding [248].



423

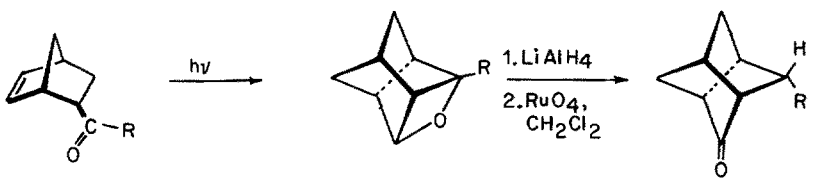


424

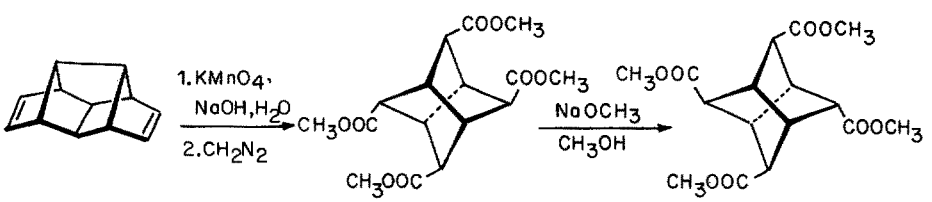
425

F Tricyclo[3.3.0.0^{3,7}]octanes

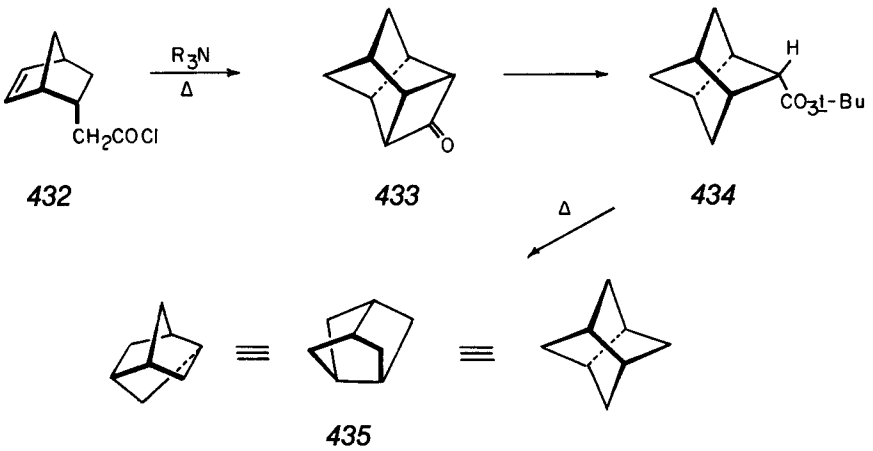
Sauers and coworkers have applied the Paterno-Büchi reaction to *endo*-5-acylnorbornenes (*426*) and observed regiospecific conversion to oxetanes of general formula *427* (Scheme XXXIV) [249]. Reductive cleavage of these products with lithium aluminium hydride is also regioselective and leads, following oxidation, to ketones



426 427 428



429 430 431



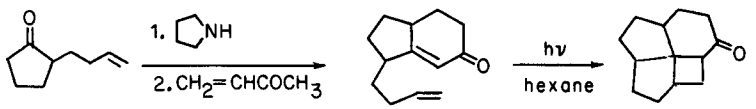
432 *433* *434* *435*

428 [249,250]. The C_{2v}- and S_4-symmetric tetraesters of tricyclo[3.3.0.0^{3,7}]octane (*430* and *431*) have been prepared by oxidation of diene *429* [251]. To access the parent hydrocarbon (*435*), acid chloride *432* was transformed to the derived ketene which undergoes intramolecular [2+2] cycloaddition [252]. The resulting cyclobutanone (*433*) serves as precursor to perester *434* whose thermal decomposition proceeds with chain transfer in competition with cleavage [252]. The unique arrangement of the carbon atoms in *435* is such that the smallest rings are all five-membered. The highly symmetric structure may be viewed as a constrained cisoid bicyclo[3.3.0]octane (as well as the symbol of NATO).

G Fenestranes

The synthesis of [4.4.4.4]fenestrane or "windowpane" has become an active area of research due to the aesthetic appeal of the hydrocarbon and the nature of its central quaternary carbon atom which is expected to be distorted from normal tetrahedral geometry [253]. Ongoing investigations have generated a number of ring-expanded triquinane and tetraquinane ([5.5.5.5]fenestrane) homologs. These molecules form the subject matter of the discussion which follows.

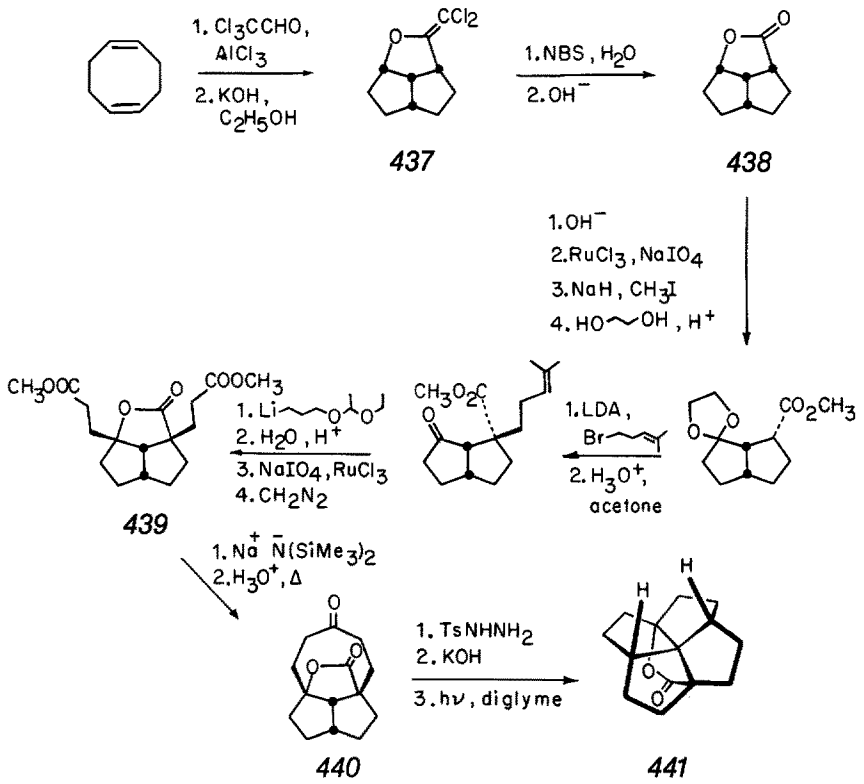
The earliest pioneering work, due to Georgian and Saltzman [254], began with Robinson annulation of *436* and intramolecular [2+2] photocyclization of the bicyclic enone.



436

Keese's group has achieved a more advanced stage of development beginning with 1,5-cyclooctadiene (Scheme XXXV) [255]. Following condensation with chloral and

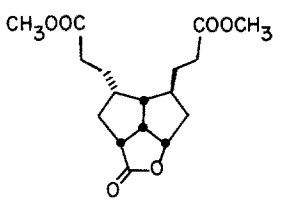
dehydrohalogenation to arrive at *437* [256], reaction with N-bromosuccinimide in the presence of water afforded a bromohydrin which in the presence of base afforded lactone *438*. This intermediate could be elaborated into the lactone diester *439* where the side-chains are configurationally fixed. Dieckmann cyclization and hydrolytic



Scheme XXXV

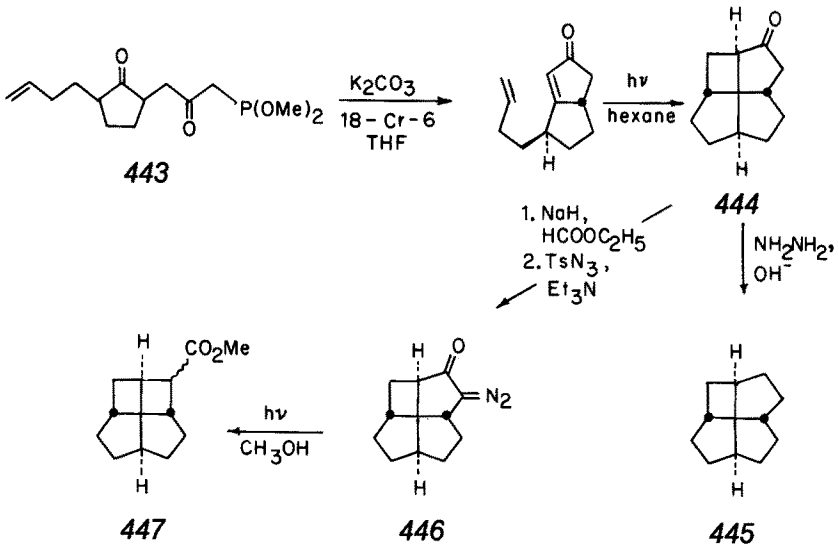
decarboxylation delivered *440*. Photolysis of the potassium salt of the tosylhydrazone in diglyme yielded the tetraquinane *441*.

Beginning with dicyclopentadiene, it has also proven possible to prepare *442* which could serve in its own right as a tetraquinane precursor [257].



442

The Dauben-Walker approach has yielded the smallest and most strained fenestrane known to date [258]. Following the intramolecular Wadsworth-Emmons cyclization of *443* which also epimerizes the butenyl sidechain to the more stable exo configuration, intramolecular photocycloaddition was smoothly accomplished to provide *444*. Wolff-Kishner reduction of this ketone afforded the C_2-symmetric hydrocarbon *445*. Application of the photochemical Wolff rearrangement to α-diazo ketone *446* gave *447*.

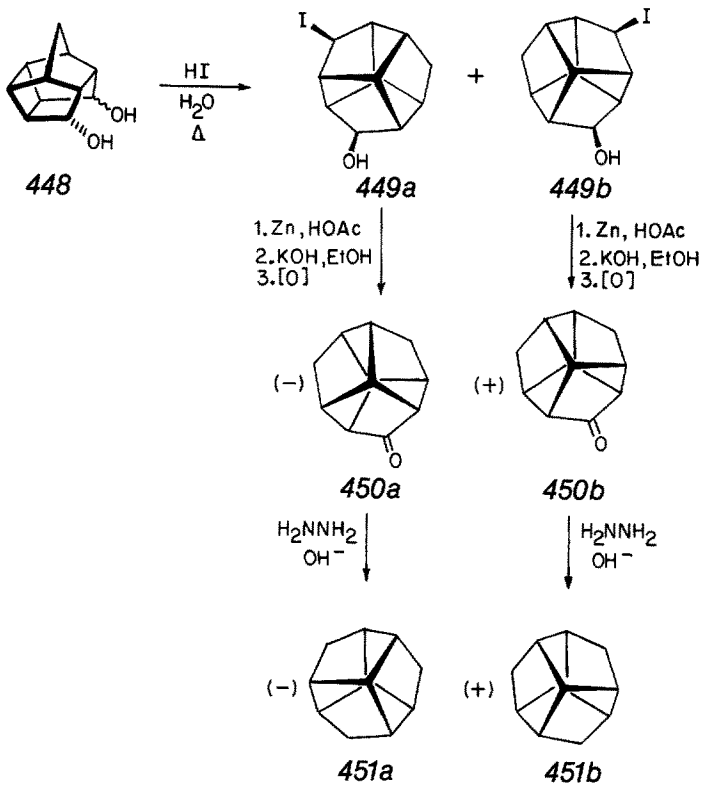


443 444 445 446 447

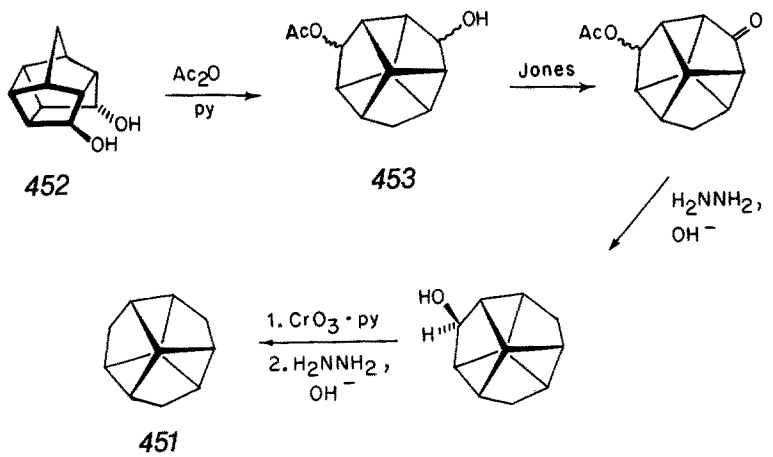
H (D_3)-Trishomocubanes and Congeners

(D_3)-Trishomocubane (*451*) is a saturated pentacyclic cage compound whose carbon skeleton is made up of fused five-membered rings. The molecule, which is intrinsically chiral, possesses the rare D_3 point group symmetry and is consequently of interest as a test system for chiroptic theories. Whereas racemic *451* has been known for more than a decade [259–261], the enantiomers have recently become available and absolute configurational assignments made [262–264]. The approach used by Helmchen and Staiger involved conversion of diol *448* with hydriodic acid into *449a* and *449b* which were separated chromatographically as their diastereomeric (—)-camphanic acid esters (Scheme XXXVI). Subsequent zinc reduction, hydrolysis, and Jones-Kiliani oxidation furnished the optically active trishomocubanones *450a* and *450b*. The hydrocarbons were arrived at by Wolff-Kishner reduction. ^{1}H NMR and x-ray methods were utilized to establish the absolute configurations [262].

Nakazaki's group also relied upon skeletal rearrangement, specifically that which occurs upon controlled acetylation of *452*. With the diastereomeric cis monoacetates *453* in hand, they proceeded to (±)-D_3-trishomocubanol which was resolved via its acid phthalate as the (+)-2-(1-aminoethyl)naphthalene salt. Collins oxidation and Wolff-Kishner reduction completed their scheme [263].



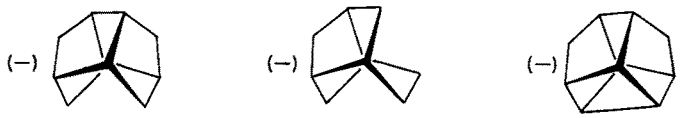
Scheme XXXVI



Eaton and Leipzig chose to resolve racemic trishomocubanone by reaction with *l*-ephedrine and separation of the diastereomers by fractional crystallization. Subsequent acid hydrolysis delivered the enantiomeric ketones [264].

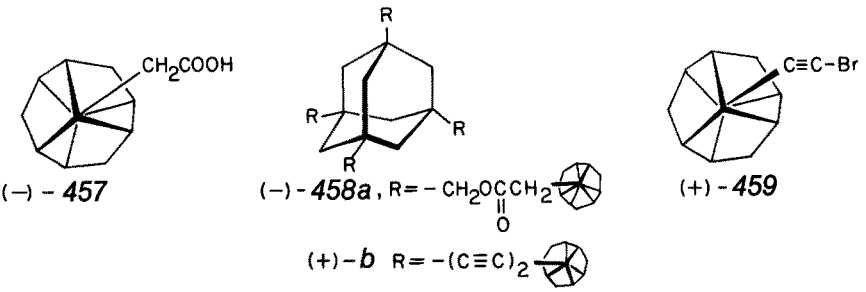
Successive removal of a diagonal CH_2 bridge from (—)-*451* furnishes (—)-ditwist-brendane (C_2 symmetry) (*454*) and (—)-twist-brendane (C_2 symmetry) (*455*). Also,

(—)-*451* may be regarded as a higher homologue of (—)-C_2-bishomocubane (*456*). The preparation of all three hydrocarbons in optically active form has recently been realized and absolute configurations assigned [263,265,266].



454 *455* *456*

By rather analogous chemistry, Nakazaki and Naemura succeeded in gaining access to (—)-2-D_3-trishomocubaneacetic acid (*457*). Esterification of this acid with 1,3,5,7-tetrakis(hydroxymethyl)adamantane gave (—)-*458a*, believed to be the first *T* symmetric organic molecule with known absolute configuration [267]. This claim was shown to be incorrect by Mislow who pointed out that asymmetry was introduced by the CH_2OCOCH_2 groups connecting the T_d adamantane core to the C_3-trishomocubane components [268]. However, Nakazaki has more recently arrived at (+)-*458b* by coupling of 1,3,5,7-tetraethynyladamantane with (+)-*459* [269]. The highest attainable static and time-averaged dynamic symmetry of this molecule are *T* and (C_3) [4].



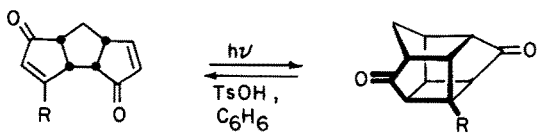
(–) - *457*

(–) - *458a*, R = $-CH_2OCCH_2$ (O)

(+) - *b* R = $-(C\equiv C)_2$

(+) - *459*

Irradiation of *cis,syn,cis*-enones *460* in ethyl acetate results in facile intramolecular cyclization to the trishomocubane diones *461*. Interestingly, these substances undergo smooth cycloreversion to *460* when exposed to catalytic amounts of *p*-toluenesulfonic acid in benzene at 30 °C [270].

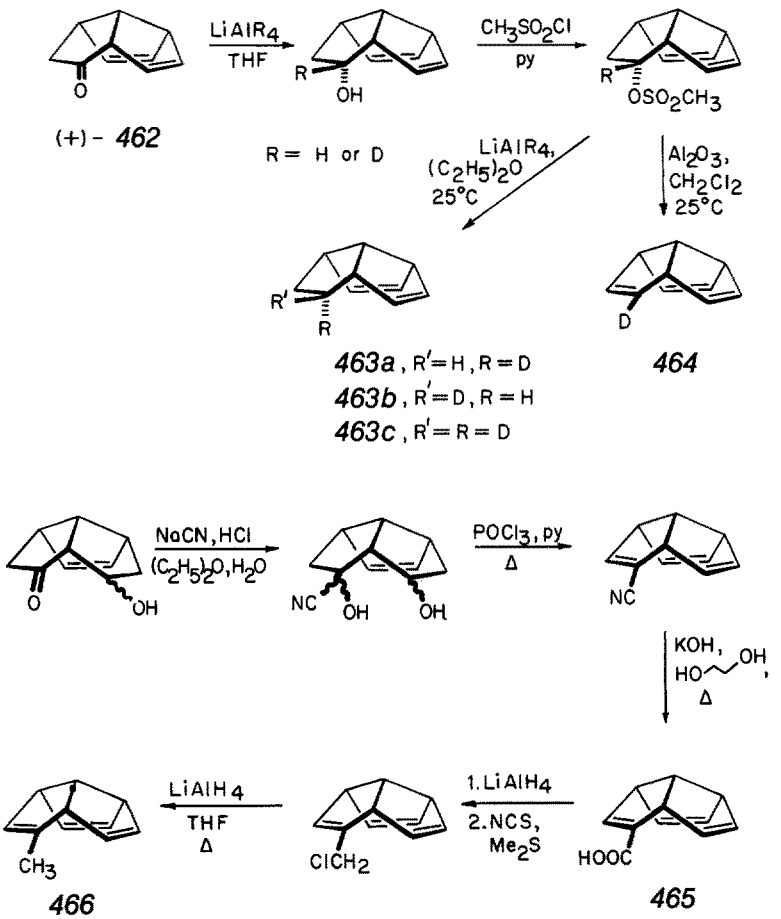


460 *461*

R = CH_3 , $CH_2CH=CH_2$, C_6H_5 , C_6H_4OMe-p

I Triquinacenes and Related Molecules

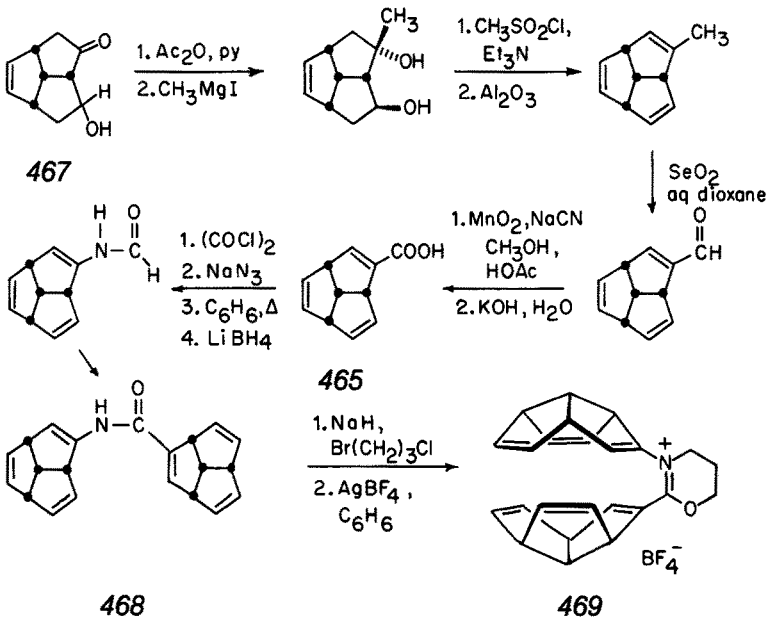
Full details have now appeared concerning the photoisomerization of triquinacene [271], its bridgehead substitution via photochlorination [272], and the S_N1 solvolytic reactivity of these halides [272]. The three deuterated, optically active 2,3-dihydrotriquinacenes *463* of known absolute configuration have been prepared from (+)-*462* (Scheme XXXVII) [273]. The dextrorotatory monodeuterated triquinacene *464* was



Scheme XXXVII

obtained from the same precursor and (—)-(1*S*)-2-methyltriquinacene (*466*) from (—)-triquinacene-2-carboxylic acid (*465*) [273]. The absorption and circular dichroism spectra of these hydrocarbons have been measured and analyzed in terms of the contributions of the composite double bonds and peripheral substituents. By this technique, triquinacene is shown not to be homoaromatic [273].

An alternative practical synthesis of triquinacene-2-carboxylic acid (as the dextrorotatory enantiomer) has been described by Deslongchamps and Soucy [274]. Their protocol begins with hydroxy ketone *467* and passes via the 2-methyl derivative (Scheme XXXVIII). Selenium dioxide oxidation of the hydrocarbon provided the aldehyde which was further oxidized and then hydrolyzed to arrive at the acid.

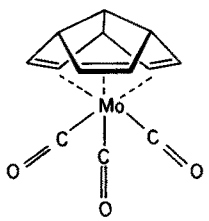


467 *465* *468* *469*

Scheme XXXVIII

Following resolution with (—)-quinine, (+)-*465* was transformed into the (+)-2-formamido derivative which was condensed with the acid chloride of (+)-*465* to give the secondary amide *468*. From this point, the cyclic imidate salt *469* was prepared, but cyclization to the dodecahedrane nucleus could not be realized [274].

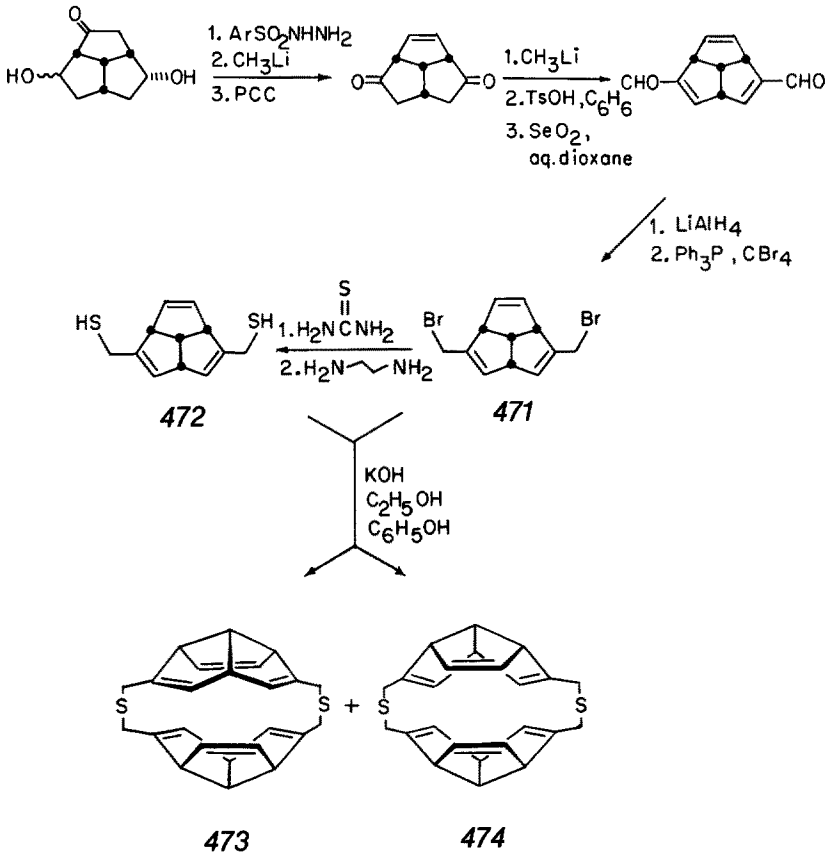
With Thiele's acid as starting material, several routes to triquinacene and 2,3-dihydrotriquinacen-2-one (*462*) have been developed [275]. Triquinacene reacts with $Mo(CO)_6$ to give tricarbonyl(triquinacene)molybdenum (*470*) and with $(CH_3CN)_3$-



470

$W(CO)_3$ to give tricarbonyl(triquinacene)tungsten [276]. X-ray analysis has revealed *470* to possess the indicated structure.

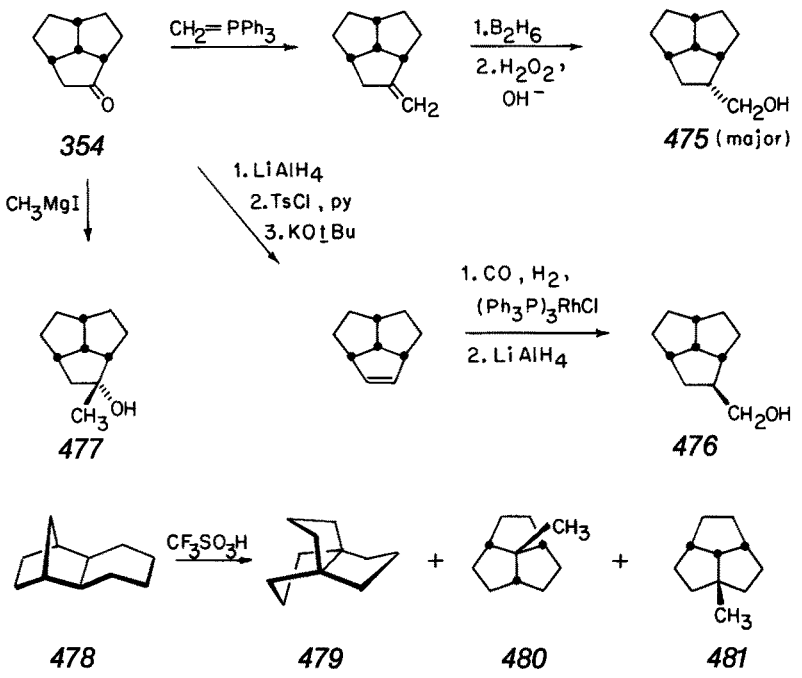
Following the preparation of 2,6-di(bromomethyl)triquinacene (*471*), dimercaptan *472* was synthesized conventionally. Coupling of these intermediates produced a 3.5 to 1 mixture of *anti-* and *syn*-triquinacenophanes *473* and *474*. These [somers were separated chromatographically and identities established by x-ray structure determination of *473* [277].



As part of a general study of the fate of perhydrotriquinacene 2-carbinyl cations, ketone *354* was converted to *475–477* [184].

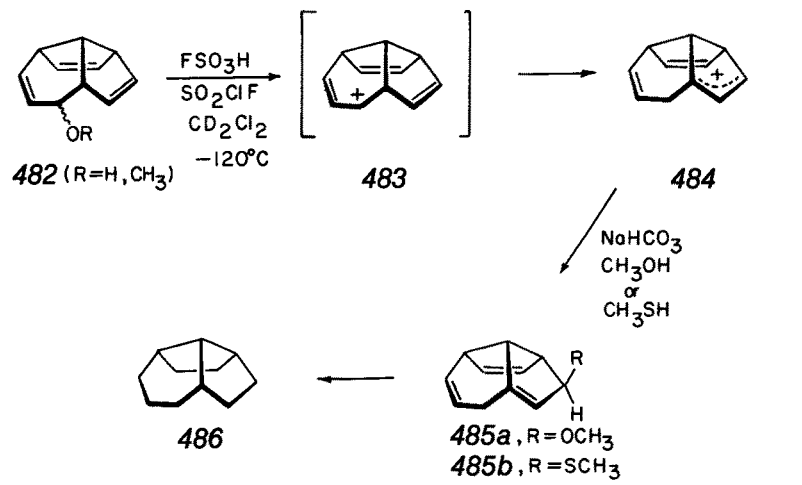
Amidst the complex mixture of products formed upon trifluoromethanesulfonic acid-catalyzed skeletal rearrangement of tricyclo[6.2.1.$0^{2,7}$]undecane (*478*) has been found [3.3.3]propellane (*479*) and the methylated perhydrotriquinacene *480* and *481* [278].

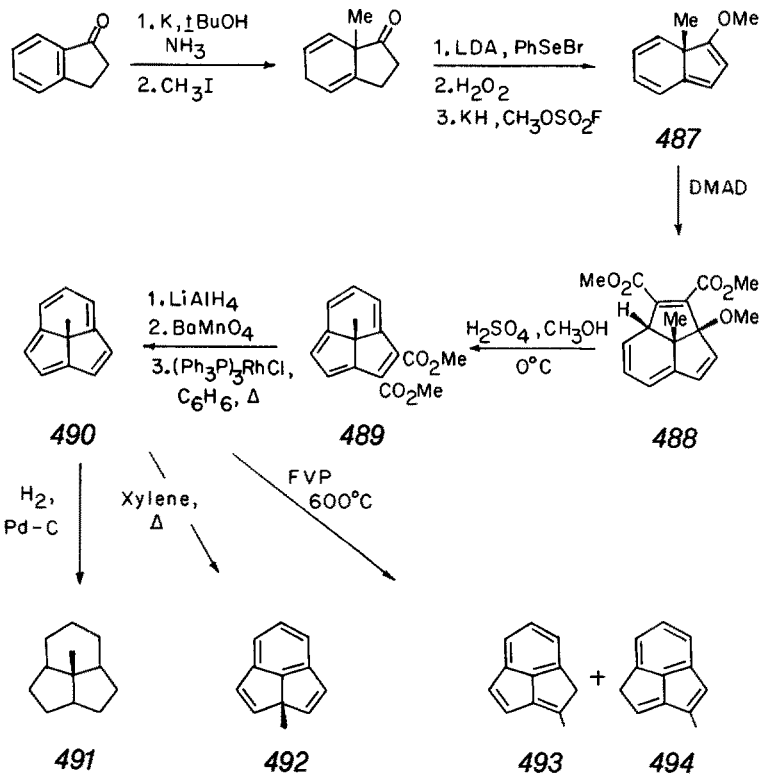
Treatment of *482* as the ether or alcohol with magic acid generates carbocation *483* which rapidly isomerizes to *484* whose spectra are observable. Quenching experiments carried out with sodium bicarbonate suspensions in methanol or methyl mercaptan at −110 °C produced *485a* and *485b*. Dissolution of *485a* in magic acid



regenerated *484*. Reduction of *485b* with Raney nickel followed by hydrogenation over 10% palladium on charcoal gave *486* as the only detectable product [279].

Following the successful preparation of 3-methoxy-3a-methyl-3a*H*-indene (*487*), cycloaddition with dimethyl acetylenedicarboxylate was found to occur across the 3- and 4-positions to give *498* [280]. Dissolution of *488* in a 1:1 mixture of concentrated sulfuric acid and methanol at 0 °C results in loss of the elements of methanol and conversion to a new tricyclic aromatic [10]annulene (Scheme XXXIX) [281]. Diester *489* was subsequently transformed into the unsubstituted system (*490*). Catalytic hydro-

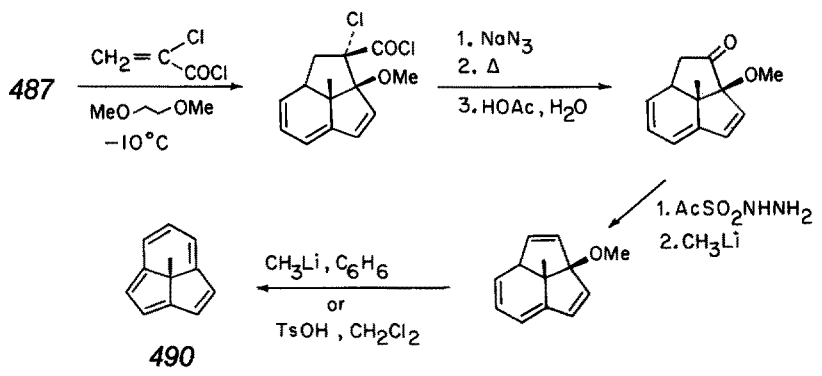


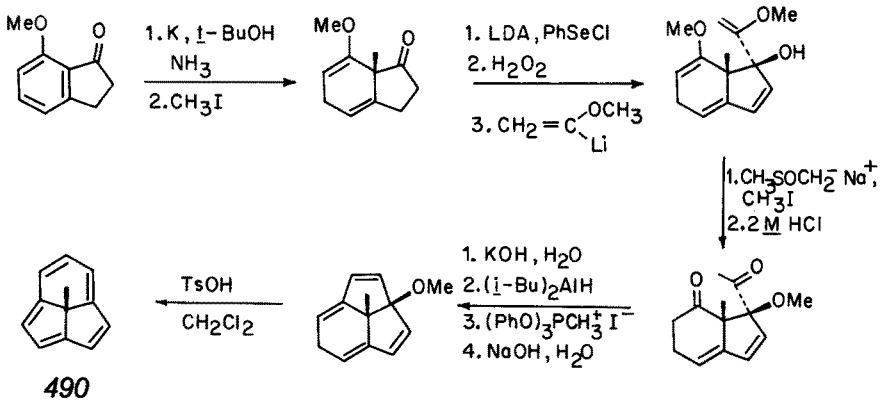


Scheme XXXIX

genation produced *491* while thermal rearrangement in refluxing xylene gave rise to *492*. Flash vacuum pyrolysis at 600 °C resulted in further isomerization and formation of *493* and *494* [282].

More recently, two improved syntheses of *490* have been realized in Rees' laboratory [283,284]. The main features of these approaches are summarized in Scheme XL.

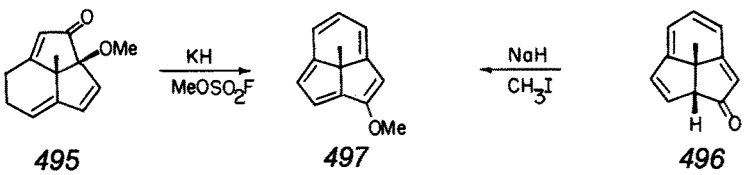




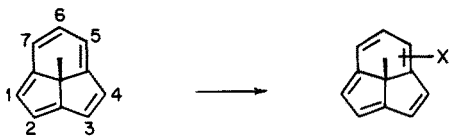
490

Scheme XL

The intermediate tricyclic ketones *495* and *496* have been transformed to the methoxy-substituted derivative *497* [284,285]. The latter ketone is subject to hydrogen-deuterium exchange only under basic conditions and appears to exist entirely in the keto form despite the ready formation of its anion and successful methylation on oxygen [285]. In agreement with the aromatic nature of *490*, the hydrocarbon undergoes electrophilic substitution reactions [283].



495 **497** **496**

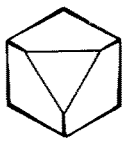


490

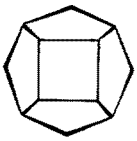
	Isomer	1-	2-	5-	6-
$Cu(NO_3)_2$, Ac_2O, 0°C					
Ac_2O, CH_2Cl_2, $BF_3 \cdot Et_2O$	X = NO_2	40	5	40	15
$Cl_2CHOBu\text{-}n$, $TiCl_4$, CH_2Cl_2	X = COMe	20	0	75	5
	X = CHO	4	0	93	3

J Peristylanes

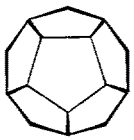
Garratt and White have pointed out the similarities in the topologies of *498–500* and their more spherical counterparts *501–503* [286]. Following Eaton's lead [287], they proposed to name *498–500* as [3]-, [4]-, and [5]-peristylanes, respectively, to reflect



498

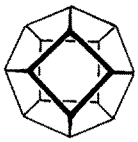


499

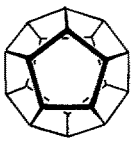


500

501



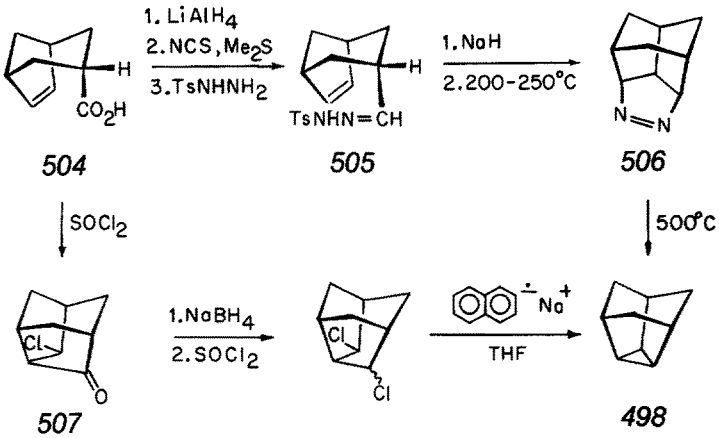
502



503

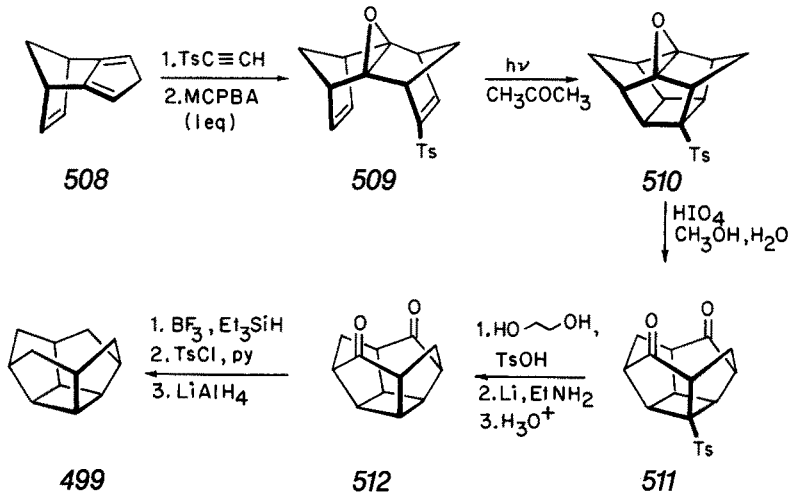
the size of the basal ring. The first member of this series to yield to synthesis was *498* and three approaches are currently available. In expedient fashion, Nickon and Pandit pyrolyzed the sodium salt of the tosylhydrazone of noradamantan-2-one [288]. Regiospecific C—H insertion leads directly and exclusively to *498*. The synthetic entries devised by Garratt and White both start from carboxylic acid *504*. Conversion to tosylhydrazone *505* and pyrolysis of its sodium salt afforded azo compound *506* which itself on pyrolysis gave *498*. Alternatively, *504* reacts with thionyl chloride to provide chloro ketone *507*. Once dichloride *508* was arrived at, reduction with sodium naphthalenide delivered *498*.

Eaton's synthesis of [5]-peristylane (*500*) [287] was discussed in our earlier review [1].



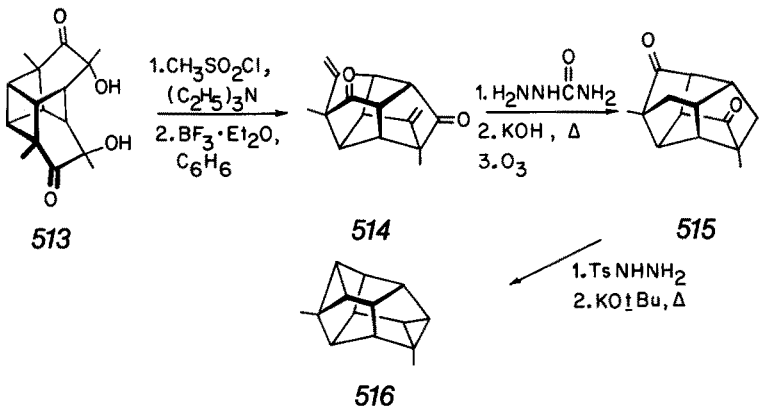
A fully stereocontrolled preparation of *499* has recently been completed by Paquette and coworkers [289]. When triene *508* was treated with *p*-toluenesulfonylacetylene, highly stereoselective addition from the endo surface occurred to deliver an adduct which was directly epoxidized (Scheme XLI). The proximity of the two π bonds in *509* allows for ready photocyclization. Oxidative cleavage of *510* afforded

diketone *511* which was desulfonylated after bisketalization. Stepwise reduction of *512* furnished the desired *499*.



Scheme XLI

A synthesis of a dimethyl derivative of *501* has also recently been announced by Hirao, et al. [290]. Following conversion of *513* to its dimesylate, Lewis acid-catalyzed rearrangement gave dienedione *514* as the major product. Heating of the disemicarbazone of *514* with powdered KOH furnished the diolefin which was transformed into *515* by ozonolysis. When the ditosylhydrazone of *515* was heated with potassium



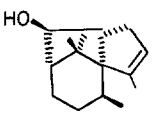
tert-butoxide in glyme, the C_2-symmetric product *516* containing two cyclopropane rings resulted.

A discussion of dodecahedrane chemistry is deferred to a later section of this review.

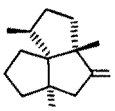
VI Natural Products Chemistry

A Isolation and Physical Properties

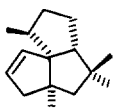
Bohlmann and his coworkers have continued their impressive pace in the isolation of polyquinane-based natural products. These include pardalianchol (*517*) [291], β-isocomene (*518*) [292], silphinene (*519*) [293,303], 13-acetoxymodhephene (*520*) [294], 5-oxosilphiperfol-6-ene (*521*) [295], 8-α-hydroxypresilphiperfolene (*522*) [296], 1-acetoxyisocomene (*523*) [297], and several additional derivatives of this ring system [298]. From other laboratories have come the characterization of such interesting substances as magellanine (*524*) [299], paniculatine (*525*) [300], arnicenone (*526*) [301], riolozatrione (*527*) [302], stoechospermol (*528*) [304], ptychanolide (*529*) [305], yuzurimine (*530*) [306,307], yuzurimine-A (*531a*) [307,308], macrodaphniphyllamine (*531b*) [309], structurally related alkaloids of this family [306–311], laurenene (*532*) [312], the only naturally occurring fenestrane molecule, and several oxygenated 1,7-diepicedrane sesquiterpenes [313].



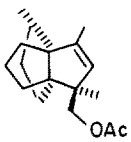
517



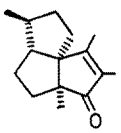
518



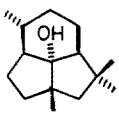
519



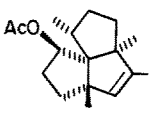
520



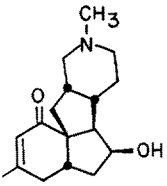
521



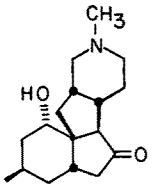
522



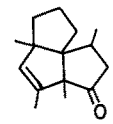
523



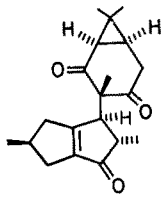
524



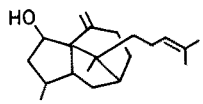
525



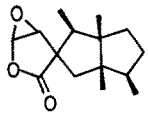
526



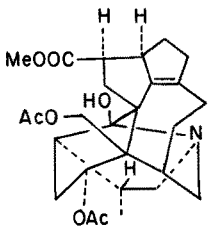
527



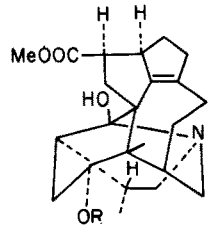
528



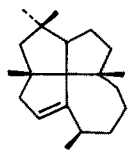
529



530



531a, R = Ac
531b, R = H

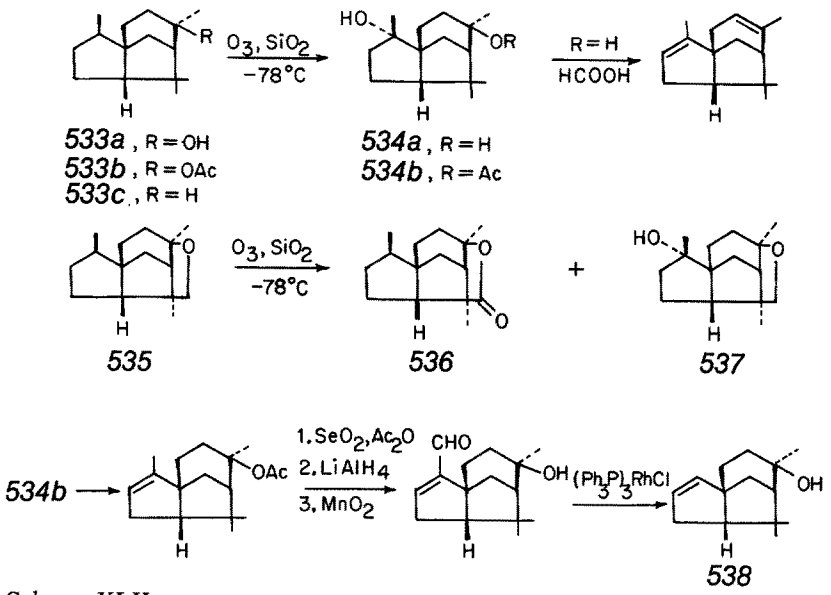


532

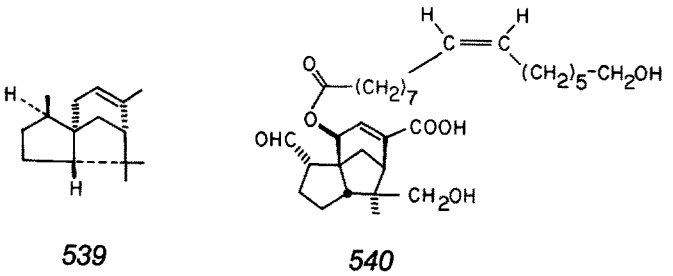
B Chemical Transformations

Cedrol (*533a*), its acetate (*533b*), and 8α*H*-cedrane (*533c*) undergo selective hydroxylation with ozone adsorbed on silica gel to produce *534a* or *b* [314]. Cedrane oxide (*535*) gives the lactone *536* (30%) and tertial alcohol *537*, thereby revealing that $-CH_2O-$ and tertiary C—H groups are of similar reactivity. The conversion of *534b* to C_{14}-norcedrenol (*538*) has also been accomplished (Scheme XLII) [314]. With $PhICl_2$, cedryl acetate affords the tertiary chloride corresponding to *534b*. The autoxidation of 8*R*-hydroxycedran-13-al has been reported [315].

Borohydride reduction of 9-oxo, 10-oxo- and 8-ene-10-oxo-cedranoids proceeds in general to give the β-hydroxy epimer [316]. Details concerning the reductive ring opening of several cedrane oxides have been disclosed, as have the circular dichroism spectra of cedran-10-ones [317]. The configuration of the bromination product of dimethyl 8,13-epoxy-9-oxocedrane-12,15-dioate has also been established [318]. One of the sesquiterpene hydrocarbons previously obtained [319] by solvolysis of the *p*-bromobenzenesulfonate of *allo*-cedrol has recently been shown to be identical with α-funebrene (*539*) [320]. The total synthesis of jalaric ester-I (*540*) has been accomplished through selective condensation of 16-hydroxy-(*Z*)-9-hexadecanoic acid and jalaric acid [321,322]. The possible importance of this compound in the elaboration of lac resin by insects has been pointed out.



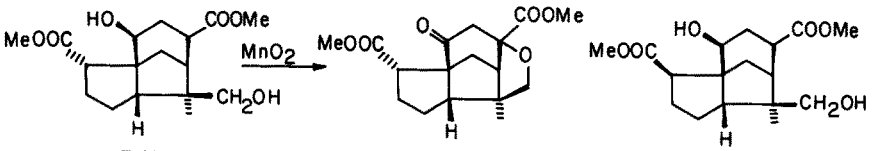
Scheme XLII



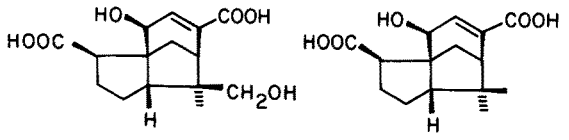
The action of activated manganese dioxide on *541* gives the oxo-ether *542* as a single product in quantitative yield. On the other hand, *543* leads under analogous conditions to a mixture of six products [323]. The configurations of shellolic (*544*) and laccishelloic acids (*545*) have been correlated by conversion of the C_{13}-hydroxymethyl function of the former into the methyl group of the latter via two routes involving reduction of an intermediate thioacetal and an iodo derivative, respectively [324].

Because of the absence of a suitably positioned C—H bond, the alkoxy radical derived from *546* cannot undergo heterocyclization. β-Fragmentation therefore ensues to give *547* along with a small amount of parent ketone. An empirical predictive rule has been developed to account for the stereoelectronic control observed in such reactions [235].

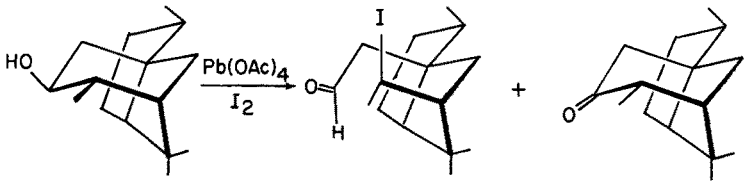
Tricyclodehydroisohumulone (*550*), detected as a new bittering component present in beer and in stored hops, is formed in low yield by boiling aqueous humulone (*549*) in air. This highly functionalized triquinane, originally believed to possess an alternative structure [326], is best prepared (30%) by reaction of *549* with lead tetra-



541 542 543

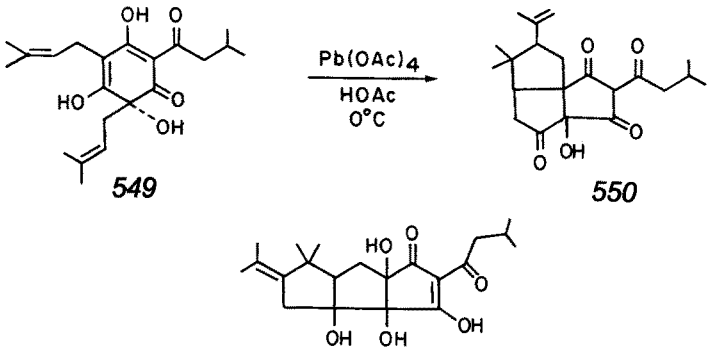


544 545



546 547 548

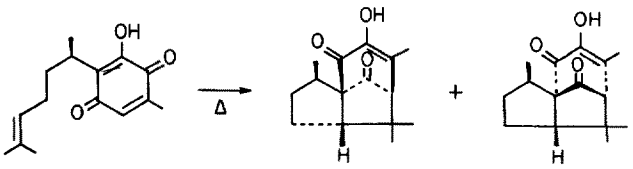
acetate [327]. On the basis of recent spectroscopic evidence the structural assignment to isohumulione A has been revised to *551* [328].



549 550 551

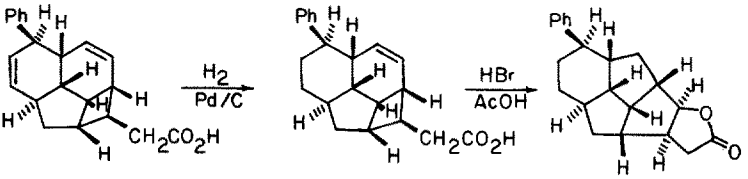
While the chirality of perezone (*552*) has been known for some time [329], that of the α- (*553*) and β-pipitzols (*554*) which are derivable from *552* by thermolysis was rigorously proven only recently by chemical transformation to cedrene and x-ray diffraction [330]. The cyclization of *552* has been shown to involve a concerted [4+2] cycloaddition which lacks stereochemical induction by the chiral center already present, since *553* and *554* are obtained in equimolar amounts [331]. However, a stepwise mechanism having higher stereoselectivity is followed by *552* in the presence

of boron trifluoride (90% of *553*) [332]. The stereochemistries of the closely related cedranolides α-, β-, and γ-perezol have been assigned from their respective ORD curves [330].



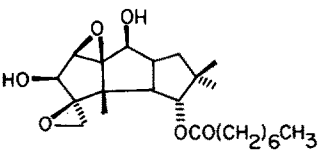
552 *553* *554*

Hydrogenation of endiandric acid (*555*) with an aged palladium catalyst afforded the dihydro derivative *556* which isomerized to the triquinane lactone *557* when heated with HBr in acetic acid [333].



555 *556* *557*

Chemical modification of coriolin B (*558*) of rather extensive scope has been described [334,335].



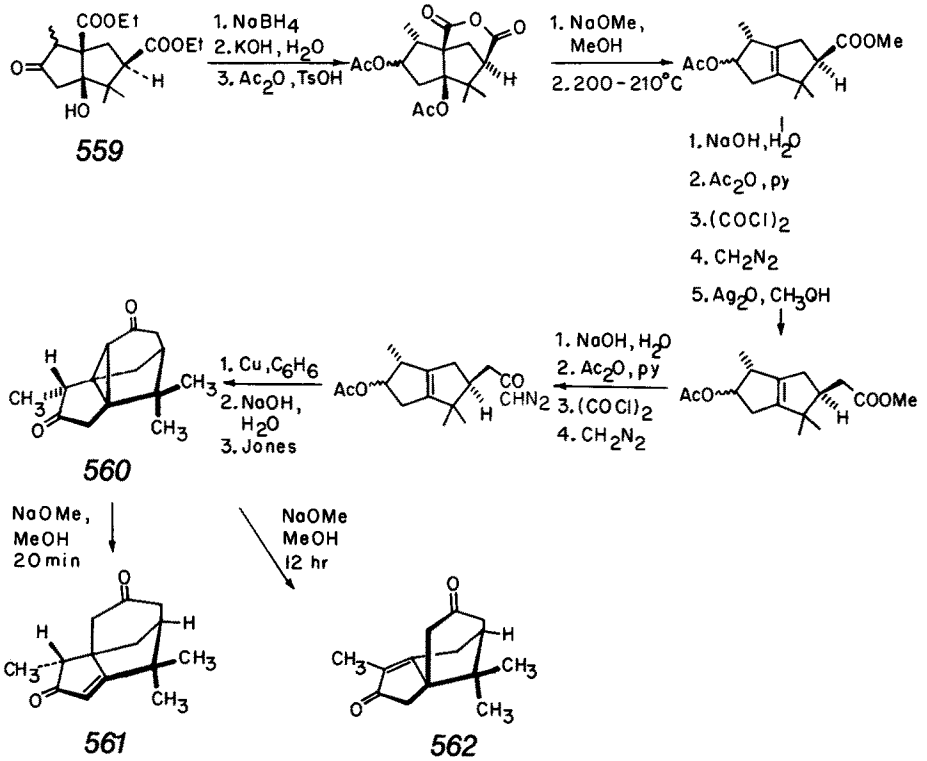
558

Experimental studies delineating an extensive number of chemical transformations of laurenene (*532*) [312,336], including the crystal structure analysis of a bromo derivative [337], have been published.

VII Synthesis of Diquinane Natural Products

A Cedranoids

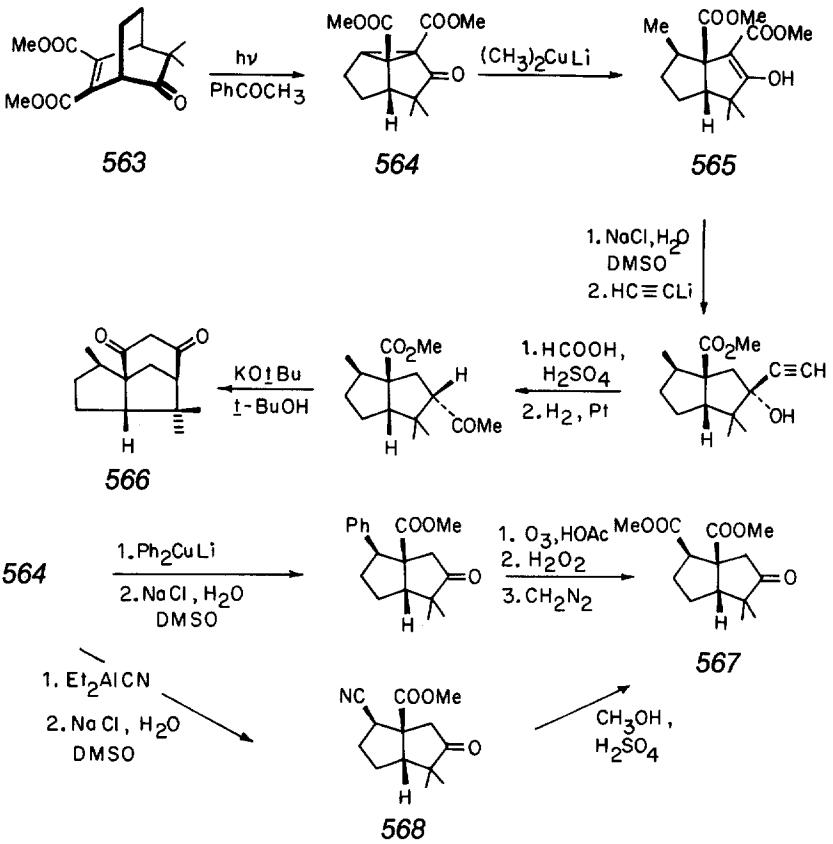
Although cedranoid sesquiterpenes have earlier been synthesized, a renewed interest in alternative methods for elaborating these frameworks has arisen. The stereospecific approach to α-cedrene and α-patchoulene skeletons designed by Deslongchamps and summarized in Scheme XLIII is a case in point [338]. Beginning with the Stork-Clarke intermediate *559*, the tetracyclic cyclopropyl diketone *560* was elaborated via a series of standard transformations. Treatment of *560* with three equivalents of sodium methoxide in methanol at room temperature for 20 min



Scheme XLIII

gave the tricyclic enedione *561* (cedrene skeleton) as the only product. When the same reaction was carried out for 12 hr, the isomeric enedione *562* (patchoulene skeleton) was formed uniquely. Thus, *561* is the kinetic product and *562* the thermodynamic product.

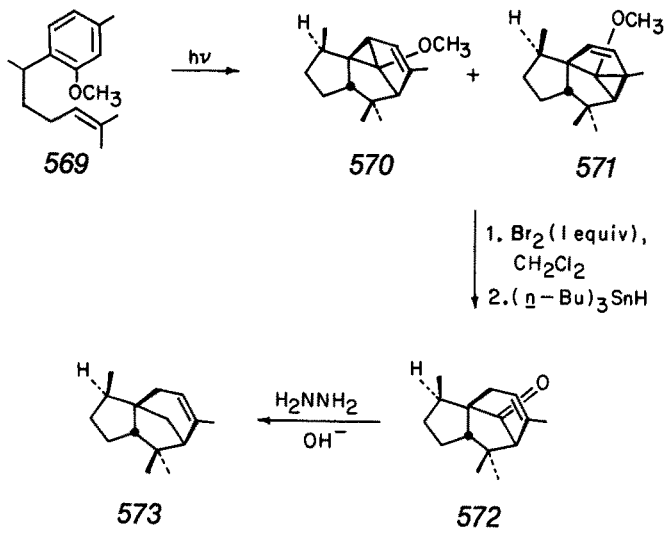
Yates and Stevens have devised an interesting synthesis of diketone *566* which is potentially adaptable to the introduction of additional functionality [339]. Taking advantage of the efficiency with which *563* enters into oxa-di-π-methane rearrangement and *564* undergoes homoconjugative addition, these workers gained access to *565*. This keto ester was subjected to Rupe rearrangement conditions which led ultimately to *566* as shown.



The viability of this synthetic approach to the introduction of a carboxylic acid function at C_2 has been demonstrated in two ways. Following lithium diphenylcuprate addition to *564*, the newly introduced phenyl group is subsequently degraded by ozonolysis to provide *567*. Alternatively, reaction of *564* with diethylaluminium cyanide in toluene gives *568* which is also conveniently transformed into *567* [339,340].

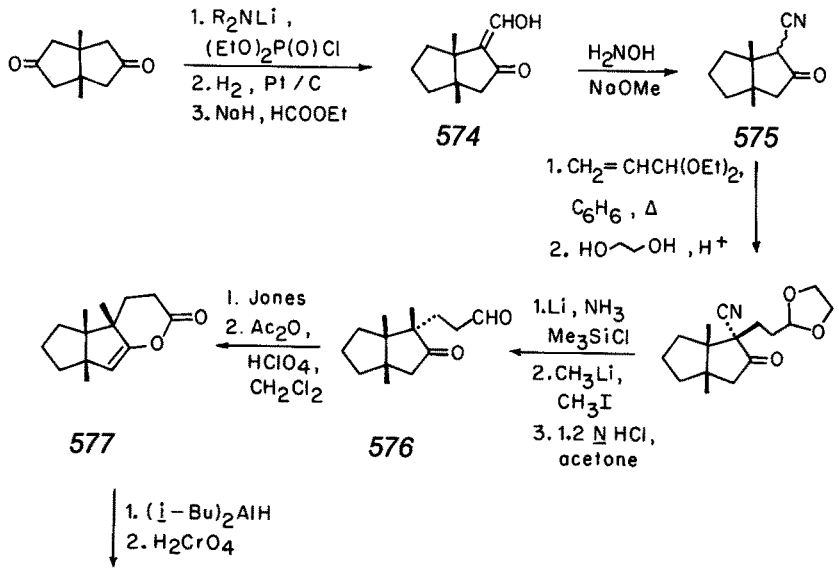
Making elegant use of the intramolecular arene-olefin meta-cycloaddition reaction, Wender and Howbert have achieved a total synthesis of (±)-cedrene (*573*) [341]. Irradiation of *569* led to an approximately equal mixture of *570* and *571* which

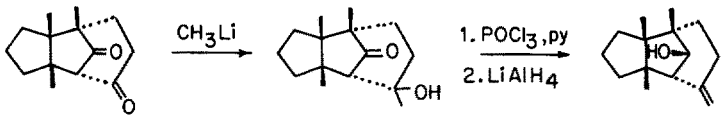
without separation were converted to cedren-11-one (*572*) by a bromination-reduction sequence. Wolff-Kishner reduction of this product gave *573* in 59% overall yield.



B Gymnomitrol

Gymnomitrol (*579*), a tricyclic sesquiterpenoid which occurs as a major metabolite of the liverwort *Gymnomitrion obtusum* (Lindb.) Pears, contains a rare 4,8-methano-azulene (diquinane) carbon skeleton with five adjacent chiral centers, three of them



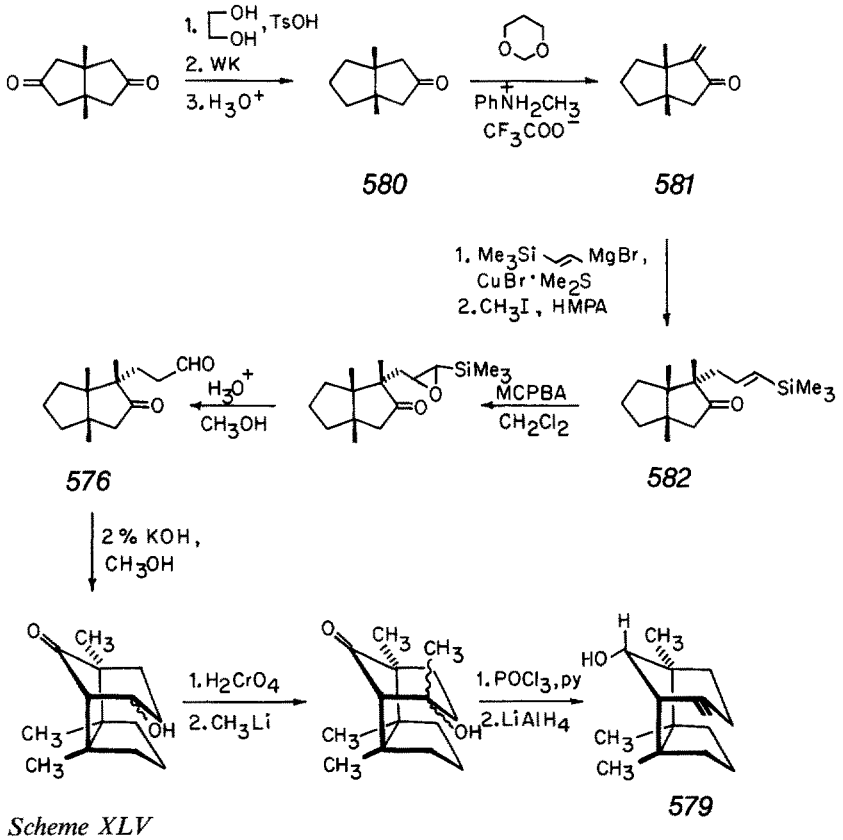


578 579

Scheme XLIV

quaternary. This molecule probably sets a record in that five different syntheses were reported in a span of only two months [342-347]. The Coates protocol (Scheme XLIV) centers about elaboration of hydroxymethylene ketone (*574*) into the tricyclic diketone (*578*). Alkylation of keto nitrile *575* proceeds exclusively cis to the angular methyl groups as does the subsequent reductive methylation. These authors were not able to achieve aldol cyclization of keto aldehyde *576* and consequently proceeded to enol lactone *577* [342]. The addition of a methyl group to *578* could be achieved regioselectively. Subsequently dehydration gave *579* and its endocyclic isomer which were separated chromatographically.

Paquette and Han chose to append their sidechain to *580* by preforming the α-methylene ketone *581* and carrying out a conjugate addition of a vinyl silane organo-

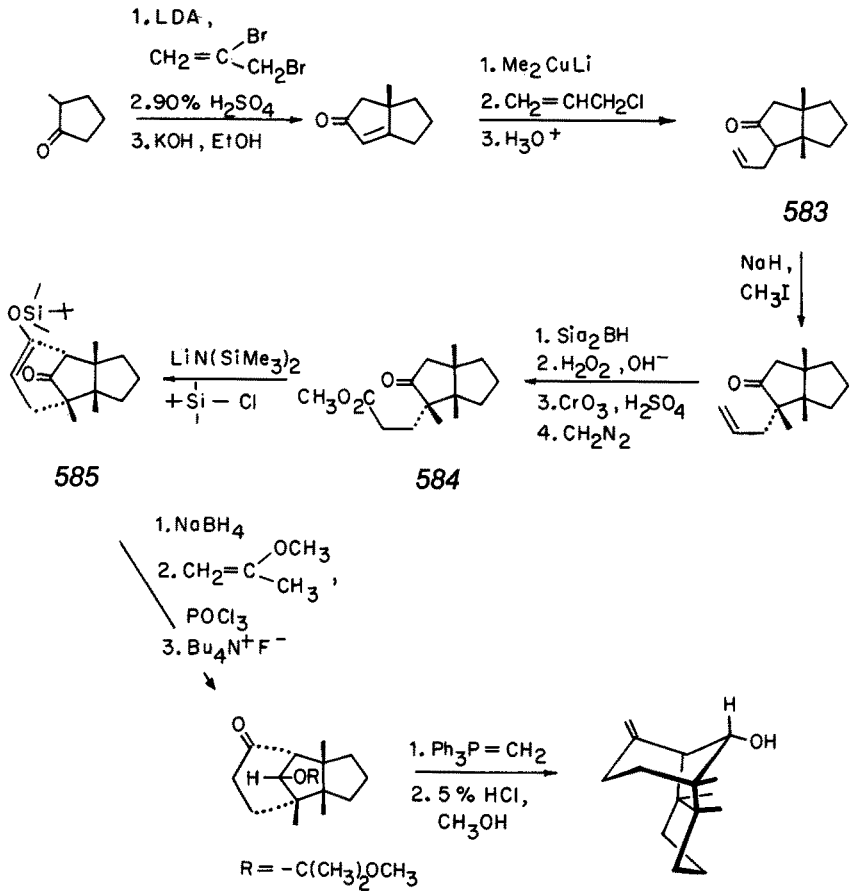


576 582 579

Scheme XLV

metallic reagent concurrent with methylation (Scheme XLV) [343]. Epoxidation and acid hydrolysis of *582* generated keto aldehyde *576* which they were able to cyclize with 2% potassium hydroxide in methanol. The remainder of the synthesis bears close similarity to the Coates approach.

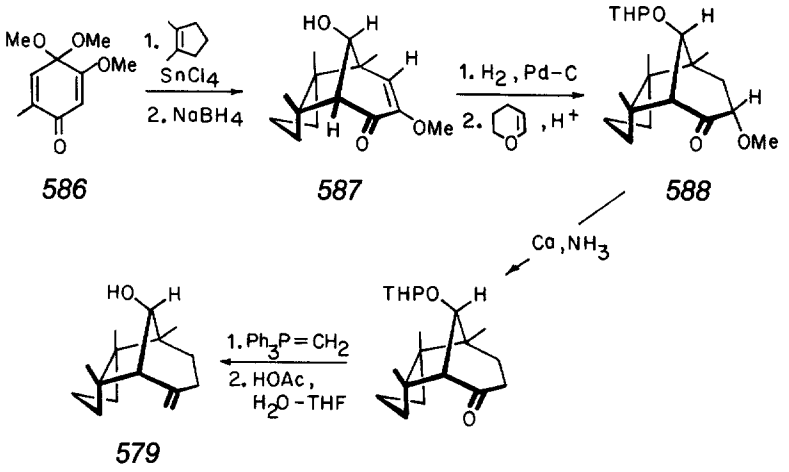
Welch's stereoselective synthesis centered about the tandem conjugate addition of a methyl group and allylation to produce *583* (Scheme XLVI) [344]. A second methylation, combined with oxidation of the allyl sidechain, gave *584* which was successfully cyclized under Claisen conditions. Trapping of the enolate as in *585* permitted differentitation between the two potential ketone carbonyl groups.



Scheme XLVI

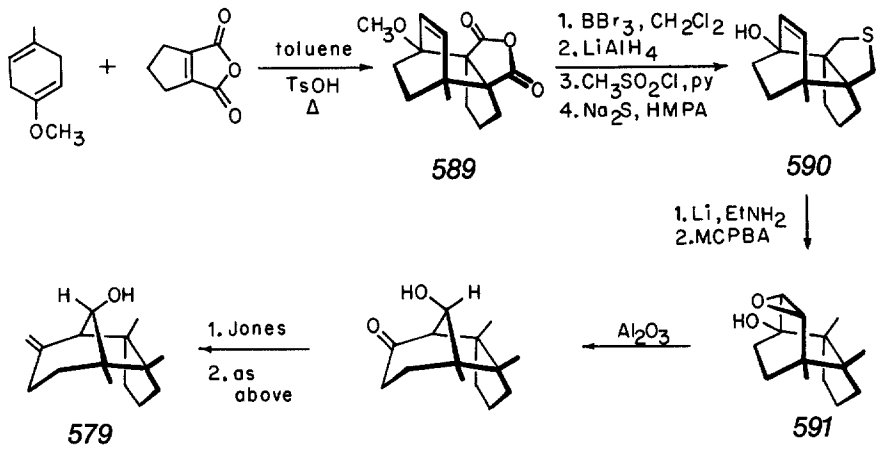
In a clever adaptation of the acid-catalyzed addition of *p*-quinone ketals to olefins [345], Büchi and Chu condensed *586* with 1,2-dimethylcyclopentene in the presence of stannic chloride and immediately reduced the two diastereomeric adducts with sodium borohydride [346]. The major alcohol *587* was separated, catalytically hydrogenated, and converted to the tetrahydropyranyl derivative *588* (Scheme XLVII).

The subsequent conversion to gymnomitrol proved uneventful and the overall sequence is the most expedient yet devised.



Scheme XLVII

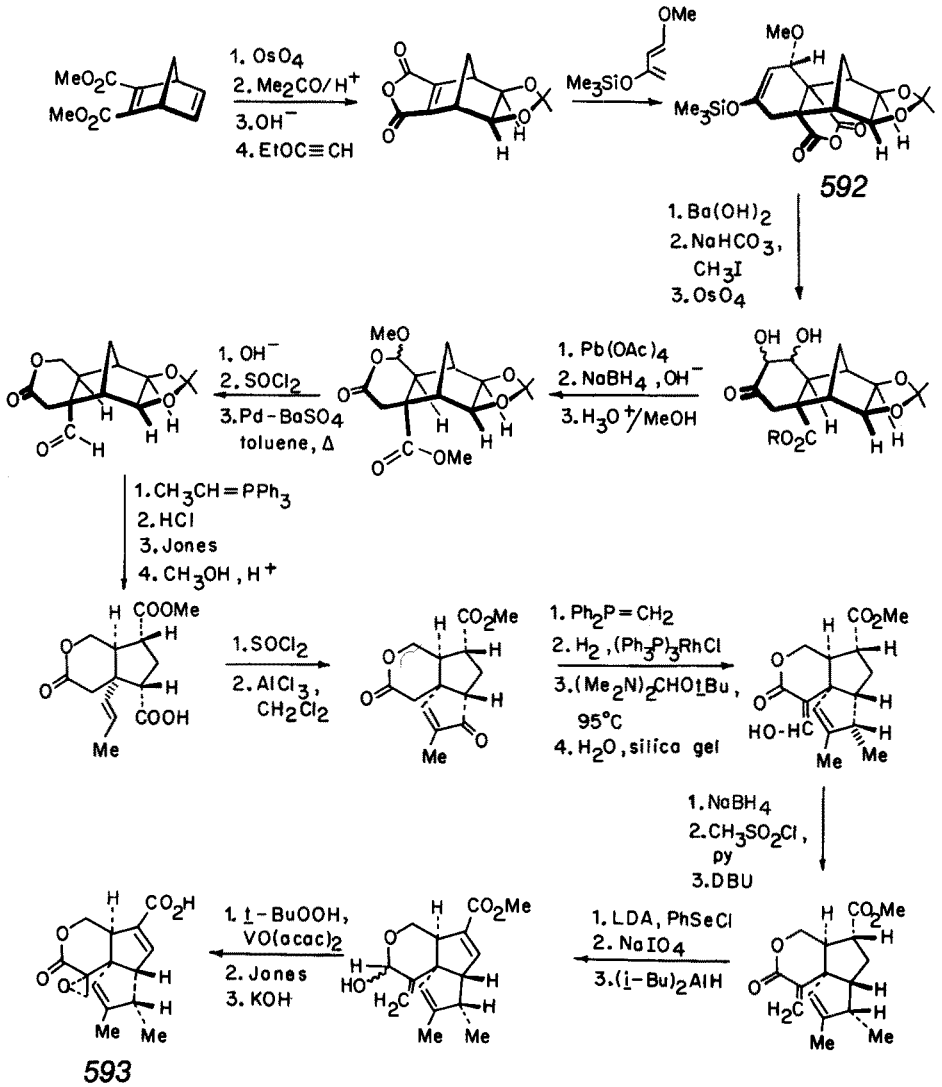
The last synthesis to evolve which is due to Ito and his coworkers is interesting in that it relies on a stereospecific skeletal rearrangement of a bicyclo[2.2.2]octane system which in turn was prepared by Diels-Alder methodology (Scheme XLVIII) [347]. Heating of a toluene solution of cyclopentene 1,2-dicarboxylic anhydride and 4-methylcyclohexa-1,4-dienyl methyl ether in the presence of a catalytic quantity of *p*-toluenesulfonic acid afforded *589*. Demethylation was followed by reduction and cyclization to sulfide *590*. Desulfurization set the stage for peracid oxidation and arrival at *591*. Chromatography of this intermediate on alumina induced isomerization to keto alcohol *592*. Jones oxidation afforded diketone *593* which had earlier been transformed into gymnomitrol.



Scheme XLVIII

C Pentalenolactone

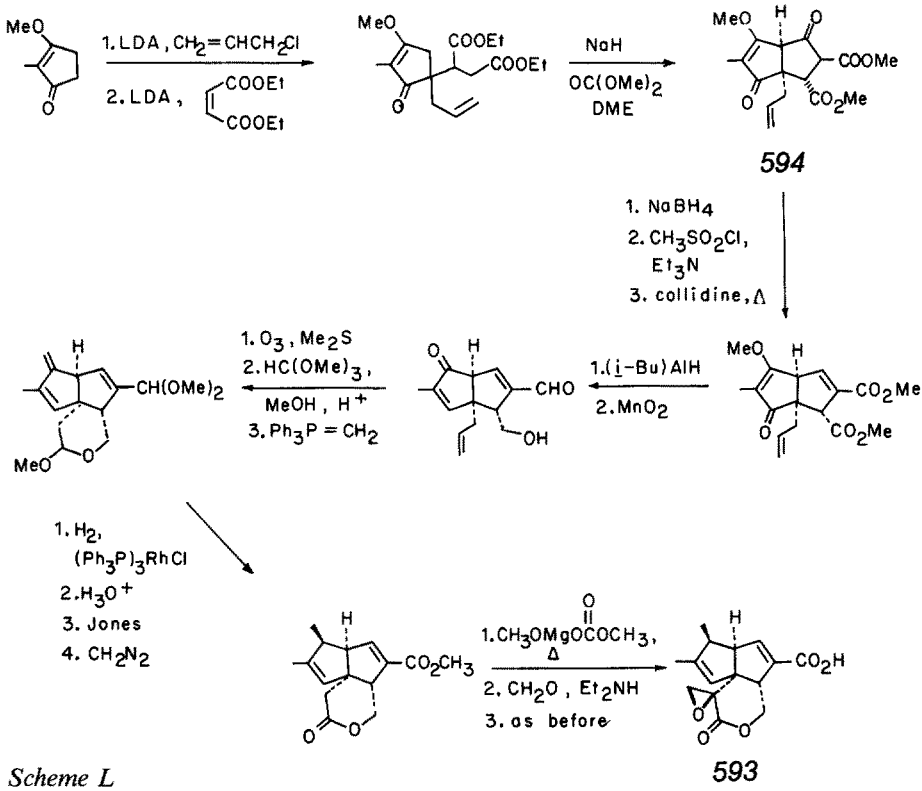
Pentalenolactone (*593*) is an antibiotic, tumor inhibitory agent whose provisional structural assignment was later revised on the basis of x-ray studies. Biosynthetic studies show pentalenolactone to be of sesquiterpenoid origin [348]. Two syntheses of *593*, due to Danishefsky [349] and Schlessinger [350], have been reported to date. In the first (Scheme IL), the operating strategy was to arrive at keto ester *592* by Diels-Alder cycloaddition. Following incorporation of the essential stereochemical information in this manner, an additional five-membered ring was crafted and the cyclo-



Scheme IL

hexenone subunit was modified so as to become the epoxy lactone portion of the natural product.

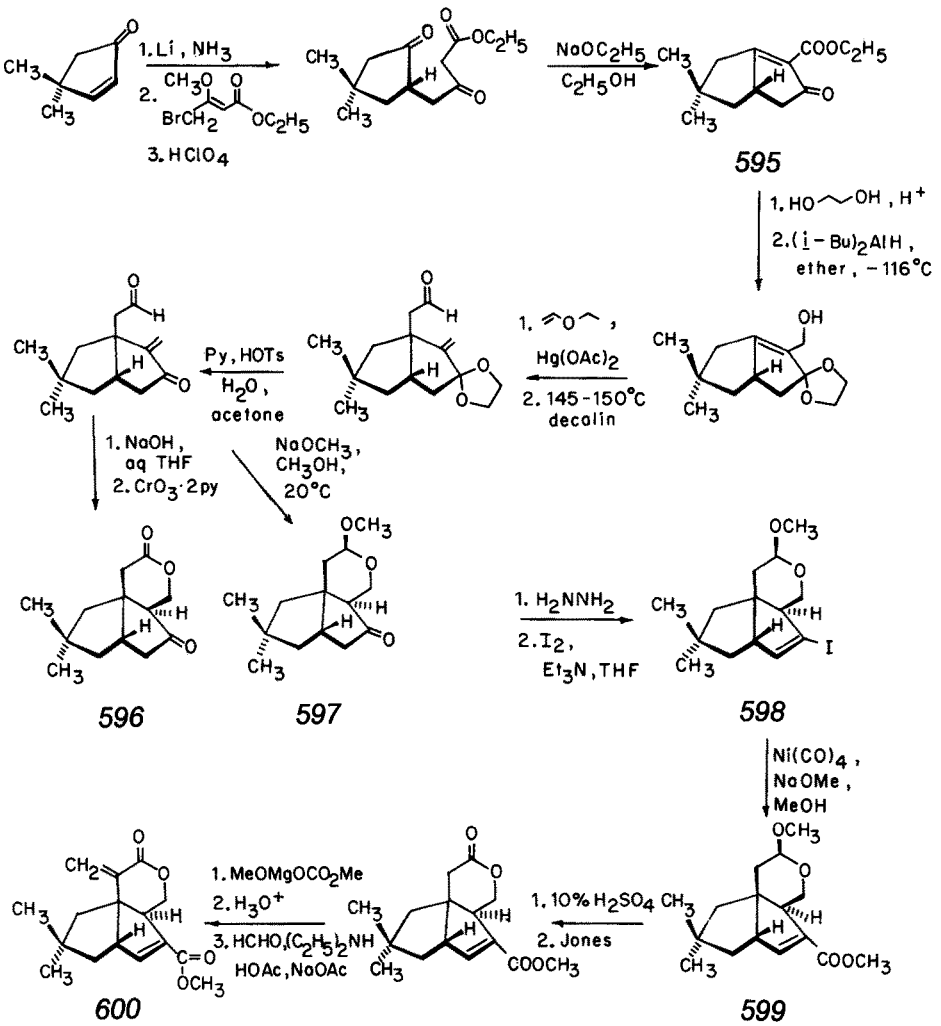
The quite different route implemented by Schlessinger commences with an expedient construction of the diquinane nucleus *594*. This accomplishment is followed by an interclude of functional group reorganization. The concluding steps are concerned with appropriate introduction of carbon atoms 14 and 10 (Scheme L).



Scheme L

D Pentalenolactone E Methyl Ester

In the course of biosynthetic experiments involving *Streptomyces* UC5319, Cane and Rossi treated the acidic fraction of an ether extract with diazomethane and obtained *600* which they called pentalenolactone E methyl ester [351]. Paquette's solution to the total synthesis of this substance (Scheme LI) [352] was founded upon a new protocol for stereocontrolled lactone annulation [353]. 4,4-Dimethylcyclopentenone was suitably annulated to give *595* which was subjected to controlled reduction. Application of the Claisen rearrangement and implementation of an intramolecular Michael addition-oxidation sequence led to the tricyclic lactone *596* or the lactol ether *597*. Once vinyl iodide *598* was produced, the nickel carbonyl-sodium methoxide reagent furnished ester *599* which served as progenitor to the target molecule.

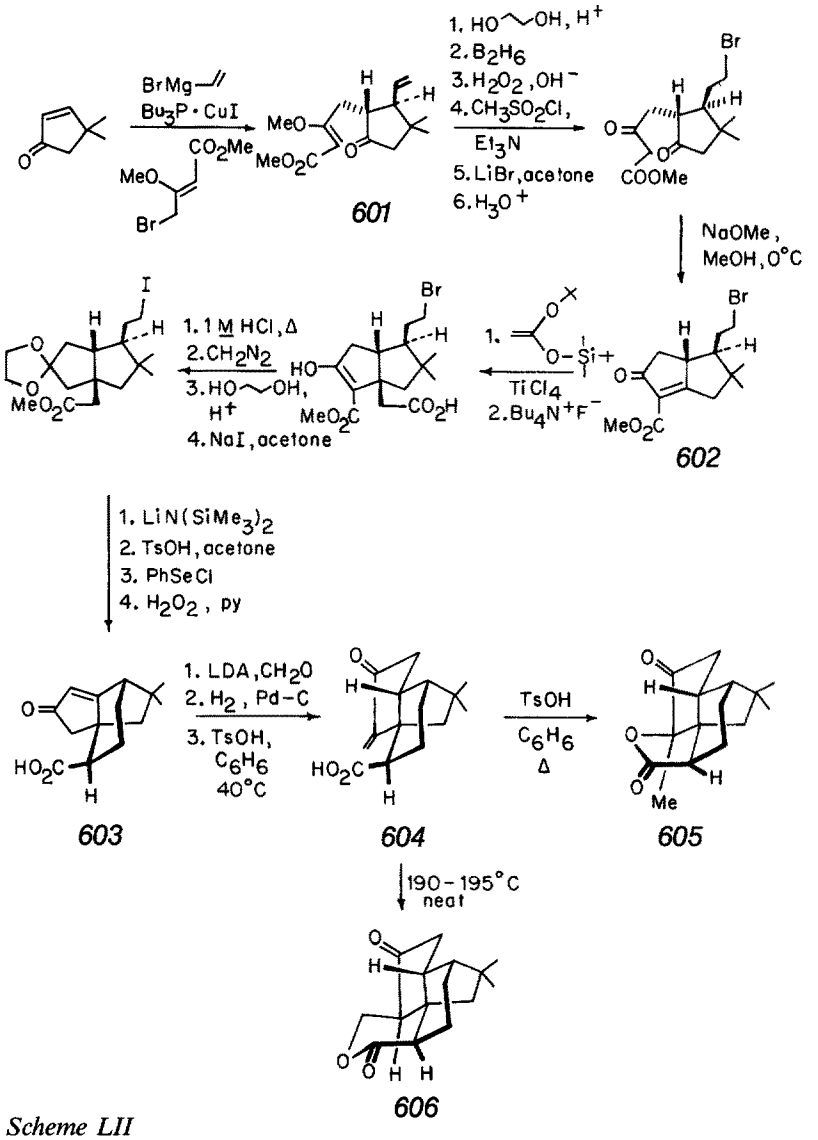


Scheme LI

E Quadrone

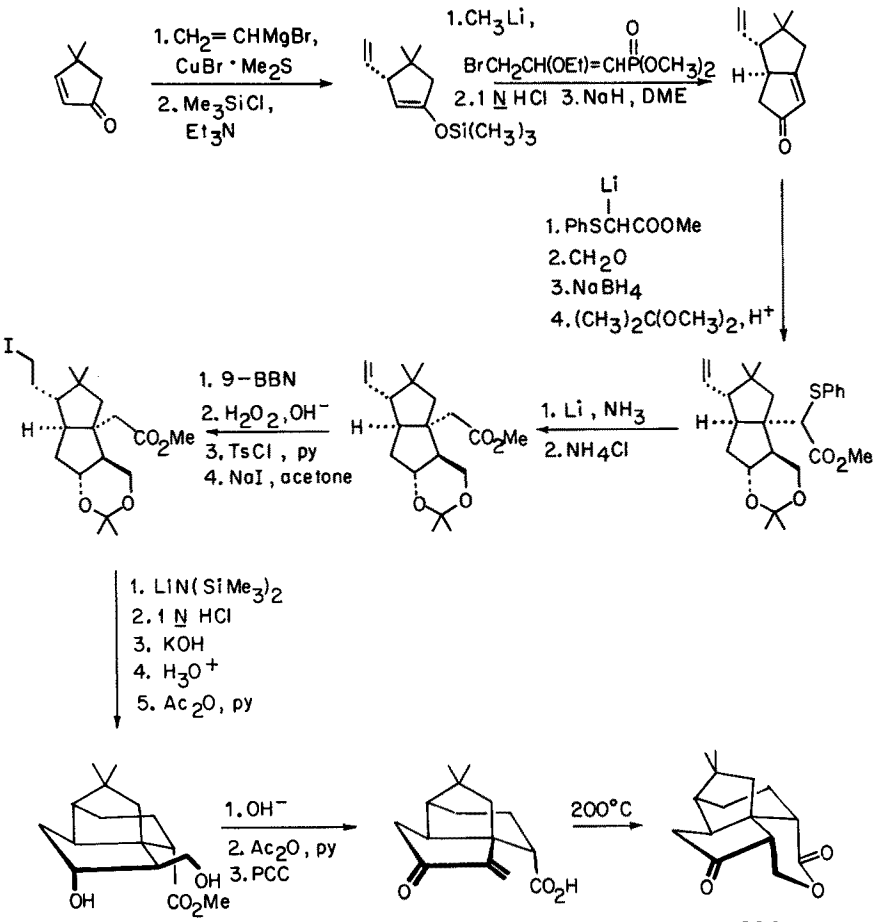
Interest in the total synthesis of the *Aspergillus terreus* derived quadrone (*606*), an antitumor agent [354], has been very intense. Success was first realized in Danishefsky's laboratory [355]. Once *601* was reached, its sidechain was elaborated and ring closure effected (Scheme LII). Condensation of *602* with 1-*tert*-butoxy-1-*tert*-butyldimethylsiloxyethylene in the presence of titanium tetrachloride and subsequent desilylation resulted in introduction of an angular acetic acid moiety. The two sidechains were next connected by intramolecular alkylation and the resulting keto acid was subjected to selenenylation in order to produce *603*. The α,β-unsaturated double bond was used to force enolization to the α' position. Indeed, *604* was

obtained conventionally. However, upon exposure to *p*-toluenesulfonic acid in refluxing benzene, *604* gave predominantly *605*, an isomer of quadrone. On the other hand, heating *604* to 190–195 °C in the absence of the solvent induced proper lactonization and resulted in the formation of *606*.



Scheme LII

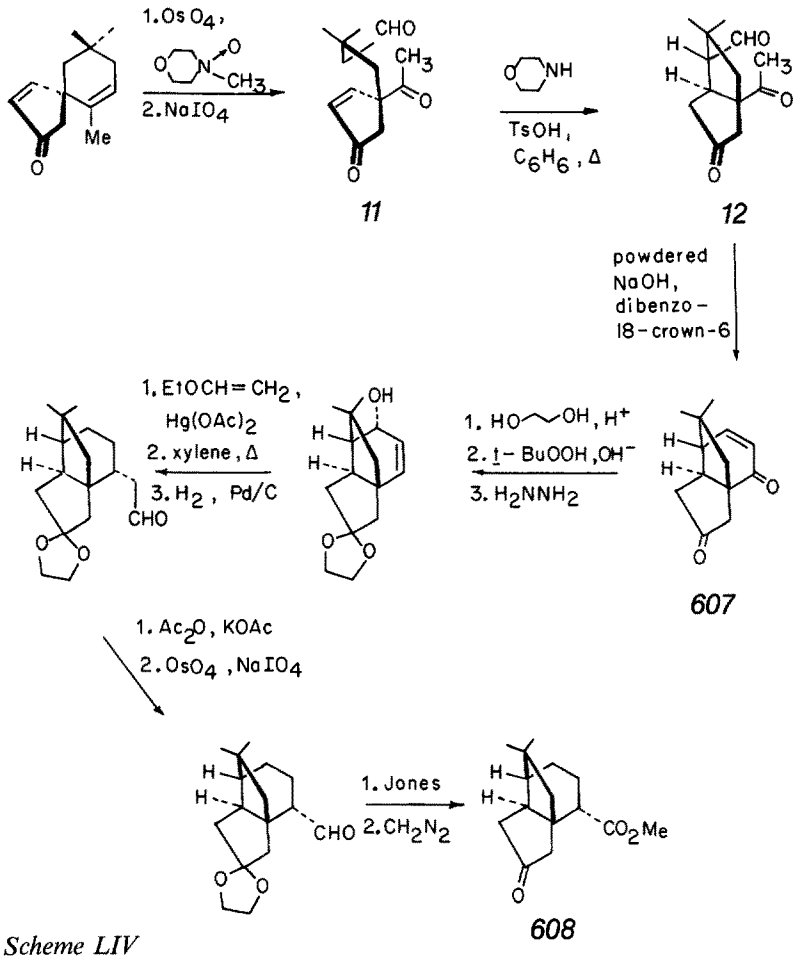
The Helquist approach to quadrone begins in the same fashion and has many close similarities to the Danishefsky effort. Importantly, however, a key element of novelty in Scheme LIII is the deplopment of a lactone annulation procedure which bypasses the regiochemical complications earlier encountered [356].



Scheme LIII

The starting material in Burke's phenomenologically different approach to quadrone was a spiro[4,5]decadienone which is readily available from 2-methyldimedone isobutyl ether (Scheme LIV) [357] Oxidative cleavage of the trisubstituted double bond in *606* set the stage for controlled intramolecular Michael addition (*11*→*12*) [12]. Once aldol cyclization to give *607* had been accomplished, the remaining major obstacle was installation of the lactone ring. The ester sidechain in *608* was introduced through combined application of Wharton and Claisen rearrangements and a one-carbon degradation scheme. Keto ester *608* linked up with both previous syntheses of quadrone.

An interestingly short total synthesis of quadrone was developed by Kende and coworkers who made application of Pd(II)-mediated cycloalkenylation of silyl enol ethers (Scheme LV) [358]. Their point of departure was *609* which was converted directly to *610*. Reaction of this silyl enol ether with palladium acetate in acetonitrile gave predominantly *611* which could be cyclized to *612*. From this intermediate, it was possible to prepare the known keto acid.

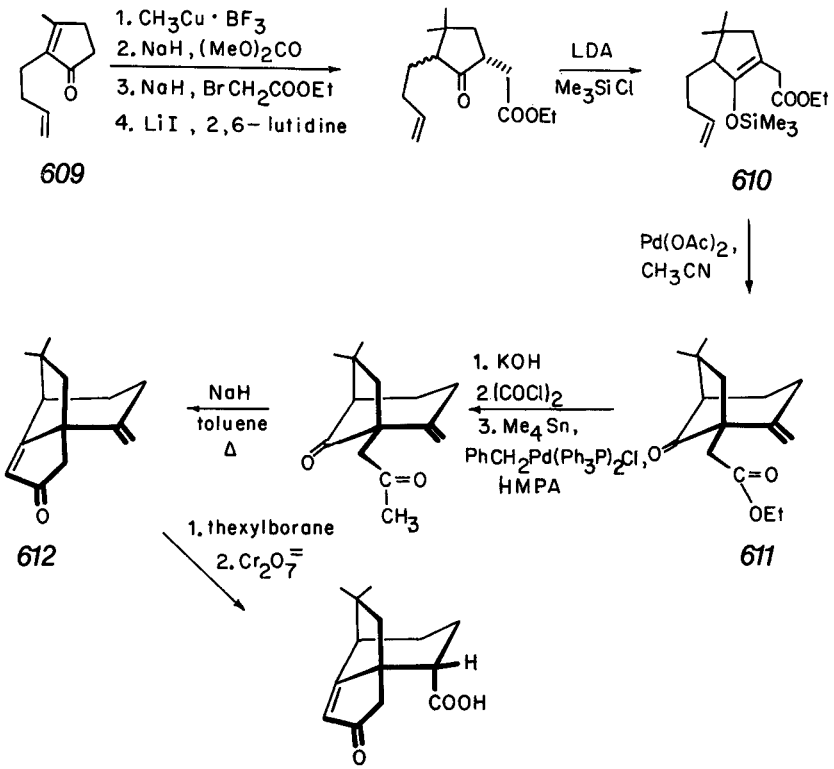


Scheme LIV

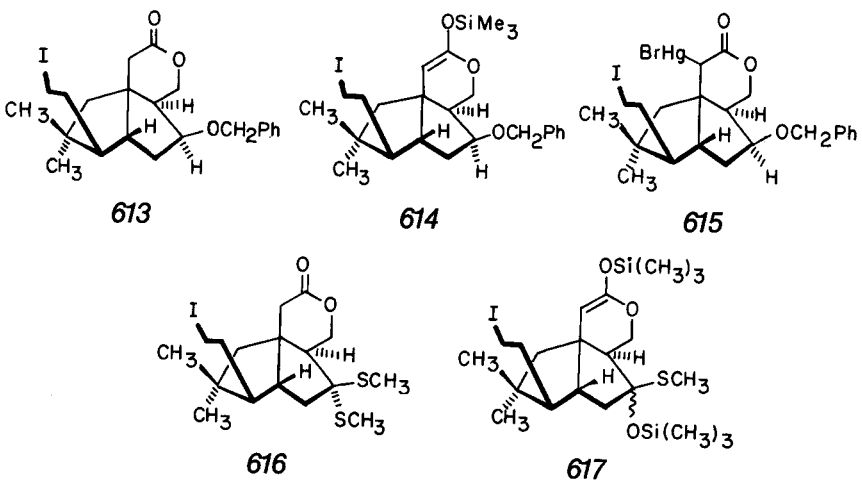
It is seemingly important that the lactone ring be formed last due to the strain present in the quadrone molecule. This conclusion is based upon Paquette's findings that cyclization of intermediates such as *613–617* could not be induced under a myriad of conditions [352].

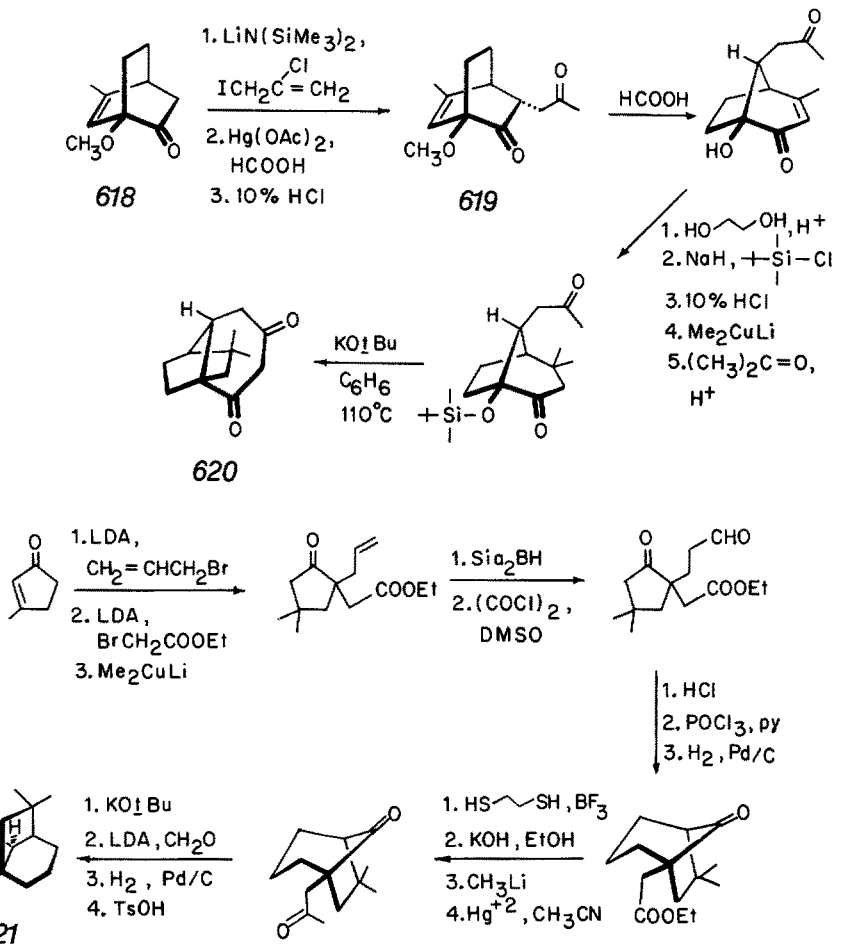
The preparation of *620*, a tricyclic intermediate suited for elaboration into quadrone, has been reported by Monti and Dean [359]. Following introduction of the proper C_{5a} stereochemistry by alkylation of *618* under kinetically controlled conditions, diketone *619* was subjected to acid-catalyzed rearrangement. After functional group manipulation, a tandem intramolecular aldol-pinacol rearrangement gave *620*.

A synthesis of descarboxylquadrone (*621*) has been described [360]. The presence of the α, β-unsaturated carbonyl system causes this substance to be biologically active, presumably in parallel with the latent α-methylene cyclopentanone functionality believed responsible for the cytotoxic activity of quadrone.


1. $CH_3Cu \cdot BF_3$
2. NaH, $(MeO)_2CO$
3. NaH, $BrCH_2COOEt$
4. LiI, 2,6-lutidine
LDA
Me_3SiCl
COOEt
OSiMe3
609
610
$Pd(OAc)_2$, CH_3CN
NaH
toluene
Δ
1. KOH
2. $(COCl)_2$
3. Me_4Sn, $PhCH_2Pd(Ph_3P)_2Cl$, HMPA
C=O
CH_3
OEt
612
611
1. thexylborane
2. $Cr_2O_7^{=}$
H
COOH

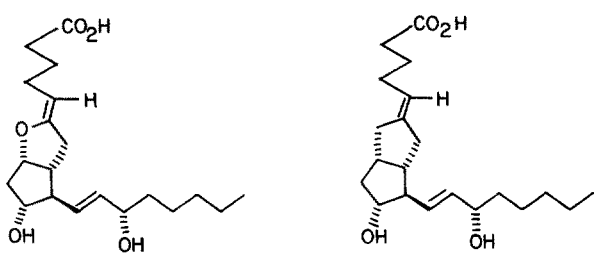
Scheme LV


I
CH_3
OCH_2Ph
H
OSiMe3
BrHg
SCH3
OSi(CH3)3
613
614
615
616
617



F Carbaprostaglandins

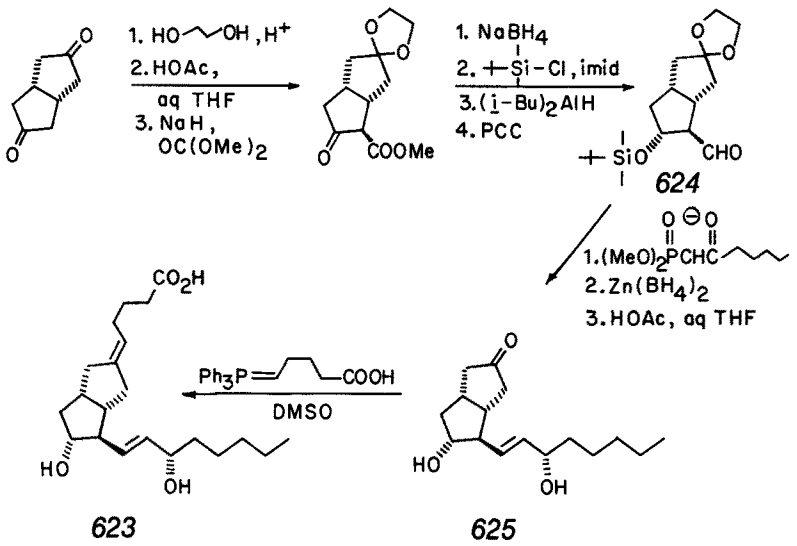
Prostacyclin (PGI_2, *622*) appears to play an important role in preventing stroke, thrombosis, and heart attack [361,362]. However, this substance is very unstable because of its labile enol ether linkage. This property has prompted intense research



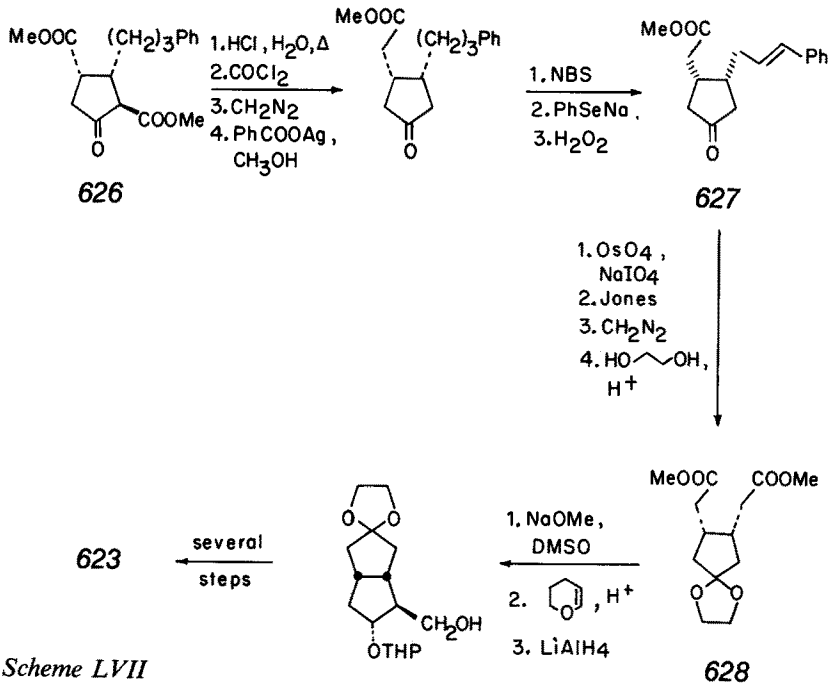
622 623

in the preparation of a chemically stable analogue whose therapeutic potential is also high. One primary focus of attention has been 6a-carbaprostaglandin I_2 (*623*).

Nicolaou's synthetic plan (Scheme LVI) begins with *cis*-bicyclo[3.3.0]octane-3,7-dione and proceeds after monoketalization to append the lower sidechain as in *625* [363].



Scheme LVI

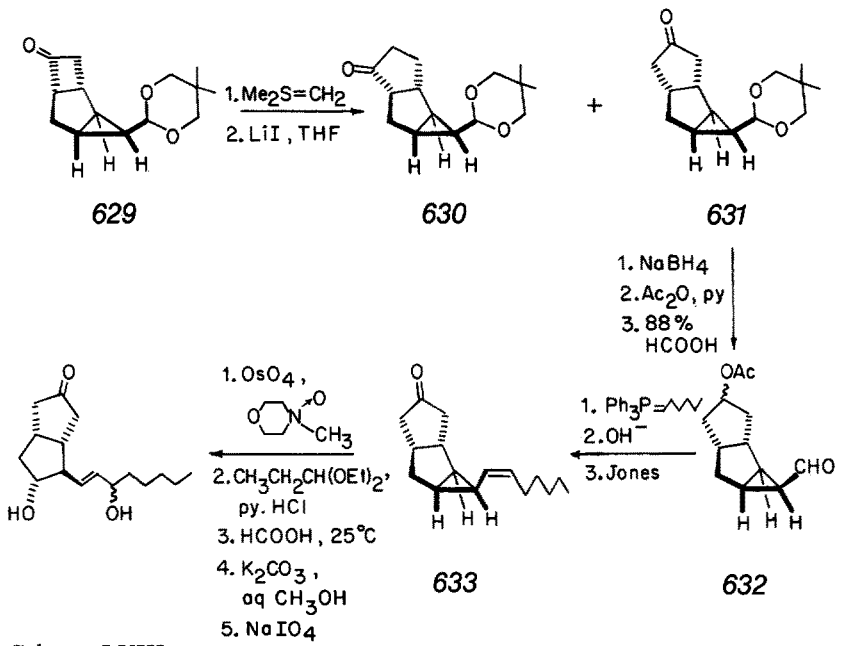


Scheme LVII

Involvement of *625* in a Wittig reaction with 4-carboxybutyl(triphenyl)phosphorane dissolved in dimethyl sulfoxide generates a mixture of double bond isomers rich in *623*.

The Kojima-Sakai approach, which makes use of trans-cis diester *626*, is summarized in Scheme LVII [364]. This intermediate was homologated by the Arndt-Eistert method, converted to olefin *627*, and oxidatively cleaved to produce ultimately the diester *628*. Dieckmann condensation was used to construct the diquinane core which was subsequently transformed to *623* by standard reactions.

The first synthesis of *623* in optically active form is due to Morton and Brokaw [365]. Reaction of resolved cyclobutanone *629* with dimethylsulfonium methylide and ring expansion with lithium iodide in tetrahydrofuran gave the isomeric cyclopentanones *630* and *631* (major) (Scheme XVIII). In the next step, *631* was reduced with sodium borohydride, acetylated, and hydrolyzed to endo aldehyde *632*. This substance was then condensed with *n*-hexylidenetriphenylphosphorane, saponified, and oxidized to generate the presolvolysis ketone *633*. Following hydroxylation, the isomeric cis glycols were treated with triethyl orthopropionate and rearranged in anhydrous formic acid. The formate mixture was hydrolyzed and exposed to sodium metaperiodate to give a keto diol which served as precursor to *623*.

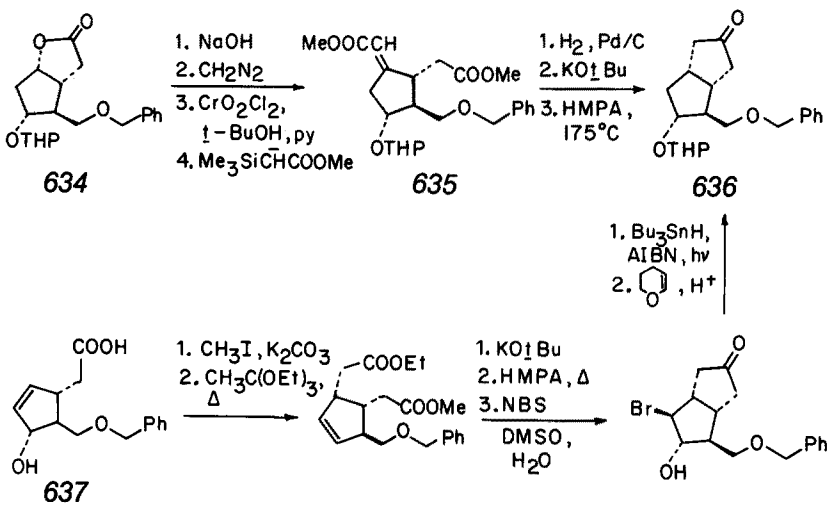


Scheme LVIII

The same feat was achieved by Hayashi and coworkers who began with the readily available, optically active lactone *634* (Scheme LIX) [366]. Cleavage of the oxygenated ring followed by reaction with excess lithio trimethylsilylacetate afforded the α,β-unsaturated ester *635*. Hydrogenation, ring closure, and demethoxycarbonylation proceeded without event to furnish ketone *636* and its epimer which were separated

chromatographically. A second route to the same ketone was realized from the optically active hydroxy acid *637*. The conversion of *636* to carbaprostacyclin followed established protocol.

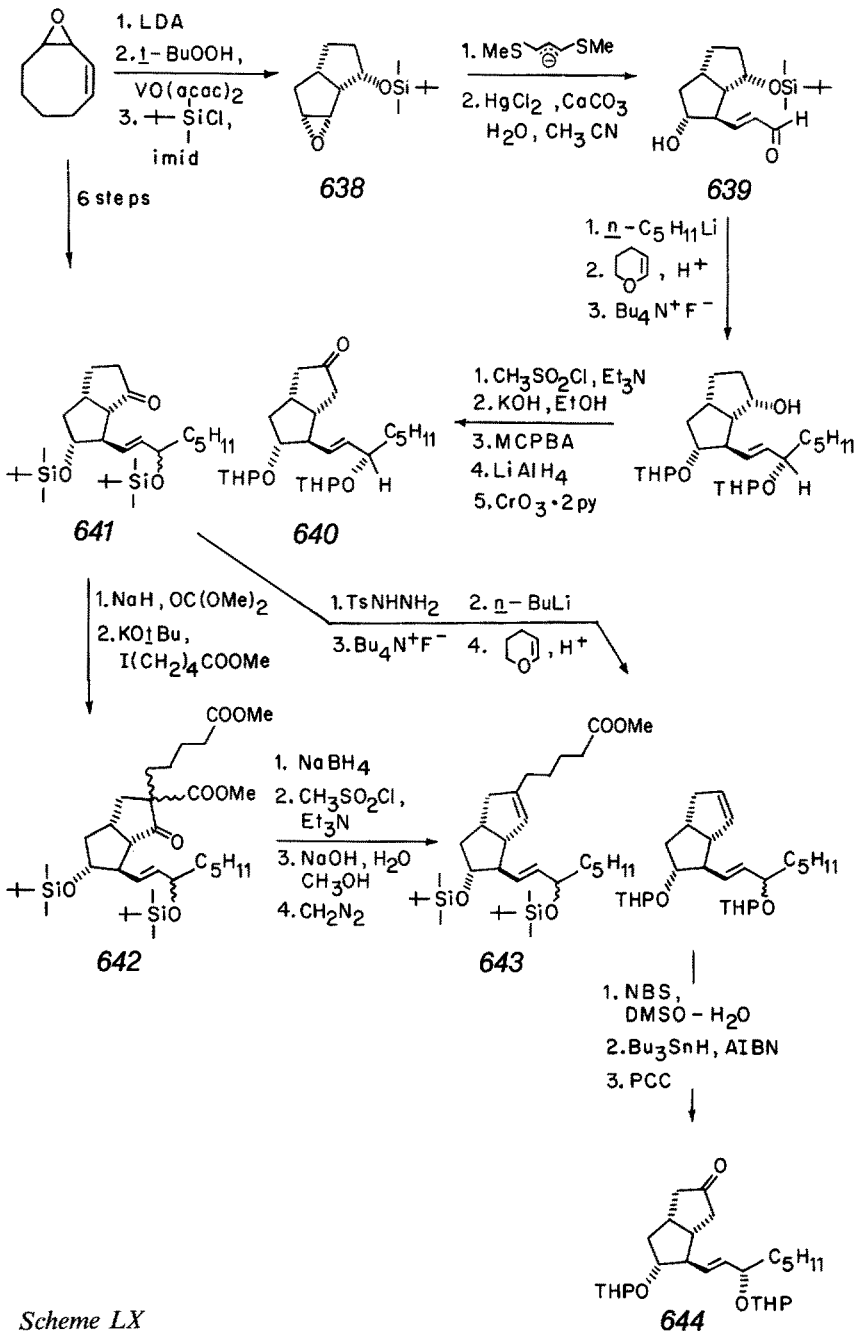
Ikegami has devised an interesting approach based upon 1,3-cyclooctadiene monoepoxide as starting material (Scheme LX) [367]. Transannular cyclization, Sharpless epoxidation, and silylation leads to *638* which is opened with reasonable regioselectivity upon reaction with 1,3-bis(methylthio)allyllithium. Once aldehyde *639* had been accessed, *n*-amyllithium addition was found to be stereoselective, perhaps because of the location of the *tert*-butyldimethylsilyloxy group. Nevertheless, *640* is ultimately produced in low overall yield. This situation is rectified in part by the initial formation of *641* and eventual decarboxylative elimination of *642* to arrive at *643*. An additional improvement has appeared in the form of a 1,2-carbonyl transposition sequence which successfully transforms *641* into *644* [368].



Scheme LIX

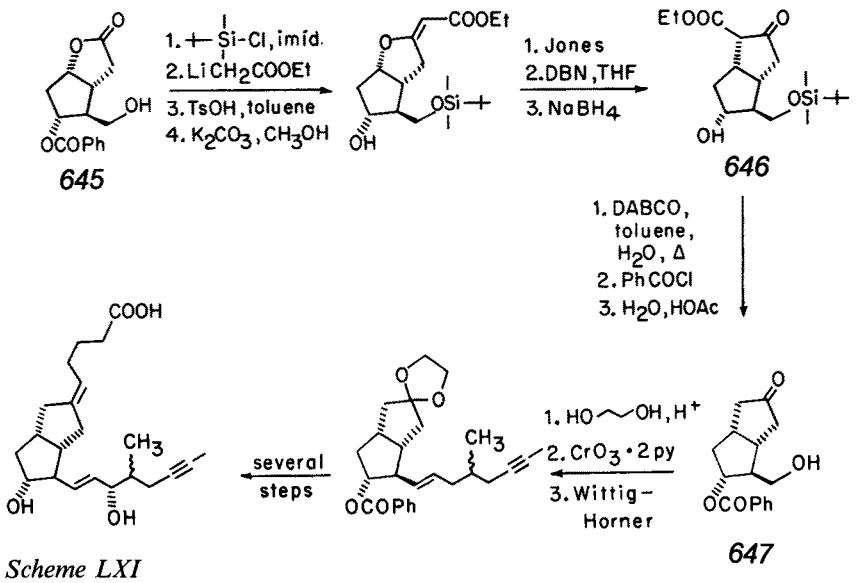
Recently, more economical routes to carbaprostaglandins have been developed. Beginning with the commercially available, optically active lactone *645*, Skuballa and Vorbrüggen achieved a clever replacement of the ring oxygen atom by a methylene group (Scheme LXI) [369]. The subsequent conversion of *646* to *647* was accomplished in 88% overall yield. After ketalization and sidechain oxidation of this intermediate, these workers prepared *648* which proved to be an analogue with the same pharmacological activity profile and efficacy as *623*. This activity is not seen with many analogues [370].

Seemingly, Aristoff has designed the most practical synthesis of prostacyclin to date. In his ingenious approach to optically active *623*, *648* was treated with



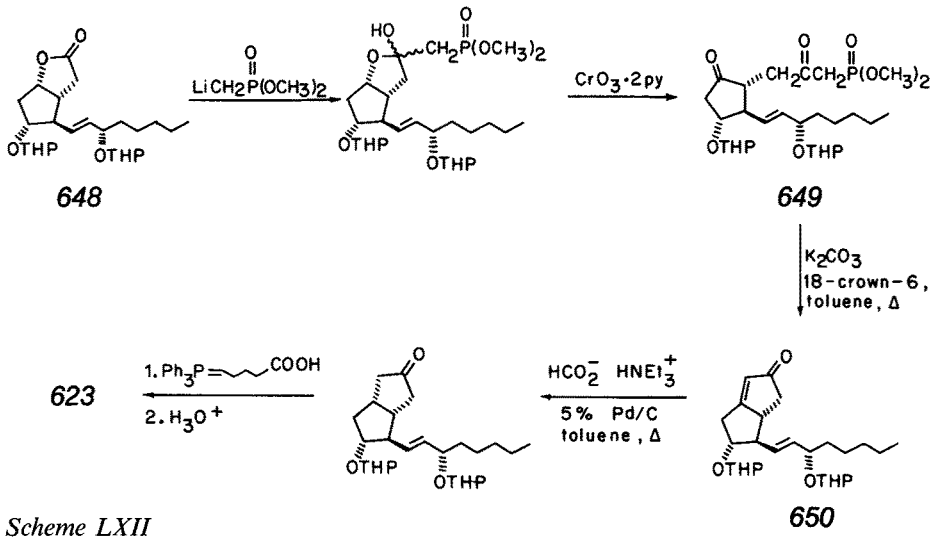
Scheme LX

lithium dimethyl methylphosphonate and subjected to modified Collins oxidation (Scheme LXII) [371]. Cyclization of *649* could not be accomplished using standard methods. However, with potassium carbonate and 18-crown-6 in warm toluene, *650*



Scheme LXI

was obtained in 77% yield. Reduction with triethylammonium formate in the presence of palladium catalyst led to the cyclopentanone derivative which was transformed to *623* by sequential Wittig reaction with (4-carboxybutyl)triphenylphosphorane and hydrolysis.



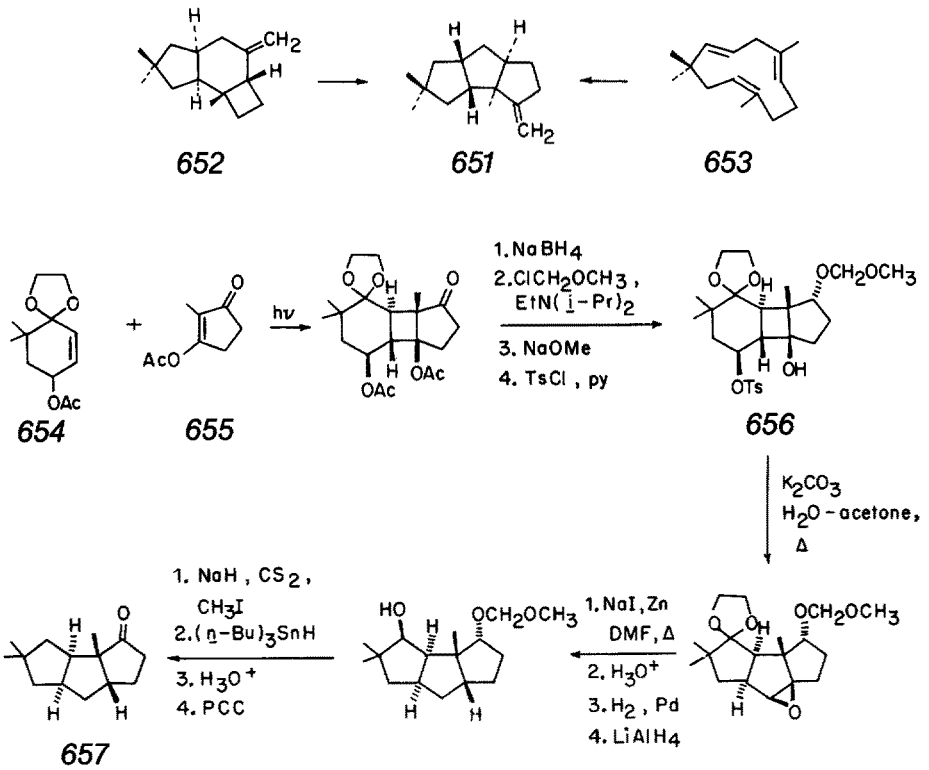
Scheme LXII

VIII Synthesis of Triquinane Natural Products

A Linear Triquinanes

1 Hirsutine

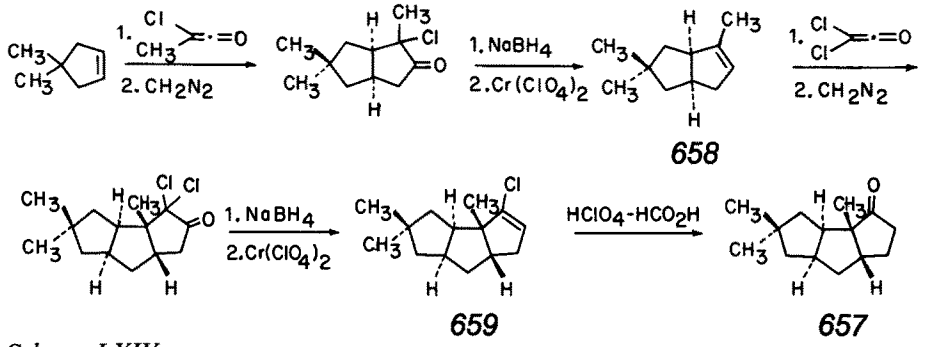
In 1976, Nozoe, et al. isolated and identified hirsutene (*651*) from an extract of the mycelium of *Coriolus consors*. Matsumoto has described the transformation of the protoilludene *652* [372,373] and humulene (*653*) into *651* and other compounds possessing this *cis,anti,cis*-tricyclo[6.3.0.$0^{2,6}$]undecane carbon skeleton [374]. Beyond this, hirsutene has proven to be a popular synthetic target and fertile testing ground for new and interesting synthetic protocols. For example, Tatsuta's elegant stereo-



Scheme LXIII

controlled synthesis (Scheme LXIII) began with the head-to-head photocycloaddition to *654* to *655* [375]. Following functionality modification to give *656*, skeletal rearrangement was effected in high yield by heating with potassium carbonate in aqueous acetone. This transformation is facilitated by the breaking of parallel C—C bonds. Once the norketone *657* was in hand, the formal synthesis was completed, since this substance had previously been transformed into *651* [376].

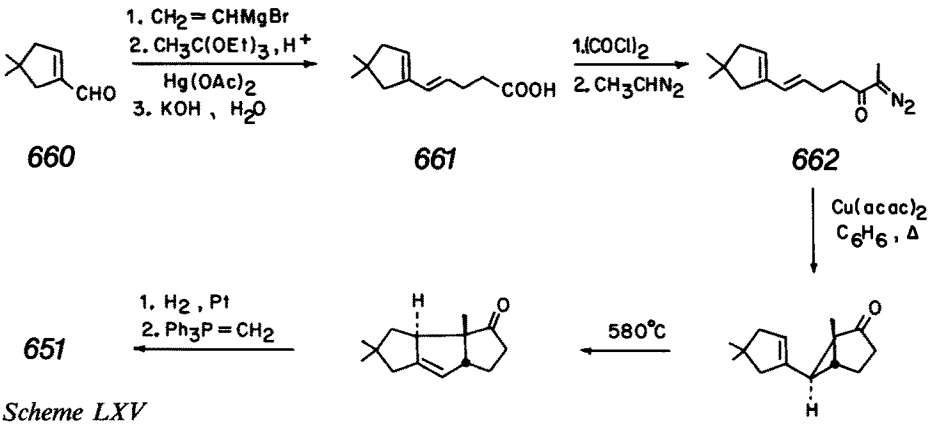
For Greene, hirsutine proved to be a molecule which could be prepared by iterative application of his three-carbon annulation procedure [377]. 4,4-Dimethylcyclopentene was cycloadded to methylchloroketene and the resulting cyclobutanone was ring expanded with diazomethane (Scheme LXIV). Once a double bond was introduced as in *658*, the sequence was repeated with dichloroketene to produce *659*. Hydrolysis ultimately led to *657*.



658 659 657

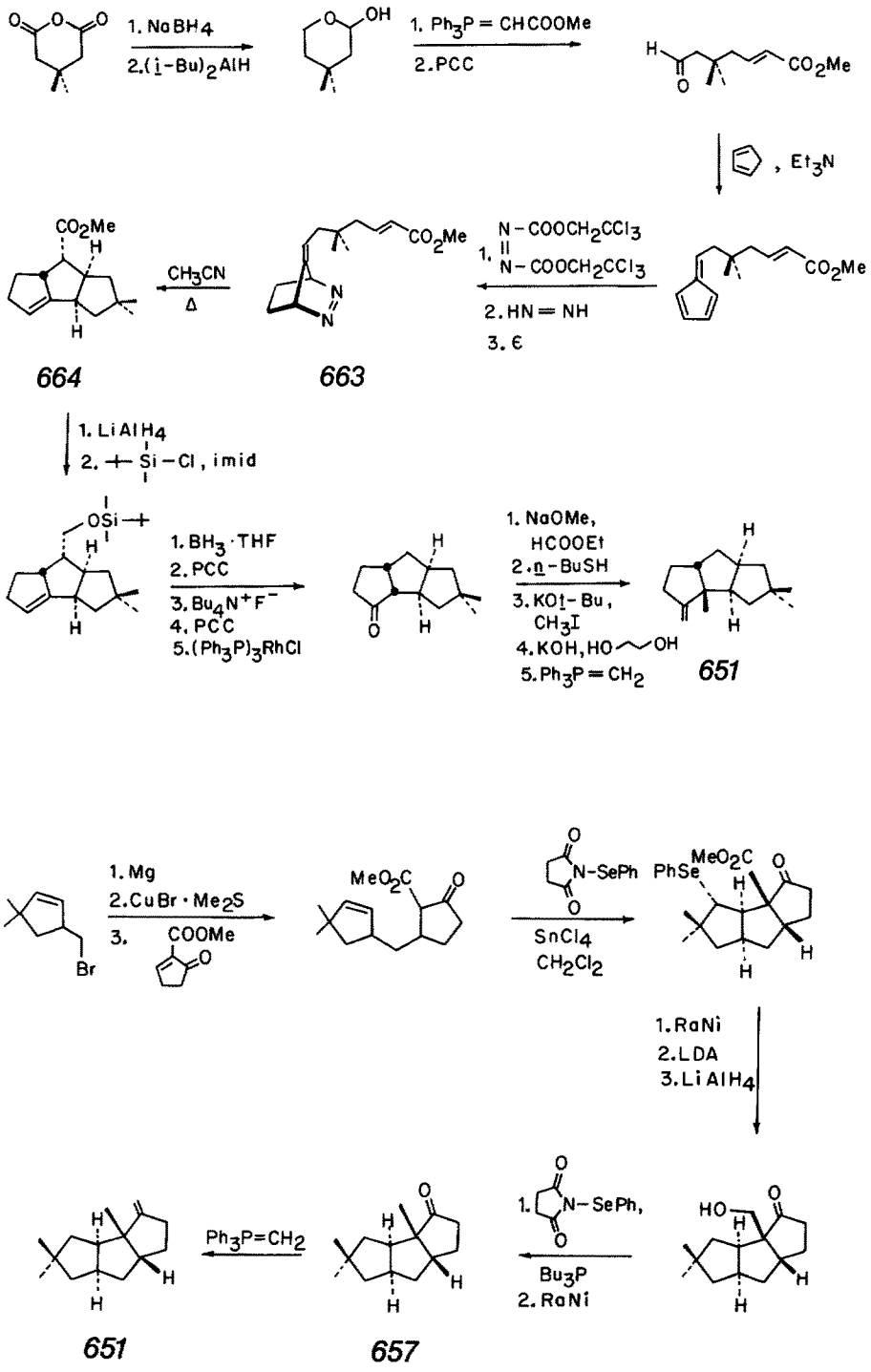
Scheme LXIV

Hudlicky saw in *651* an occasion to apply α-diazo ketone cyclization methodology [378]. With cyclopentene aldehyde *660* as the starting point, dienyl carboxylic acid *661* was elaborated and transformed into *662* (Scheme LXV). Cyclization, thermal isomerization, and catalytic hydrogenation gave *657* and ultimately hirsutine.



660 661 662 651

Scheme LXV

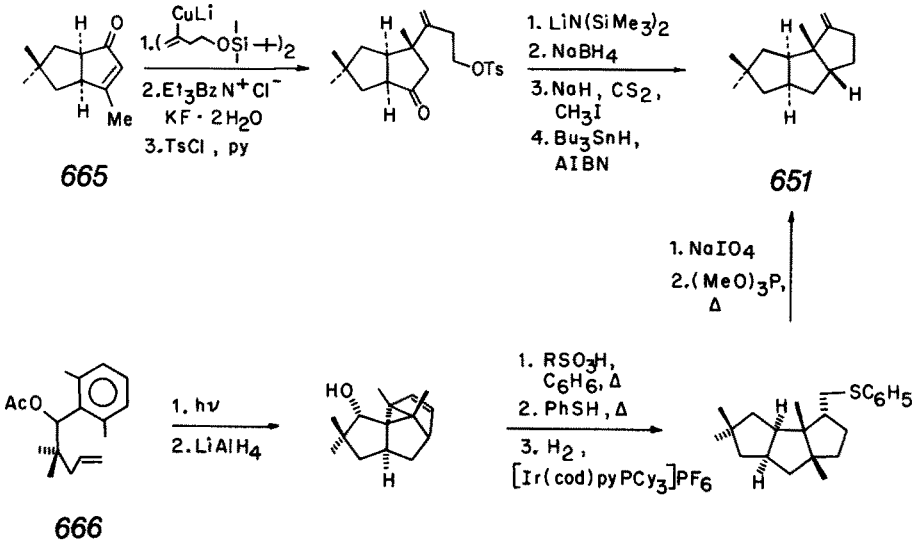


Scheme LXVII

With the intent of exploiting the intramolecular 1,3-diyl trapping reaction, Little and Muller prepared azo compound *663* and decomposed the substance in refluxing acetonitrile (Scheme LXVI) [379]. Triquinane *664*, isolated in 85% yield, was then degraded to a saturated ketone which was methylated in the angular position prior to olefination.

Ley and Murray have developed a short synthesis of hirsutine in which the key step involves intramolecular cyclization of a β-oxoester to an alkene with N-phenylselenophthalimide and stannic chloride (Scheme LXVII) [380].

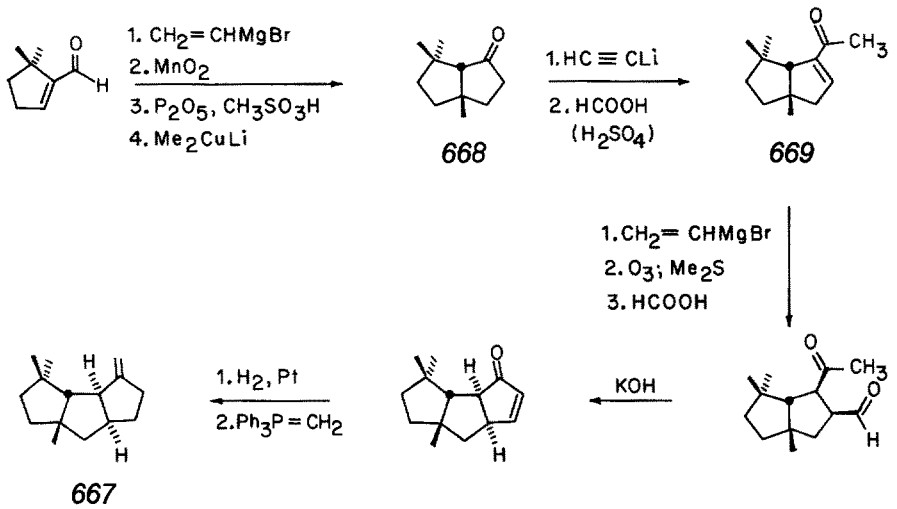
The bicyclic enone *665* (see Scheme IX) has been utilized as a precursor to hirsutene [381]. The mold metabolite has also been attained in clever fashion from *666* using meta-photocycloaddition methodology [382].



2 The Capnellene Group

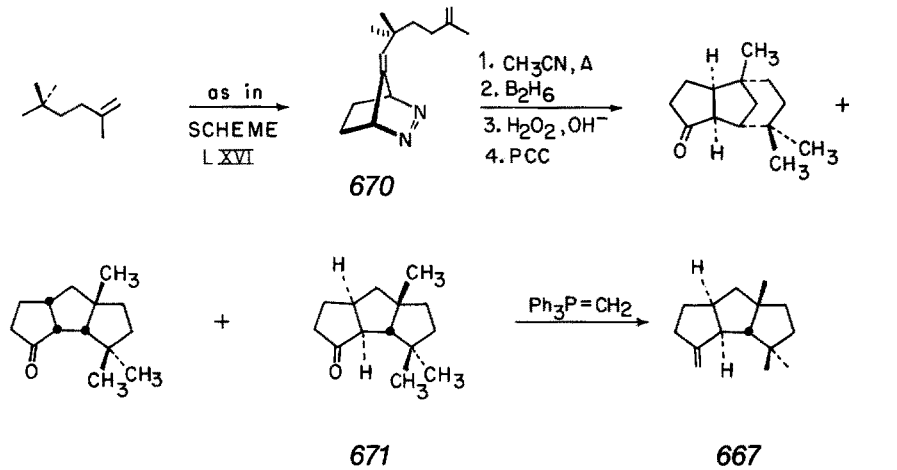
Capnellane is the generic name applied to a group of sesquiterpene alcohols and the hydrocarbon isolated from the soft coral *Capnella imbricata* [383]. $\Delta^{9(12)}$-Capnellene (*667*), the presumed biosynthetic precursor of the capnellenols, was first synthesized in 1981 by Stevens and Paquette [384]. Their synthetic plan called for the construction of bicyclic ketone *668* and its appropriate annulation. The latter event was achieved by application of the Rupe rearrangement to *668*, conjugate addition of a vinyl group to *669*, ozonolysis, and cyclization (Scheme LXVIII). Hydrogenation and olefination completed the sequence.

More recently, Little has synthesized *667* [385] during his studies of the applicability of 1,3-diyl trapping reactions to the construction of tricyclopentanoids [386]. Capitalizing on a reversal of the "normal" regioselective mode of these transformations which gives rise to linearly fused triquinanes, he decomposed diazene *670* in refluxing acetonitrile and immediately subjected the product mixture to a hydroboration-



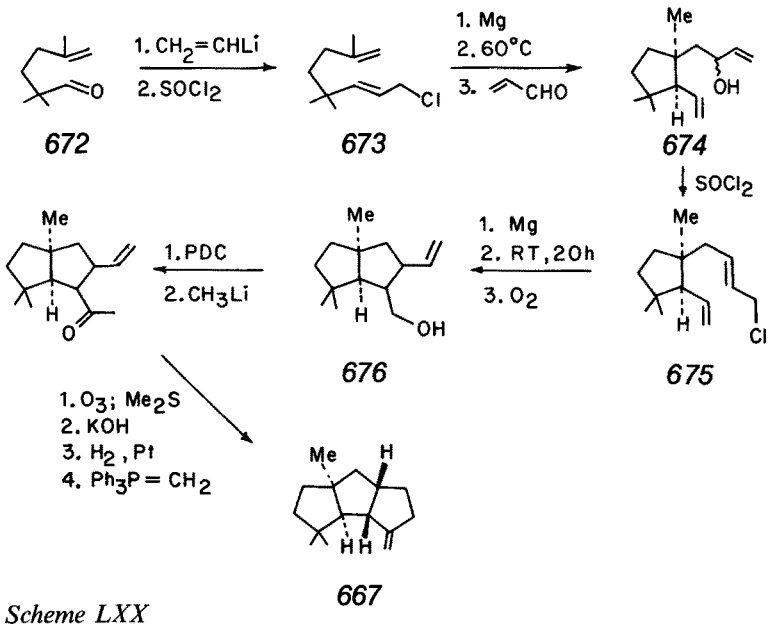
Scheme LXVIII

oxidation sequence (Scheme LXIX). The less dominant ketone *671* gave $\Delta^{9(12)}$-capnellene upon Wittig olefination.



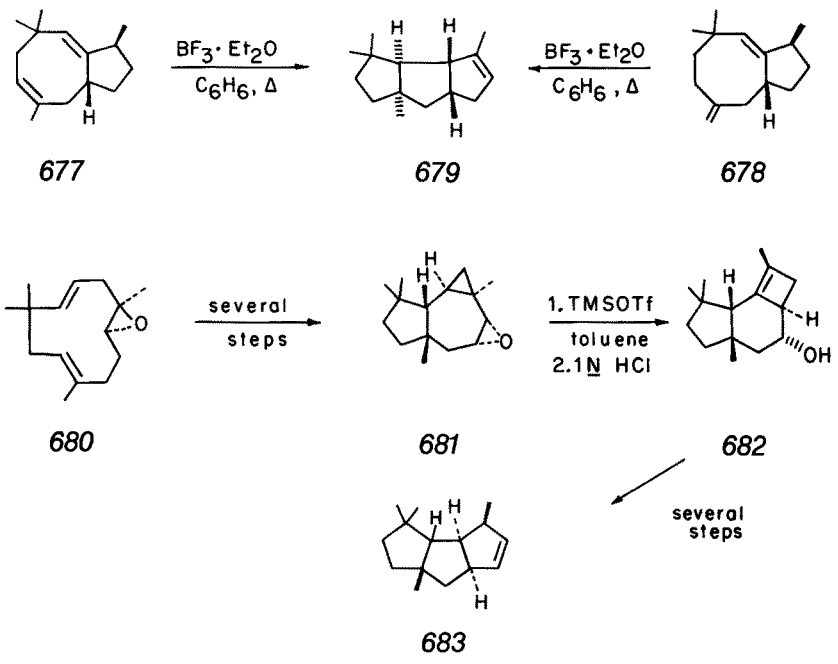
Scheme LXIX

Oppolzer and Bättig have prepared the marine sesquiterpene via ingenious application of iterative intramolecular "magnesium-ene" reactions [387]. Aldehyde *672* was converted to the allylic chloride *673*, the Grignard of which was heated at 60 °C for 23 hours and subsequently treated with acrolein to furnish alcohol *674* (Scheme LXX). An analogous sequence transformed *675* to *676* and set the stage for final transformations which were patterned after earlier work.



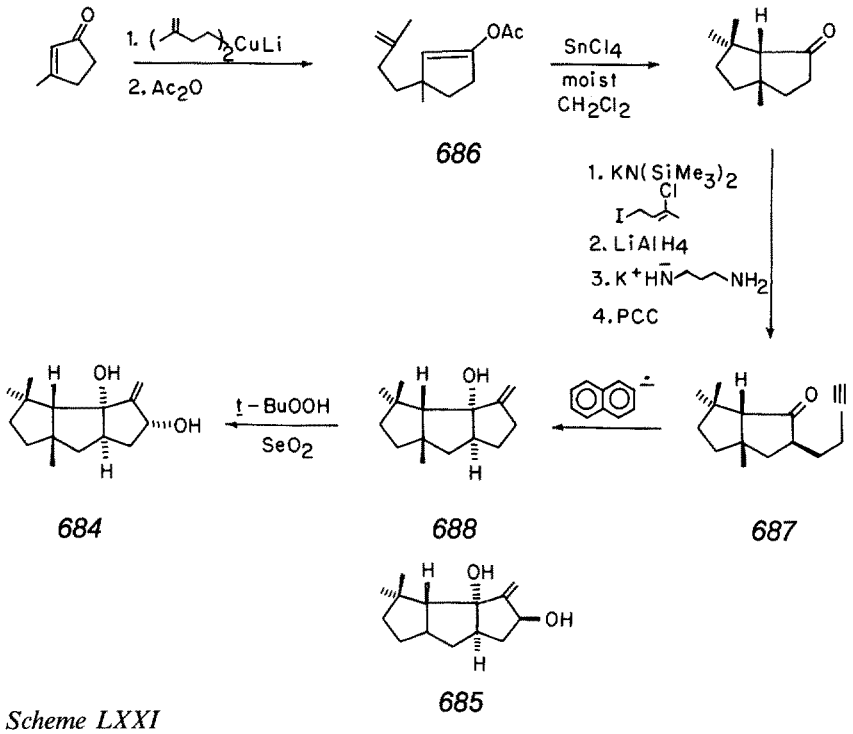
Scheme LXX

Two transannular cyclizations have been reported which lead to isomers of *677*. Thus, treatment of *677* or *678* with boron trifluoride etherate gives rise to $\Delta^{8(9)}$-capnellene (*679*) [388]. Also, conversion of humulene 6,7-oxide (*680*) to tricyclic epoxide *681* [389] has provided the opportunity for trimethylsilyl triflate-promoted



isomerization to the methyl migrated product *682*, from which Δ^7-capnellene (*683*) was fashioned [390].

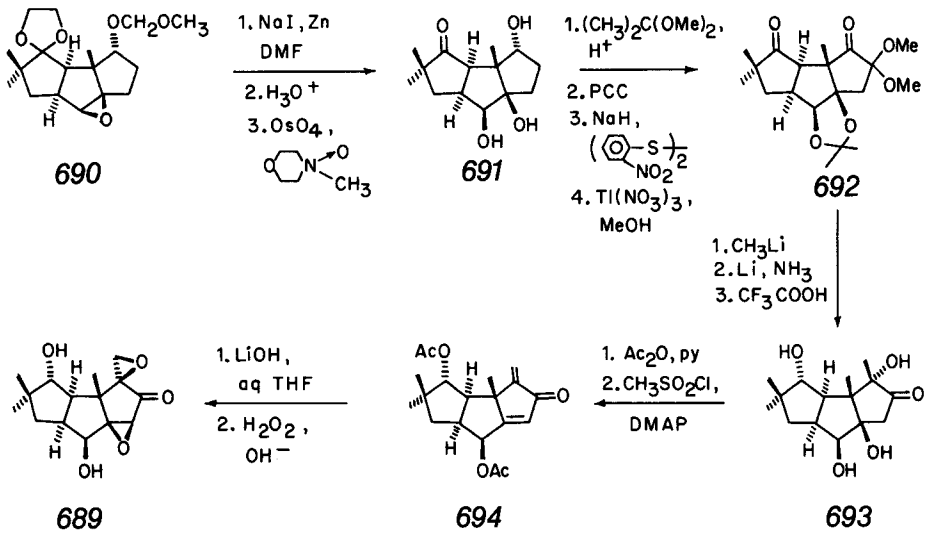
Pattenden and Teague have prepared tricyclic diol *684* which is epimeric to the naturally occurring $\Delta^{9(12)}$-capnellene-8β,10α-diol (*685*) [391]. Their strategy, which is summarized in Scheme LXXI, encompasses two critical cyclization steps. The first is the Lewis acid-catalyzed ring closure of enol acetate *686* and the second involves reductive closure of acetylenic ketone *687*. It is of interest that the oxidation of *688* proved to be stereospecific.



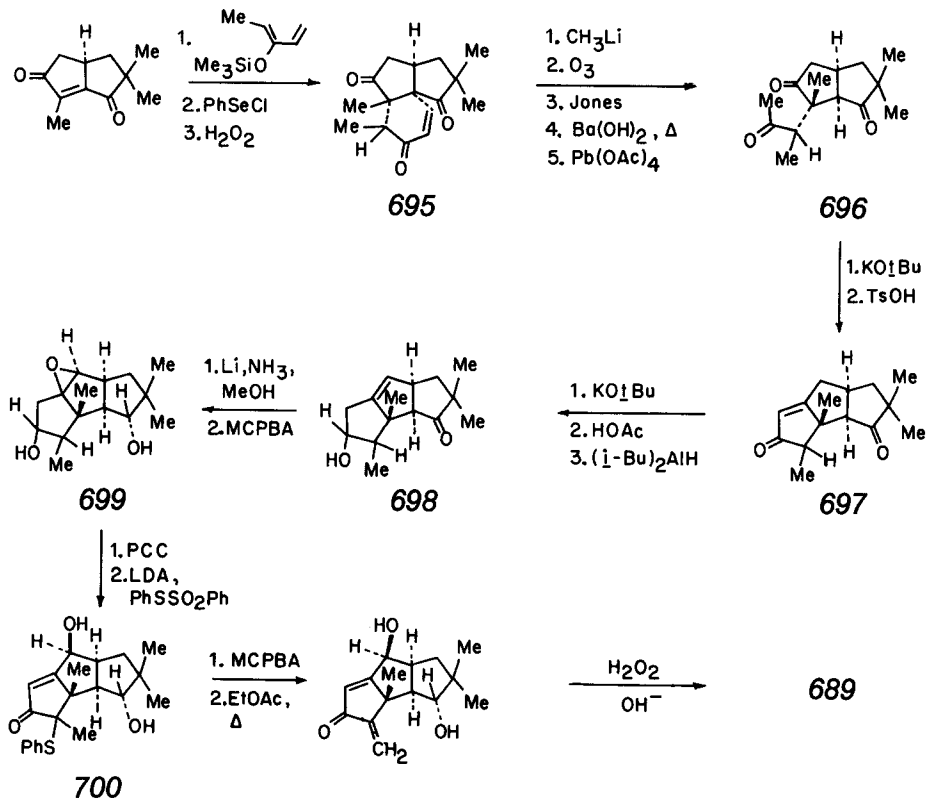
Scheme LXXI

3 Coriolin

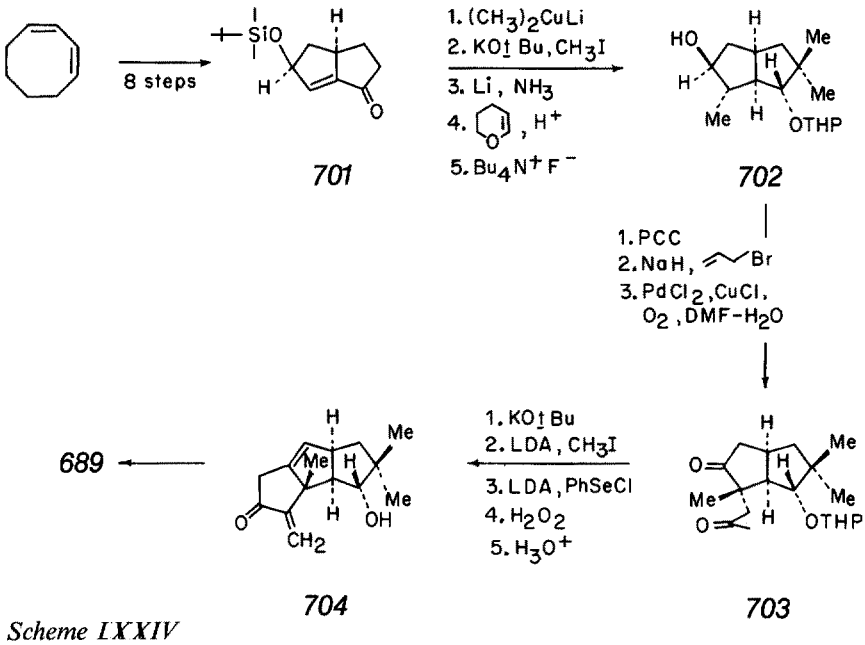
Coriolin (*689*), a metabolite of the Basidiomycete *Coriolus consors*, has attracted widespread interest because of its unusual anti-tumor activity and highly functionalized triquinane structure. Accordingly, a number of syntheses of *689* have appeared on the scene. One of the earliest, due to Tatsuta, et al., begins with epoxide *690*, whose preparation had been earlier realized in connection with their work on hirsutine (see Scheme LXIII). Deoxygenation of *690*, hydrolysis, and cis-hydroxylation provided keto triol *691* (Scheme LXXII) [392]. The derived acetonide was transformed via *692* into tetraol *693* which could be selectively acetylated and dehydrated on both flanks of the carbonyl group. Deacetylation of *694* followed by epoxidation completed the synthesis.



Scheme LXXII

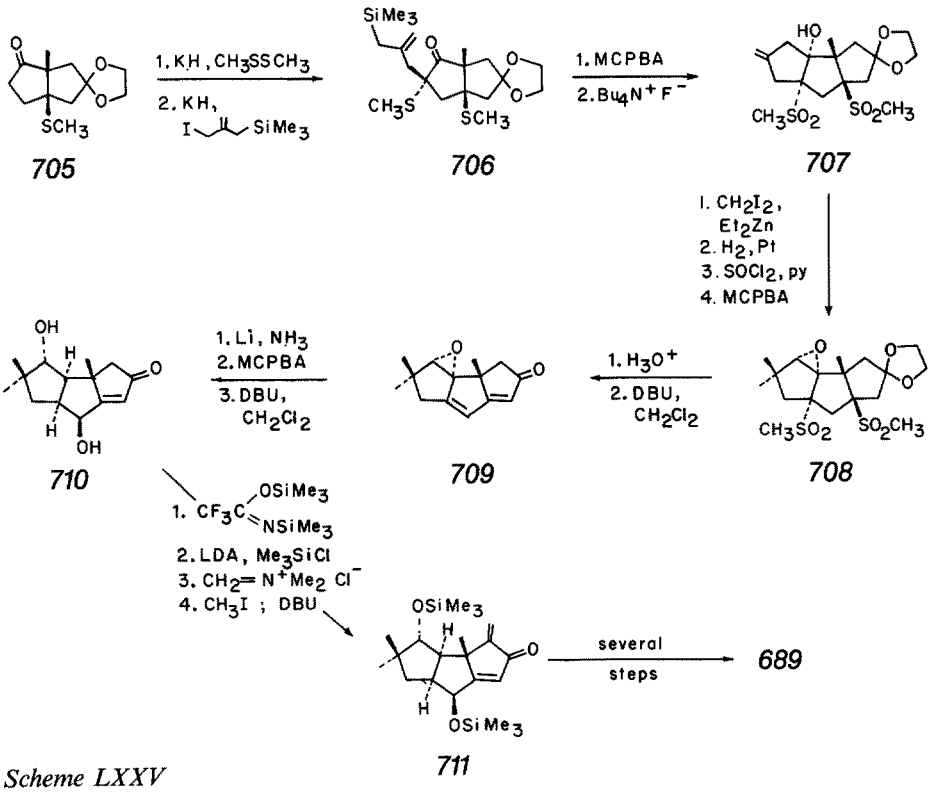


Scheme LXXIII



701 702 703 704

Scheme LXXIV

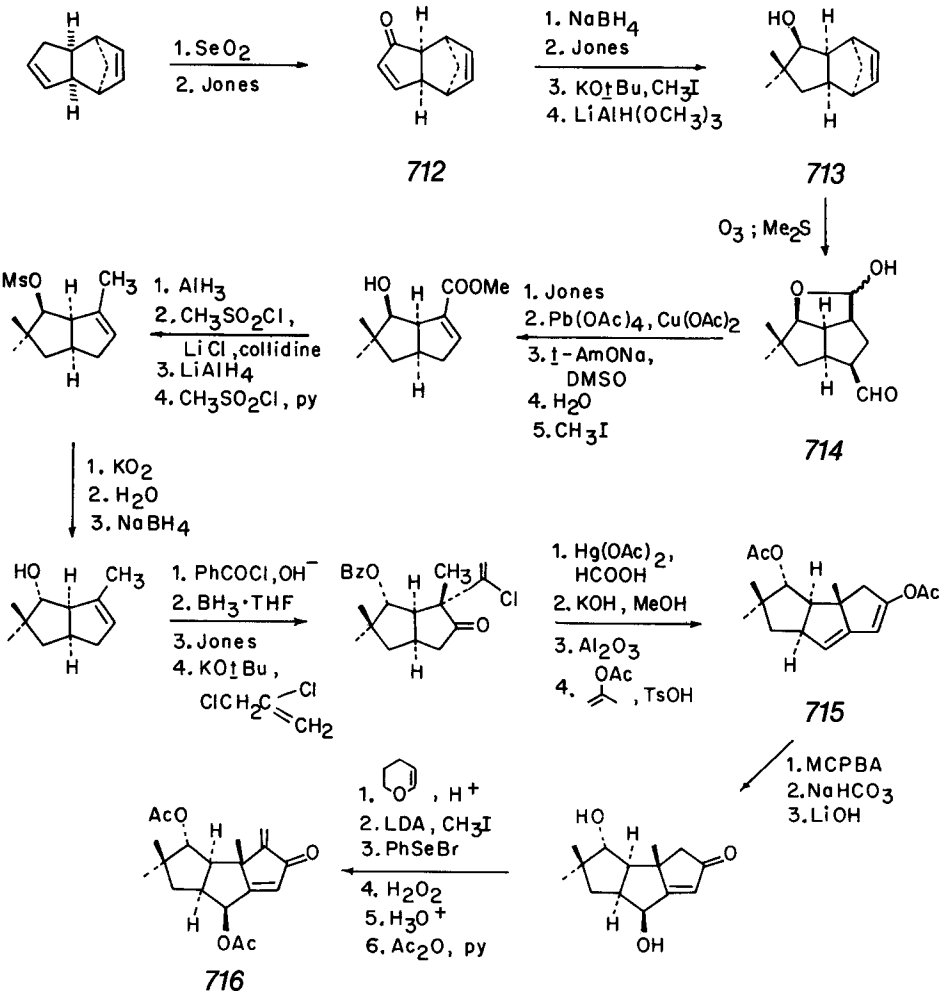


705 706 707 708 709 710 711

Scheme LXXV

To arrive at racemic coriolin, Danishefsky and coworkers chose to add an acetonyl fragment to a bicyclic enedione by Diels-Alder chemistry (Scheme LXXIII) [393,394]. Treatment of the resulting adduct *695* sequentially with a series of conventional reagents produced the key intermediate *696*. Suitable aldolization delivered *697*, the functionality in which was adjusted by deconjugation and reduction. Further reduction of *698* with lithium in liquid ammonia and methanol followed by epoxidation afforded *699*. Selective oxidation of the more accessible hydroxyl group and phenylsulfenylation gave *700* which experiences smooth elimination to *701* after conversion to the sulfoxide. As before, epoxidation completed the sequence.

In a manner paralleling somewhat their strategy for carbaprostaglandin synthesis (Scheme LX), Ikegami, et al., have realized a coriolin total synthesis starting from 1,3-cyclooctadiene. With *701* in hand, they proceeded to elaborate the functionalized



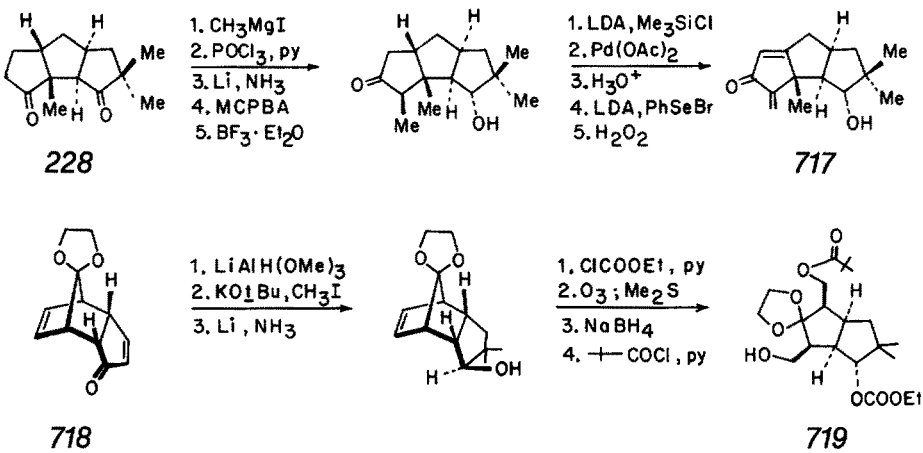
Scheme LXXVI

diquinanes *702* and *703* (Scheme LXXIV) [395]. Once the tricyclic enone *704* had been attained, introduction of the remaining functionality proved to be straightforward.

The Trost-Curran coriolin synthesis makes use of *705* as starting material (Scheme LXXV) [396]. Monosulfenylation and alkylation of this intermediate provided *706* which was oxidized and subjected to fluoride-induced cyclization. To introduce the gem-dimethyl group, *707* was cyclopropanated and hydrogenolyzed. The derived dehydration product was epoxidized to provide *707* from which the sulfone groups could be removed by exposure to catalytic quantities of DBU. To introduce the needed secondary hydroxyl group, *709* was reduced under dissolving metal conditions, epoxidized, and directly isomerized to allylic alcohol *710*. Once its hydroxyl groups were silylated, the kinetic enol silyl ether of *710* was generated and treated with Eschenmoser's salt. Elimination and deblocking afforded the customary penultimate intermediate to coriolin.

The diacetate of *711* has also been produced in stereoselective fashion via a route beginning with dicyclopentadiene (Scheme LXXVI) [397]. Ketone *712* was transformed into dimethylated alcohol *713* whose ozonolysis provided *714*. Following Jones oxidation, decarboxylation with concomitant introduction of a double bond was realized by application of Kochi's procedure. A lengthy sequence of steps to adjust functionality led up to annulation by a modified Wichterle sequence. The conversion of *715* to *716* was accomplished by standard reactions.

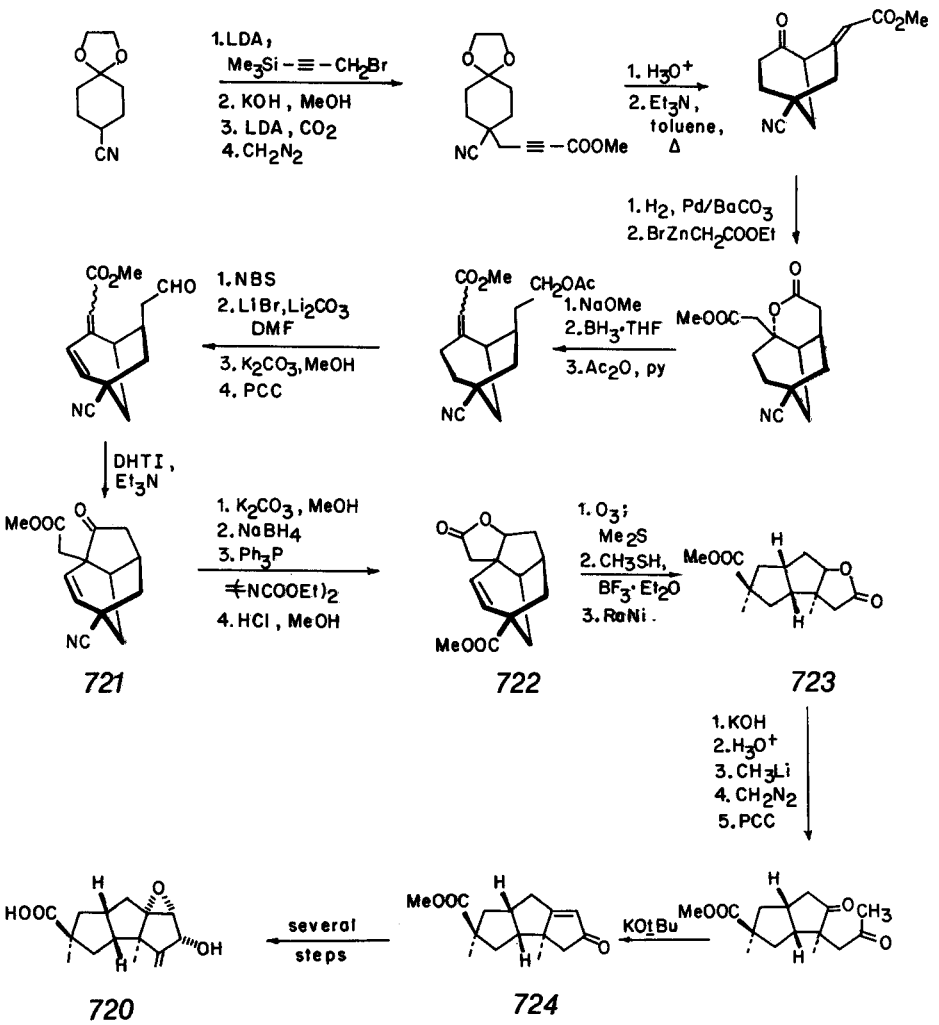
Diketone *228*, prepared by Mehta in conjunction with another study, has been transformed into *717* in a clever sequence of reactions which required no protection steps [398]. The conversion of methanoindene *718* into the highly functionalized intermediate *719* that might be serviceable as a coriolin precursor has been published [399].



4 Hirsutic Acid

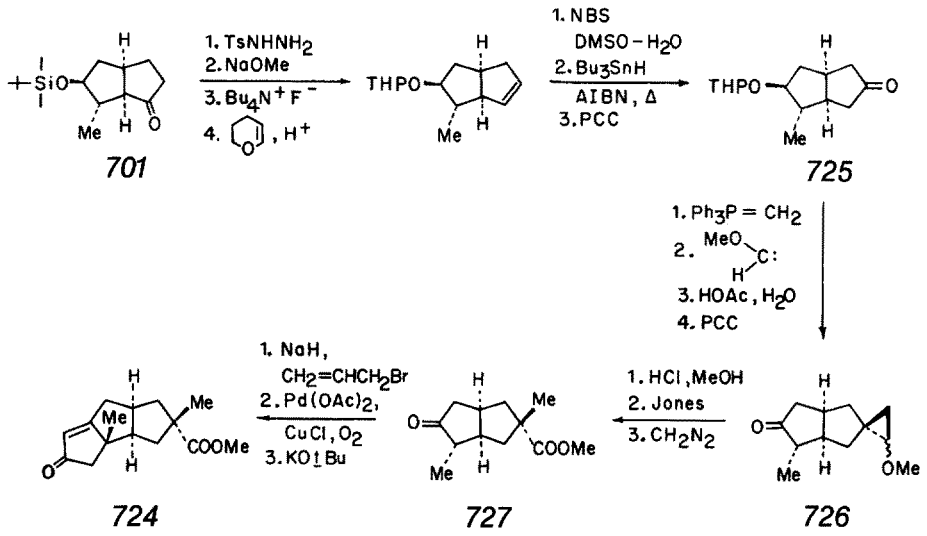
The first stereocontrolled synthesis of (±)-hirsutic acid (*720*) was achieved by Trost [400]. In this work, four of the seven asymmetric centers are fixed in the correct relative stereochemistry in bridged bicyclic compound *721* which in turn is formed by

two intramolecular Michael addition reactions (Scheme LXXVII). This key intermediate was reduced, hydrolyzed, and lactonized. Hydrolysis of the nitrile to give *722* set the stage for conversion of the double bond to methyl groups. Tricyclic lactone *723* was hydrolyzed and transformed conventionally to a known methyl ketone. Aldolization furnished *724* which earlier had been transformed to hirsutic acid.



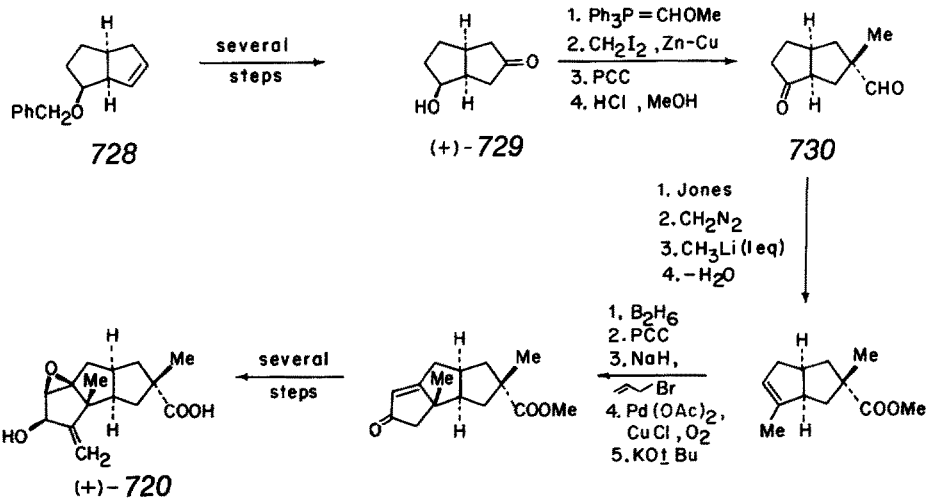
Scheme LXXVII

Ikegami's successful synthesis of racemic *720* materialized by initial conversion of *701* to *725* via a 1,2-carbonyl transposition sequence (Scheme LXXVIII) [401]. Treatment of *725* with methoxycarbene, deprotection, and oxidation provided *726*. Acid-promoted cyclopropane ring cleavage and added functional group manipulation led to *727* which could be allylated stereoselectively. The tricyclic enone *724* was subsequently produced conventionally.



Scheme LXVIII

More recently, the same group achieved a simple, highly stereocontrolled total synthesis of (+)-hirsutic acid (Scheme LXXIX)[402]. This chirally directed effort developed subsequent to reaction of *dl-728* with (+)-di-3-pinanylborane, alkaline hydrogen peroxide oxidation, chromatography, PCC oxidation, and hydrogenolysis. The dextrorotatory hydroxy ketone *729* was nicely crafted into keto aldehyde *730* from which *720* was readily obtained. Once again, the Wacker oxidation played an instrumental role in annulation of the third five-membered ring. The remainder of the asymmetric synthesis was completed as before.

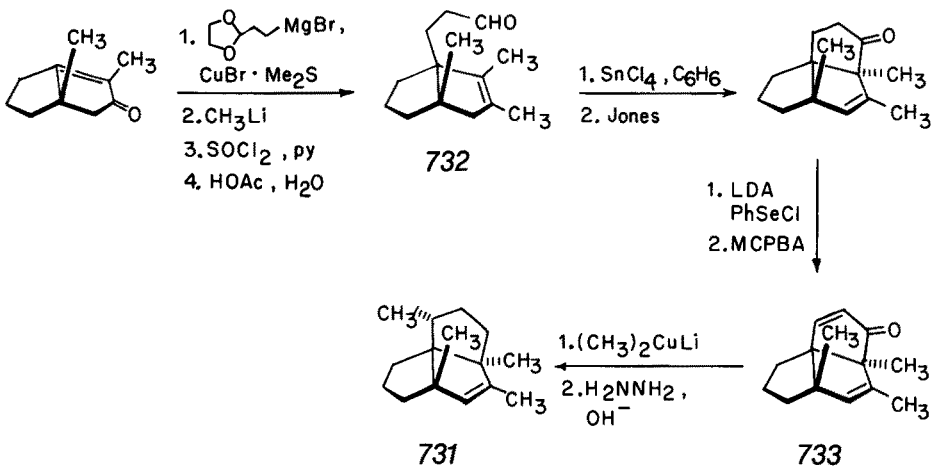


Scheme LXXIX

B Angular Triquinanes

1 Isocomene

The first naturally occurring tricyclo[6.3.0.$0^{4,8}$]undecane to be synthesized was isocomene (*731*), a colorless oily sesquiterpene hydrocarbon isolated from several plant sources. In 1979, Paquette and Han reported an efficient, stereospecific approach starting with a preformed bicyclic enone, to which the third five-membered ring was appended with proper attention to stereochemistry and position of unsaturation (Scheme LXXX) [403]. The pivotal steps are seen to be the stannic chloride-induced cyclization of aldehyde *732* and the conjugate addition of lithium dimethylcuprate to *733* which sets the stereochemistry of the last methyl group.

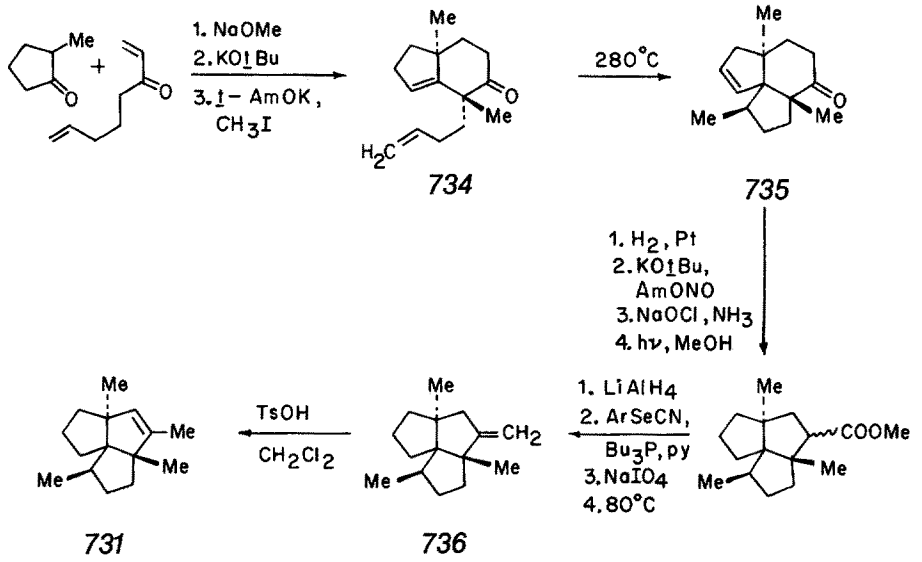


Scheme LXXX

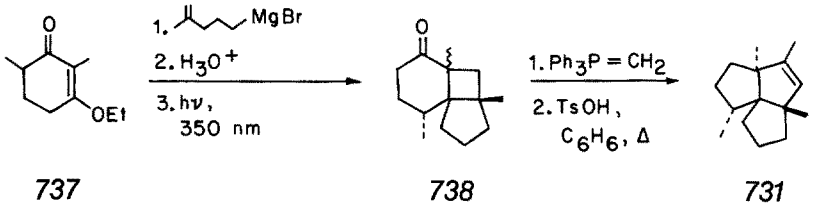
Concurrently, two other approaches to isocomene made their appearance. The first of these due to Oppolzer, et al., features as its key step an intramolecular thermal ene reaction which converts *734* to *735* (Scheme LXXXI) [404]. Another point of interest is the fact that penultimate intermediate *736* is also a natural product (β-isocomene).

The Pirrung synthesis is notable for its brevity and clever amalgamation of [2 + 2] photocycloaddition and Wagner-Meerwein rearrangement chemistry [405]. Enol ether *737* was reacted with the Grignard reagent from 5-bromo-2-methyl-1-pentene, subjected to acid hydrolysis, and irradiated to generate the tricycle *738*. Wittig olefination of this ketone and treatment with *p*-toluenesulfonic acid provided racemic isocomene.

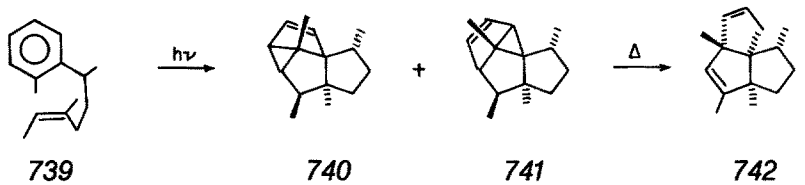
A purportedly expedient synthesis of isocomene outlined by Chatterjee is unquestionably bogus [403,405]. However, success in arriving at *731* has been enjoyed by several other research groups. For Wender and Dreyer, the meta-photocycloaddition



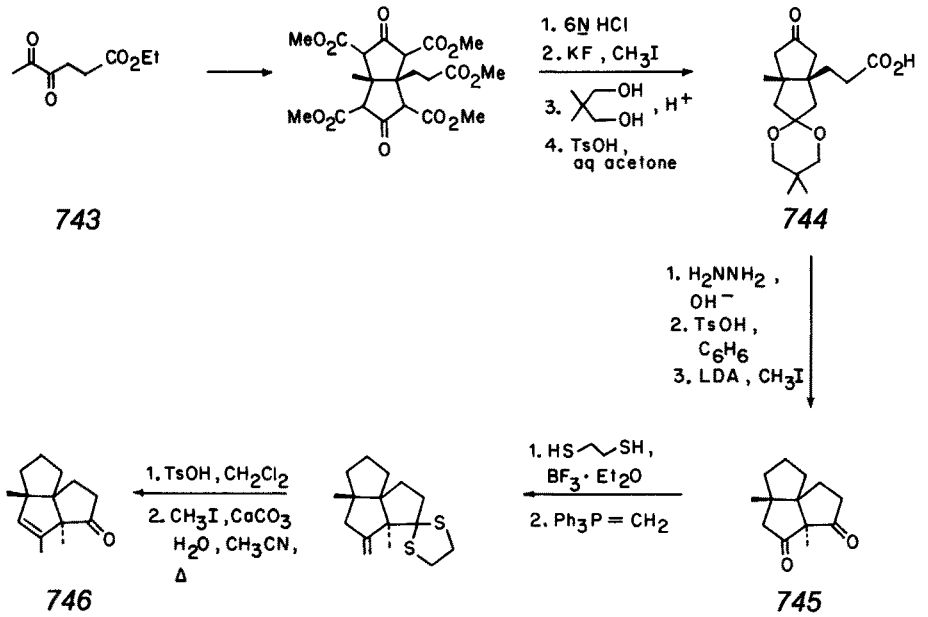
Scheme LXXXI



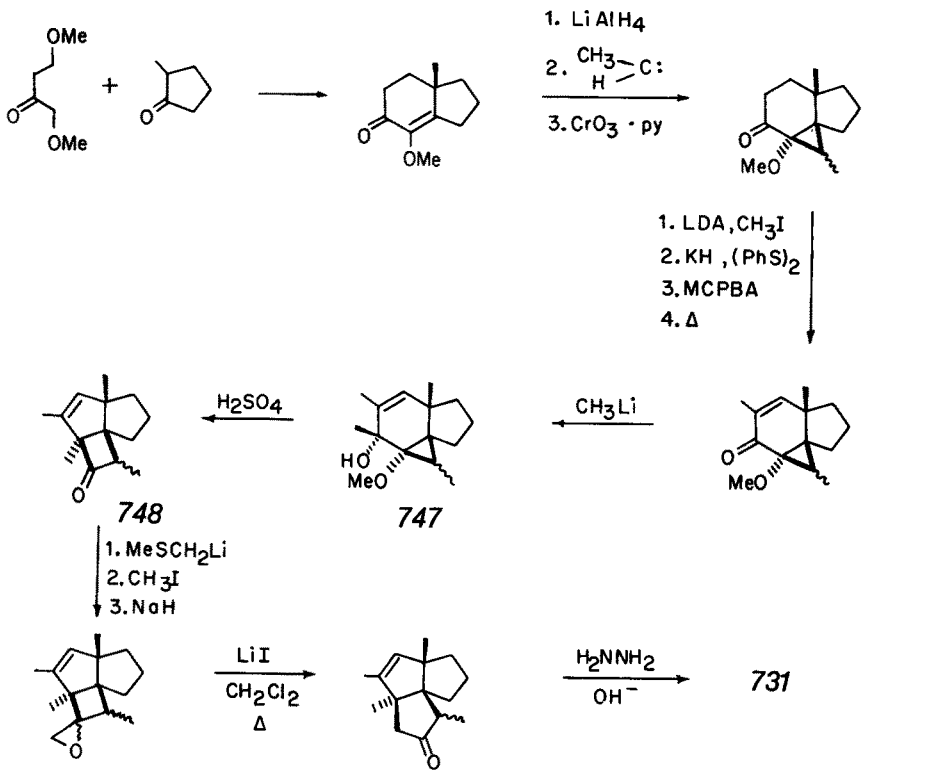
of *739* proved magnificently serviceable [407]. When this aromatic olefin was irradiated, conversion to *740* and *741* ensued in varying ratios dependent upon conditions. Thermolysis of either substance in toluene provided dehydroisocomene (*742*), controlled hydrogenation of which led to *731*.



The approach to *731* developed by Dauben and Walker, outlined in Scheme LXXXII, begins with the Weiss-Cook condensation of *743* and proceeds after hydrolysis and monoketalization to furnish keto acid *744*. Wolff-Kishner reduction, cyclization, and methylation of this intermediate provided diketone *745* which was transformed by standard means to *746*, a molecule which had previously been carried on to *731* (Scheme LXXX).



Scheme LXXXII

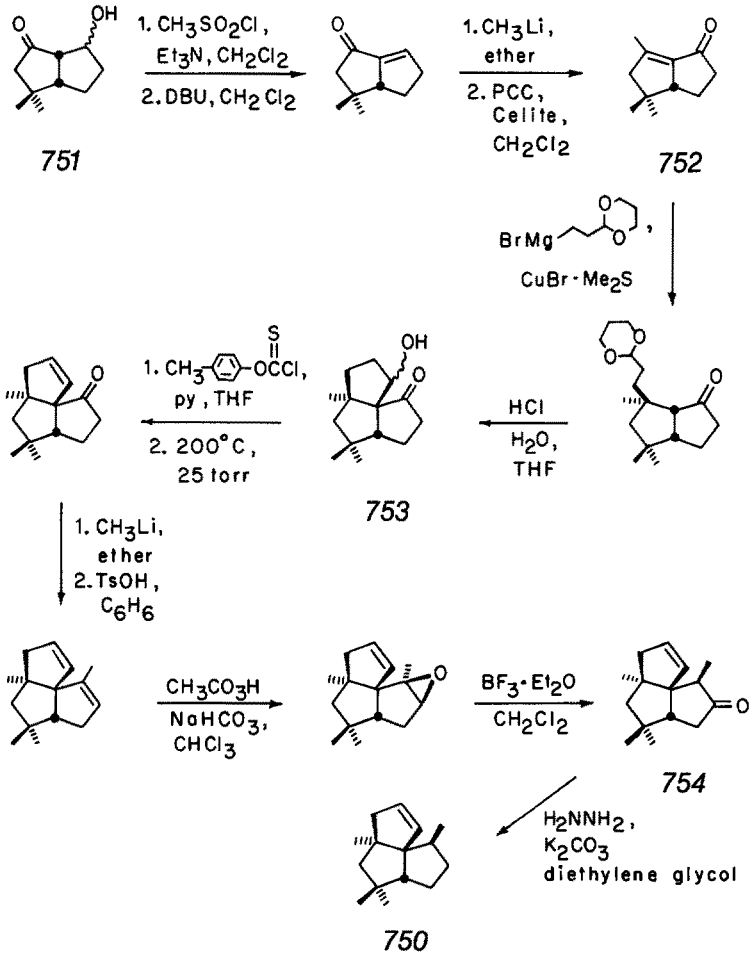


Scheme LXXXIII

In work which remains unpublished, Wenkert has succeeded in cleverly transforming 2-methylcyclopentanone into isocomene [409]. The key elements of his strategy (Scheme LXXXIII) are the acid-catalyzed ring expansion of methoxycyclopropane *747* to *748* and the regiospecific homologation of the cyclobutanone to *749*. Unfortunately, the Wolff-Kishner reduction of this penultimate intermediate affords both *731* and its epimer.

2 Silphinene

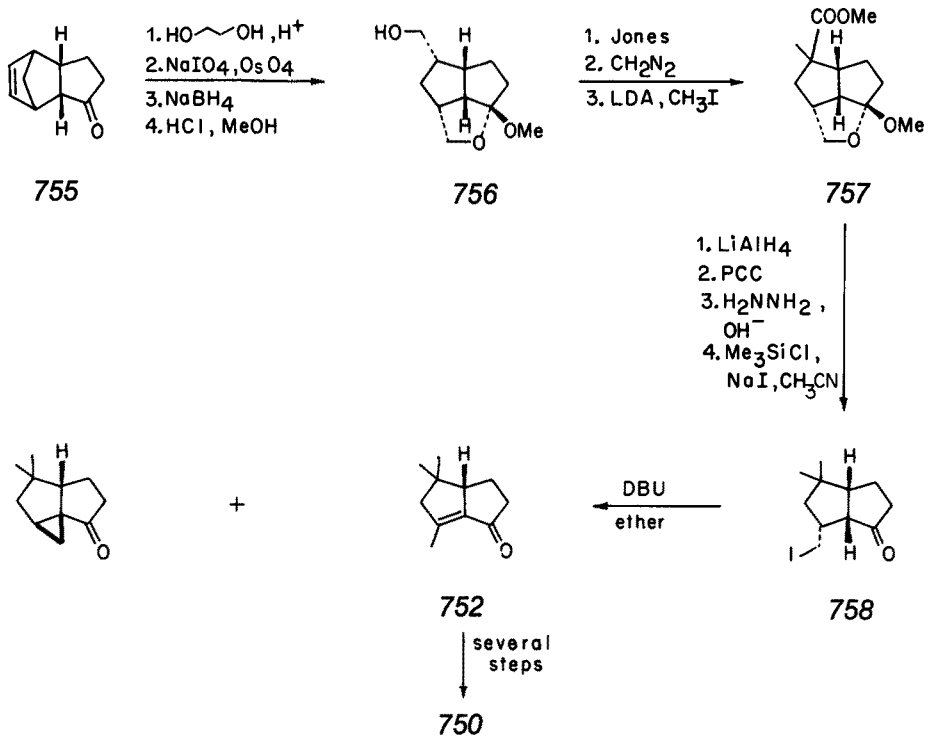
Silphinene (*750*), an angularly fused triquinane isolated by Bohlmann and Jakupovic from *Silphium perfoliatum* in 1980 [410] has a substitution pattern entirely different from that of isocomene and pentalenene. Entirely different synthetic protocols are consequently required. Two successful approaches to *750* have so far been devised. That due to Leone-Bay and Paquette [411], makes use of an iterative annulation scheme



Scheme LXXXIV

for fusion of the second and third five-membered rings. Beginning with *751*, which was prepared in the manner outlined earlier for *8*, sequential dehydration and alkylative carbonyl transposition was effected to provide *752* (Scheme LXXXIV). This intermediate was subjected to the identical annulation procedure used to access *751*. Following the isolation of *753*, suitable functional group manipulation delivered ketone *754* stereospecifically. No loss of stereochemical integrity was lost in the final conversion to *750*.

Itô's regio- and stereoselective total synthesis relied on dicyclopentadiene as starting material [412]. The derived ketone *755* was cleaved to provide *756* which was crafted into *757* (Scheme LXXXV). Following reduction of the carbomethoxy group, conversion to iodo ketone *758* was realized with trimethylsilyl iodide. Reaction of *758* with DBU resulted chiefly in conversion to *752* which was transformed into silphinene essentially as described above.

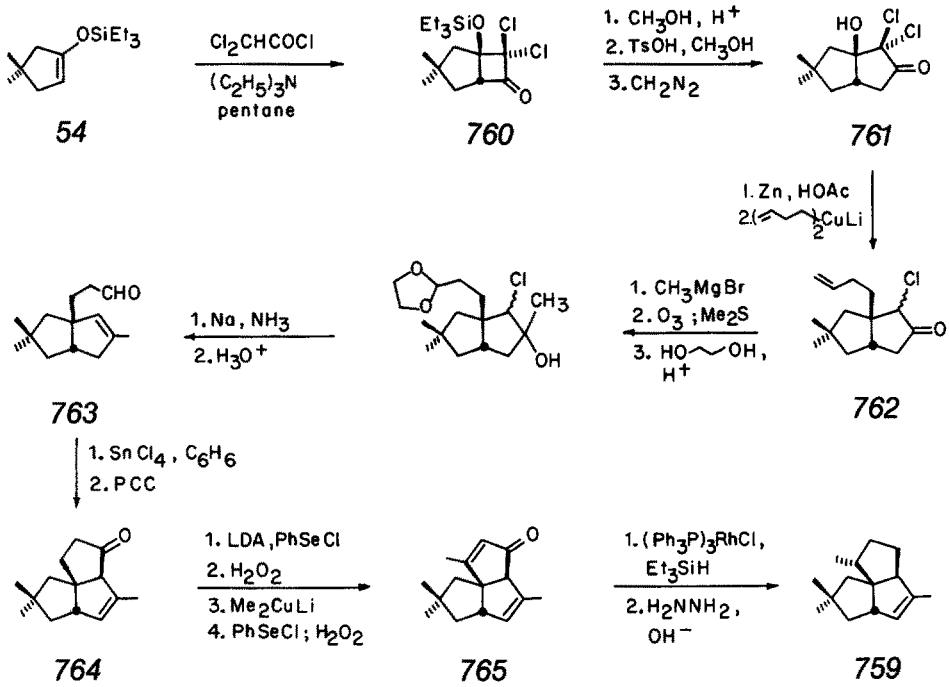


Scheme LXXXV

3 Pentalenene

Recently, the oxygen-free neutral precursor to the pentalenolactone family of metabolites was isolated, identified as *759*, and named pentalenene [413]. Annis and Paquette have since devised a synthesis of *759* which efficiently elaborates its ring junction quaternary center and three angularly fused cyclopentane rings [414]. Condensation

of silyl enol ether *54* with dichloroketene and regiocontrolled ring expansion made *761* available (Scheme LXXXVI). Zinc reduction led to introduction of a double bond and set the stage for conjugate addition of an angular allyl group. Conventional conversion of *762* to *763* made possible Lewis acid-catalyzed ene cyclization to give *764*. At this point, the α,β-unsaturated ketone *765* was prepared and reduced in two steps to *759*.



54 *760* *761*

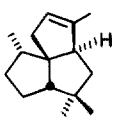
763 *762*

764 *765* *759*

Scheme LXXXVI

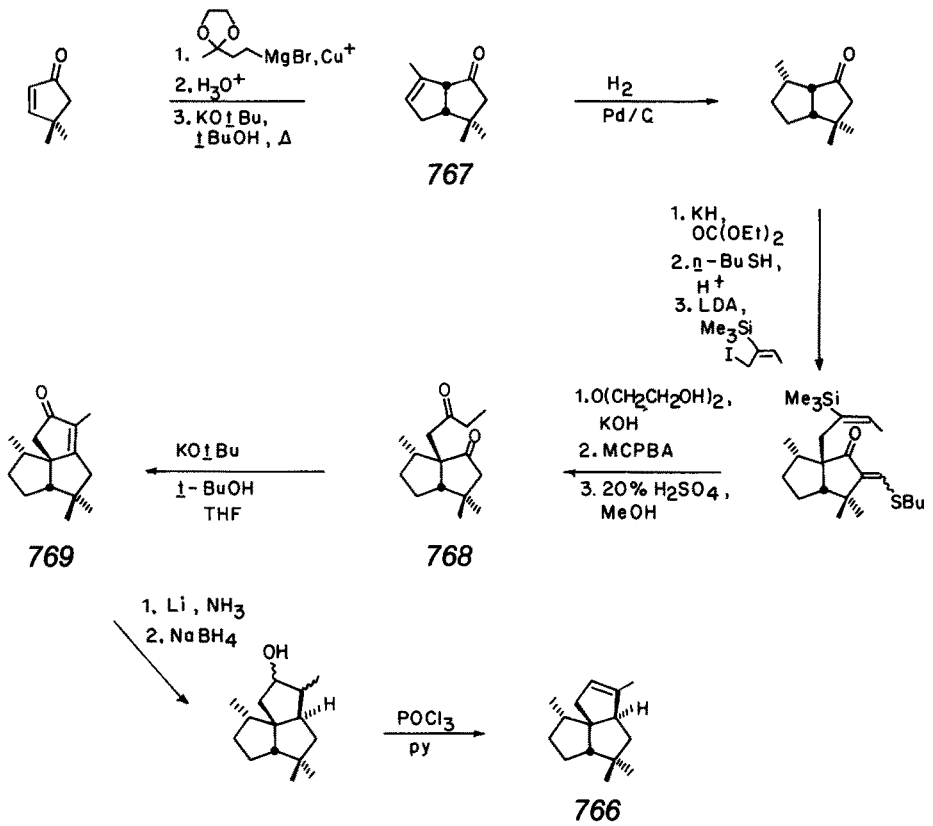
4 Senoxydene

In 1979, Bohlmann and Zdero reported the isolation and an unusual sesquiterpene hydrocarbon from *Senecio oxyodontus* [415]. This substance was formulated as *766* on the basis of its spectral characteristics and called senoxydene. However, Galemmo and Paquette have recently prepared this particular compound and determined that it is not identical to the natural product. Their pathway, which is summarized in Scheme LXXXVII, begins by transforming 4,4-dimethylcyclopentenone into bicyclic



766

α,β-unsaturated ketone *767* which is hydrogenated to set the stereochemistry of the secondary methyl group [416]. A vinylsilane sidechain is next introduced which, after deblocking, is modified to introduce a second carbonyl group. Cyclization of diketone *768* delivers *769* which is subjected to dissolving metal reduction in order to fix the last chiral center appropriately. Finally, the double bond is generated regiospecifically. The finding that *766* is not senoxydene requires, of course, that structural revision be made and this action is currently pending.

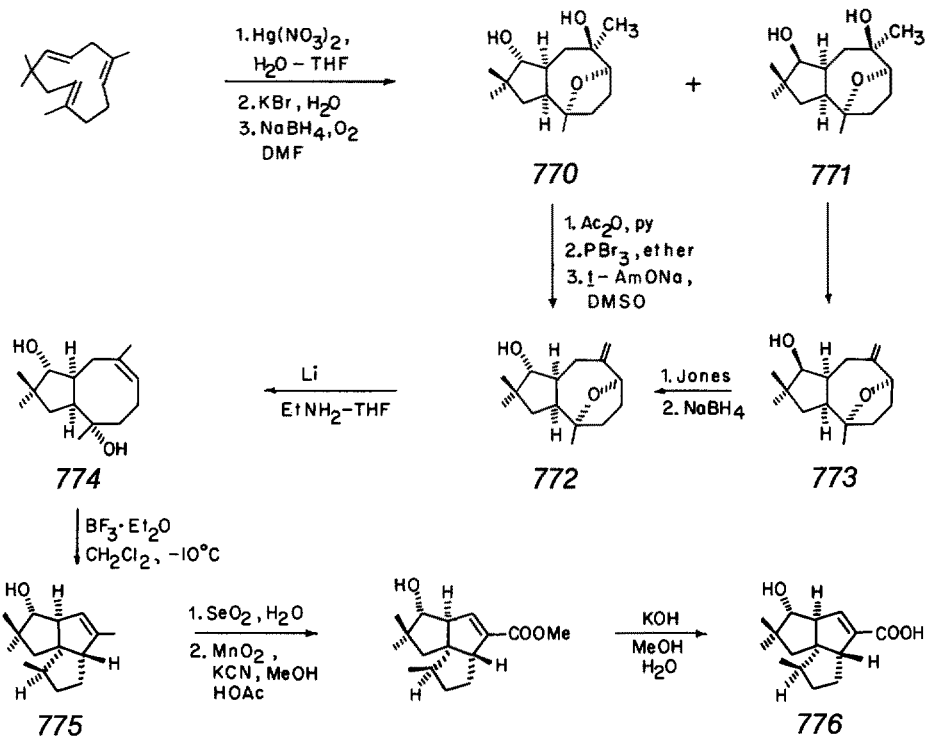


Scheme LXXXVII

5 Pentalenic Acid

The fermentation broth of various *Streptomyces* species can be separated into an acidic fraction shown to contain pentalenic acid (*776*) [417]. The somewhat less oxidized pentalenolactone precursor has been independently prepared from humulene from which is is probably derived biogenetically [418]. Thus, treatment of humulene with mercuric nitrate followed by aqueous potassium bromide solution gave two bromomercury derivatives which were oxygenated in the presence of sodium borohydride. The resulting pair of diols (*770* and *771*) were separately converted to exo methylene

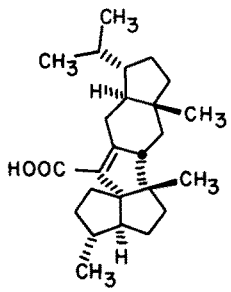
derivatives *772* and *773*, respectively, and *773* was transformed under standard conditions to *772* (Scheme LXXXVIII). Reduction of *772* with lithium in ethylamine furnished *774* which was cyclized under Lewis acid conditions. 10α-Hydroxypentalenene (*775*), formed (20%) alongside four other compounds, was subjected to conditions which oxidized its allylic methyl group first to the aldehyde level and ultimately to the methyl ester. Hydrolysis of this material delivered pentalenic acid, identical to the natural product.



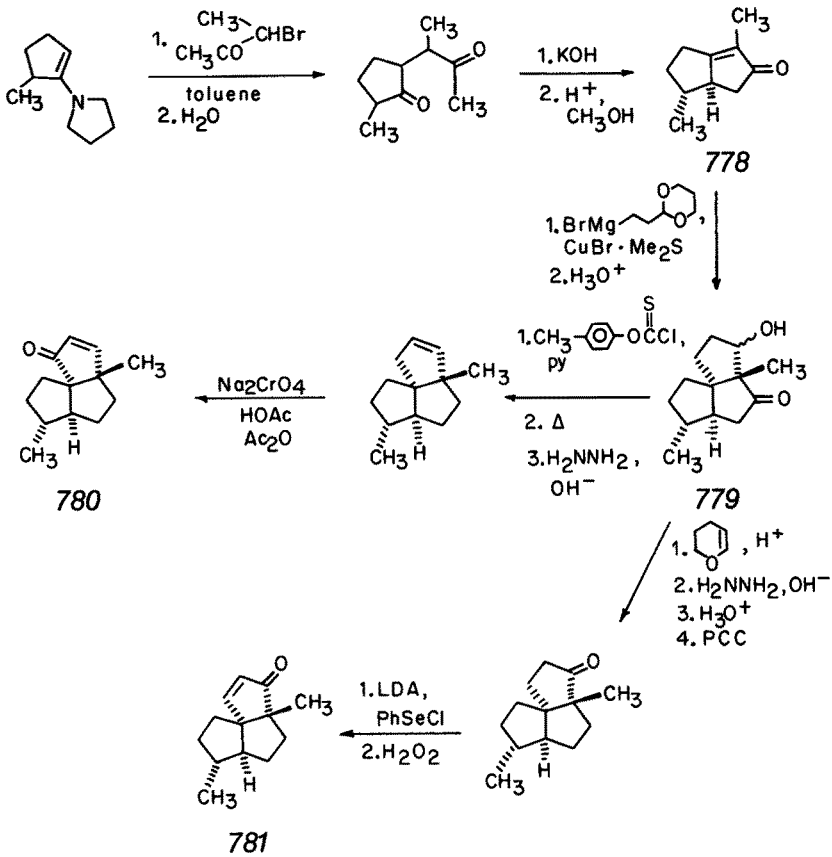
Scheme LXXXVIII

6 Retigeranic Acid

A pentacyclic sesterterpene having eight chiral centers and five quaternary carbon atoms, retigeranic acid (*777*) is a topologically unique polyquinane system. Although its total synthesis has not yet been achieved, the lower triquinane segment of the molecule has been prepared in racemic and optically active form [419]. Enones *780* and *781* were obtained by initial conversion of 2-methylcyclopentanone to *778* followed by cyclopentannulation of this substrate to produce *779* (Scheme LXXXIX). With the indicated tricyclic α,β-unsaturated ketones in hand, the proper fusion of rings D and E should be forthcoming.

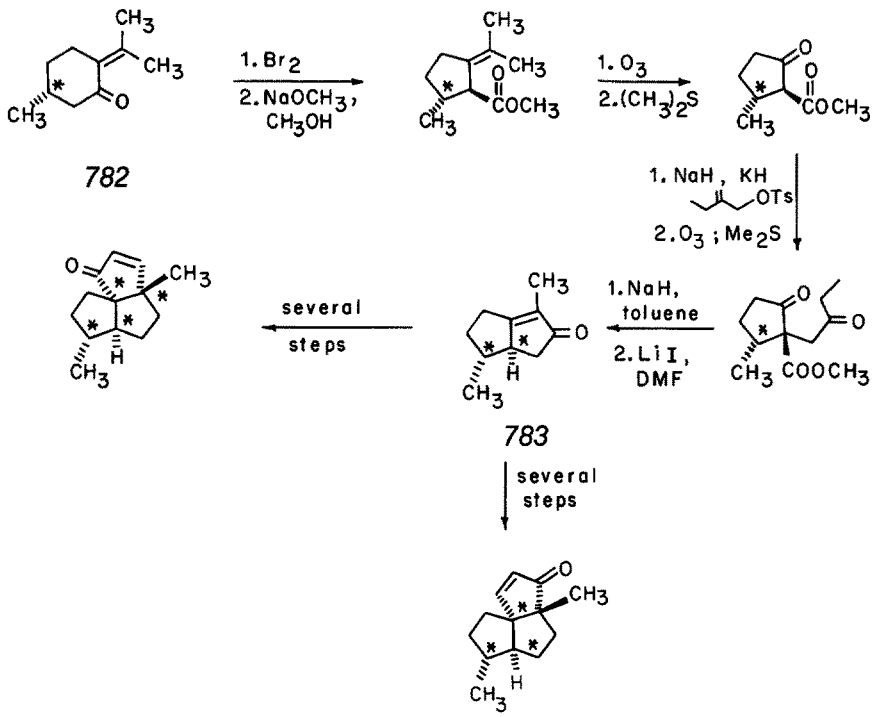


777



Scheme LXXXIX

For the optically active analogues, (+)-pulegone (*782*) was utilized as the chiral pool source [419]. Since its methyl substituted carbon atom is not perturbed during the conversion to *783* and beyond (Scheme XC), this stereocenter is fixed. Three additional asymmetric centers were then introduced as previously outlined.



Scheme XC

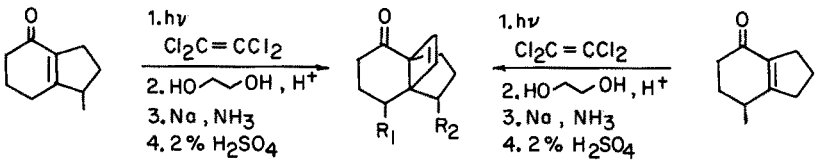
C Propellane Structures

1 Modhephene

In 1977, Zalkow and associates reported the isolation and characterization of isocomene (*784*), a novel tricyclo[6.3.0.$0^{4,8}$]undecane featuring a bridged spirane arrangement of three cyclopentane rings [420]. At a later date, Bohlmann described the successful efforts of his group in isolating *784* [421]. Such a great deal of attention has been paid to the total synthesis of *784* that a detailed analysis of the convergency of the various pathways has been reported [422].

The strategy deployed by Smith and Jerris (Scheme XCI) converged upon formation of the [3.3.3]propellenone *786* which in turn was derived from acid-catalyzed rearrangement of tricyclic enones *785* [423]. Following an alkylative 1,3-carbonyl transposition, conjugate addition of lithium dimethylcuprate, Wittig olefination, and double bond isomerization, *784* and its epimer were obtained.

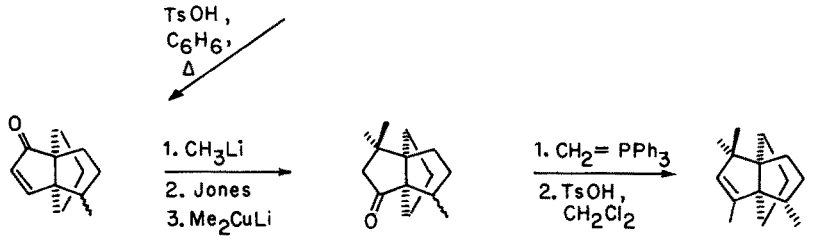
The approach chosen by Schostarez and Paquette (Scheme XCII) was fully regiocontrolled and designed to generate modhephene and epimodhephene independently [424]. Bicyclic enone *787* was transformed by conjugate addition into *788* or *789*. When the first substrate was thermolyzed, ene chemistry locked the secondary methyl sub-



785

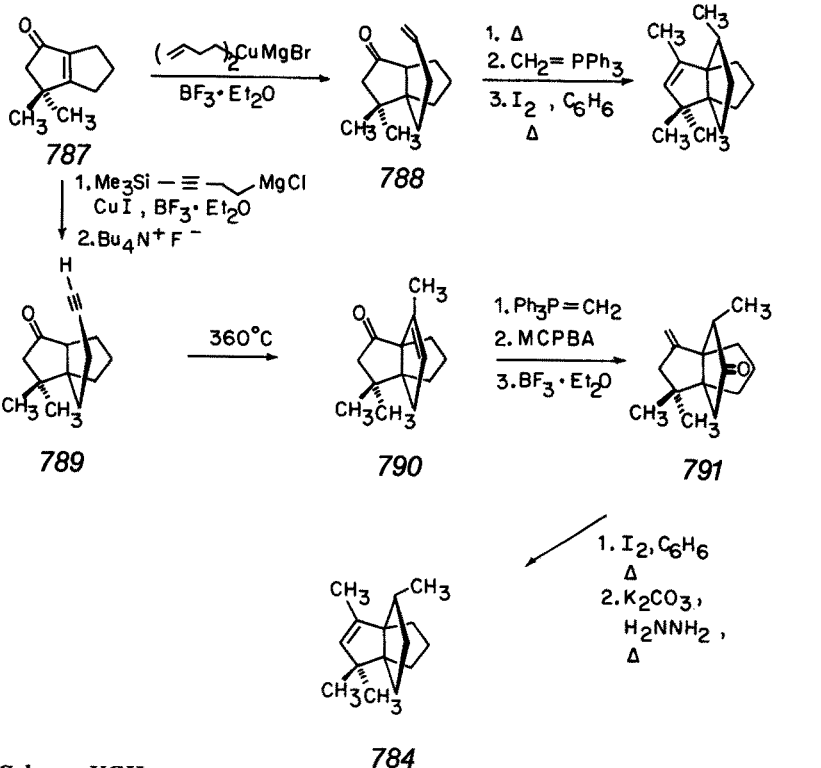
$R_1 = H$, $R_2 = CH_3$

$R_1 = CH_3$, $R_2 = H$



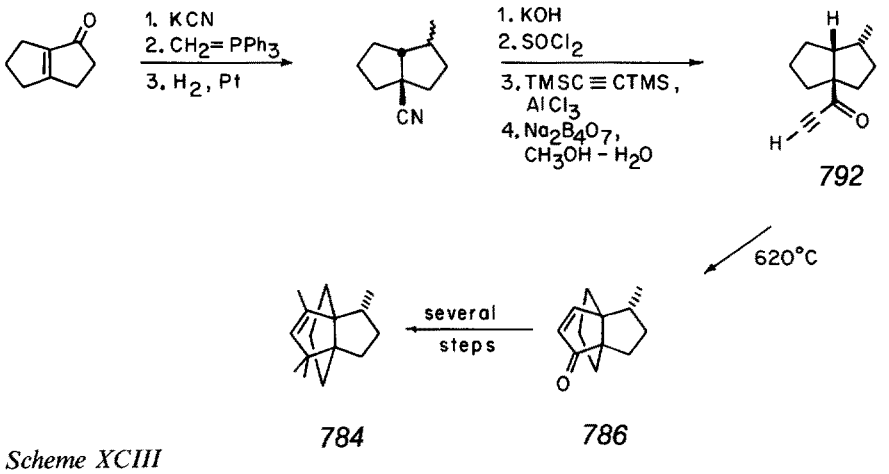
786 784

Scheme XCI

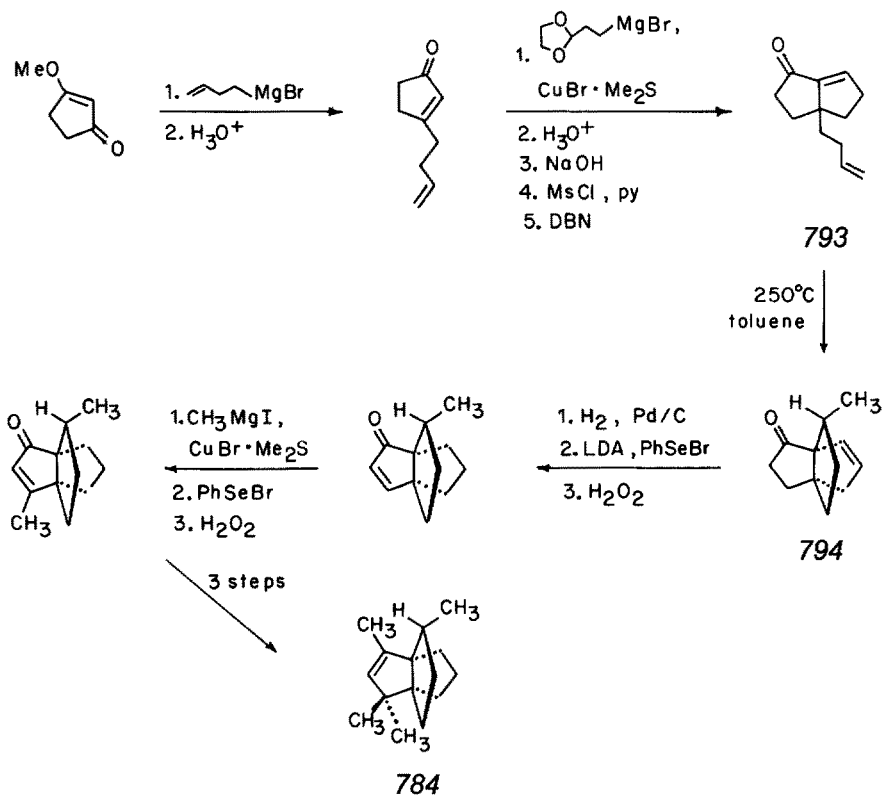


Scheme XCII

stituent into a syn relationship to the carbonyl group. Comparable pyrolysis of *789* led to the formation of *790* which was epoxidized and isomerized with full stereocontrol to give *791*. Double bond isomerization and Wolff-Kishner reduction completed the synthesis.



Scheme XCIII

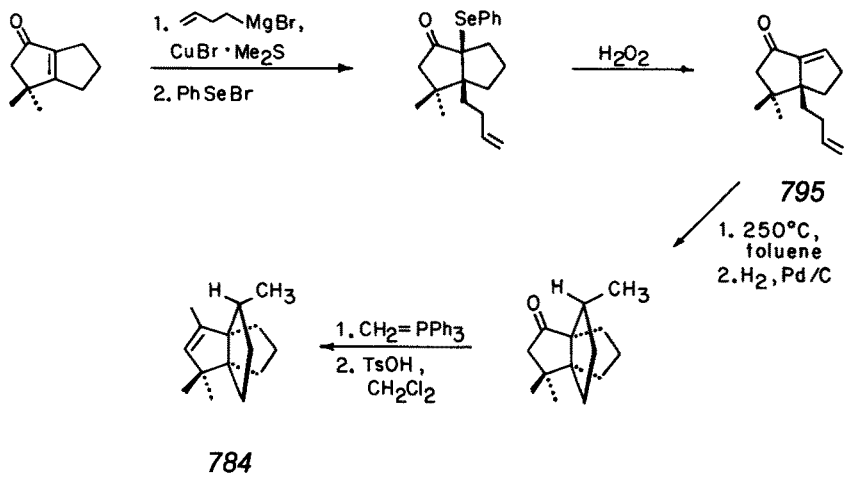


Scheme XCIV

Karpf and Dreiding arrived at modhephene by thermal α-alkynone cyclization (Scheme XCIII) [425]. The synthesis of key intermediate *792* was unfortunately plagued by isomer problems. Also, the pyrolysis of *792* did not afford *786* cleanly. With the availability of this last intermediate, arrival at modhephene followed earlier precedent.

Oppolzer has designed two approaches to modhephene, both of which are based on the high level of stereochemical control attainable in intramolecular thermal ene reactions. In the first (Scheme XCIV), α,β-unsaturated ketone *793* is obtained by aldol methodology and heated at 250 °C in toluene to produce *794* [426]. A methyl group and double bond are next introduced in standard fashion prior to arrival at the final sesquiterpene stage.

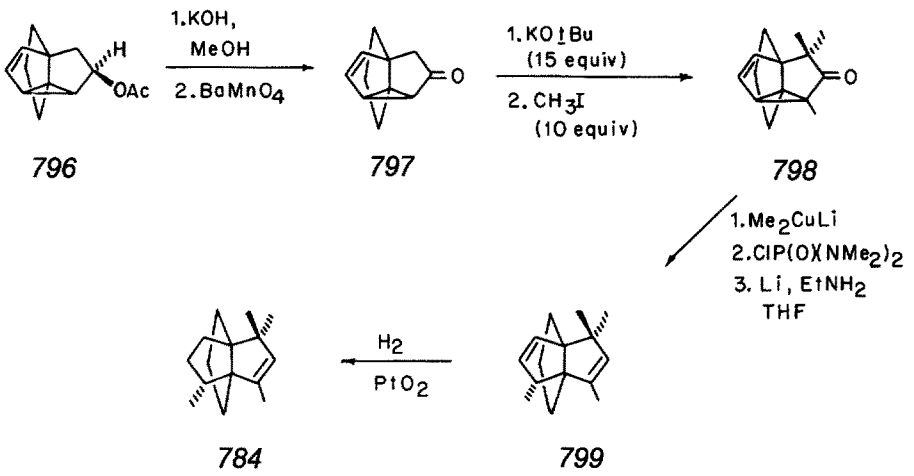
The far more expedient pathway involves gaining direct access to *795* by cuprate addition-selenation and subsequent elimination (Scheme XCV). In this way, modhephene can be produced in only six steps.



Scheme XCV

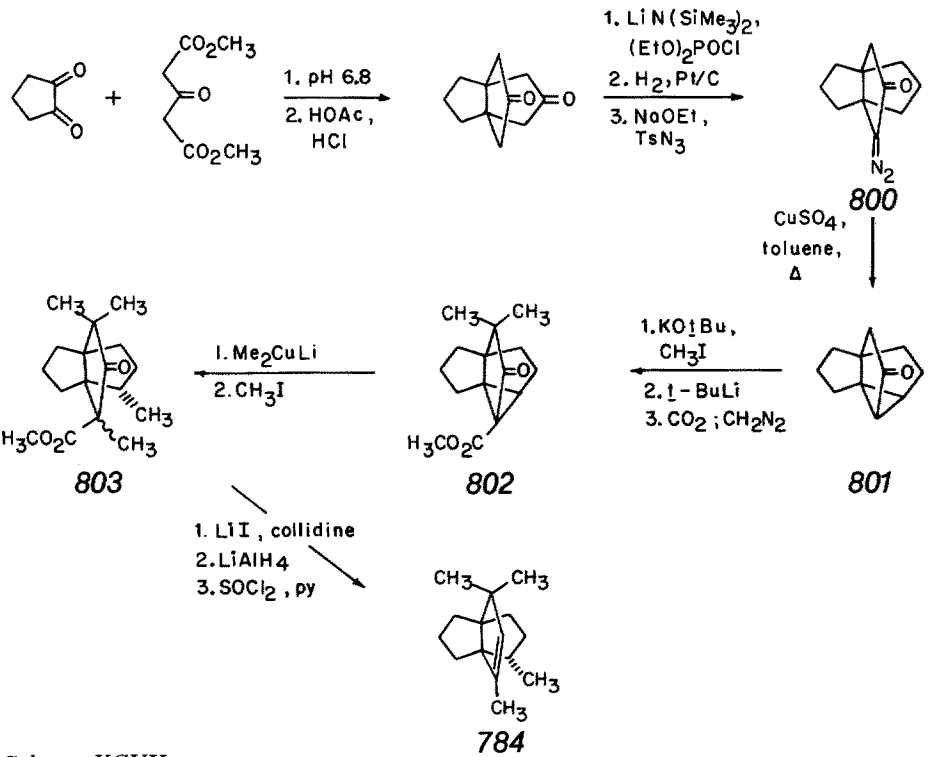
Wender and Dreyer have demonstrated that meta-arene photocycloaddition chemistry can lead expediently to modhephene [428]. Acetate *796*, a photoproduct derived from indane and vinyl acetate was converted to tetracyclic ketone *797* (Scheme XCVI). Because the enolate of *797* partakes of the dynamic behavior of semibullvalenes, it proved possible to trimethylate the substance to produce *798*. A fourth methyl group was introduced by conjugate addition and the carbonyl was simultaneously converted to an olefinic center. Selective hydrogenation of *799* provided modhephene in seven steps.

A regio- and stereospecific synthesis of modhephene has also been achieved beginning with the Weiss-Cook reaction [429]. As illustrated in Scheme XCVII, cyclopentane-1,2-dione can be readily crafted into α-diazo ketone *800*, copper-catalyzed decomposition of which delivers tricyclic ketone *801*. Following the dimethylation of this intermediate, carbomethoxylation was accomplished to give *802* and provide



Scheme XCVI

the opportunity for controlled ring opening with lithium dimethyl cuprate. Once this final stereocenter had been introduced, conventional methodology was utilized to convert *803* to *784*.



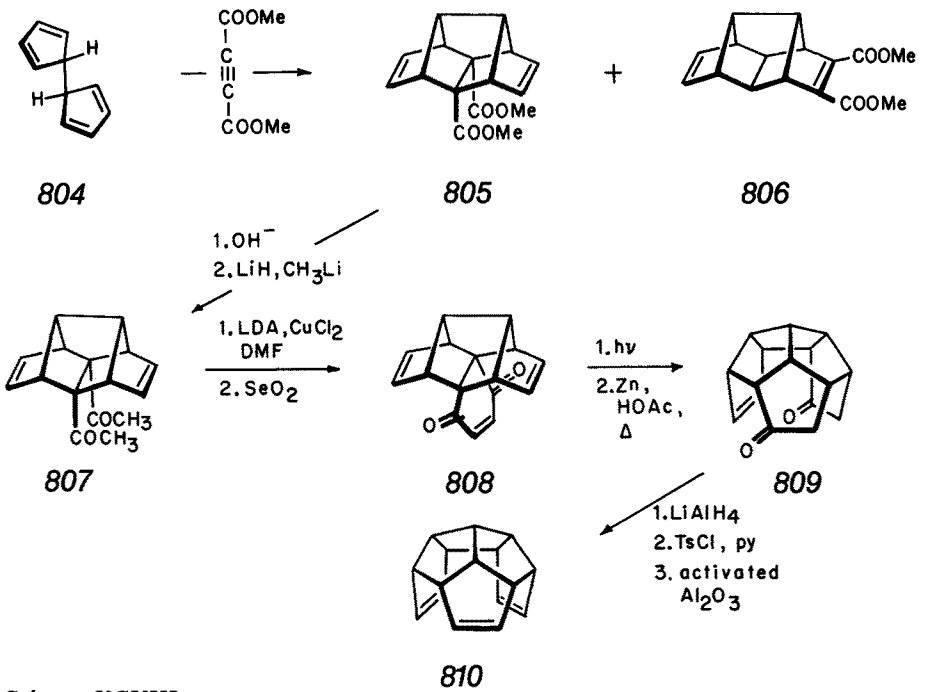
Scheme XCVII

IX The Quest for Dodecahedrane

A C_{16}-Hexaquinacene

1 Synthesis and Properties

When unstable 9,10-dihydrofulvalene (*804*) is allowed to react with dimethyl acetylenedicarboxylate, a separable mixture of the adducts *805* and *806* is produced [430]. The diacid derived from *805* can be readily transformed into diketone *807* and subsequently into triene dione *808* (Scheme XCVIII) [431,432]. Once the intramolecular photocyclization of this intermediate has been carried out, two sigma bonds can be ruptured by reduction with zinc. X-ray analysis of *809* showed its three unsubstituted cyclopentane rings to be essentially planar and the other three to have half-chair conformations [433].

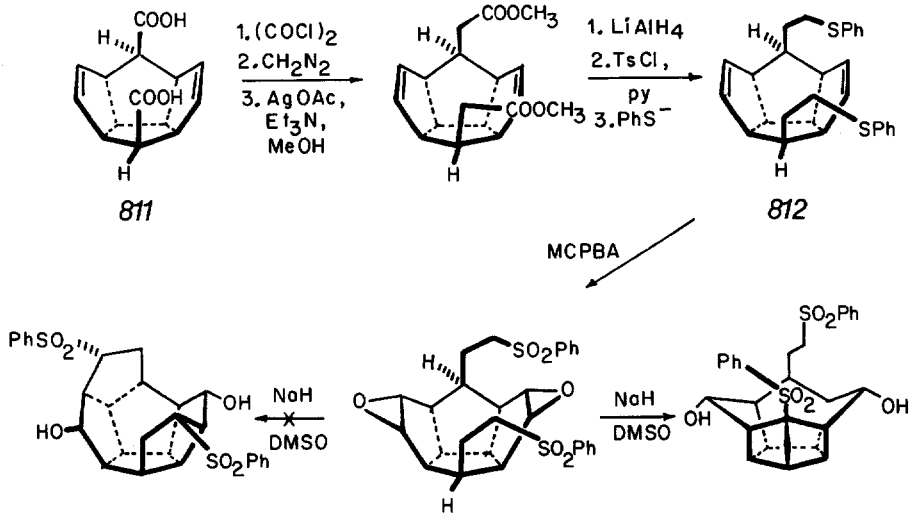


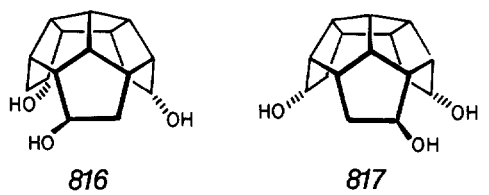
Scheme XCVIII

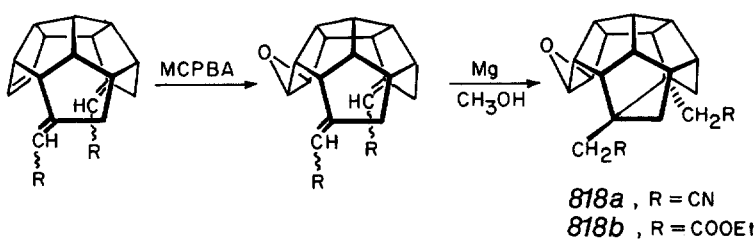
When the remaining two double bonds are introduced to give *810*, a high level of sphericality is achieved. However, the three sites of unsaturation do not engage in homoconjugative overlap [431,432,434].

2 Functionalization Reactions

Hales and Paquette have observed that sequential reduction and hydrolysis of *805* can lead efficiently to *endo,endo* diacid *811* [435]. Arndt-Eistert homologation, conventional elaboration of bis(thioether) *813*, and exhaustive oxidation was utilized to arrive at *813*. The plan was to deploy the dianion of *813* in a manner which would lead to *814*. However, the principal product proved to be the unwanted *815*.

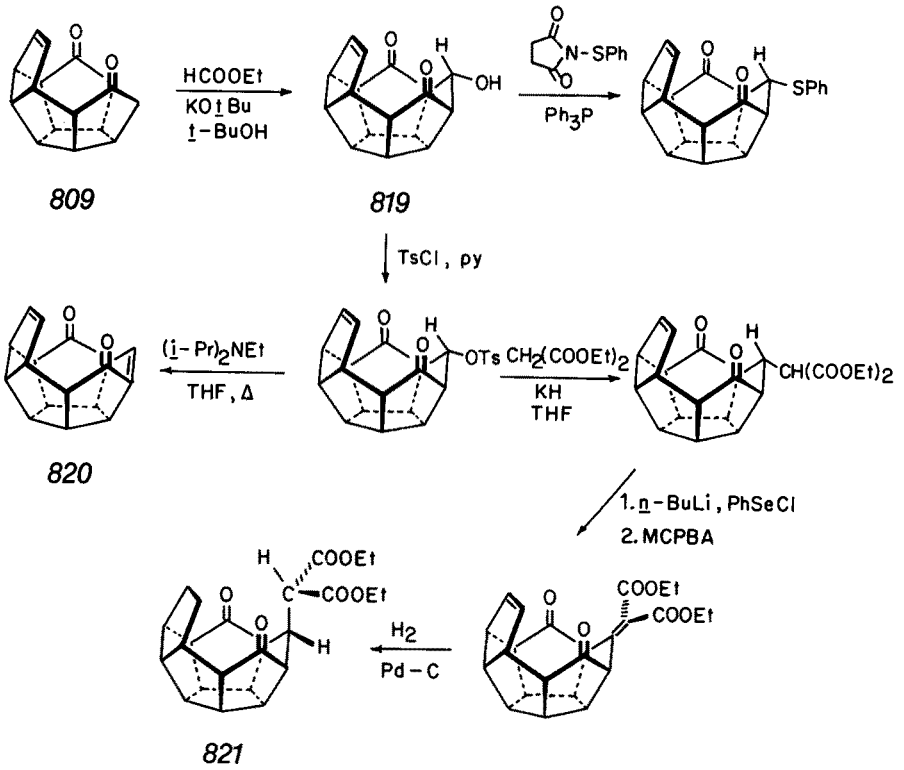






The exhaustive hydroboration of C_{16}-hexaquinacene (*810*) has been investigated and the isomeric *exo*[3]-triols *816* and *817* isolated [436]. Also, diketone *809* has been functionalized as in *818a* and *818b*, but these epoxides resisted intramolecular cyclization [436, 437].

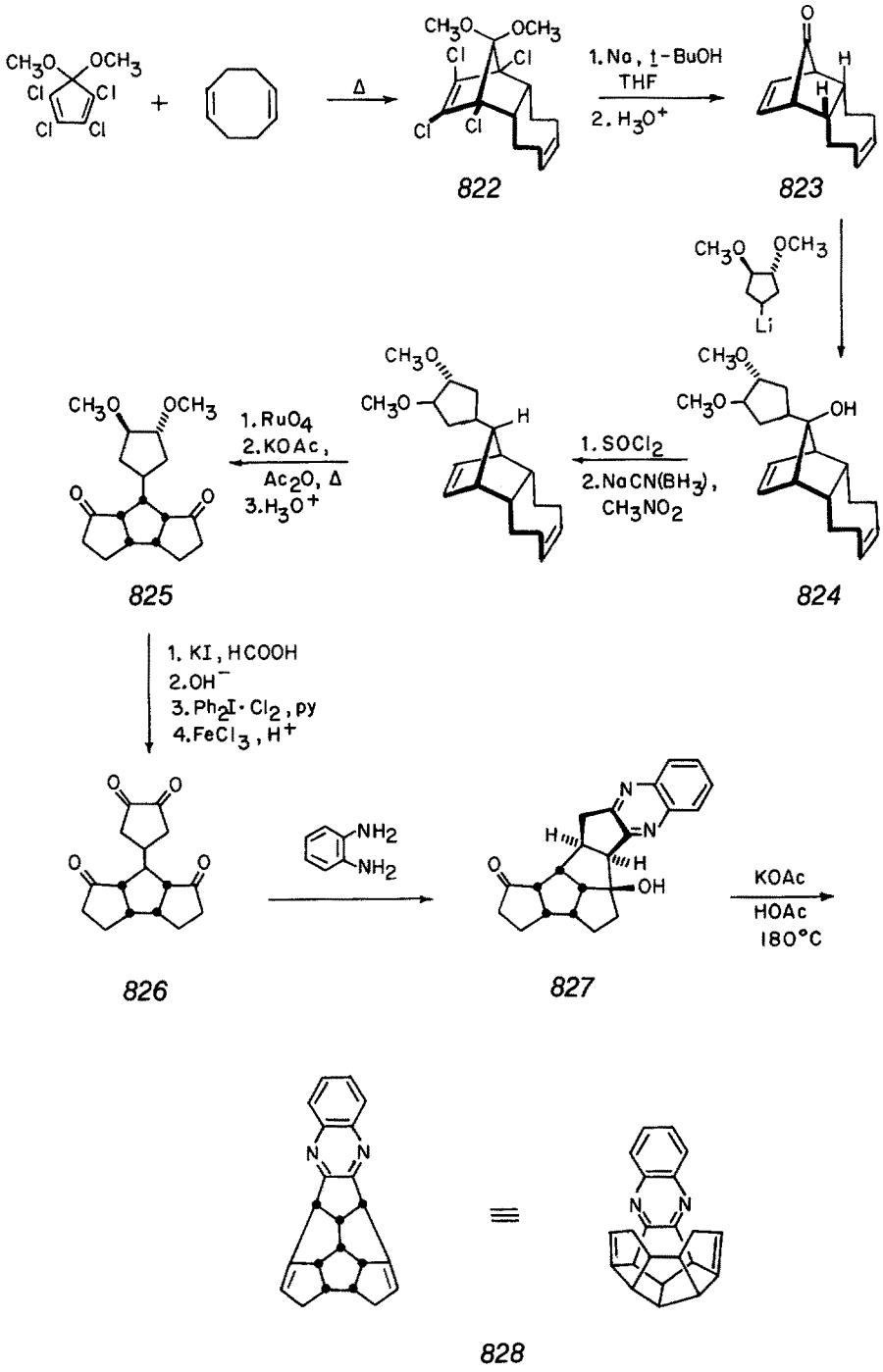
The same hexacyclic enedione has been converted to a series of C_{17}-heptaquinane derivatives via the alcohol *819* which is produced by condensation with ethyl formate in base [438]. The hydroxyl group in *819* can be readily functionalized, although loss of water to arrive at *820* occurs remarkably readily, despite the inherent strain of this system (Scheme XCIX). The conjugated double bond in *820* is understandably a good Michael acceptor, a property which was utilized to prepare *821*.



Scheme XCIX

B Alternative Approach to Hexaquinanes

In a vastly different approach to C_{16}-hexaquinanes, Eaton and coworkers prepared the Diels-Alder adduct *822* and transformed it into ketone *823* in preparation for reaction with *trans*-3,4-dimethoxycyclopentyllithium (Scheme C) [439]. Reductive removal of the tertiary hydroxyl group in *824*, followed by oxidative cleavage of the double bonds, cyclization and decarboxylation afforded *825*. The methoxyl groups in *825* were cleaved and the resulting diol oxidized stepwise to produce

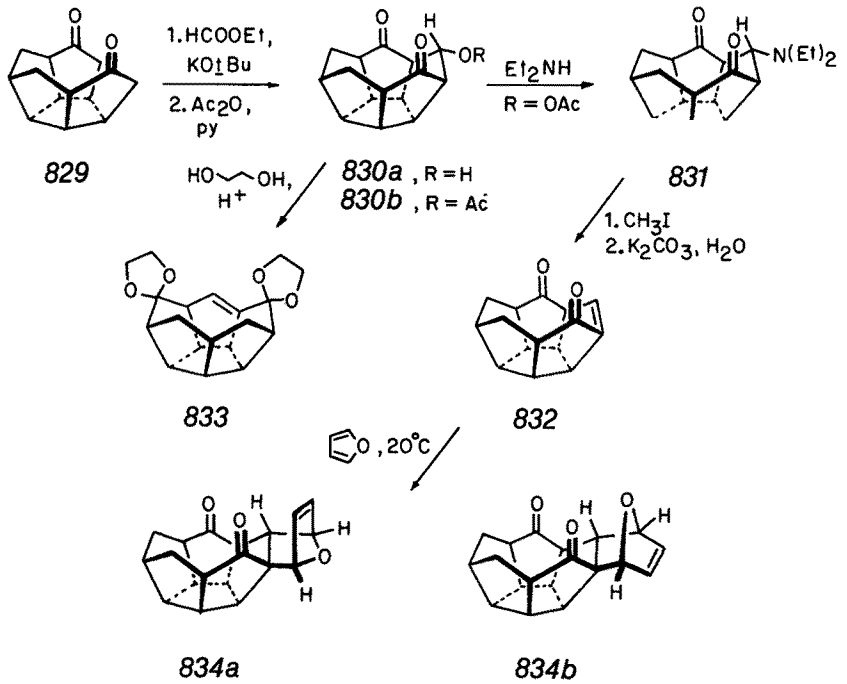

CH3O
OCH3
Cl
Cl
Cl
Cl
Δ
1. Na, t-BuOH
THF
2. H3O+
822
823
Li
824
1. SOCl2
2. NaCN(BH3),
CH3NO2
1. RuO4
2. KOAc,
Ac2O, Δ
3. H3O+
825
1. KI, HCOOH
2. OH−
3. Ph2I· Cl2, py
4. FeCl3, H+
826
NH2
NH2
827
KOAc
HOAc
180°C
828

Scheme C

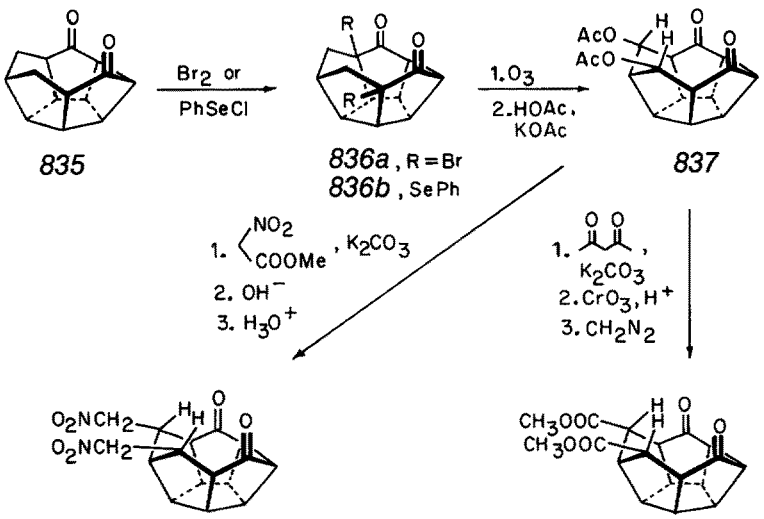
tetraketone *826*, which was trapped by reaction with *o*-phenylenediamine. During the latter reaction, an additional C—C bond was unexpectedly formed and the unsymmetrical quinoxaline *827* was obtained. However, when *827* was heated with potassium acetate and acetic acid at 180 °C in a sealed tube, ring opening preceded twofold dehydration and delivered the attractive hexaquinane heterocycle *828*.

C Peristylenones and Norperistylenones

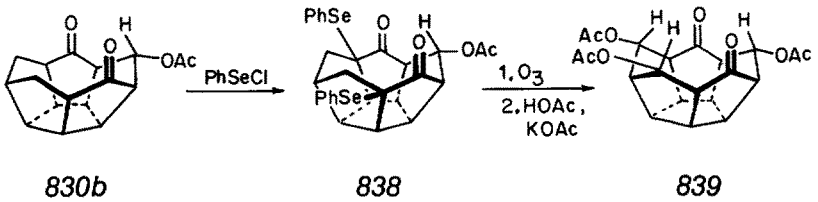
Diketone *829* closely parallels *820* in its chemical reactivity. Introduction of a functionalized bridging carbon can be achieved with ethyl formate and base [440]. The acetate group in *830b* is remarkably easily replaced with retention by simple nucleophiles, e.g. the conversion to *831*. The implicated peristyl-3-ene-2,6-dione (*832*) can in fact be obtained as a colorless crystalline compound. Also, *830a* spontaneously dehydrates during ketalization to produce *833*. The strained double bond in *832* enters readily into Diels-Alder reaction with furan to furnish a 3:1 mixture of *834a* and *834b*.



Bromination of norperistylane-5,11-dione (*835*) gives rapidly and quantitatively the C_{2v}-symmetric dibromide *836a*. Similarly, reaction with phenylselenyl chloride delivers *836b* [420]. Decomposition of the bis(selenoxide) in glacial acetic acid led to diketo diacetate *837*. This product enters into twofold exchange reactions with representative nucleophiles.



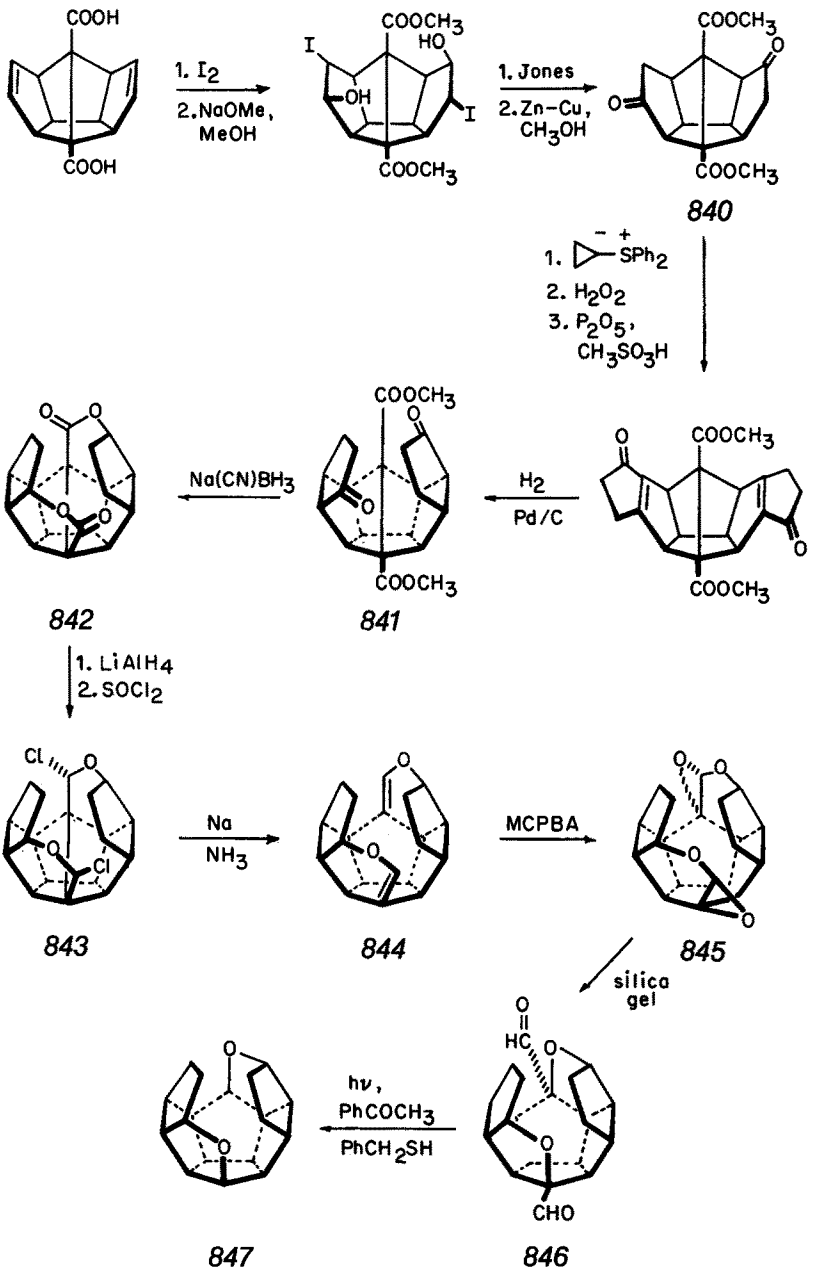
Peristylane derivative *839b* behaves in a totally analogous manner, as seen by its conversion via *838* to *839* [440].



D C_2-Dioxa-C_{20}-octaquinane

Cross-corner oxygenation of the diacid derived from *805* can be realized by sequential iodoloactonization, methoxide-promoted ring opening of the dilactone at room temperature, oxidation, and reductive deiodination (Scheme CI) [441]. Cyclopentenone annulation of *840* and catalytic hydrogenation delivered *841* whose hydride reduction gave *842*. This intermediate was readily converted to the highly reactive bis(chloroether) *843* which was transformed into *844* by reduction with sodium in liquid ammonia [442]. At this stage, extrusion of the trigonal carbon atoms α to the oxygen atoms in *844* was accomplished by epoxidation and acid-catalyzed rearrangement. Photodecarbonylation of dialdehyde *846* led to *847*, a heterocyclic trisecodecahedrane.

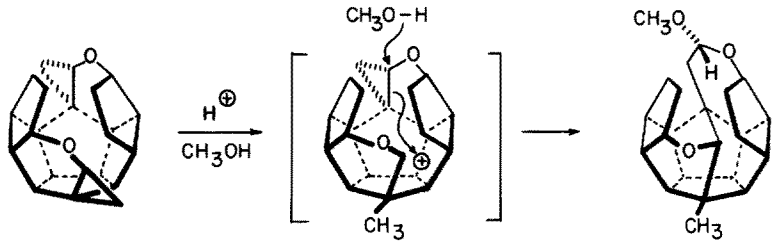
The isomerization of *845* contrasts in a striking way with the response of biscyclopropyl ether *848* to electrophilic ring cleavage. In acidic methanol, cleavage of the cyclopropane ring toward oxygen results to give *849* [442].



Scheme CI

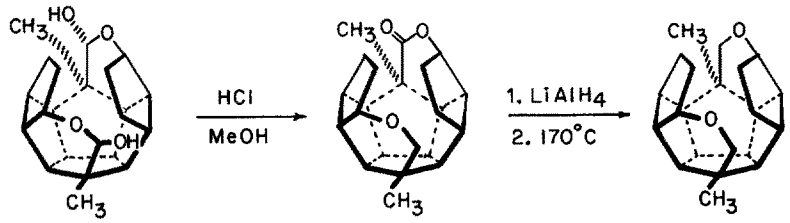
X-ray crystal structure analysis of *847* revealed the unusual conformation adopted by this molecule. Its two oxygen atoms are puckered toward the inner regions of the sphere in a manner which causes the methylene carbons to tilt outward from the cavity in order to achieve nonbonded strain minimization [443].

The high propensity of these molecules for structural rearrangement was again



848 849

made apparent in the case of *850* which, in acidic methanol, suffers internal oxidation-reduction (*851*) [444]. Deuterium-labeling studies substantiated that transannular hydride migration was operative. If *851* is subsequently reduced and dehydrated at 170 °C, the bishomologue of *847* is arrived at in the form of *852*.

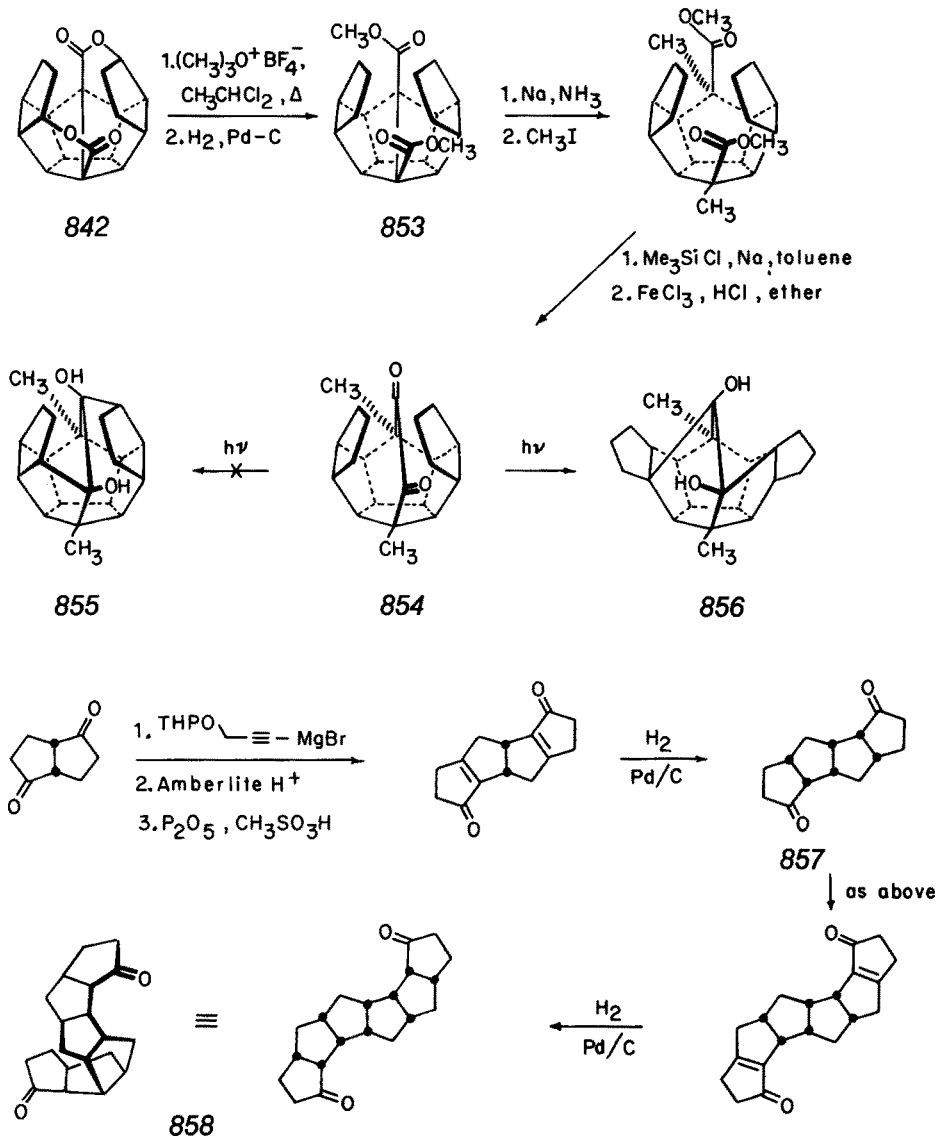


850 851 852

E Approaches to Higher Polyquinanes

When heated with trimethyloxonium fluoroborate in 1,1-dichloroethane, dilactone *842* experiences cleavage of both lactone rings to give a mixture of diene diesters, catalytic reduction of which produced *853* [445]. Reductive methylation of *853* proceeded with installation of the methyl groups on the exterior face for obvious steric reasons. Acyloin condensation followed by ferric cloride oxidation furnished α-diketone *854* which proved to be highly responsive to photoexcitation. However, irradiation of *854* did not provide *855* as expected. Rather, a most unusual reaction pathway was followed to deliver diol *856*.

McKervey and coworkers have developed an elegantly simple pathway for the conversion of *cis*-bicyclo[3.3.0]octane-2,6-dione to (C_2)-C_{20}-hexaquinane diketone *858* (Scheme CII) [446]. Twofold cyclopentenone annulation and hydrogenation rapidly led to the tetraquinane *857*. Repetition of the same steps then afforded *858*, the x-ray analysis of which showed the molecule to have an "opened out" conformation as the direct result of severe intramolecular overcrowding.



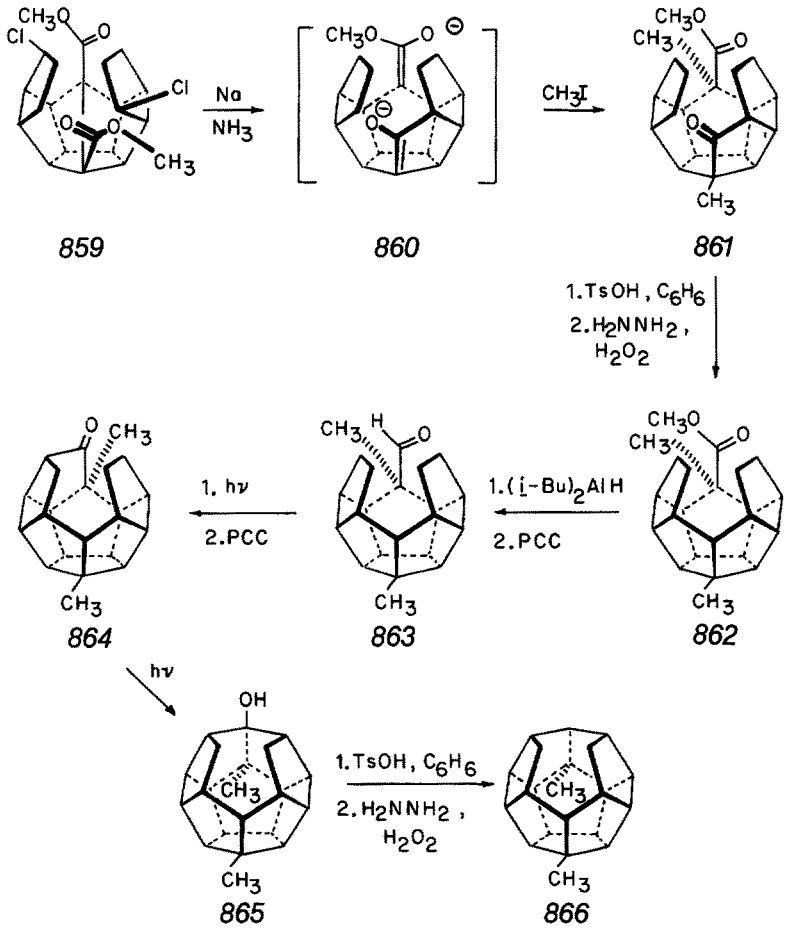
Scheme CII

F Pentagonal Dodecahedranes

1 The 1,16-Dimethyl Derivative

In an amazing reaction, dissolving metal reduction of dichloro diester *859* generates dianion *860* which can be conventionally methylated (Scheme CIII)[47]. Irradiation of keto ester *861* introduces yet another framework bond. Dehydration of the newly

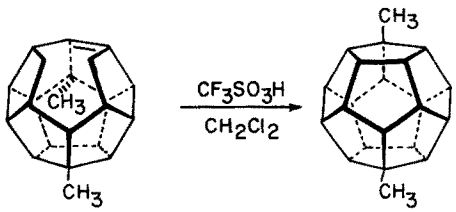
formed tertiary alcohol and diimide reduction made *862* available. After functional group manipulation, aldehyde *863* was photolyzed to induce "homo-Norrish" cyclization and generation of the first disecododecahedrane derivative [447,448]. With PCC oxidation, ketone *864* was produced and again photocyclized. Subsequent removal of the tertiary hydroxyl group in *865* proved to be a simple feat. The resulting C_{2v}-symmetric hydrocarbon *866* proved to have pronounced internal stresses as revealed by x-ray analysis [449].



Scheme CIII

When the olefinic precursor to *866* was treated briefly with trifluoromethanesulfonic acid in dichloromethane solution, cyclization occurs with installation of the final dodecahedrane framework bond. The predominant product proved to be *867* in which methyl group migration has also taken place [448,450]. The D_{3d} symmetry of this first dodecahedrane was apparent from its spectral properties and nicely detailed

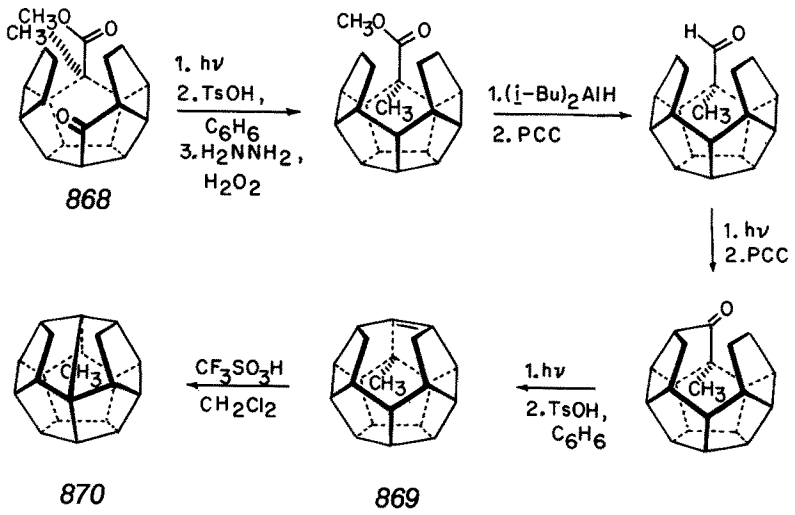
in its x-ray structure. In particular, the two alkyl groups are seen to cause only small distortions from pure dodecahedral symmetry.



867

2 Monomethyl Dodecahedrane

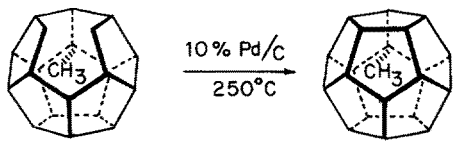
Paquette and coworkers have demonstrated that monoalkylation of dianion *860* proceeds with a kinetic preference for electrophilic capture at the ester enolate site. Thus, addition of limited amounts of methyl iodide to *860* affords *868* in 46 % isolated yield [451–453]. With this keto ester in hand, it proved an easy matter to elaborate secododecahedrene *869* in a manner paralleling that detailed above (Scheme CIV). When this olefin was exposed to strongly acidic conditions, however, a myriad of products resulted. Curiously, the "isododecahedrane" *870* proved to be the most prevalent of these. It will be noted that a new sigma bond has indeed been introduced, but at right angles to the desired direction! The total polyquinane nature of *870* was confirmed by x-ray analysis [454]. By this technique, the twinned norbornyl character of its methano bridges was noted to project the associated internal hydrogens well beyond intramolecular contact range. Evidently, the release of very serious nonbonded interactions provides the necessary driving force for its unusual process.



868 *870* *869*

Scheme CIV

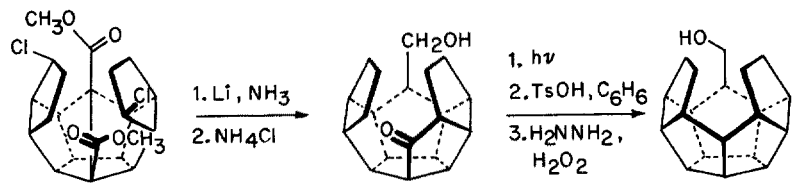
This complication was nicely bypassed by subjecting secododecahedrane *871* to dehydrogenation. Heating an intimate mixture of *871* with 50 times its weight of 10% Pd—C (previously saturated with hydrogen) at 250 °C produces the desired *872* in 35–40% yield [451, 454].



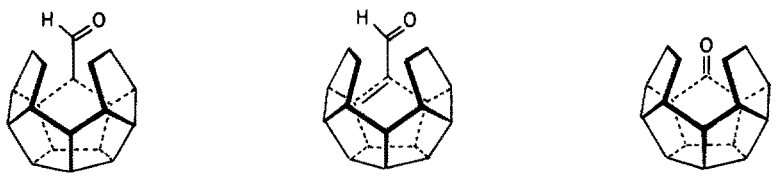
871 *872*

3 The Parent $C_{20}H_{20}$ Hydrocarbon

By suitable modification of reaction conditions, it was found possible to reduce *859* to keto alcohol *873* [455]. The subsequent conversion of this intermediate to *874* proceeded without event. However, *874* could not be oxidized to aldehyde *875*. Overoxidation to produce *876* or *877* (Jones conditions) invariably was observed due to the extreme sensitivity of *874*. This potentially expedient route to dodecahedrane therefore had to be abandoned and recourse made to blocking group methodology.

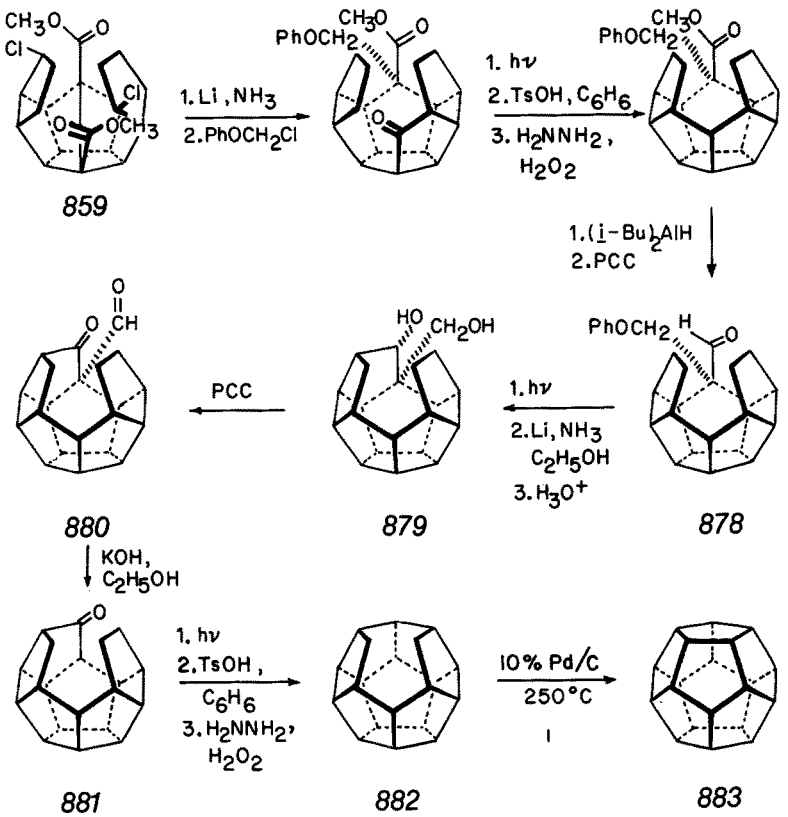


859 *873* *874*



875 *876* *877*

The phenoxymethyl group was selected as the pendant sidechain because it could be introduced via S_N2 methodology, should survive those chemical transformations required to construct framework bonds, and not encourage photodecarbonylation of the tertiary triseco aldehyde. These expectations were fulfilled as outlined in Scheme CV [455]. Furthermore, reduction of *878* under Birch conditions and subsequent acid hydrolysis gave diol *879* whose oxidation led to keto aldehyde *880*. Retroaldol cleavage within *880* afforded *881* which was transformed via *882* into the highly symmetric target *883*.



Scheme CV

In line with expectation, the ^{1}H and ^{13}C NMR spectra of dodecahedrane (in $CDCl_3$) are characterized by singlets (δ 3.38; 66.93 ppm). Only 3 infrared and 8 Raman bands are observed. The crystal dynamics of this substance which are witnessed upon heating to >400 °C are fascinating [455].

X References

1. Paquette, L. A.: Topics in Current Chemistry *79*, 41 (1979)
2. Froborg, J., Magnusson, G.: J. Am. Chem. Soc. *100*, 6728 (1978)
3. Danishefsky, S., Etheredge, S. J.: J. Org. Chem. *47*, 4791 (1982)
4. Becker, D., Brodsky, N. C., Kalo, J.: ibid. *43*, 2557 (1978)
5. Geetha, G., Raju, N., Rajagopalan, K., Swaminathan, S.: Ind. J. Chem. *B20*, 238 (1981)
6. Klipa, D. K., Hart, H. J.: J. Org. Chem. *46*, 2815 (1981)
7. Trost, B. M., Vincent, J. E.: J. Am. Chem. Soc. *102*, 5680 (1980)
8. Begley, M. J., Cooper, K., Pattenden, G.: Tetrahedron Lett. 257 (1981): Tetrahedron *37*, 4503 (1981)
9. Marfat, A., Helquist, P.: Tetrahedron Lett. 4217 (1978)
10. Leone-Bay, A., Paquette, L. A.: J. Org. Chem. *47*, 4173 (1982)
11. Barco, A., Benetti, S., Pollini, G. P., Baraldi, P. G., Gandolfi, C.: ibid. *45*, 4776 (1980)
12. Burke, S. D., Murtiashaw, C. W., Dike, M. S.: ibid. *47*, 1349 (1982)
13. Harre, M., Winterfeldt, E.: Chem. Ber. *115*, 1437 (1982)
14. Quesada, M. L., Schlessinger, R. H., Parsons, W. H.: J. Org. Chem. *43*, 3968 (1978)
15. Tice, C. M., Heathcock, C. H.: ibid. *46*, 9 (1981)
16. House, H. O., Sayer, T. S. B., Yau, C. C.: ibid. *43*, 2153 (1978)
17. Knapp, S., O'Connor, U., Mobilio, D.: Tetrahedron Lett. 4557 (1980)
18. Gandhi, P.: Chem. Ind. (London) 290 (1980)
19. Marino, J. P., Linderman, R. J.: J. Org. Chem. *46*, 3696 (1981)
20. Trost, B. M., Curran, D. P.: J. Am. Chem. Soc. *102*, 5699 (1980)
21. Trost, B. M., Curran, D. P.: Tetrahedron Lett. 4929 (1981)
22. Brooks, D. W., Grothans, P. G., Irwin, W. L.: J. Org. Chem. *47*, 2820 (1982)
23. Crandall, J. K., Magaha, H. S., Widener, R. K., Tharp, G. A.: Tetrahedron Lett. 4807 (1980); Crandall, J. K., Magaha, H. S., Henderson, M. A., Widener, R. K., Tharp, G. A.: J. Org. Chem. *47*, 5372 (1982)
24. Garst, M. E., Johnson, A. T.: Tetrahedron Lett. 4811 (1980); Garst, M. E., McBride, B. J., Johnson, A. T.: J. Org. Chem. *48*, 8 (1983)
25. Weiss, U., Edwards, J. M.: Tetrahedron Lett. 4885 (1968)
26. Bertz, S. H., Rihs, G., Woodward, R. B.: Tetrahedron *38*, 63 (1982)
27. Gawish, A., Mitschka, R., Cook, J. M., Weiss, U.: Tetrahedron Lett. 211 (1981)
28. Avasthi, K., Deshpande, M. N., Han, W.-C., Cook, J. M., Weiss, U.: ibid. 3475 (1981)
29. Mitschka, R., Oeldrich, J., Takahashi, K., Cook, J. M., Weiss, U., Silverton, J. V.: Tetrahedron *37*, 4521 (1981); Han, W. C., Takahashi, K., Cook, J. M., Weiss, U., Silverton, J. F.: J. Am. Chem. Soc. *304*, 318 (1982)
30. Trost, B. M.: Tetrahedron *33*, 2615 (1977); Pure Appl. Chem. *51*, 787 (1979)
31. Trost, B. M., Chan, D. M. T.: J. Am. Chem. Soc. *101*, 6429 (1979)
32. Trost, B. M., Chan, D. M. T.: ibid. *103*, 5972 (1981)
33. Trost, B. M., Chan, D. M. T.: ibid. *104*, 3733 (1982)
34. Binger, P., Bentz, P.: Angew. Chem., Int. Ed. Engl. *8*, 622 (1982)
35. Wollenberg, R. H., Goldstein, J. E.: Synthesis 757 (1980)
36. Chan, T. H., Baldassarre, A., Massuda, D.: ibid. 801 (1976)
37. Taylor, R. T., Degenhardt, C. R., Melega, W. P., Paquette, L. A.: Tetrahedron Lett. 159 (1977)

38. Chamberlin, A. R., Stemke, J. E., Bond, F. T.: J. Org. Chem. *43*, 147 (1978)
39. Fristad, W. E., Dime, D. S., Bailey, T. R., Paquette, L. A.: Tetrahedron Lett. 1999 (1979); Paquette, L. A., Fristad, W. E., Dime, D. S., Bailey, T. R.: J. Org. Chem. *45* 3017 (1980)
40. Cooke, F., Moerck, R., Schwindeman, J., Magnus, P.: ibid. *45*, 1046 (1980)
41. Magnus, P., Quagliato, D. A., Huffman, J. C.: Organometallics *1*, 1240 (1982)
42. Denmark, S. E., Jones, T. K.: J. Am. Chem. Soc. *104*, 2642 (1982)
43. Danheiser, R. L., Carini, D. J., Basak, A.: ibid. *103*, 1604 (1981)
44. Smith, A. B., III, Toder, B. H., Branca, S. J., Dieter, R. K.: ibid. *103*, 1996 (1981)
45. Basu, B., Maity, S. K., Mukherjee, D.: Synth. Commun. *11*, 803 (1981)
46. Callant, P., De Wilde, H., Vandewalle, M.: Tetrahedron *37*, 2079 (1981)
47. Callant, P., Ongena, R., Vandewalle, M.: ibid. *37*, 2085 (1981)
48. Greene, A. E., Deprés, J.-P.: J. Am. Chem. Soc. *101*, 4003 (1979)
49. Annis, G. D., Paquette, L. A.: ibid. *104*, 4504 (1982)
50. Knapp, S., Trope, A. F., Ornaf, R. M.: Tetrahedron Lett. 4301 (1980)
51. Paquette, L. A., Farkas, E., Galemmo, R.: J. Org. Chem. *46*, 5434 (1981)
52. Roberts, M. R., Schlessinger, R. H.: J. Am. Chem. Soc. *101*, 7626 (1979)
53. Ogino, T., Mochizuki, K.: Chem. Lett. 443 (1979)
54. Whitesell, J. K., Minton, M. A., Flanagan, W. G.: Tetrahedron *37*, 4451 (1981)
55. Apparu, M., Barrelle, M.: ibid. *34*, 1817 (1978)
56. Haufe, G., Kleinpeter, E., Muhlstadt, M., Graffe, J.: Monatsh. Chem. *109*, 575 (1978)
57. Tolstikov, G. A., Kanzafarov, F. Y., Dzhemilev, U. M., Sangalov, Y. A.: Neftekhimiya *20*, 674 (1980)
58. Snider, B. B., Rodini, D. J., Kirk, T. C., Cordova, R.: J. Am. Chem. Soc. *104*, 555 (1982)
59. Nagendrappa, G.: Tetrahedron *38*, 2429 (1982)
60. Gausing, W., Wilke, G.: Angew. Chem., Int. Ed. Engl. *17*, 371 (1978)
61. Petersen, H., Meier, H.: Chem. Ber. *113*, 2383 (1980)
62. Daniels, R. G., Paquette, L. A.: J. Org. Chem. *46*, 2901 (1981)
63. Baird, M. S., Nethercott, W., Reese, C. B.: J. Chem. Soc., Chem. Commun. 224 (1982)
64. Hudlicky, T., Sheth, J. P., Gee, V., Barnvos, D.: Tetrahedron Lett. 4889 (1979)
65. Hudlicky, T., Koszyk, F. J.: ibid. 2487 (1980)
66. Hudlicky, T., Koszyk, F. J., Kutchan, T. M., Sheth, J. P.: J. Org. Chem. *45*, 5020 (1980)
67. Beckwith, A. L. J., Phillipou, G., Serelis, A. K.: Tetrahedron Lett. 2811 (1981)
68. Wolff, S., Agosta, W. C.: J. Chem. Res. 578 (1981)
69. Schore, N. E., Croudace, M. C.: J. Org. Chem. *46*, 5436 (1981)
70. Brulé, D., Chalchat, J.-C., Garry, R.-P., Lacroix, G., Michet, A., Vessière, R.: Bull. Soc. Chim. France, II-57 (1981)
71. Trost, B. M., Schudder, P. H.: J. Org. Chem. *46*, 506 (1981)
72. Paquette, L. A., Wells, G. J., Horn, K. A., Yan, T.-H.: Tetrahedron Lett. 263 (1982)
73. Paquette, L. A., Wells, G. J., Horn, K. A., Yan, T.-H.: Tetrahedron, *39*, 913 (1983)
74. Drouin, J., Leyendecker, F., Conia, J. M.: ibid. *36*, 1195 (1980)
75. Drouin, J., Leyendecker, F., Conia, J. M.: ibid. *36*, 1203 (1980)
76. Plavac, F., Heathcock, C. H.: Tetrahedron Lett. 2115 (1979)
77. Trost, B. M., Warner, R. W.: J. Am. Chem. Soc. *304*, 6112 (1982)
78. Karpf, M., Dreiding, A. S.: Helv. Chim. Acta *62*, 852 (1979)
79. Karpf, M., Huguet, J., Dreiding, A. S.: ibid. *65*, 13 (1982)
80. Japenga, J., Klumpp, G. W., Schakel, M.: Tetrahedron Lett. 1869 (1982)
81. Hoffmann, H. M. R., Vathke-Ernst, H.: Chem. Ber. *114*, 2898 (1981)
82. Strapersma, J., Rood, I. D. C., Klumpp, G. W.: Tetrahedron *38*, 2201 (1982)
83. Shea, K. J., Wise, S.: Tetrahedron Lett. 2283 (1978)
84. Kirmse, W., Richarz, U.: Chem. Ber. *111*, 1883, 1895 (1978)
85. Graham, S. H., James, H. A., Suavansri, T.: J. Chem. Res. (S), 292 (1980)
86. Nee, M., Roberts, J. D.: J. Org. Chem. *46*, 67 (1981)
87. Olah, G. A., Fung, A. P., Rawdah, T. N., Surya Prakash, G. K.: J. Am. Chem. Soc. *103*, 4646 (1981)
88. Huston, R., Rey, M., Dreiding, A. S.: Helv. Chim. Acta *65*, 1563 (1982)
89. Sakkers, P. J. D., Vankan, J. M. J., Klunder, A. J. H., Zwanenburg, B.: Tetrahedron Lett. 897 (1979)

90. Sasaki, K., Kushida, T., Iyoda, M., Oda, M.: ibid. 2117 (1982)
91. Oda, M., Oikawa, H., Kanao, Y., Yamamuro, A.: ibid. 4905 (1978)
92. Hayano, K., Ohfune, Y., Shirahama, H., Matsumoto, T.: Chem. Lett. 1301 (1978)
93. Hayano, K., Ohfune, Y., Shirahama, H., Matsumoto, T.: Helv. Chim. Acta *64*, 1347 (1981)
94. Balasubramanian, R., Chandrasekhar, S., Rajagopalan, K., Swaminathan, S.: Tetrahedron *34*, 1561 (1978)
95. Geetha, K. Y., Rajagopalan, K., Swaminathan, S.: ibid. *34*, 2201 (1978)
96. Oppolzer, W., Bird, T. G. C.: Helv. Chim. Acta *62*, 1199 (1979)
97. Danheiser, R. L., Martinez-Davila, D., Auchus, R. J., Kadonaga, J. T.: J. Am. Chem. Soc. *103*, 2443 (1981)
98. Heine, H. G., Hartmann, W.: Angew. Chem., Int. Ed. Engl. *14*, 698 (1975)
99. Demuth, M., Raghavan, P. R., Carter, C., Nakano, K., Schaffner, K.: Helv. Chim. Acta *63*, 2434 (1980)
100. Mehta, G., Srikrishna, A.: Tetrahedron Lett. 3187 (1979)
101. Lyle, T. A., Frei, B.: Helv. Chim. Acta *64*, 2598 (1981)
102. Yoshioka, M., Ishii, K., Wolf, H. R.: ibid. *63*, 571 (1980)
103. Salomon, R. G., Ghosh, S., Zagorski, M. G., Reitz, M.: J. Org. Chem. *47*, 829 (1982)
104. Osuka, A.: ibid. *47*, 3131 (1982)
105. Cantrell, T. S.: ibid. *46*, 2674 (1981)
106. Saito, I., Shimozono, K., Matsuura, T.: J. Am. Chem. Soc. *102*, 3948 (1980); *105*, 963 (1983)
107. Woolsey, N. F., Radonovich, L. H., Saad, F. M., Koch, F. J.: J. Org. Chem. *44*, 2483 (1979)
108. Goto, S., Takamuku, S., Sakurai, H., Inoue, Y., Hakushi, T.: J. Chem. Soc. Perkin II, 1678 (1980)
109. Brandes, D., Lange, F., Sustmann, R.: Tetrahedron Lett. 265 (1980)
110. Brinker, U. H., Fleischhauer, I.: Angew. Chem., Int. Ed. Engl. *19*, 304 (1980); Tetrahedron *37*, 4495 (1981)
111. Kulagowski, J. J., Moody, C. J., Rees, C. W.: J. Chem. Soc., Chem. Commun., 548 (1982)
112. McRae, J., Moss, V. A., Raphael, R. A.: Tetrahedron *38*, 2097 (1982)
113. Hafner, K., Lindner, H. J., Ude, W.: Angew. Chem., Int. Ed. Engl. *18*, 161 (1979)
114. Hafner, K., Lindner, H. J., Ude, W.: ibid. *18*, 162 (1979)
115. Slongo, M., Kronig, P., Neuenschwander, M.: Makromol. Chem. *180*, 259 (1979)
116. Schore, N. E., LaBelle, B. E.: J. Org. Chem. *46*, 2306 (1981)
117. Bryce-Smith, D., Gilbert, A.: Tetrahedron *33*, 2459 (1977);
Gilbert, A.: Pure Appl. Chem. *52*, 2669 (1980)
118. Bryce-Smith, D., Foulger, B., Forrester, J., Gilbert, A., Orger, B. H., Tyrrell, H. M.: J. Chem. Soc. Perkin I, 55 (1980)
119. Gilbert, A., Wahid bin Samsudin, M.: ibid. 1118 (1980)
120. Jans, A. W. H., van Arkel, B., van Dijk-Knepper, J. J., Cornelisse, J.: Tetrahedron Lett. 3827 (1982)
121. Jans, A. W. H., van Dijk-Knepper, J. J., Cornelisse, J.: Rec. Trav. Chim. Pays-Bas *101*, 275 (1982)
122. Jans, A. W. H., Cornelisse, J.: ibid. *100*, 213 (1981)
123. Sheridan, R. S.: Tetrahedron Lett. 267 (1982)
124. Bryce-Smith, D., Fenton, G. A., Gilbert, A.: ibid. 2697 (1982)
125. Pallmer, M., Morrison, H.: J. Org. Chem. *45*, 798 (1980)
126. Gilbert, A., Taylor, G. N.: J. Chem. Soc. Perkin I, 1761 (1980)
127. Rule, M., Lazzara, M. G., Berson, J. A.: J. Am. Chem. Soc. *101*, 7091 (1979)
128. Salinaro, R. F., Berson, J. A.: ibid. *101*, 7091 (1979)
129. Corwin, L. R., McDaniel, D. M., Bushby, R. J., Berson, J. A.: ibid. *102*, 276 (1980)
130. Duncan, C. D., Corwin, L. R., Davis, J. H., Berson, J. A.: ibid. *102*, 2350 (1980)
131. Siemionko, R., Show, A., O'Connell, G., Little, R. D., Carpenter, B. K., Shen, L., Berson, J. A.: Tetrahedron Lett. 3529 (1978)
132. Salinaro, R. F., Berson, J. A.: ibid. 1447 (1982)
133. Rule, M., Salinar, R. F., Pratt, D. R., Berson, J. A.: J. Am. Chem. Soc. *104*, 2223 (1982)
134. Little, R. D., Brown, L.: Tetrahedron Lett. 2203 (1980)
135. Little, R. D., Myong, S. O.: ibid. 3339 (1980)
136. Gund, P., Gund, T. M.: J. Am. Chem. Soc. *103*, 4458 (1981)

137. Hudlicky, T., Short, R. P.: J. Org. Chem. *47*, 1522 (1982)
138. Burke, S. D., Grieco, P. A.: Org. React. *26*, 361 (1979)
139. Ceccherelli, P., Curini, M., Tingoli, M., Pellicciari, R.: J. Chem. Soc. Perkin I 1924 (1980)
140. Hudlicky, T., Kutchen, T.: Tetrahedron Lett. 691 (1980)
141. Satyanarayana, G. O. S. V., Kanjilal, P. R., Ghatak, U. R.: J. Chem. Soc., Chem. Commun. 746 (1981);
Satyanarayana, G. O. S. V., Roy, S. C., Ghatak, U. R.: J. Org. Chem. *47*, 5353 (1982);
Roy, S. C., Satyanarayana, G. O. S. V., Ghatak, U. R.: ibid. *47*, 5361 (1982)
142. Little, R. D., Bukhari, A., Venegas, M. G.: Tetrahedron Lett. 305 (1979)
143. Little, R. D., Muller, G. W.: J. Am. Chem. Soc. *101*, 7129 (1979)
144. Kueh, J. S. H., Mellor, M., Pattenden, G.: J. Chem. Soc. Chem. Commun. 5 (1978); J. Chem. Soc. Perkin I 1052 (1981)
145. Mehta, G., Reddy, A. V.: J. Chem. Soc. Chem. Commun. 756 (1981)
146. Mehta, G., Srikrishna, A., Reddy, A. V., Nair, M. S.: Tetrahedron *37*, 4543 (1981)
147. Mehta, G., Rao, K. S., Bhadbhade, M. M., Venkatesan, K.: J. Chem. Soc. Chem. Commun. 755 (1981)
148. Mehta, G., Reddy, A. V., Srikrishna, A.: Tetrahedron Lett. 4863 (1979)
149. Tamaru, Y., Yoshida, A.: J. Org. Chem. *44*, 1188 (1979)
150. Demuth, M., Raghavan, P. R.: Helv. Chim. Acta *62*, 2338 (1979)
151. Demuth, M., Mikhail, G., George, M. V.: ibid. *64*, 2759 (1981)
152. Miller, R. D., McKean, D. R.: J. Org. Chem. *46*, 2412 (1982)
153. Kon, K., Isoe, S.: Tetrahedron Lett. 3399 (1980)
154. Trigo, G. G., Avendano, C., Santos, E., Edward, J. T., Wong, S. C.: Can. J. Chem. *57*, 1456 (1979)
155. Brown, H. C., Hammar, W. J.: Tetrahedron *34*, 3405 (1978)
156. Docken, A. M.: J. Org. Chem. *46*, 4097 (1981)
157. Trost, B. M., Curran, D. P.: Tetrahedron Lett. 5023 (1981)
158. Tsuzuki, K., Hashimoto, H., Shirahama, H., Matsumoto, T.: Chem. Lett. 1469 (1977)
159. Crow, A. B., Borden, W. T.: J. Am. Chem. Soc. *101*, 6666 (1979)
160. Trost, B. M., Buhlmayer, P., Mao, M.: Tetrahedron Lett. 1443 (1982)
161. Trost, B. M., Mao, M. K. T.: ibid. *3523* (1980)
162. Nicolaou, K. C., Magolda, R. L., Sipio, W. J.: Synthesis 982 (1979)
163. Rao, R. R., Bhattacharya, S., Panigrahi, R.: Ind. J. Chem. *18B*, 28 (1979)
164. Rao, R. R., Bhattacharya, S., Panigrahi, R.: ibid. *18B*, 117 (1979)
165. Rao, R. R., Panigrahi, R.: ibid. *15B*, 681 (1977)
166. Whitesell, J. K., Helbling, A. M.: J. Org. Chem. *45*, 4135 (1980)
167. Whitesell, J. K., Matthews, R. S., Minton, M. A., Helbling, A. M.: J. Am. Chem. Soc. *103*, 3468 (1981)
168. Kopecky, K. R., Lockwood, P. A., Gomez, R. R., Ding, J.: Can. J. Chem. *59*, 851 (1981)
169. Garratt, D. G., Kabo, A.: ibid. *58*, 1030 (1980)
170. Corey, E. J., Kabo, A.: ibid. *58*, 1030 (1980)
171. Kuritani, H., Takaoka, Y., Shingu, K.: J. Org. Chem. *44*, 452 (1979)
172. Salomon, M. F., Pardo, S. N., Salomon, R. G.: J. Am. Chem. Soc. *102*, 2473 (1980)
173. Pardo, S. N., Ghosh, S., Salomon, R. G.: Tetrahedron Lett. 1885 (1981)
174. Demuth, M., Chandrasekhar, S., Nakano, K., Raghavan, P. R., Schaffner, K.: Helv. Chim. Acta *63*, 2440 (1980)
175. Haslanger, M. F., Ahmed, S.: J. Org. Chem. *46*, 4808 (1981)
176. Shibasaki, M., Iseki, K., Ikegami, S.: Synth. Commun. *10*, 545 (1980)
177. Gardette, D., Lhomme, J.: J. Org. Chem. *44*, 2315 (1979)
178. Danishefsky, S., Kahn, M.: Tetrahedron Lett. 485 (1981)
179. Danishefsky, S., Kahn, M.: ibid. 489 (1981)
180. Sugihara, Y., Sugimura, T., Murata, I.: J. Am. Chem. Soc. *103*, 6738 (1981)
181. Marini-Bettolo, G., Sahoo, S. P., Poulton, G. A., Tsai, T. Y. R., Wiesner, K.: Tetrahedron *36*, 719 (1980)
182. Exon, C., Noobs, M., Magnus, P.: ibid. *37*, 4519 (1981)
183. Laishev, V. Z., Petrov, M. L., Petrov, A. A.: Zh. Org. Khim (USSR) *18*, 514 (1982)
184. Fujikura, Y., Takaishi, N., Inamoto, Y.: Tetrahedron *37*, 4465 (1981)

185. Danishefsky, S., Vaughan, K., Gadwood, R. C., Tsuzuki, K., Springer, J. P.: Tetrahedron Lett. 2625 (1980)
186. Bell, T. W., Cheng, P. G., Newcomb, M., Cram, D. J.: J. Am. Chem. Soc. *104*, 5185 (1982)
187. Whitesell, J. K., Matthews, R. S.: J. Org. Chem. *42*, 3878 (1977)
188. Hudlicky, T., Koszyk, F. J., Dochwat, D. M., Cantrell, G. L.: ibid. *46*, 2911 (1981)
189. Venegas, M. G., Little, R. D.: Tetrahedron Lett. 309 (1979)
190. Takeuchi, S., Ogawa, Y., Yonehara, H.: ibid. 2737 (1969)
191. Kuritani, H., Imajo, S., Shingu, K., Nakagawa, M.: ibid. 1697 (1979)
192. Nakajima, T., Toyota, A., Kataoka, M.: J. Am. Chem. Soc. *104*, 5610 (1982)
193. Bischof, P., Gleiter, R., Hafner, K., Knauer, K. H., Spanget-Larsen, J., Süss, H. U.: Chem. Ber. *111*, 932 (1978)
194. Fürderer, P., Gerson, F., Hafner, K.: Helv. Chim. Acta *61*, 2974 (1978)
195. Fürderer, P., Gerson, F., Rabinovitz, M., Willner, I.: ibid. *61*, 2981 (1978)
196. Harris, P. G., Howard, J. A. K., Knox, S. A. R., McKinney, R. J., Phillips, R., Stone, F. G. A., Woodward, P.: J. Chem. Soc. Dalton 403 (1978)
197. McGhinchey, M. J.: Inorg. Chim. Acta *49*, 125 (1981)
198. Rull, M., Serratosa, F., Vilarrasa, J.: Tetrahedron Lett. 4549 (1977); An. Quim., Ser. C *76*, 226 (1980)
199. Paquette, L. A., Doehner, R. F., Jr., Jenkins, J. A., Blount, J. F.: J. Am. Chem. Soc. *102*, 1188 (1980)
200. Askani, R., Littmann, M.: Tetrahedron Lett. 3651 (1982)
201. Quast, H., Christ, J., Görlach, Y., von der Saal, W.: ibid. 3653 (1982)
202. Quast, H., Görlach, Y., Meichsner, G., Peters, K., Peters, E.-M., von Schnering, H. G.: ibid. 4677 (1982)
203. Askani, R., Kirsten, R., Dugall, B.: Tetrahedron *37*, 4437 (1981)
204. Askani, R., Kirsten, R.: Tetrahedron Lett. 1491 (1979)
205. Stapersma, J., Knipers, P., Klumpp, G. W.: Rec. Trav. Chim. Pays-Bas *101*, 213 (1982)
206. Bender, C. O., Bengtson, D. L., Dolman, D., Herle, C. E. L., O'Shea, S. F.: Can. J. Chem. *60*, 1942 (1982)
207. Birnberg, G. H., Paquette, L. A.: J. Org. Chem. *45*, 5379 (1980)
208. Nickon, A., Kwasnik, H., Swartz, T., Williams, R. O., DiGiorgio, J. B.: J. Am. Chem. Soc. *87*, 1613 (1965)
209. Nickon, A., Kwasnik, H. R., Methew, C. T., Swartz, T. D., Williams, R. O., DiGiorgio, J. B.: J. Org. Chem. *43*, 3904 (1978)
210. Bartlett, P. D., Blakeney, A. J., Kimura, M., Watson, W. H.: J. Am. Chem. Soc., *102*, 1383 (1980)
211. Paquette, L. A., Carr, R. V. C., Böhm, M. C., Gleiter, R.: ibid. *102*, 1186 (1980); *102*, 6218 (1980)
212. Watson, W. H., Galloy, J., Bartlett, P. D., Roof, A. A. M.: ibid. *103*, 2022 (1981)
213. Paquette, L. A., Hayes, P. C., Charumilind, P., Böhm, M. C., Gleiter, R.: ibid. *105*, 3148 (1983)
214. Paquette, L. A., Charumilind, P., Böhm, M. C., Gleiter, R., Bass, L. S., Clardy, J.: ibid. *105*, 3136 (1983)
215. Paquette, L. A., Schaefer, A., Blount, J. F.: ibid. *105*, 3642 (1983)
216. Pinkerton, A. A., Schwarzenbach, D., Stibbard, J. H. A., Carrupt, P.-A., Vogel, P.: ibid. *103* 2095 (1981)
217. Paquette, L. A., Ohkata, K., Carr, R. V. C.: ibid. *102*, 3303 (1980)
218. Paquette, L. A., Carr, R. V. C.: ibid. *102*, 7553 (1980)
219. Bartlett, P. D., Roof, A. A. M., Winter, W. J.: ibid. *103*, 6520 (1981)
220. Paquette, L. A., Kravetz, T. M., Böhm, M. C., Gleiter, R.: J. Org. Chem. *48*, 1250 (1983)
221. Hagenbuch, J.-P., Vogel, P., Pinkerton, A. A., Schwarzenbach, D.: Helv. Chim. Acta *64*, 1818 (1981)
222. Paquette, L. A., Charumilind, P.: J. Am. Chem. Soc. *104*, 3749 (1982)
223. Paquette, L. A.: in Stereochemistry and Reactivity of Pi Systems, (Watson, W. H., ed.), Verlag Chemie, in press
224. Gleiter, R., Paquette, L. A.: Accounts Chem. Res., *16*, 328 (1983)

225. Paquette, L. A., Charumilind, P., Kravetz, T. M., Böhm, M. C., Gleiter, R.: J. Am. Chem. Soc. *105*, 3126 (1983)
226. Subramanyam, R., Bartlett, P. D., Watson, W. H., Galloy, J.: J. Org. Chem. *47*, 4491 (1982)
227. Paquette, L. A., Williams, R. V., Carr, R. V. C., Charumilind, P., Blount, J. F.: ibid. *47*, 4566 (1982)
228. Wiseman, J. R., Vanderbilt, J. J., Butler, W. M.: ibid. *45*, 667 (1980)
229. Jäggi, F. J., Ganter, C.: Helv. Chim. Acta *63*, 2087 (1980)
230. Majerski, Z., Djigas, S., Vinkovic, V.: J. Org. Chem. *44*, 4064 (1979)
231. Jäggi, F. J., Buchs, P., Ganter, C.: Helv. Chim. Acta *63*, 872 (1980)
232. Majerski, Z., Janjatovic, J.: Tetrahedron Lett. 2977 (1979)
233. Schleyer, P. von R., Grubmüller, P., Meier, W. F., Vostrowsky, O.: ibid. 921 (1980)
234. Jäggi, F. J., Ganter, C.: Helv. Chim. Acta *63*, 214 (1980)
235. Aumann, L., Averbeck, H.: J. Organometal. Chem. *160*, 241 (1978)
236. Jäggi, F. J., Ganter, C.: Helv. Chim. Acta *63*, 866 (1980)
237. Schleyer, P. von R., Grubmüller, P., Maier, W. F., Skattebol, L., Holm, K. H.: Tetrahedron Lett. 921 (1980)
238. Cargill, R. L., Peet, N. P., Pond, D. M., Bundy, W. A., Sears, A. G.: J. Org. Chem. *45*, 3999 (1980)
239. Bishop, R., Landers, A. E.: Austr. J. Chem. *32*, 2675 (1979)
240. Cargill, R. L., Dalton, J. R., O'Connor, S., Michels, D. G.: Tetrahedron Lett. 4465 (1978)
241. Cargill, R. L., Bushey, D. F., Dalton, J. R., Prasad, R. S., Dyer, R. D., Bordner, J.: J. Org. Chem. *46*, 3389 (1981)
242. Eaton, P. E., Jobe, P. G., Nyi, K.: J. Am. Chem. Soc. *102*, 6636 (1980)
243. Tobe, Y., Hayauchi, Y., Odaira, Y.: J. Org. Chem. *46*, 5219 (1981)
244. Maggio, J. E., Simmons, H. E. III, Kouba, J. K.: J. Am. Chem. Soc. *103*, 1579 (1981)
245. Simmons, H. E., III, Maggio, J. E.: Tetrahedron Lett. 287 (1981)
246. Paquette, L. A., Vazeux, M.: ibid. 291 (1981)
247. Bennér, S. A., Maggio, J. E., Simmons, H. E. III: J. Am. Chem. Soc. *103*, 1581 (1981)
248. Lipkowitz, K. B., Larter, R. M., Boyd, D. B.: ibid. *102*, 85 (1980)
249. Sauers, R. R., Schinski, W., Mason, M. M.: Tetrahedron Lett. 79 (1969);
Sauers, R. R., Sickles, B. R.: ibid. 1067 (1970);
Sauers, R. R., Kelly, K. W., Sickles, B. R.: J. Org. Chem. *37*, 537 (1972)
250. Windhorst, J. C. A.: Ph. D. Dissertation, Univ. of Leiden, 1975
251. Park, H., Paquette, L. A.: J. Org. Chem. *45*, 5378 (1980)
252. Sauers, R. R., Kelly, K. W.: ibid. *45*, 5378 (1980)
253. Wiberg, K. B., Ellison, G. B., Wendolski, J. J.: J. Am. Chem. Soc. *98*, 1212 (1976)
254. Georgian, V., Saltzman, M.: Tetrahedron Lett. 4315 (1972)
255. Keese, R., Pfenninger, A., Roesle, A.: Helv. Chim. Acta *62*, 326 (1979)
256. Fritz, H., Weis, C. D., Winkler, T.: ibid. *58*, 1345 (1975)
257. Schori, H., Patil, B. B., Keese, R.: Tetrahedron *37*, 4457 (1981)
258. Dauben, W. G., Walker, D. M.: Tetrahedron Lett. 711 (1982)
259. Underwood, G. R., Ramamoorthy, B.: ibid. 4125 (1970)
260. Godleski, S. A., Schleyer, P. von R., Osawa, E., Kent, G. J.: J. Chem. Soc. Chem. Commun. 976 (1974)
261. Eaton, P. E., Hudson, R. A., Giordano, C.: ibid. 978 (1974)
262. Helmchen, G., Staiger, G.: Angew. Chem., Int. Ed. Engl. *16*, 116 (1977)
263. Nakazaki, M., Naemura, K., Arashiba, N.: J. Org. Chem. *43*, 689 (1978)
264. Eaton, P. E., Leipzig, B.: ibid. *43*, 2483 (1978)
265. Naemura, K., Nakazaki, M.: Bull. Chem. Soc. Japan *46*, 888 (1973);
Nakazaki, M., Naemura, K., Harite, S.: ibid. *48*, 1907 (1975)
266. Nakazaki, M., Naemura, K., Nakahara, S.: J. Org. Chem. *43*, 4745 (1978)
267. Nakazaki, M., Naemura, K.: ibid. *46*, 106 (1981)
268. Mislow, K.: J. Chem. Soc. Chem. Commun. 234 (1981)
269. Nakazaki, M., Naemura, K., Hokura, Y.: ibid. 1245 (1982)
270. Mehta, G., Srikrishna, A.: ibid. 218 (1982)
271. Bosse, D., deMeijere, A.: Chem. Ber. *111*, 2223 (1978)
272. Bosse, D., deMeijere, A.: ibid. *111*, 2243 (1978)

273. Paquette, L. A., Kearney, F. R., Drake, A. F., Mason, S. F.: J. Am. Chem. Soc. *103*, 5064 (1981)
274. Deslongchamps, P., Soucy, P.: Tetrahedron *37*, 4385 (1981)
275. Deslongchamps, P., Cheriyan, U. O., Lambert, Y., Mercier, J.-C., Ruest, L., Russo, R., Soucy, P.: Can. J. Chem. *56*, 1687 (1978)
276. Codding, P. W., Kerr, K. A., Oudeman, A., Sorensen, T. S.: J. Organometal. Chem. *232*, 193 (1982)
277. Roberts, W. P., Shoham, G.: Tetrahedron Lett. 4895 (1981)
278. Inamoto, Y., Aigami, K., Fujikura, Y., Takaishi, N., Tsuchihashi, K.: J. Org. Chem. *44*, 854 (1979)
279. DuVernet, R. B., Glanzmann, M., Schröder, G.: Tetrahedron Lett. 3071 (1978)
280. Gilchirst, T. L., Reese, C. W., Tuddenham, D.: J. Chem. Soc. Chem. Commun. 689 (1980)
281. Gilchrist, T. L., Rees, C. W., Tuddenham, D., Williams, D. J.: ibid. 691 (1980)
282. Gilchrist, T. L., Tuddenham, D., McCague, R., Moody, C. J., Rees, C. W.: ibid. 657 (1981)
283. McCague, R., Moody, C. J., Rees, C. W.: ibid. 497 (1982)
284. Lidert, Z., Rees, C. W.: ibid. 499 (1982)
285. McCague, R., Moody, C. J., Rees, C. W.: ibid. 622 (1982); Rzepa, H. S.: J. Chem. Res. (S), 324 (1982)
286. Garratt, P. J., White, J. F.: J. Org. Chem. *42*, 1733 (1977)
287. Eaton, P. E., Mueller, R. H.: J. Am. Chem. Soc. *94*, 1014 (1972)
288. Nickon, A., Pandit, G. D.: Tetrahedron Lett. 3663 (1968)
289. Paquette, L. A., Browne, A. R., Doecke, C. W., Williams, R. V.: J. Am. Chem. Soc., *105*, 4113 (1983)
290. Hirao, K., Ohuchi, Y., Yonemitsu, O.: J. Chem. Soc. Chem. Commun. 99 (1982)
291. Bohlmann, F., Abraham, W. R.: Phytochemistry *18*, 668 (1979)
292. Bohlmann, F., Van, N. L., Pham, T. V. C., Jakupovic, J., Schuster, A., Zabel, V., Watson, W. H.: ibid. *18*, 1831 (1979)
293. Bohlmann, F., Jakupovic, J.: ibid. *19*, 259 (1980)
294. Bohlmann, F., Zdero, C., Bohlmann, R., King, R. M., Robinson, H.: ibid. *19*, 579 (1980)
295. Bohlmann, F., Suding, H., Cuatrecasas, J., Robinson, H., King, R. M.: ibid. *19*, 2399 (1980)
296. Bohlmann, F., Zdero, C., Jakupovic, J., Robinson, H., King, R. M.: ibid. *20*, 2239 (1981)
297. Bohlmann, F., Zdero, C.: ibid. *20*, 2529 (1981)
298. Bohlmann, F., Zdero, C.: ibid. *21*, 139 (1982)
299. Castillo, M., Loyola, L. A., Morales, G., Singh, I., Calvo, C., Holland, H. L., MacLean, D. B.: Can. J. Chem. *54*, 2893 (1976)
300. Loyola, L. A., Morales, G., Castillo, M.: Phytochemistry *18*, 1721 (1979)
301. Schmitz, R., Frahm, A. W., Kating, H.: ibid. *19*, 1477 (1980)
302. Dominquez, X. A., Cano, G., Franco, R., Villarreal, A. M., Watson, W. H., Zabel, V.: ibid. *19*, 2478 (1980)
303. Teresa, J. deP., SanFeliciano, A., Barrero, A. F., Medarde, M., Tome, F.: ibid. *20*, 166 (1981)
304. Solimabi, Fernandes, L., Kamat, S. Y., Paknikar, S. K.: Tetrahedron Lett. 2249 (1980)
305. Takeda, R., Naoki, H., Iwashita, T., Hirose, Y.: ibid. 5307 (1981)
306. Sakurai, H., Sakabe, N., Hirata, Y.: ibid. 6309 (1966)
307. Irikawa, H., Yamamura, S., Hirata, Y.: Tetrahedron *28*, 3727 (1972)
308. Sakurai, H., Irikawa, H., Yamamura, S., Hirata, Y.: Tetrahedron Lett. 2883 (1967)
309. Nakano, T., Saeki, Y.: ibid. 4791 (1967)
310. Toda, M., Irikawa, H., Yamamura, S., Hirata, Y.: Nippon Kagaku Zasshi *91*, 103 (1970)
311. Yamamura, S., Hirata, Y.: Tetrahedron Lett. 2849 (1974)
312. Corbett, R. E., Lauren, D. R., Weavers, R. T.: J. Chem. Soc. Perkin I 1774 (1979)
313. Piovetti, L., Combaut, G., Diara, A.: Phytochemistry, *19*, 2117 (1980)
314. Trifilieff, E., Band, L., Narula, A. S., Ourisson, G.: J. Chem. Res. (M), 601 (1978); (S), 64 (1978)
315. Kuo, Y.-H.: J. Chin. Chem. Soc. (Taipei) *27*, 177 (1980)
316. Subramanian, G. B. V., Mahajan, V. K., Ganesh, K. N.: Ind. J. Chem. *19B*, 169 (1980)
317. Subramanian, G. B. V., Chander, Y.: ibid. *20B*, 963 (1981)

318. Subramanian, G. B. V., Majajan, V. K., Ganesh, K. N.: ibid. *20B*, 967 (1981)
319. Tomita, B., Hirose, Y.: Phytochemistry *12*, 1409 (1973)
320. Kirtany, J. K., Paknikar, S. K.: Ind. J. Chem. *20B*, 438 (1981)
321. Singh, A. N., Mhaskar, V. V., Dev, S.: Tetrahedron *34*, 595 (1978)
322. See also Subramanian, G. B. V., Chander, Y., Nuzhat, R.: Proc. Ind. Acad. Sci. Chem. Sci. *90*, 61 (1981);
Subramanian, G. V. B., Majumdar, U., Nuzhat, R., Mahajan, V. K., Ganesh, K. N.: J. Chem. Soc. Perkin I, 2167 (1979)
323. Subramanian, G. B. V., Igbal, J., Mahajan, V. K., Nuzhat, R., Chander, Y., Jajumdar, U.: Ind. J. Chem. *18B*, 320 (1979)
324. Subramanian, G. B. V., Nuzhat, R., Mahajan, V. K.: ibid. *19B*, 173 (1980)
325. Bensadoun, N., Brun, P., Casanova, J., Waegell, B.: J. Chem. Res. *8*, 2601 (1981)
326. Elvidge, J. A., Laws, D. R. J., McGuinness, J. D., Shannon, P. V. R.: Chem. Ind. (London) 573, 671 (1974)
327. Elvidge, J. A., Laws, D. R. J., McGuinness, J. D., Davis, A.-M., Shannon, P. V. R.: Tetrahedron Lett. 2633 (1978); J. Chem. Soc. Perkin I, 1791 (1982)
329. Arigoni, D., Jeger, O.: Helv. Chim. Acta *37*, 881 (1954)
330. Joseph-Nathan, P., Roman, L. U., Hernandez, J. D., Taira, Z., Watson, W. H.: Tetrahedron *36*, 731 (1980)
331. Joseph-Nathan, P., Mendoza, V., Garcia, E.: ibid. *33*, 1573 (1977)
332. Sanchez, I. H., Yanez, R., Enriquez, R., Joseph-Nathan, P.: J. Org. Chem. *46*, 2818 (1981)
333. Bandaranayake, W. M., Banfield, J. E., Black, D. St. C., Fallon, G. D., Gatehouse, B. M.: Austr. J. Chem. *34*, 1655 (1981)
334. Nishimura, Y., Koyama, Y., Umezawa, S., Takeuchi, T., Ishizuka, M., Umezawa, H.: J. Antibiot. *4*, 404 (1980)
335. Nishimura, Y., Koyama, Y., Umezawa, S., Takeuchi, T., Ishizuka, M., Umezawa, H.: ibid. *4*, 393 (1980)
336. Nathu, N. K., Weavers, R. T.: Austr. J. Chem. *33*, 1589 (1980);
Eaton, P. J., Fawcett, J. M., Jogia, M. K., Weavers, R. T.: ibid. *33*, 371 (1980);
Eaton, P. J., Lauren, D. R., O'Connor, A. W., Weavers, R. T.: ibid. *34*, 1303 (1981)
337. Corbett, R. E., Couldwell, C. M., Lauren, D. R., Weavers, R. T.: J. Chem. Soc. Perkin I, 1791 (1979)
338. Deslongchamps, P., Lafontaine, J., Ruest, L., Soucy, P.: Can. J. Chem. *55*, 4117 (1977)
339. Stevens, K. E., Yates, P.: J. Chem. Soc. Chem. Commun. 990 (1980);
Yates, P., Stevens, K. E.: Tetrahedron *37*, 4401 (1981)
340. Yates, P., Stevens, K. E.: Can. J. Chem. *60*, 825 (1982)
341. Wender, P. A., Howbert, J. J.: J. Am. Chem. Soc. *103*, 668 (1981)
342. Coates, R. M., Shah, S. K., Mason, R. W.: ibid. *101*, 6765 (1979); *104*, 2198 (1982)
343. Han, Y.-K., Paquette, L. A.: J. Org. Chem. *44*, 3731 (1979);
Paquette, L. A., Han, Y.-K.: J. Am. Chem. Soc. *103*, 1831 (1981)
344. Welch, S. C., Chayabunjonglard, S.: J. Am. Chem. Soc. *101*, 6768 (1979);
Welch, S. C., Chayabunjonglard, S., Prakasa Rao, A. S. C.: J. Org. Chem. *45*, 4086 (1980)
345. Büchi, G., Mak, C.-P.: J. Am. Chem. Soc. *99*, 8073 (1977);
Buchi, G., Chu, P.-S.: J. Org. Chem. *43*, 3717 (1978)
346. Büchi, G., Chu, P.-S.: J. Am. Chem. Soc. *101*, 6767 (1979); Tetrahedron *37*, 4509 (1981)
347. Kodama, M., Kurihara, T., Sasaki, J., Ito, S.: Can. J. Chem. *57*, 3343 (1979)
348. Seto, H., Sasaki, T., Yonehara, H., Uzawa, J.: Tetrahedron Lett. 923 (1978)
349. Danishefsky, S., Hirama, M., Gombatz, K., Harayama, T., Berman, E., Schuda, P.: J. Am. Chem. Soc. *100*, 6536 (1978); *101*, 7020 (1979)
350. Parsons, W.-H., Schlessinger, R. H., Quesada, M. L.: ibid. *102*, 889 (1980)
351. Cane, D. E., Rossi, T.: Tetrahedron Lett. 2973 (1979)
352. Paquette, L. A., Schostarez, H., Annis, G. D.: J. Am. Chem. Soc. *103*, 6525 (1981);
Paquette, L. A., Annis, G. D., Schostarez, H.: ibid. *104*, 6646 (1982)
353. Paquette, L. A., Annis, G. D., Schostarez, H., Blount, J. F.: J. Org. Chem. *46*, 3768 (1981)
354. Ranieri, R. L., Calton, G. J.: Tetrahedron Lett. 499 (1978);
Calton, G. J., Ranieri, R. L., Espenshade, M. A.: J. Antibiot. *31*, 38 (1978)

355. Danishefsky, S., Vaughan, K., Gadwood, R. C., Tsuzuki, K.: J. Am. Chem. Soc. *102*, 4262 (1980); *103*, 4136 (1981)
356. Bornack, W. K., Bhagwat, S. S., Ponton, J., Helquist, P.: ibid. *103*, 4647 (1981)
357. Burke, S. D., Murtiashaw, C. W., Saunders, J. O., Dike, M. S.: ibid. *104*, 872 (1982)
358. Kende, A. S., Roth, B., Sanfilippo, P. G., Blacklock, T. J.: ibid. *104*, 5808 (1982)
359. Monti, S. A., Dean, T. R.: J. Org. Chem. *47*, 2679 (1982)
360. Smith, A. B., III, Wexler, B. A., Slade, J.: Tetrahedron Lett. 1631 (1982)
361. Moncada, S., Gryglewski, R., Buntnig, S., Vane, J. R.: Nature *263*, 663 (1976)
362. Moncada, S., Vane, J. R.: J. Med. Chem. *23*, 591 (1980)
363. Nicolaou, K. C., Sipio, W. J., Magolda, R. L., Seitz, S., Barnette, W. E.: J. Chem. Soc. Chem. Commun. 1067 (1978)
364. Kojima, K., Sakai, K.: Tetrahedron Lett. 3743 (1978)
365. Morton, D. R., Jr., Brokow, F. C.: J. Org. Chem. *44*, 2880 (1979)
366. Konishi, Y., Kawamura, M., Arai, Y., Hayashi, M.: Chem. Lett. 1437 (1979); Konishi, Y., Kawamura, M., Iguchi, Y., Arai, Y., Hayashi, M.: Tetrahedron *37*, 4391 (1981)
367. Shibasaki, M., Ueda, J., Ikegami, S.: Tetrahedron Lett. 433 (1979); Shibasaki, M., Iseki, K., Ikegami, S.: ibid. 169 (1980)
368. Yamazaki, M., Shibasaki, M., Ikegami, S.: Chem. Lett. 1245 (1981)
369. Skuballa, W., Vorbrüggen, H.: Angew. Chem., Int. Ed. Engl. *20*, 1046 (1981)
370. Newton, R. F., Wadsworth, A. H.: J. Chem. Soc. Perkin I, 823 (1982)
371. Aristoff, P. A.: J. Org. Chem. *46*, 1954 (1981)
372. Ohfune, Y., Shirahama, H., Matsumoto, T.: Tetrahedron Lett. 2795 (1976); Hayano, K., Ohfune, Y., Shirahama, H., Matsumoto, T.: ibid. 1991 (1978)
373. Ohfune, Y., Shirahama, H., Matsumoto, T.: ibid. 2869 (1976)
374. Misumi, S., Ohtsuka, T., Ohfune, Y., Sugita, K., Shirahama, H., Matsumoto, T.: ibid. 31 (1979); Misumi, S., Matsushima, H., Shirahama, H., Matsumoto, T.: Chem. Lett. 855 (1982)
375. Tatsuta, K., Akimoto, K., Kinoshita, M.: J. Am. Chem. Soc. *101*, 6116 (1979)
376. Nozoe, S., Furukawa, J., Sankawa, U., Shibata, S.: Tetrahedron Lett. 195 (1976)
377. Greene, A. E.: ibid. 3059 (1980)
378. Hudlicky, T., Kutchen, T. M., Wilson, S. R., Mao, D. T.: J. Am. Chem. Soc. *102*, 6351 (1980)
379. Little, R. D., Muller, G. W.: ibid. *103*, 2744 (1981)
380. Ley, S. V., Murray, P. J.: J. Chem. Soc. Chem. Commun. 1252 (1982)
381. Magnus, P., Quagliato, D. A.: Organometallics *1*, 1243 (1982)
382. Wender, P. A., Howbert, J. J.: Tetrahedron Lett. 3983 (1982)
383. Sheikh, Y. M., Singy, G., Kaisin, M., Eggert, H., Djerassi, C., Tursh, B., Daloze, D., Braekman, J. C.: Tetrahedron *32*, 1171 (1976); Ayanoglu, E., Gebreyesus, T., Beecham, C. M., Djerassi, C., Kaisin, M.: Tetrahedron Lett. 1671 (1978)
384. Stevens, K. E., Paquette, L. A.: Tetrahedron Lett. 4393 (1981)
385. Little, R. D., Carroll, G. L., Petersen, J. L.: J. Am. Chem. Soc. *105*, 928 (1983)
386. Little, R. D., Muller, G. W., Venegas, M. G., Carroll, G. L., Bukhari, A., Patton, L., Stone, K.: Tetrahedron *37*, 4371 (1981)
387. Oppolzer, W., Bättig, K.: Tetrahedron Lett. 4669 (1982)
388. Birch, A. M., Pattenden, G.: ibid. 991 (1982)
389. Shirahama, H., Murata, S., Fujita, T., Chhabra, B. R., Noyori, R., Matsumoto, T.: Bull. Chem. Soc. Japan, in press
390. Fujita, T., Ohtsuka, T., Shirahama, H., Matsumoto, T.: Tetrahedron Lett. 4091 (1982)
391. Pattenden, G., Teague, S. J.: ibid. 5471 (1982)
392. Tatsuta, K., Akimoto, K., Kinoshita, M.: J. Antibiot. *33*, 100 (1980)
393. Danishefsky, S., Zamboni, R., Kahn, M., Etheredge, S. J.: J. Am. Chem. Soc. *102*, 2097 (1980); *103*, 3469 (1981)
394. Danishefsky, S., Zamboni, R.: Tetrahedron Lett. 3439 (1980)
395. Shibasaki, M., Iseki, K., Ikegami, S.: ibid. 3587 (1980); Iseki, K., Yamasaki, M., Shibasaki, M., Ikegami, S.: Tetrahedron *37*, 4411 (1981)
396. Trost, B. M., Curran, D. P.: J. Am. Chem. Soc. *103*, 7380 (1981)

397. Ito, T., Tomiyoshi, N., Nakamura, K., Azuma, S., Izawa, M., Moruyama, F., Yanagiya, M., Shirahama, H., Matsumoto, T.: Tetrahedron Lett. 1721 (1982)
398. Mehta, G., Reddy, A. V., Murthy, A. N., Reddy, D. S.: J. Chem. Soc. Chem. Commun. 540 (1982)
399. Schuda, P. F., Ammon, H. L., Heimann, M. R., Bhattacharjee, S.: J. Org. Chem. *47*, 3434 (1982)
400. Trost, B. M., Shuey, C. D., DiNinno, F., Jr.: J. Am. Chem. Soc. *101*, 1284 (1979)
401. Yamazaki, M., Shibasaki, M., Ikegami, S.: Chem. Lett. 1245 (1981)
402. Shibasaki, M., Yamazaki, M., Iseki, K., Ikegami, S.: Tetrahedron Lett. 5311 (1982)
403. Paquette, L. A., Han, Y.-K.: J. Org. Chem. *44*, 4014 (1979); J. Am. Chem. Soc. *103*, 1835 (1981)
404. Oppolzer, W., Bättig, K., Hudlicky, T.: Helv. Chim. Acta *62*, 1493 (1979); Tetrahedron *37*, 4359 (1981)
405. Pirrung, M. C.: J. Am. Chem. Soc. *101*, 7130 (1979); *103*, 82 (1981)
406. Chatterjee, S.: J. Chem. Soc. Chem. Commun. 620 (1979)
407. Wender, P. A., Dreyer, G. B.: Tetrahedron *37*, 4445 (1981)
408. Dauben, W. G., Walker, D. M.: J. Org. Chem. *46*, 1103 (1981)
409. Wenkert, E.: private communication
410. Bohlmann, F., Jakupovic, J.: Phytochemistry *19*, 259 (1980)
411. Leone-Bay, A., Paquette, L. A.: J. Org. Chem. *47*, 4173 (1982); Paquette, L. A., Leone-Bay, A.: J. Am. Chem. Soc. in press
412. Tsunoda, T., Kodama, M., Itô, S.: Tetrahedron Lett. 83 (1983)
413. Seto, H., Yonehara, H.: J. Antibiot. *33*, 92 (1980)
414. Annis, G. D., Paquette, L. A.: J. Am. Chem. Soc. *104*, 4504 (1982); Paquette, L. A., Annis, G. D.: J. Am. Chem. Soc. in press
415. Bohlmann, F., Zdero, C.: Phytochemistry *18*, 1747 (1979)
416. Galemmo, R., Paquette, L. A.: J. Am. Chem. Soc. in press
417. Seto, H., Sasaki, T., Uzawa, J., Takeuchi, S., Yonehara, H.: Tetrahedron Lett. 4411 (1978)
418. Sakai, K., Ohtsuka, T., Misumi, S., Shirahama, H., Matsumoto, T.: Chem. Lett. 355 (1981)
419. Roberts, R. A., Paquette, L. A.: unpublished results
420. Zalkow, L. H., Harris, R. N., III, Van Derveer, D., Bertrand, J. A.: J. Chem. Soc. Chem. Commun. 456 (1977); Zalkow, L. H., Harris, R. N., III, Burke, N. I.: J. Nat. Prod. *42*, 96 (1979)
421. Bohlmann, F., Van, N. L., Pham, T., Jacupovic, J., Schuster, A., Zabel, V., Watson, W. H.: Phytochemistry *18*, 1831 (1979)
422. Bertz, S. H.: J. Am. Chem. Soc. *104*, 5801 (1982)
423. Smith, A. B., III, Jerris, P.: J. Am. Chem. Soc. *103*, 194 (1981); J. Org. Chem. *47*, 1845 (1982)
424. Schostarez, H., Paquette, L. A.: J. Am. Chem. Soc. *103*, 722 (1981); Tetrahedron *37*, 4431 (1981)
425. Karpf, M., Dreiding, A. S.: Tetrahedron Lett. 4569 (1980); Helv. Chim. Acta *64*, 1123 (1981)
426. Oppolzer, W., Marazza, F.: Helv. Chim. Acta *64*, 1575 (1981)
427. Oppolzer, W., Bättig, K.: ibid. *64*, 2489 (1981)
428. Wender, P. A., Dreyer, G. B.: J. Am. Chem. Soc. *104*, 5805 (1982)
429. Wrobel, J., Takahashi, K., Honkan, V., Lannoye, G., Cooke, J. M., Bertz, S. H.: J. Org. Chem. *48*, 139 (1983)
430. Paquette, L. A., Wyvratt, M. J., Berk, H. C., Moerck, R. E.: J. Am. Chem. Soc. *100*, 5845 (1978)
431. Christoph, G. G., Muthard, J. L., Böhm, M. C., Gleiter, R.: ibid. *100*, 7782 (1978)
432. Paquette, L. A., Snow, R. A., Muthard, J. L., Cynkowski, T.: ibid. *101*, 6991 (1979)
433. Engel, P.: Zeitschr. für Kristallogr. *152*, 169 (1980)
434. Houk, K. N., Gandour, R. W., Strozier, R. W., Rondan, N. G., Paquette, L. A.: J. Am. Chem. Soc. *101*, 6797 (1979)
435. Hales, N. J., Paquette, L. A.: J. Org. Chem. *44*, 4603 (1979)
436. Osborn, M. E., Kuroda, S., Muthard, J. L., Kramer, J. D., Engel, P., Paquette, L. A.: ibid. *46*, 3379 (1981)
437. Osborn, M. E., Pegues, J. F., Paquette, L. A.: ibid. *45*, 167 (1980)
438. Sobczak, R. L., Osborn, M. E., Paquette, L. A.: ibid. *44*, 4886 (1979)

439. Eaton, P. E., Sidhu, R. S., Langford, G. E., Cullison, D. A., Pietruszewski, C. L.: Tetrahedron *37*, 4479 (1981)
440. Eaton, P. E., Andrews, G. D., Krebs, E.-P., Kunai, A.: J. Org. Chem. *44*, 2824 (1979)
441. Paquette, L. A., Wyvratt, M. J., Schallner, O., Muthard, J. L., Begley, W. J., Blankenship, R. M., Balogh, D.: ibid. *44*, 3616 (1979)
442. Balogh, D., Begley, W. J., Bremner, D., Wyvratt, M. J., Paquette, L. A.: J. Am. Chem. Soc. *101*, 749 (1979);
Paquette, L. A., Begley, W. J., Balogh, D., Wyvratt, M. J., Bremner, D.: J. Org. Chem. *44*, 3630 (1979)
443. Paquette, L. A., Balogh, D., Engel, P.: Heterocycles *15*, 271 (1981)
444. Balogh, D. W., Paquette, L. A.: J. Org. Chem. *45*, 3043 (1980)
445. Balogh, D. W., Paquette, L. A., Engel, P., Blount, J. F.: J. Am. Chem. Soc. *103*, 226 (1981)
446. McKervey, M. A., Vibuljan, P., Ferguson, G., Siew, P. Y.: J. Chem. Soc. Chem. Commun. 912 (1981)
447. Paquette, L. A., Balogh, D. W.: J. Am. Chem. Soc. *103*, 228 (1981)
448. Paquette, L. A., Balogh, D. W.: ibid. *104*, 774 (1982)
449. Christoph, G. G., Engel, P., Usha, R., Balogh, D. W., Paquette, L. A.: ibid. *104*, 784 (1982)
450. Paquette, L. A., Balogh, D. W., Usha, R., Kountz, D., Christoph, G. G.; Science *211*, 575 (1981)
451. Paquette, L. A., Ternansky, R. J., Balogh, D. W.: J. Am. Chem. Soc. *104*, 4502 (1982)
452. Paquette, L. A.: Proc. Natl. Acad. Sci. USA *79*, 4495 (1982)
453. Paquette, L. A., Balogh, D. W., Ternansky, R. J., Begley, W. J., Banwell, M. G.: J. Org. Chem. *48*, 3282 (1983)
454. Paquette, L. A., Ternansky, R. J., Balogh, D. W., Taylor, W. J.: J. Am. Chem. Soc. *105*, 5441 (1983)
455. Ternansky, R. J., Balogh, D. W., Paquette, L. A.: J. Am. Chem. Soc. *104*, 4503 (1982);
Paquette, L. A., Ternansky, R. J., Balogh, D. W., Kentgen, G.: ibid. *105*, 5446 (1983)

Subject Index

Author Index Volumes 101–119

Contents of Vols. 50–100 see Vol. 100
Author and Subject Index Vols. 26–50 see Vol. 50

The volume numbers are printed in italics