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CHAPTER 7

The photochemistry of dienes and polyenes: Application to the synthesis of complex molecules

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I. INTRODUCTION

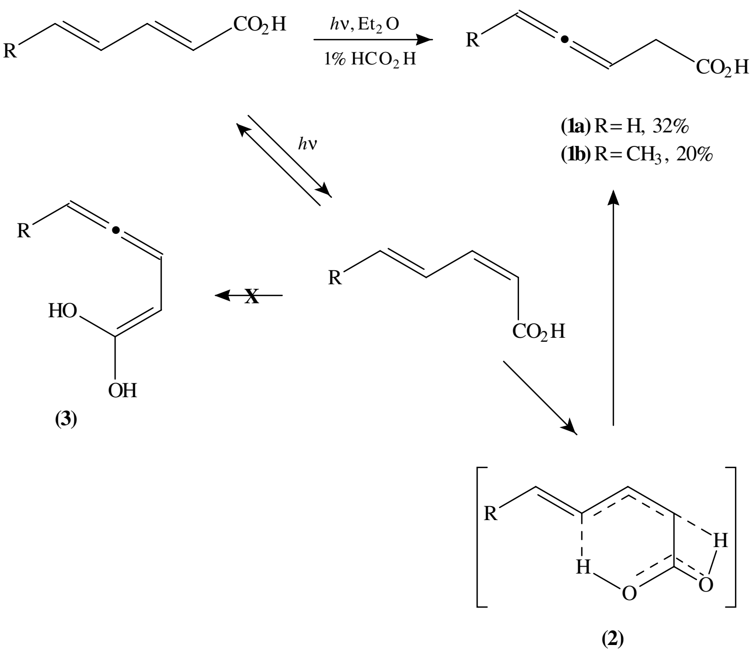
Organic photochemistry has typically been approached from a physical/mechanistic perspective, rather than a synthetic one. This may result from a certain reluctance on the part of synthetic chemists to employ reactions which often produce many products. Nonetheless, careful design of substrates can lead to high levels of chemoselectivity. In fact, there have been many recent examples of the successful application of photochemical reactions to the synthesis of complex targets[1]. In many cases, these processes provide access to unique modes of reactivity, or offer unrivaled increases in molecular complexity[2].

The literature of diene and polyene photochemistry provides many cases of synthetically useful reactions. As a result, certain arbitrary decisions have been made regarding what is covered in this chapter. For example, intramolecular [2 + 2]-photocycloaddition reactions of α,ω-dienes can be formally included under the general rubric of diene photochemistry. However, we have chosen to restrict our discussion to dienes and polyenes which constitute a self-contained chromophore, viz. conjugated, cross-conjugated and 1,4-diene systems. Likewise, arene-olefin photocycloadditions will not be considered. These two broad classes of photoreactions have been applied extensively in synthesis, and have been the subject of recent reviews[3,4].

II. PHOTOREARRANGEMENTS OF DIENES AND POLYENES

A. Bond Migration

Photoenolization is a frequently encountered process for aromatic and α,β-unsaturated carbonyl compounds[5]. Typically, an allylic or benzylic γ-hydrogen is abstracted by the

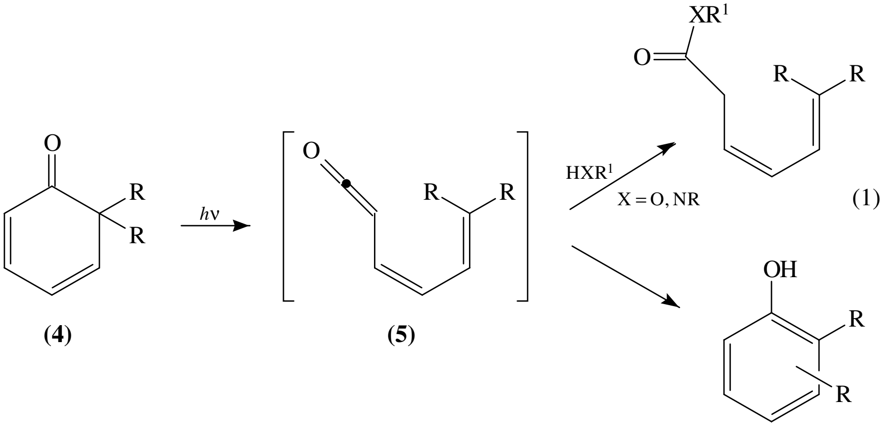


SCHEME 1

oxygen of the photochemically excited carbonyl. In contrast to their saturated counterparts, which produce a 1,4-diradical capable of either fragmentation or closure to cyclobutanol, these systems lead to dienols, also referred to as photoenols. These intermediates can then undergo ketonization to give the isomeric β,γ-unsaturated carbonyls, or take part as diene partners in Diels-Alder cycloadditions. In the case of $\alpha,\beta,\gamma,\delta$-unsaturated carbonyls, the vinylic γ-hydrogen is presumably somewhat less reactive. However, Crowley reported that irradiation of sorbic acid or 2,4-pentadienoic acid in the presence of formic acid furnishes **1**, presumably involving prior photochemical *cis/trans* isomerization of the C-2/C-3 alkene (Scheme 1)[6]. This leads to a net deconjugation of the unsaturated carbonyl, with concomitant creation of an allene. This process does not occur with the corresponding carboxylate salts, and only in low yields with methyl sorbate. To explain these differences, a transition state **(2)** involving simultaneous transfer of the γ- and carboxyl hydrogens was invoked, rather than photoenolization to give **3**, followed by tautomerization.

B. Electrocyclic Ring Opening of Cyclic Dienes

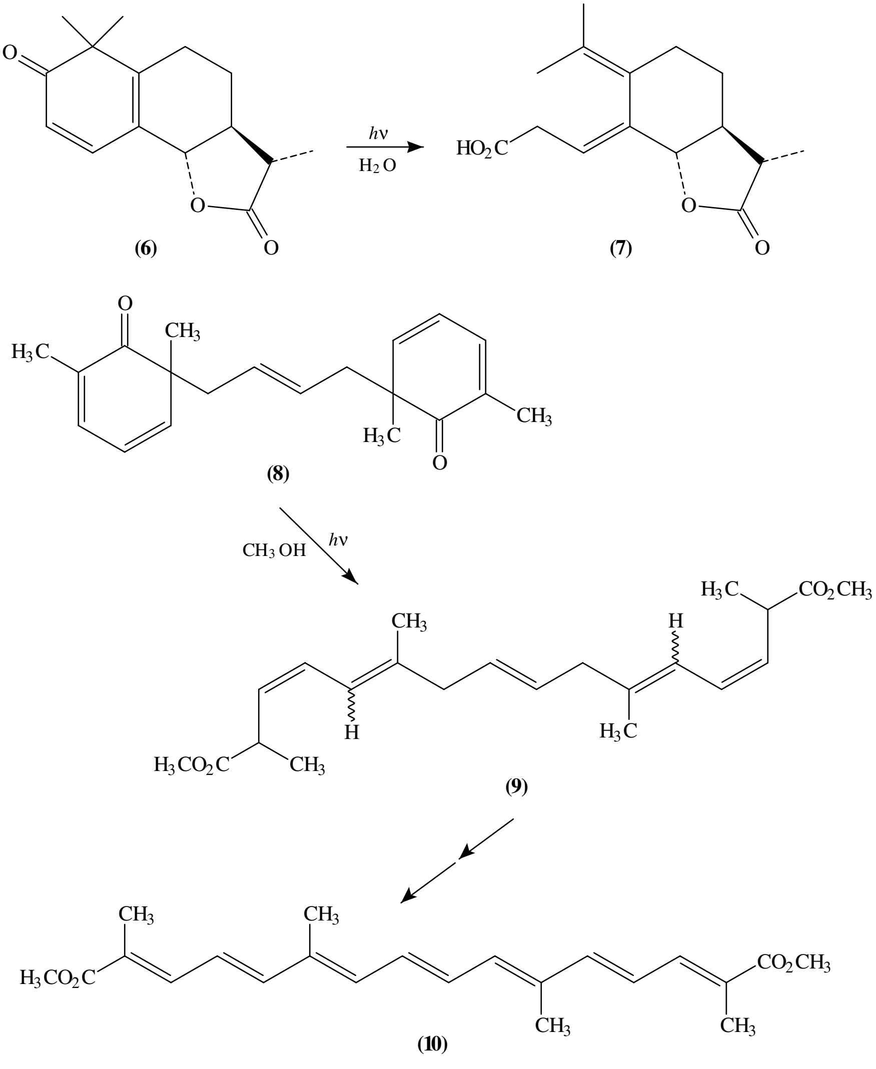
The photochemistry of linearly conjugated 2,4-cyclohexadiene-1-ones (e.g. **4**) has been studied extensively[7]. These linearly conjugated systems generally photorearrange to a (*Z*)-dienylketene **5** (equation 1); this process is usually reversible, so that in the absence of a nucleophile little change is observed. In the presence of amines or alcohols, however, amides and esters are typically isolated. In the presence of weaker nucleophiles a slow formation of phenol derived products is usually observed.



(4) **(5)** (1)

An early example of this process is typified by the formation of photosantonic acid **7**, isolated in high yield when **6** is irradiated in aqueous solution (Scheme 2)[8]. Barton and Quinkert have also utilized this ring opening/trapping process in the synthesis of dimethylcrocetin, **10**, as well as other derivatives of this diapocarotenoid[9]. Double C-alkylation of the 2,6-dimethylphenol with 1,4-dibromobut-2-ene affords the requisite (bis)cyclohexadieneone **8** in modest yield. Irradiation of **8** in methanol affords a mixture of isomeric dimethyltetrahydrocrocetins **(9)**, which on dehydrogenation with DDQ leads to a mixture of compounds from which the naturally occurring dimethylcrocetin **10** can be isolated.

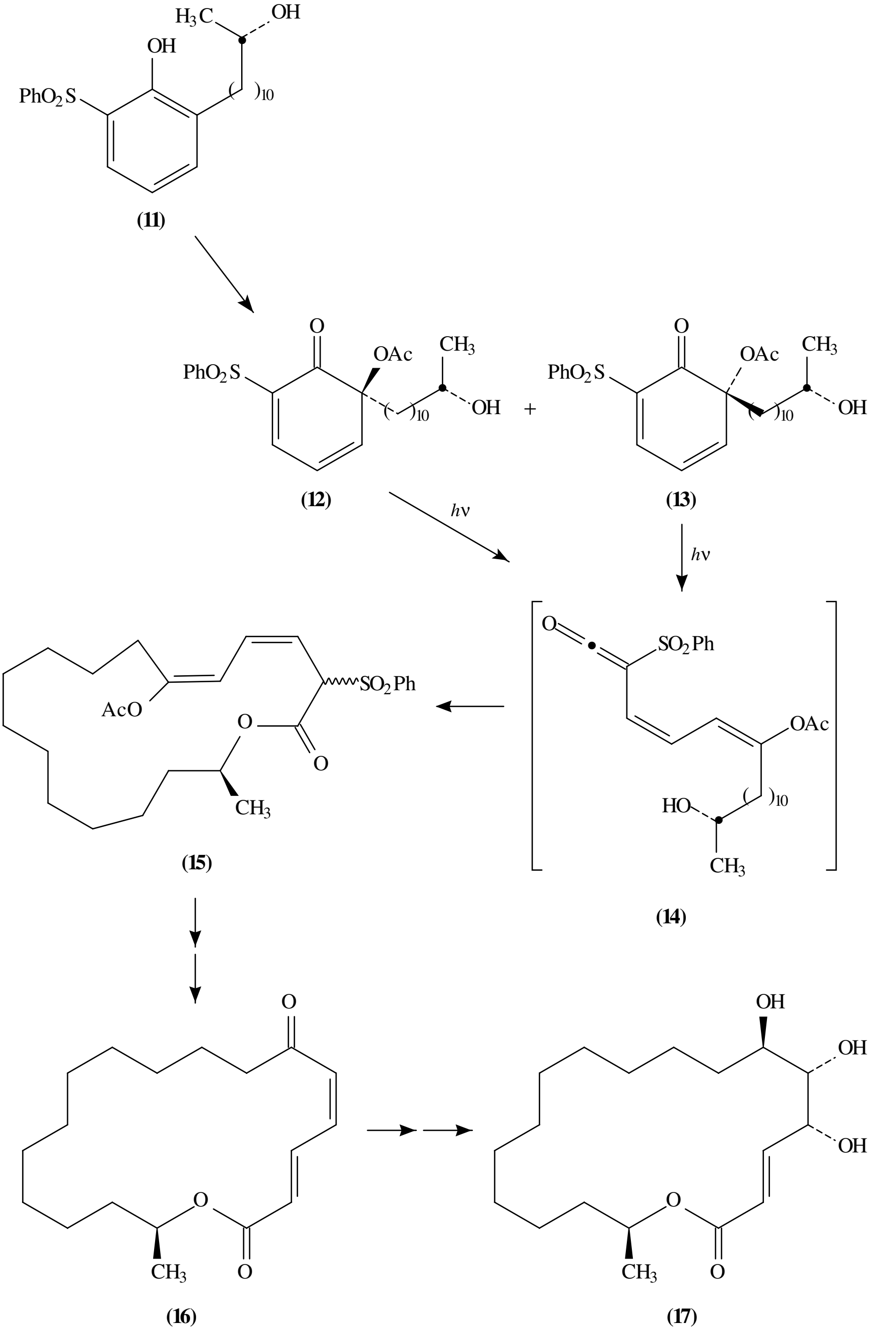
Quinkert and coworkers have also described a clever synthesis of the lichen macrolide (+)-aspicilin **(17)** using this ring opening/trapping strategy in which the trapping is done intramolecularly by a remote hydroxyl functionality, affording a macrolide product



SCHEME 2

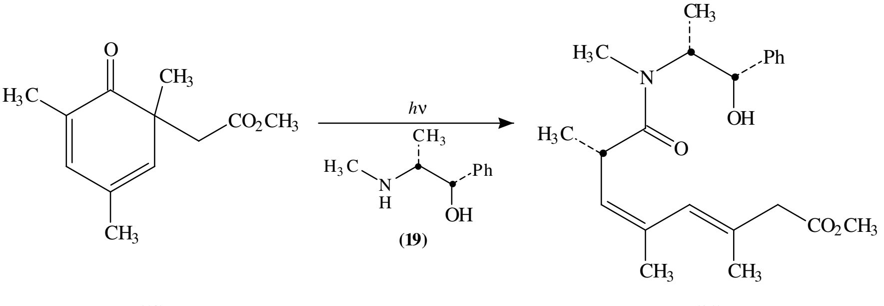
(Scheme 3)[10]. Indeed, independent photolysis of 2,4-cyclohexadien-1-ones **12** and **13** afforded the macrolides **15**. These reactions likely proceed via a common intermediate, in this case dienylketene **14**, which is trapped intramolecularly by the pendant hydroxyl group. Adjustment of the oxidation level and functional group interconversion then led efficiently to the desired macrolide **17**. The sulfonyl group was used for two reasons: first, to easily transform lactones **15** into dienyl lactones **16** needed for **17**, and secondly, to control the regiochemistry of the Wessely oxidation of phenolic precursor needed to produce the photolysis substrates **12** and **13**.

Schultz and Kulkarni have explored the possibilities of using this process in asymmetric synthesis by trapping the ketene generated from these photochemical ring-opening


H3C
OH
OH
PhO2S
( )10
(11)
O
PhO2S
OAc
CH3
( )10
OH
+
(12)
(13)
hν
hν
O
SO2Ph
OAc
HO
( )10
CH3
(14)
AcO
SO2Ph
O
O
CH3
(15)
O
O
CH3
O
(16)
OH
OH
OH
O
CH3
O
(17)

SCHEME 3

reactions with a chiral, nonracemic amine or alcohol (Scheme 4)[11]. Preliminary studies indicated that irradiation of **18** in the presence of a chiral, nonracemic amine (or amino alcohol) led to only moderate yields of the amide or ester products. The best chiral modifier in this case is the (D)-ephedrine, **19**, which gave a *ca* 70:30 ratio of diastereomers. The authors did show, however, that this method is preparatively useful, as multigram quantities of optically pure **20** can be produced easily.



(18) **(19)** **(20)**

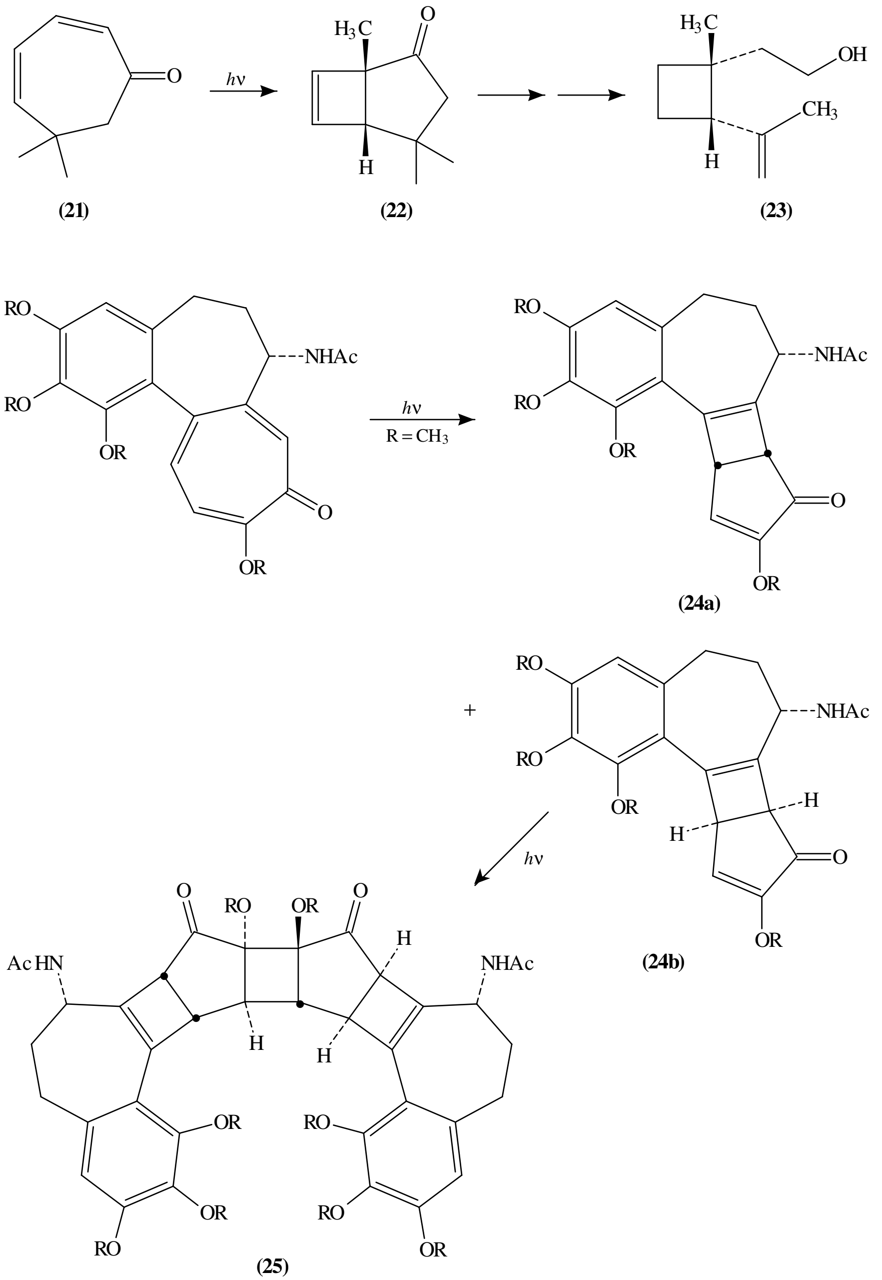
SCHEME 4

C. Electrocyclic Closure of Dienes and Trienes

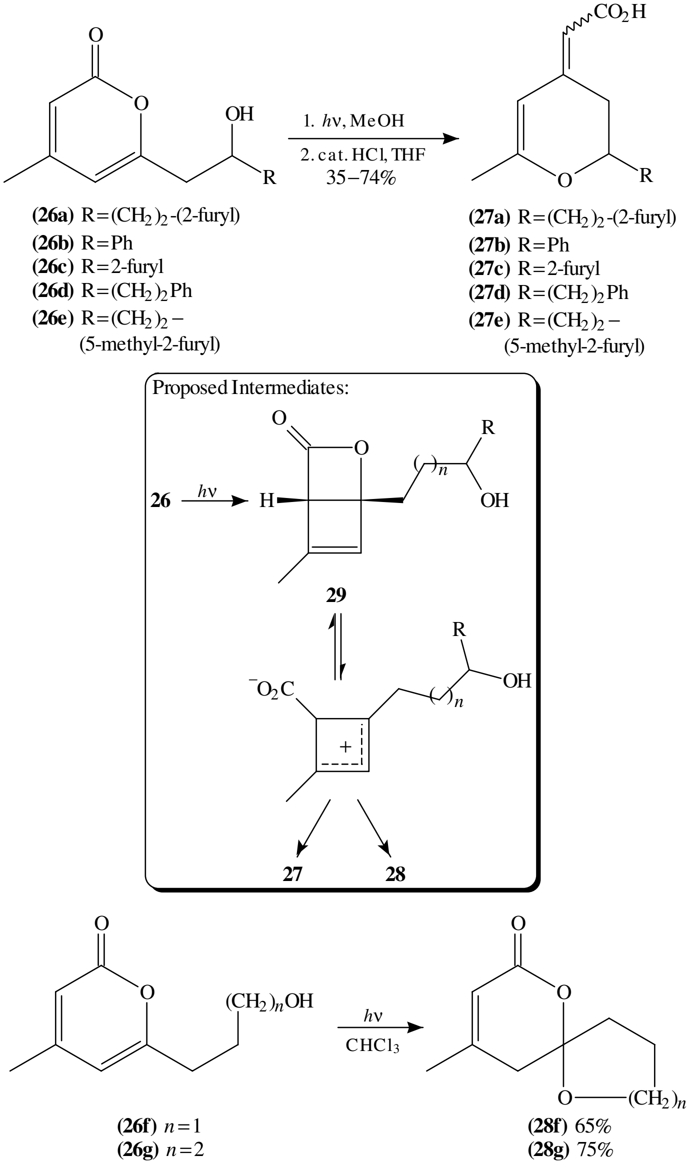
Electrocyclic closure of butadiene units encased within cycloheptane rings has been used to obtain bicyclo[3.2.0]heptene systems (Scheme 5)[12]. For example, irradiation of eucarvone **21** led to the formation of adduct **22** in 52% yield via a disrotatory ring closure[12a]. This adduct was used as a key intermediate in the synthesis of the pheromone grandisol, **23**, which proceeded in 20% overall yield from **22**. In their synthesis of α-lumicolchicine, Chapman and coworkers utilized a photochemically initiated four-electron disrotatory photocyclization of colchicine to produce β-lumicolchicine **24a** and its γ-isomer **24b** in a 2:1 ratio[12b]. These adducts were then converted, in a second photochemical step, to the *anti* head-to-head dimer α-lumicolchicine **25**.

In conjunction with studies probing [4 + 4]-photocycloaddition chemistry of 2-pyrones (*vide infra*), West and coworkers recently reported observations regarding alternative rearrangement pathways[13]. Irradiation of 6-hydroxyethylpyran-2-ones **26** furnished novel dihydropyrans **27** (Scheme 6). Although the details of the mechanism are not available, initial closure to bicyclic 'Dewar pyrone' **29** is considered to be a likely pathway[14]. When the length of the tether connecting the pendant alcohol to the 2-pyrone was increased, spirocyclic products **28** were formed instead.

The hexatriene/cyclohexadiene isomerization has been extensively studied and has been the topic of numerous reviews and monographs[15]; this section will attempt to deal only with applications of these reactions to synthesis, and in particular the use of these reactions for the synthesis of natural products. Much of the early work in this area was done by Havinga and coworkers during the course of their detailed work on the stereochemical consequences of the thermal and photochemical conversions in the vitamin D field[16]; this work provided much of the impetus for the development and elaboration of the Woodward–Hoffman rules (Scheme 7)[17]. The reversible photochemical ring opening of provitamin **30** to precalciferol **(31)** and the photochemical ring closure of **31** to lumisterol **32** can be explained by consecutive photochemically allowed conrotatory processes[16].

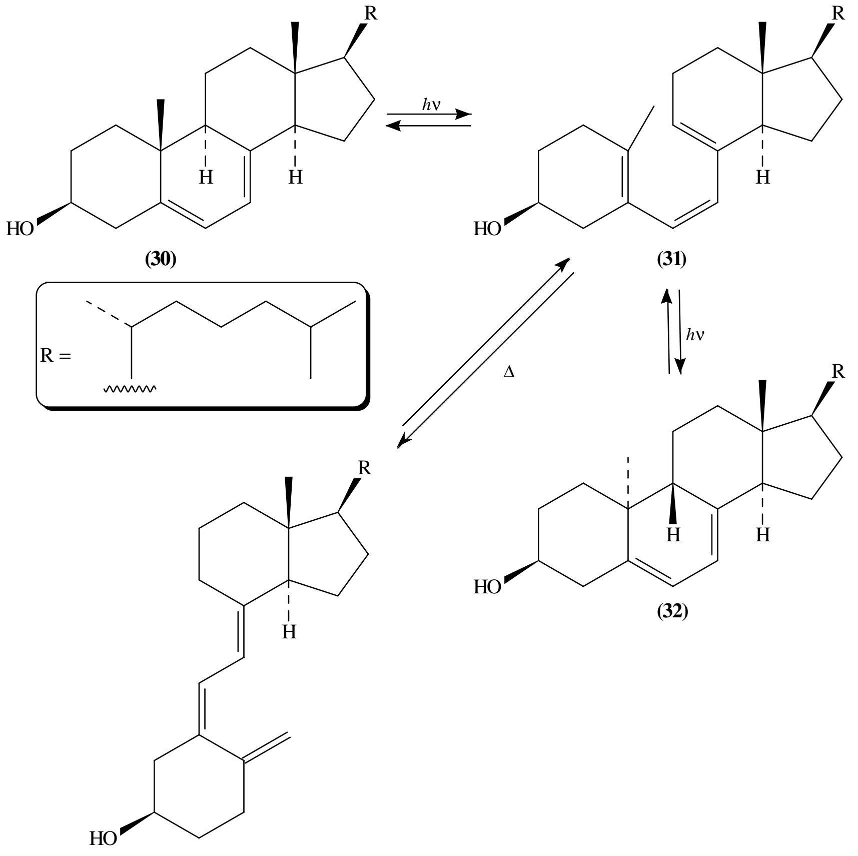


SCHEME 5

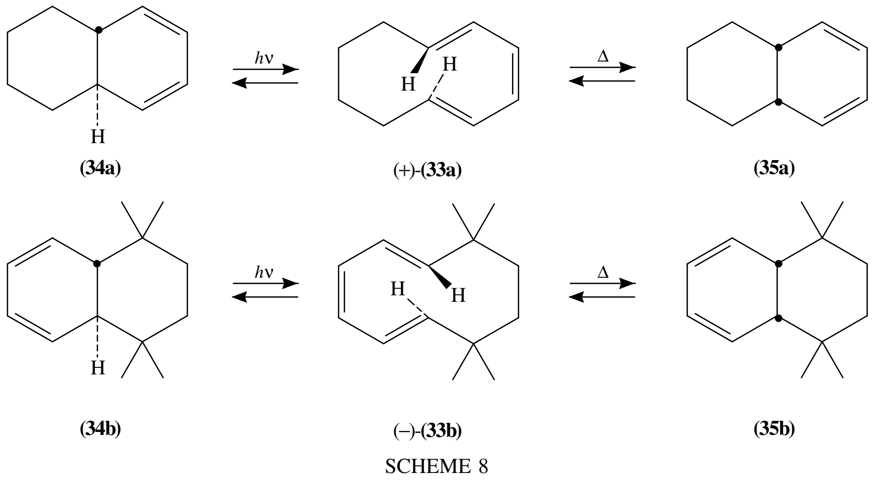


SCHEME 6

In an interesting illustration of these reactions, the two disymmetric trienes (+)-**33a** and (−)-**33b** were found to preserve their chirality upon photolysis at 193 K and provide cyclohexadienes **34a** and **34b**, respectively (Scheme 8)[18]. Upon warming above 205 K, however, they lose their chiral integrity by competitive disrotatory cyclization to the achiral dienes **35a** and **35b**. The thermal disrotatory closure to the *cis*-fused ring isomer is generally found to be extremely facile in these systems.

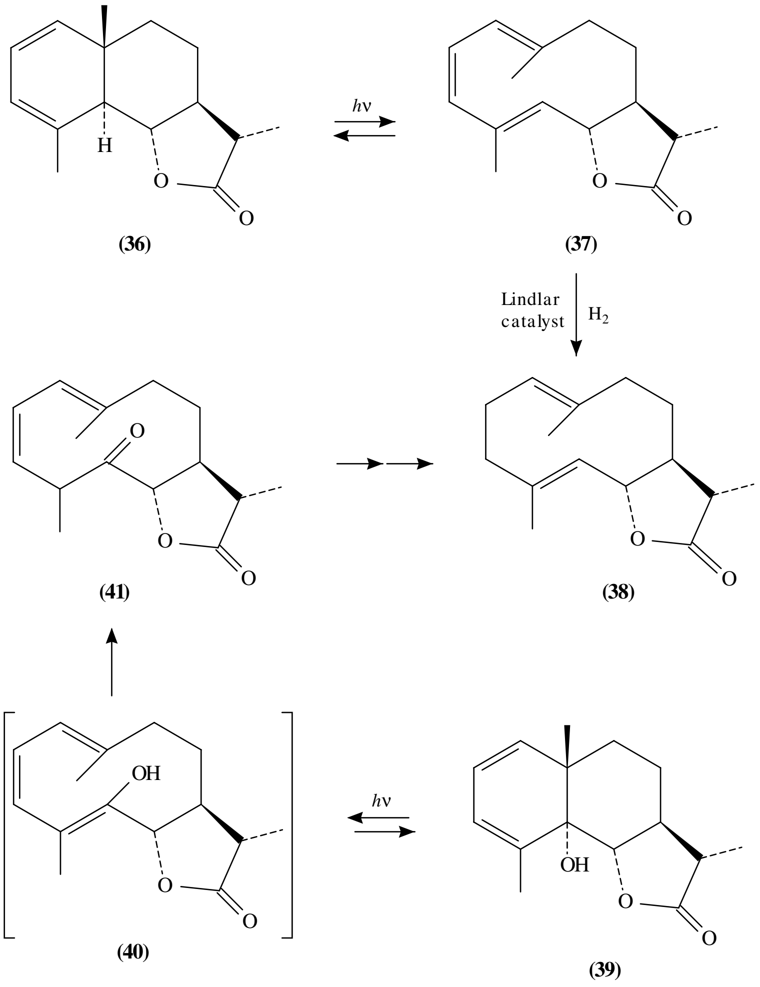


SCHEME 7



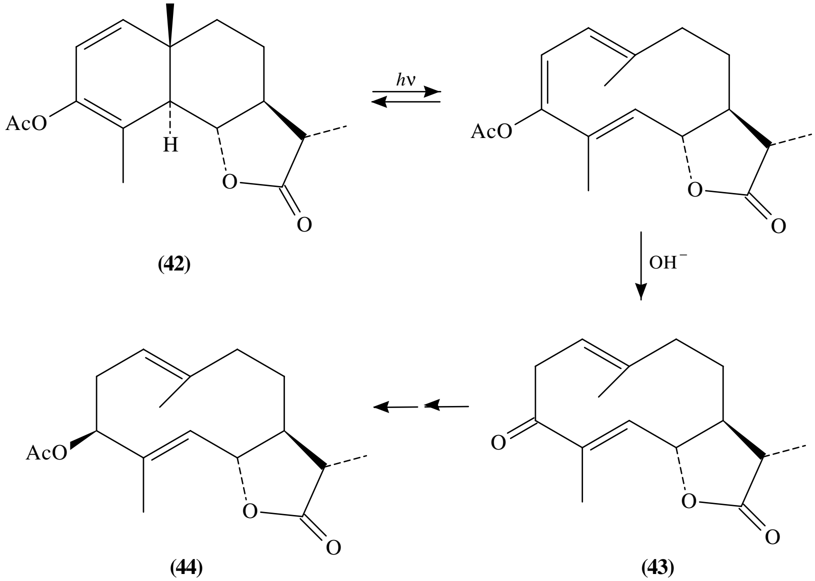
SCHEME 8

In one of the earliest applications of this type of process to complex molecule synthesis, Corey and Hortmann, in their synthesis of dihydrocostunolide **38**, found that photolysis of **36** afforded a photostationary state of **36** and **37** (Scheme 9)[19]. Hydrogenation of this mixture then gave **38**. A recent modification of this synthesis, which avoids the photostationary equilibrium between eudesmane **(36)** and germacrane **(37)** forms, was realized using a modified substrate, **39**[20]. Irradiation of **39** provided a 77% yield of a mixture of diastereomeric ketones **41**; these are produced via tautomerization of the intially produced trienol **40**. Dienone **41** was then easily converted to **38** via a series of conventional steps (Scheme 9).



SCHEME 9

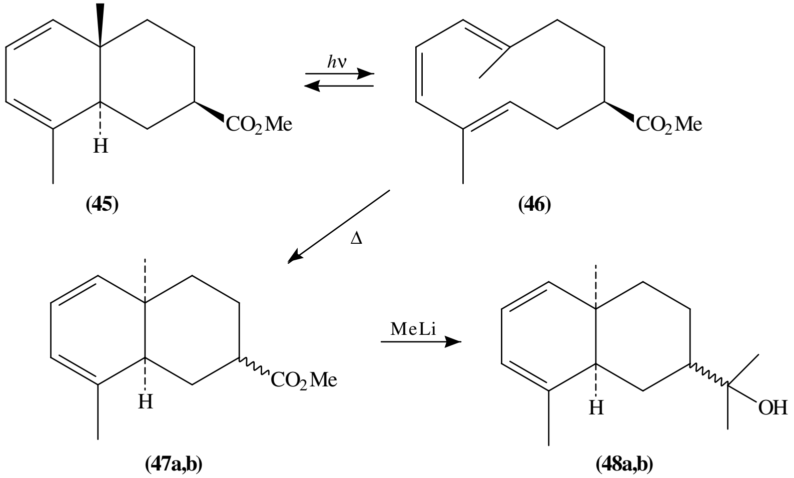
A similar strategy has been employed in a clever synthesis of the sesquiterpene dihydronovanin **(44)**[21]. Enol acetate **42** was irradiated in cold methanol to prevent thermal closure to the *cis*-fused system via a facile disrotatory electrocyclization (Scheme 10).



SCHEME 10

This was followed by immediate saponification of the enol ester to afford dieneone **43**, which could be easily elaborated to **44**.

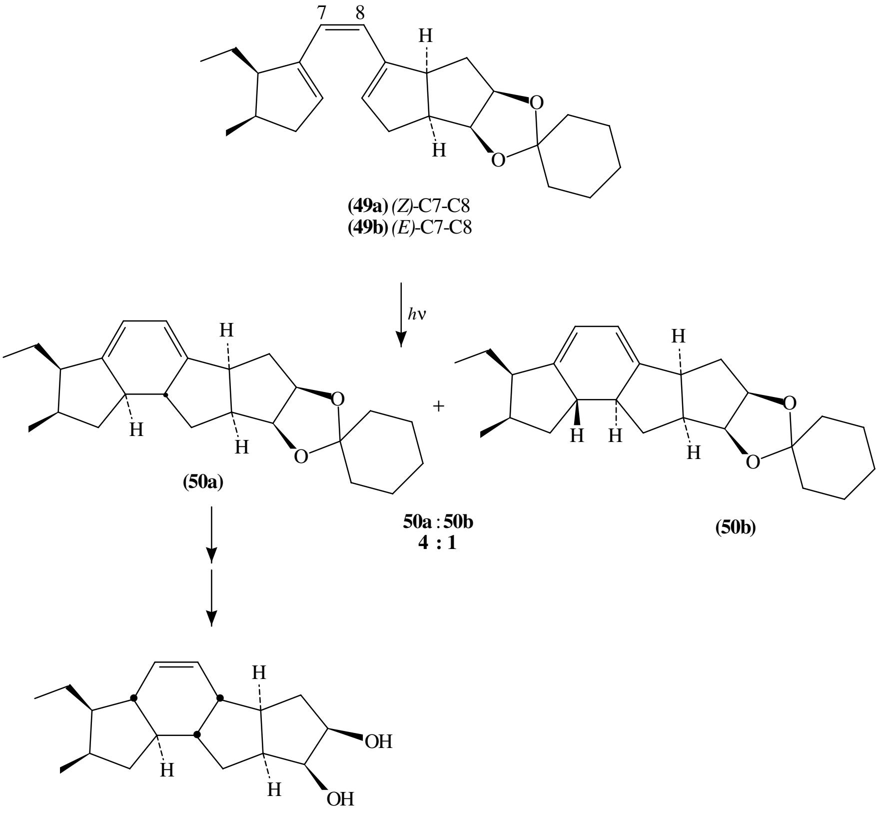
The *trans–cis* isomerization process observed in the eudesmane/germacrane ring system has been utilized for the synthesis of the *cis*-fused sesquiterpene occidentalol, **48a**, and its 7-epi isomer, **48b** (Scheme 11)[22]. Photolysis of the *trans*-fused diene **45** at −78 °C afforded triene **46**, which upon warming underwent disrotatory electrocyclization to give **47a** and **47b** as a 1:2 mixture of diastereomers. Apparently, the carboalkoxy group imparts



SCHEME 11

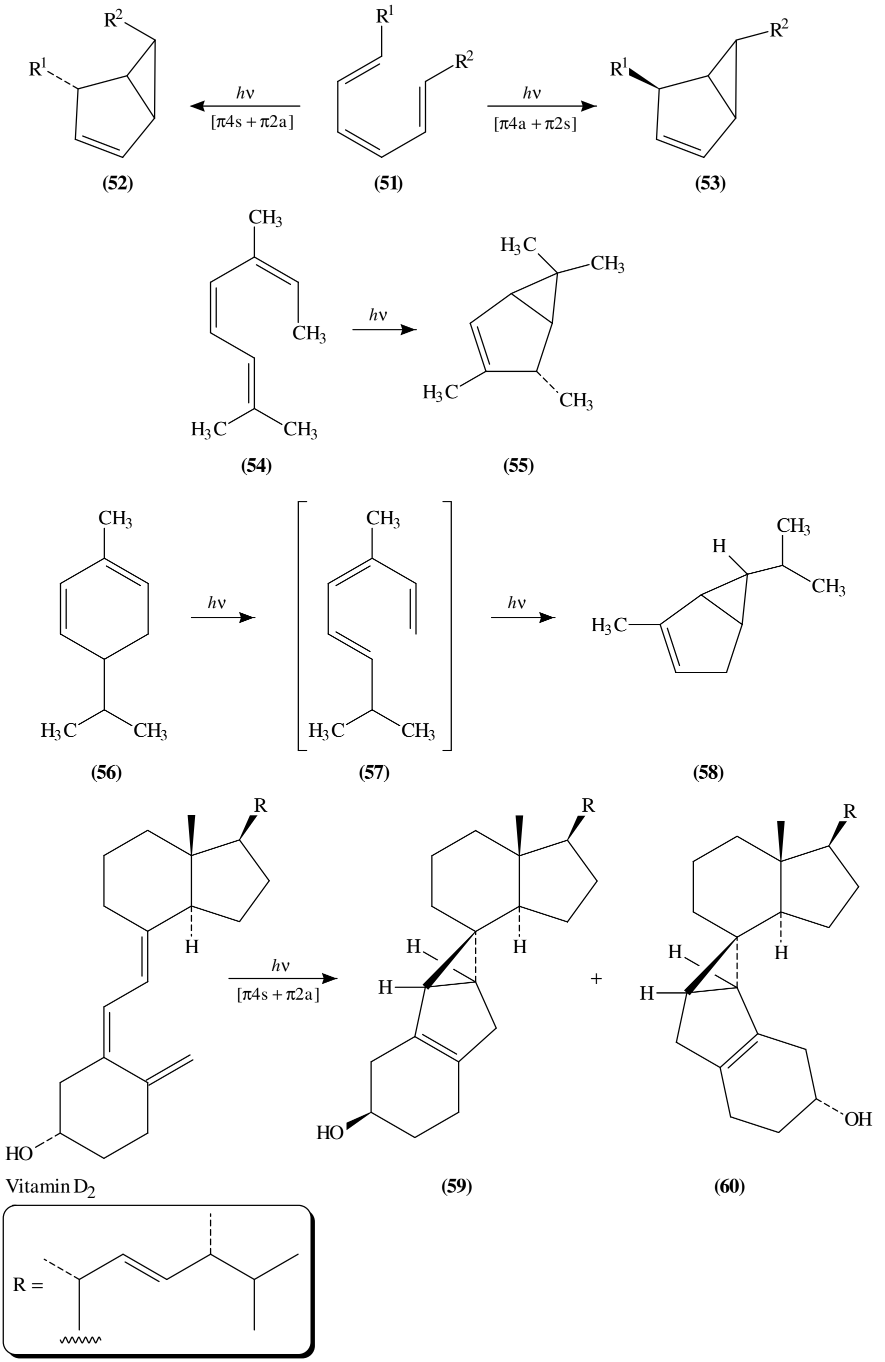
little stereoinduction in the electrocyclization of triene **46**. These diastereomers could be separated and they reacted with methyllithium to afford **48a** and **48b** in good yield.

Whitesell and Minton have reported an ingenous synthesis of the antimicrobial and amoebicidal agent ikarugamycin which utilizes a photochemically initiated conrotatory electrocyclization as its critical step (Scheme 12)[23]. These workers found that photolysis of a *ca* 2:1 mixture of the trienes **49a** and **49b** led to a 4:1 mixture of the two possible conrotatory closure products **50a** and **50b** in near-quantitative yield. This product ratio most likely reflects the conformational bias in the ground state of the (*Z*)-triene **49a**, as it is likely that one conformer reacts to give **50a** while the other conformer reacts to give **50b**. Triene **49b** is assumed to photochemically equilibrate with **49a**, followed by conversion to **50a** and **50b**. Glycol **50a** functioned as a key intermediate in the synthesis of the target compound.



SCHEME 12

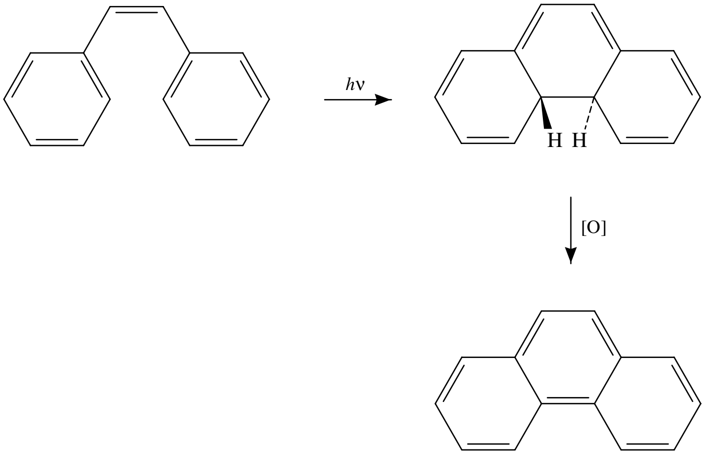
Irradiation of conjugated trienes such as **51** can also lead to the formation of bicyclo[3.1.0]hexanes (**52** or **53**) via a process that can be considered as a formal [$\pi 4s + \pi 2a$] or [$\pi 4a + \pi 2s$] cycloaddition (Scheme 13)[17,24]. Thus, triene **51** affords **52** and **53** via symmetry-allowed processes[17]. For example, allocimene **54** gave **55** (with other photoproducts)[25], while α-phellandrene **(56)** gave **57**, which upon further irradiation afforded **58**[26]. These reactions would be of little interest were it not for the observation


R1
R2
hν
[π4s + π2a]
hν
[π4a + π2s]
(52)
(51)
(53)
CH3
H3C
CH3
hν
(54)
(55)
(56)
(57)
(58)
H
hν
Vitamin D2
R
HO
OH
[π4s + π2a]
+
(59)
(60)
R =

SCHEME 13

that upon irradiation Vitamin D_2 (calciferol) undergoes photocyclization to afford suprasterols **59** and **60**[27]. The formation of these adducts, and their stereochemistry, can be nicely rationalized by a $[\pi 4s + \pi 2a]$ process.

The photocyclization of stilbenes to phenanthrene derivatives and related conjugated arylalkenes to polycyclic aromatic derivatives constitutes one of the most widely used applications of organic photochemistry to organic synthesis, owing primarily to the plethora of natural products containing a phenanthrene unit[28]. This reaction, in accordance with the accepted mechanism, starts from the excited state of the stilbene, which undergoes a six-electron, conrotatory electrocyclization to afford the dihydrophenanthrene (Scheme 14). In the majority of cases, however, this dihydrophenanthrene is unstable and undergoes either oxidation to the aromatic system (in the presence of oxygen or an oxidant such as iodine) or, less commonly, converts to the isomeric 9,10-dihydrophenanthrene by a hydrogen shift. Though somewhat outside the scope of the present discussion, this type of cyclization has been utilized effectively for the synthesis of a wide variety of complex systems; the reader is referred to numerous excellent review articles for further discussions of this subject[28].

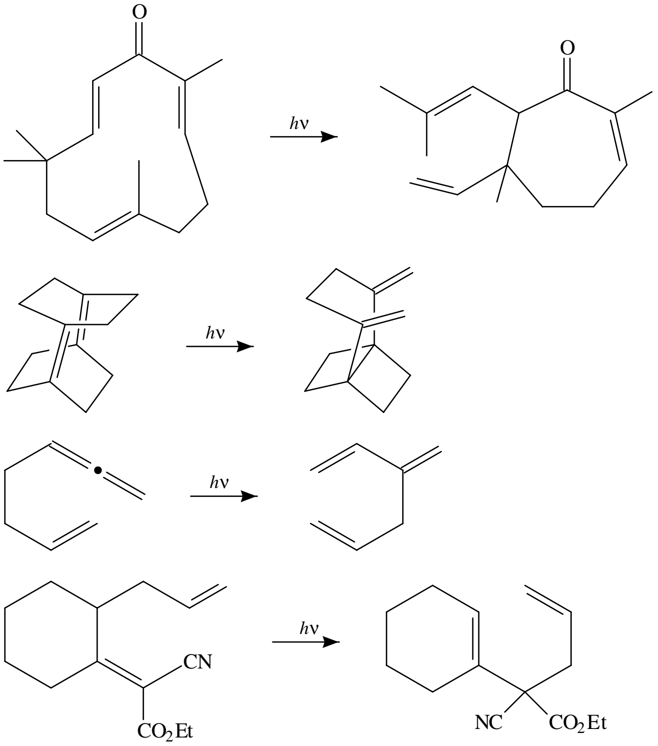


SCHEME 14

D. Sigmatropic Rearrangements

The Cope and Claisen rearrangements are the most widely utilized sigmatropic rearrangements from the standpoint of complex molecule synthesis. It has been found that the Cope rearrangement is frequently subject to great rate enhancements in the presence of catalysts; these most frequently have been either metal salts or acids[29]. However, there are several examples of the use of light to catalyze the [3,3] sigmatropic rearrangement of a 1,5-diene[30]. Some of these are shown in Scheme 15. The examples reported to date are a fairly random collection and it is not clear what factors facilitate the observed photochemical rearrangements, but it should be noted that in at least one case (**61** to **62**) photolysis reverses the normal equilibrium[30d].

In what is one of the few examples of utilization of a higher order sigmatropic hydrogen shift in the synthesis of complex molecules, Eschenmoser, in studies directed toward the synthesis of Vitamin B_{12}, found that an antarafacial [1,16] H-shift could be utilized to effect closure of secocorrin **63** to corrin **65** (Scheme 16)[31]. An intermediate biradical



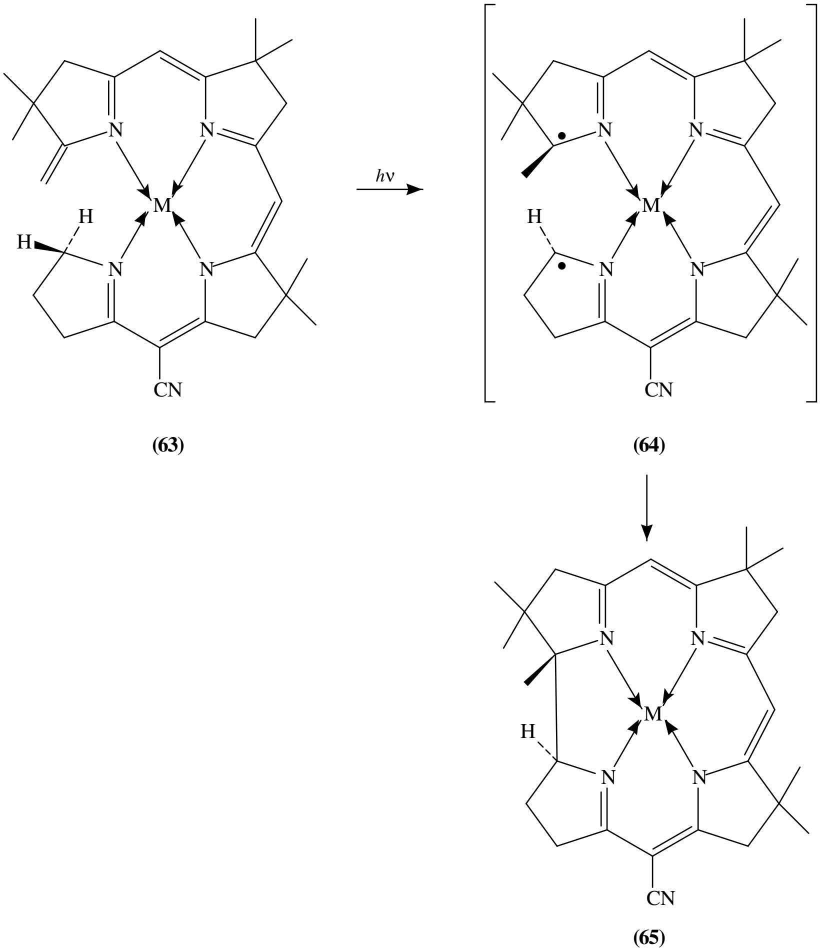
(61) **(62)**

SCHEME 15

64 is formed following the photochemically allowed H-shift. This then undergoes an antarafacial electrocyclic closure to form the desired product **65**. The process has been found to be dependent upon the metal ion used, as reaction occurred with Li, Na, Mg, Ca, Zn, Cd, Pd or Pt ion present but failed to proceed with Co, Ni or Cu ion as the chelating agent.

E. Di-π-methane Rearrangements

While not formally conjugated, the electronic nature of 1,4-dienes is such that they participate in a wide variety of photochemical reactions and have a rich photochemical history. In particular, the photochemical rearrangement of a 1,4-diene to a vinylcyclopropane (**66** to **67**), the so-called di-π-methane (DPM) rearrangement, is one of the most extensively studied photochemical rearrangements (Scheme 17)[32]. This process could be viewed as a formal 1,2-shift of a vinyl group with inversion of configuration of the migrating carbon atom[32a]. In reality, the mechanism is quite complex and has been investigated in exhaustive detail; the reader is referred to other articles for a detailed discussion of these aspects of this reaction. While this rearrangement has been utilized for the synthesis of a wide variety of unusual nonnaturally occurring ring systems, in particular the semibullvalenes and related compounds (e.g. **68** to **69**)[33], its use in the synthesis of natural products has been quite limited. In fact, it is quite surprising, given the level at which the di-π-methane rearrangement has been studied and is understood, that this reaction has not

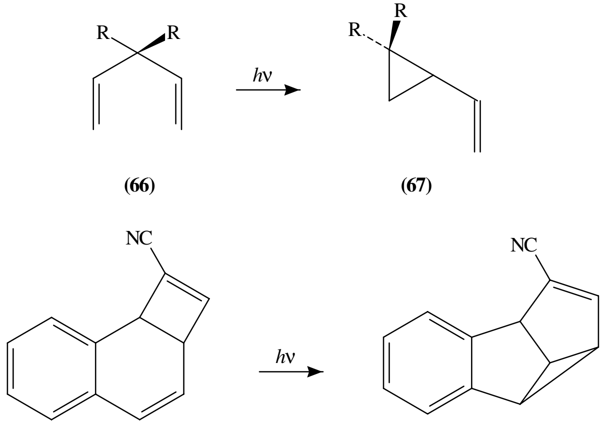


SCHEME 16

been utilized more in complex molecule synthesis, especially given that the products of this rearrangement, namely vinylcyclopropanes, are quite valuable synthetic commodities[34].

The first reported use of the DPM rearrangement in natural product synthesis can be found in the synthesis of methyl chrysanthemate, **71**, reported by Pattenden and Whybrow (Scheme 18)[35]. This is produced directly by photolysis of 1,4-diene **70**. While it should be noted that this reaction gave **71** in only 12% yield, it did furnish the desired product in a single step, with the correct relative stereochemistry. Bullivant and Pattenden also used a DPM rearrangement to form an advanced intermediate in the synthesis of the dideoxy derivative of the sesquiterpene taylorione, **74**[36]. Irradiation of **72** afforded **73** in 45% isolated yield; this was then simply converted to **74** using standard transformations.

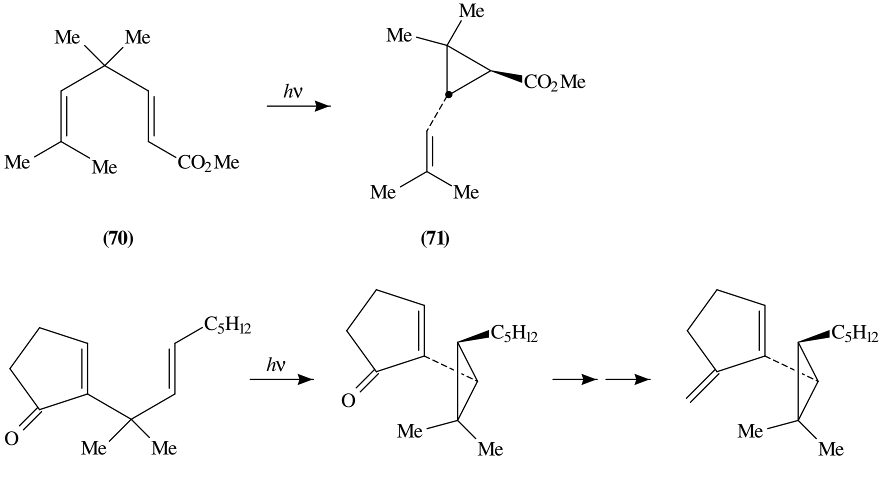
Armesto, Horspool and coworkers have extensively studied the related rearrangement of β,γ-unsaturated imine derivatives, the so-called aza-di-π-methane rearrangement[37]. A particularly interesting example is seen by the rearrangement of **75** to **76** (Scheme 19). Adduct **76** furnished chrysanthemic acid following a simple series of steps. It has been



(66) (67)

(68) (69)

SCHEME 17



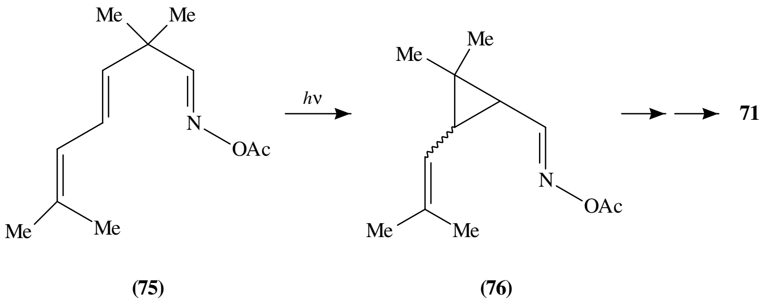
(70) (71)

(72) (73) (74)

SCHEME 18

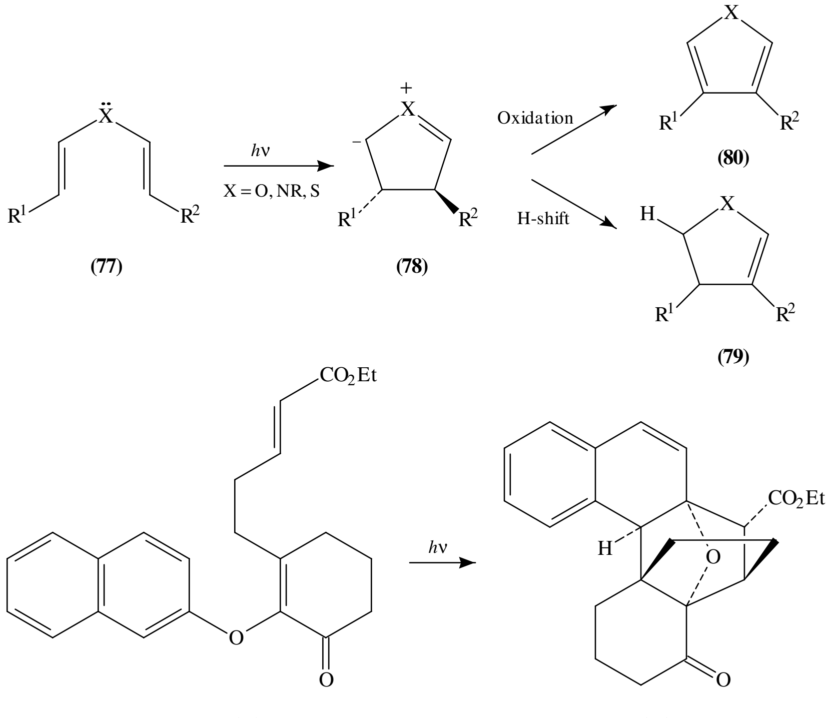
found that, in general, oxime derivatives undergo this rearrangement much more efficiently than do the corresponding imine or hydrazone derivatives.

Electrocyclization of 1,4-dienes is an efficient process when a heteroatom with a lone pair of electrons is placed in the 3-position, as in **77** (Scheme 20)[38]. Photoexcitation of these systems generally results in efficient formation of a C−C bond via 6e conrotatory cyclization to afford the ylide **78**. These reactive intermediates can undergo a variety of processes, including H-transfer (via a suprafacial 1,4-H transfer) to **79** or oxidation to **80**. In a spectacular example of reaction, and the potential it holds for complex molecule synthesis, Dittami and coworkers found that the zwitterion formed by photolysis of divinyl ether **81** could be efficiently trapped in an intramolecular [3 + 2] cycloaddition by the



(75) **(76)**

SCHEME 19



(77) **(78)** **(80)** **(79)**

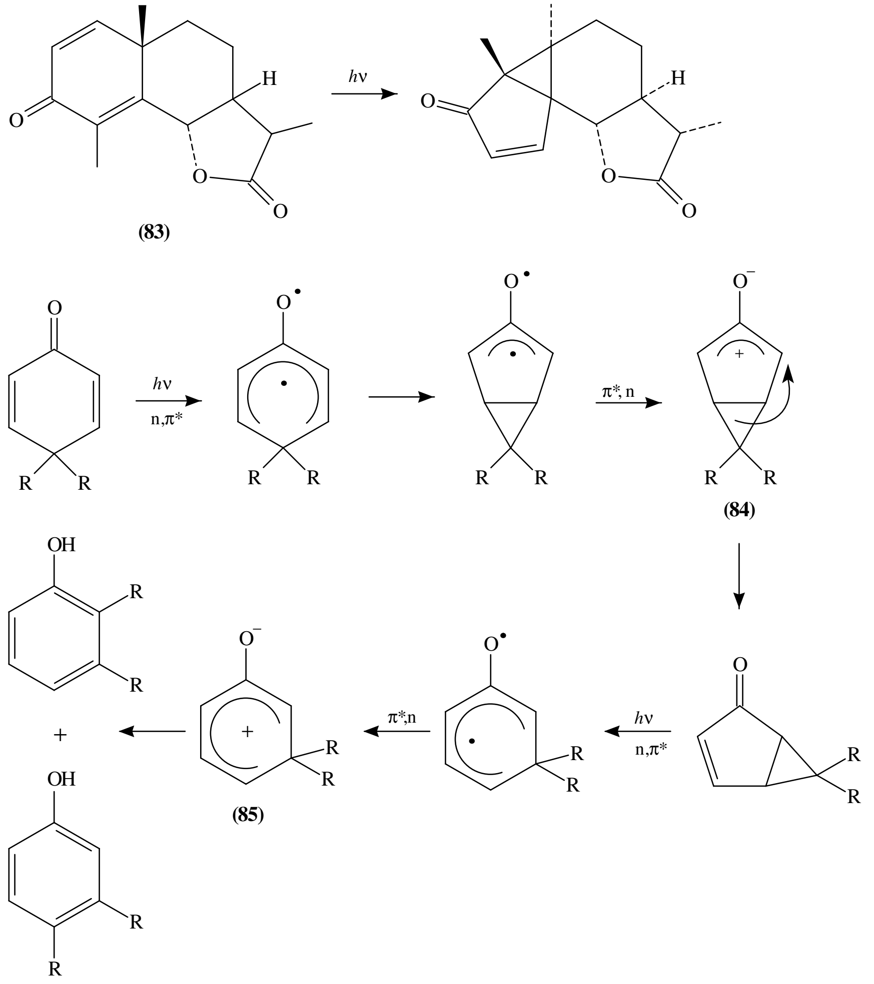
(81) **(82)**

SCHEME 20

pendant acrylate to afford **82** in 85% yield[39]. In general, these electrocyclizations are quite efficient and have been extensively utilized for the synthesis of a variety of complex molecules.

F. Rearrangements of Cross-conjugated Dienones

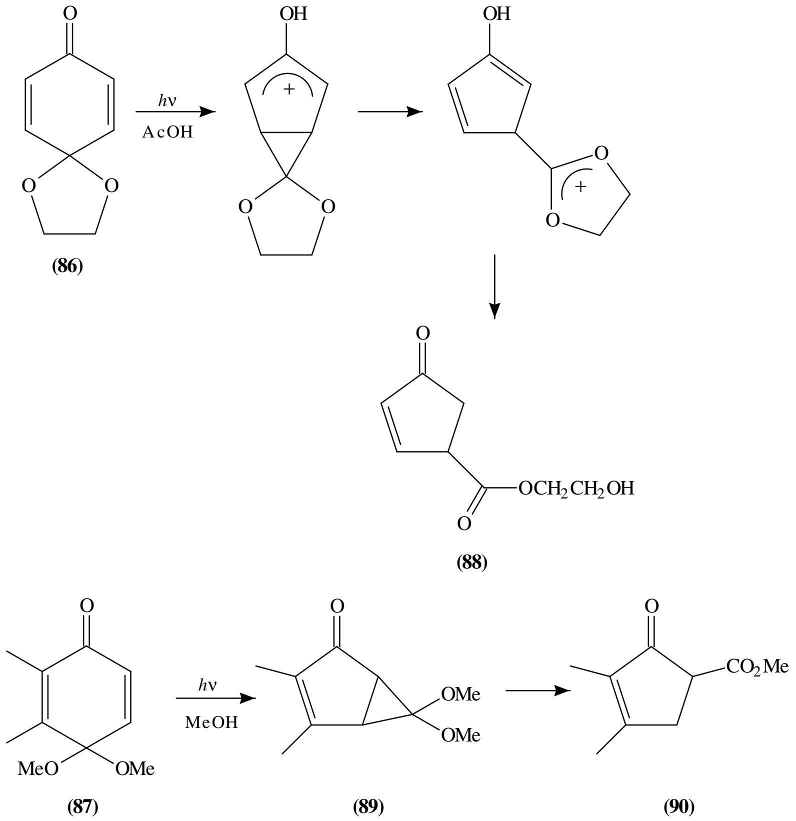
The mechanistic photochemistry of cross-conjugated 2,5-cyclohexadienones has been comprehensively examined (Scheme 21). The photochemical isomerization of the



SCHEME 21

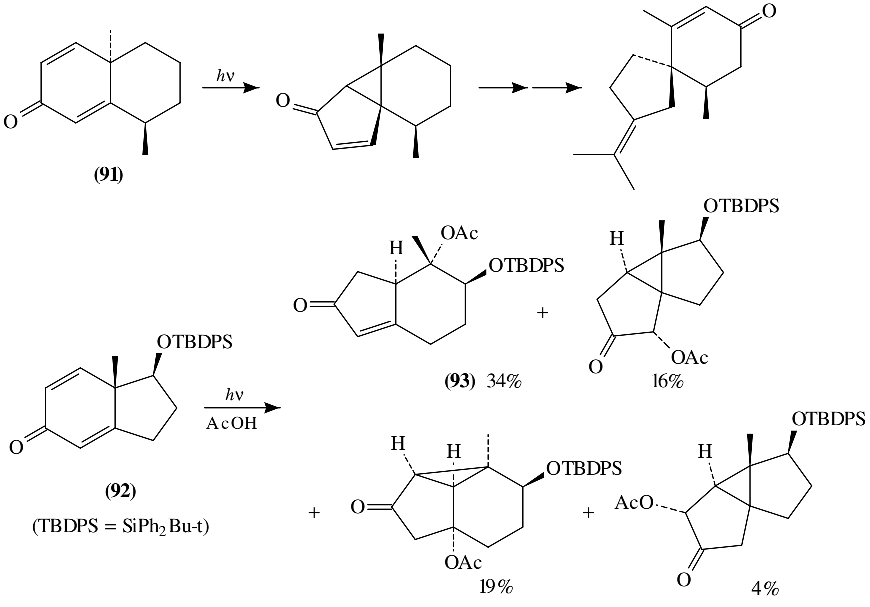
sesquiterpene santonin **83** was first noted more than a century ago. It was later found that these systems undergo photochemical rearrangement to 'lumiketones', with a net extrusion of C-4 and concomitant formation of a new cyclopropane ring[40]. The generally accepted mechanism for this rearrangement[41,42] involves singlet n,π^* excitation, intersystem crossing to the longer-lived triplet state, bonding of the β-carbons of the dienone system, electron demotion to a high-energy zwitterionic ground state and thermal [1,4]-rearrangement of the bicyclic zwitterion. Irradiation of the primary photoproduct gives phenolic secondary photoproducts. This appears to occur via fission of the ring-fusing cyclopropane bond to give a second, conjugated oxyallyl zwitterion **85**, which then suffers [1,2]-migration of one of the substituents on the quaternary carbon. Evidence for 1,5-zwitterion **85** includes formation of the same products following its independent generation under non-photochemical conditions[43].

With the considerable degree of bond reorganization inherent in this rearrangement, it is not surprising that several laboratories have sought to exploit dienone photochemistry in synthesis. Simple, readily accessible quinone monoketals **86** and **87**, which possess the cross-conjugated dienone chomophore, have been examined (Scheme 22)[44]. Upon irradiation, substrate **86** rearranged via the bicyclic oxyallyl intermediate to give the ethylene glycol monoester **88** of cyclopentenone-4-carboxylic acid[44a]. The presence of the electron-rich ketal unit allows for facile fragmentation of the cyclopropane ring of the intermediate. On the other hand, the corresponding dimethyl ketal **87** underwent photochemical conversion to 5-methoxycarbonylcyclopentenones **90**, suggesting the intermediacy of dimethoxycyclopropane **89**[44b].

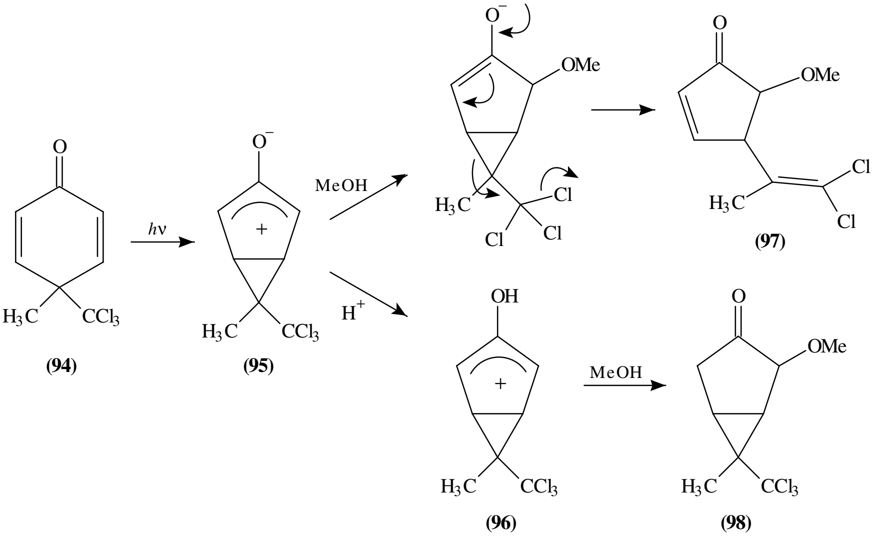


SCHEME 22

In the 1960s, Kropp showed that fused bicyclic dienones structurally related to santonin could potentially serve as synthetically useful precursors to either spirocyclic skeletons or hydroazulenones[45]. One of these cases, **91**, was successfully used by Marshall and Johnson as the starting point in an elegant synthesis of the spirocyclic sesquiterpene β-vetivone (Scheme 23)[46]. More recently, a variety of bicyclic cyclohexadienones have been studied by Caine and coworkers. For example, bicyclic dienone **92** could be photochemically rearranged to the oxygenated bicyclo[4.3.0]nonenone system **93**, along with other rearrangement products, via acetic acid solvolysis of the cyclopropyl ketone intermediate[47].

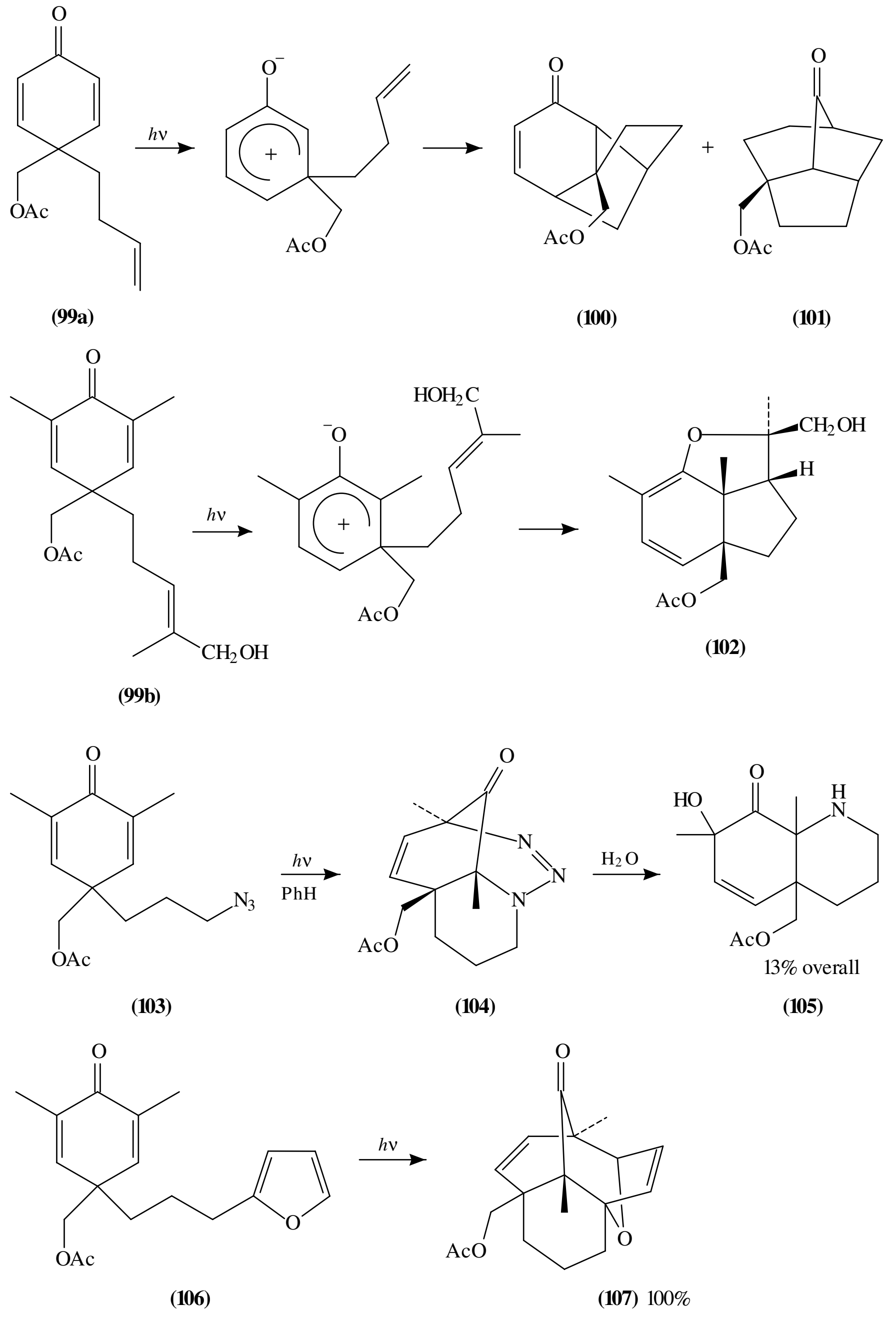


SCHEME 23



SCHEME 24

Direct interception of the initially formed bicyclic oxyallyl zwitterion derived from cyclohexadienones is difficult, due to its facile rearrangement to cyclopropyl ketone. One notable exception is the observation that 4-trichloromethyl-substituted dienone **94** gave solvent adduct **97** when irradiated in methanol, and both **97** and **98** upon irradiation in acidic methanol (Scheme 24)^{48}. It was proposed that **97** arises either from a facile

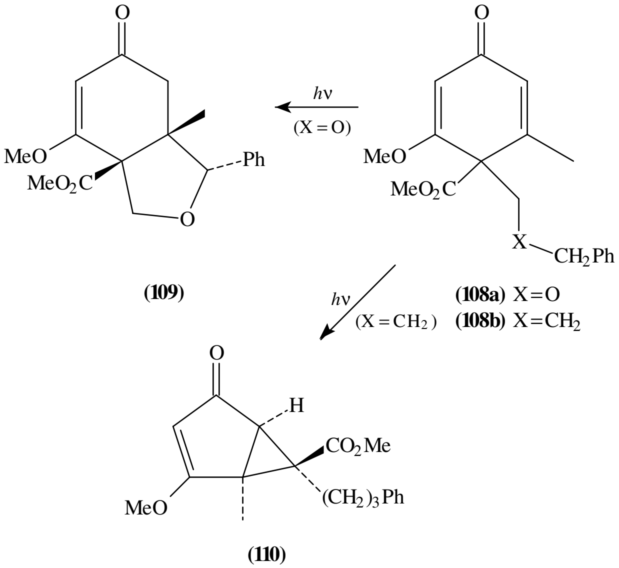

(99a)
hν
(100)
(101)
(99b)
hν
(102)
(103)
hν
PhH
(104)
H₂O
(105)
13% overall
(106)
hν
(107) 100%

SCHEME 25

fragmentation pathway available to the zwitterion **95**, or by solvent capture of **95** followed by fragmentation. Irradiation in an acidic medium would likely involve hydroxyallyl cation **96**, which would undergo solvent capture without fragmentation to give **98**.

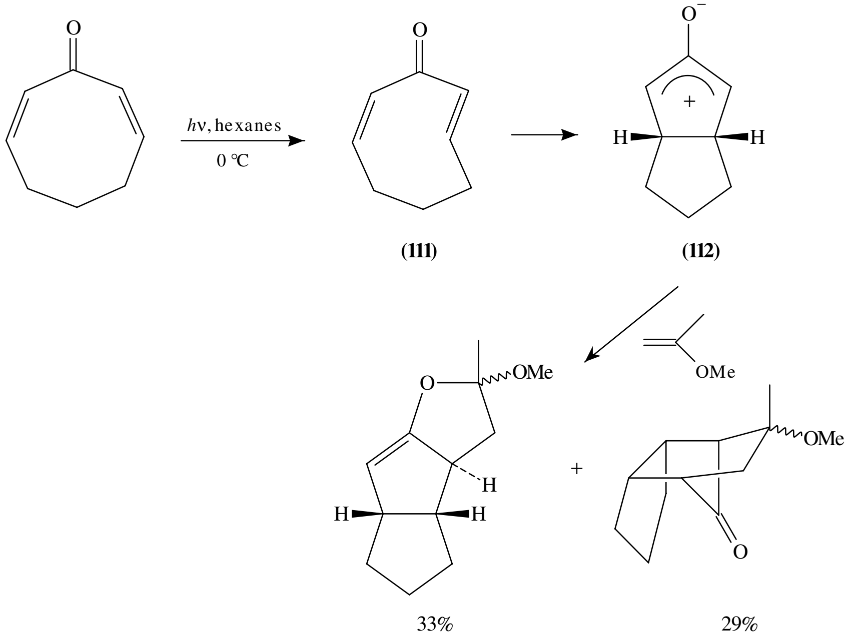
Given the typically rapid rearrangement of the first zwitterion, Schultz and coworkers have focused on trapping processes involving the 1,5-zwitterion arising from secondary photochemistry of the initially formed cyclopropyl ketone (Scheme 25)[49]. Pendant alkenes, as exemplified by substrates **99a** and **99b**, can intercept the zwitterion in a variety of modes, leading to both bridged and fused polycyclic products **100**–**102**[49c]. Formal 3 + 2 cycloadducts **101** and **102** almost certainly arise from a stepwise pathway with initial cationic cyclization, followed by ring closure with either C—O or C—C bond formation. Pendant 4π traps can also be used to capture the zwitterion in a concerted cycloaddition process. For example, azide **103** could be converted to the highly functionalized triazine **104**, which underwent an unusual, water-mediated loss of dinitrogen to furnish hexahydroquinolone **105**[49a]. Likewise, furan-containing substrate **106** gave [4 + 3]-adduct **107** in excellent yield.

More recently, Schultz and coworkers have reported competing hydrogen abstraction chemistry for dienone substrates containing a 4-alkoxymethylene substituent[50]. For example, benzyl ether **108a** was efficiently converted into bicyclic ether **109** as a single diastereomer (Scheme 26). This presumably proceeds through transfer of a benzylic hydrogen to the α-position of the excited dienone, followed by collapse of the resulting biradical. In contrast, dienone **108b**, containing an all-carbon side-chain, underwent typical dienone photochemistry to produce **110**.

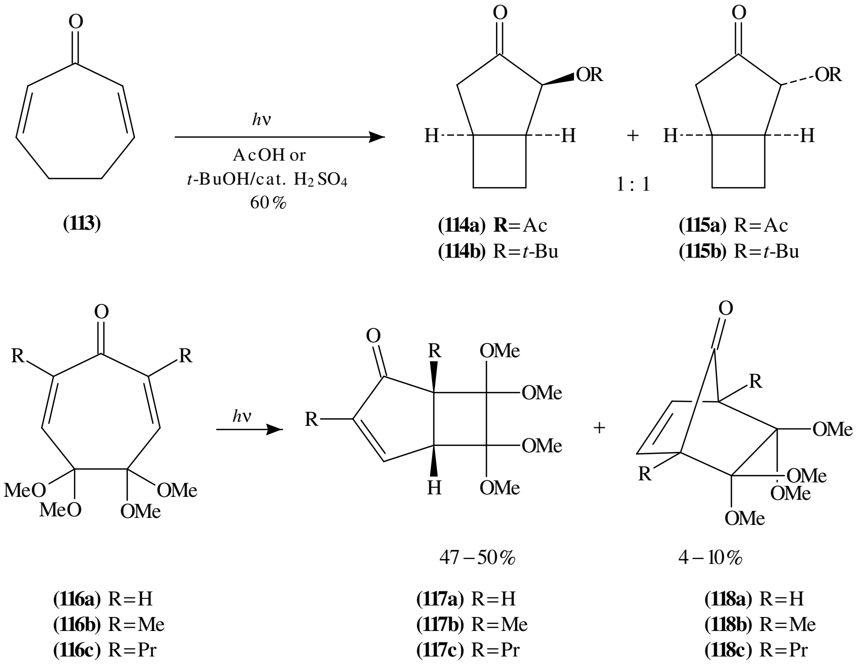


SCHEME 26

Analogous olefin trapping chemistry employing 2,7-cyclooctadienone has been investigated[51]. With this substrate, the oxyallyl zwitterion **112** could be intercepted intermolecularly with simple alkenes in a (presumably stepwise) 3 + 2 manner (Scheme 27). Importantly, intermediate **112** differs from 2,5-cyclohexadienone-derived zwitterions in terms of its lack of a facile rearrangement pathway. An interesting side-issue



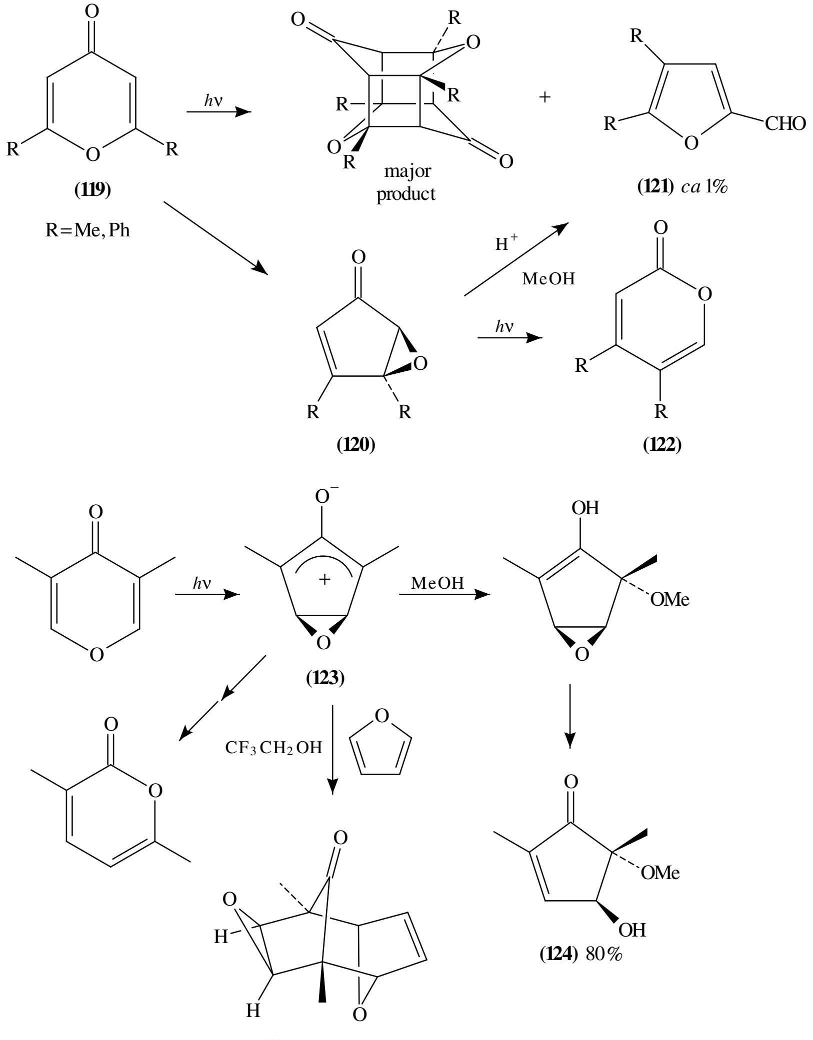
SCHEME 27



SCHEME 28

concerns the mechanism by which **112** is generated, which may differ from the pathway described above (Scheme 21). The authors report evidence for the prior formation of a short-lived, ground-state intermediate at low temperature, which then rearranges to **112** upon warming, and propose highly strained *E*,*Z*-dienone **111** as a candidate for this intermediate.

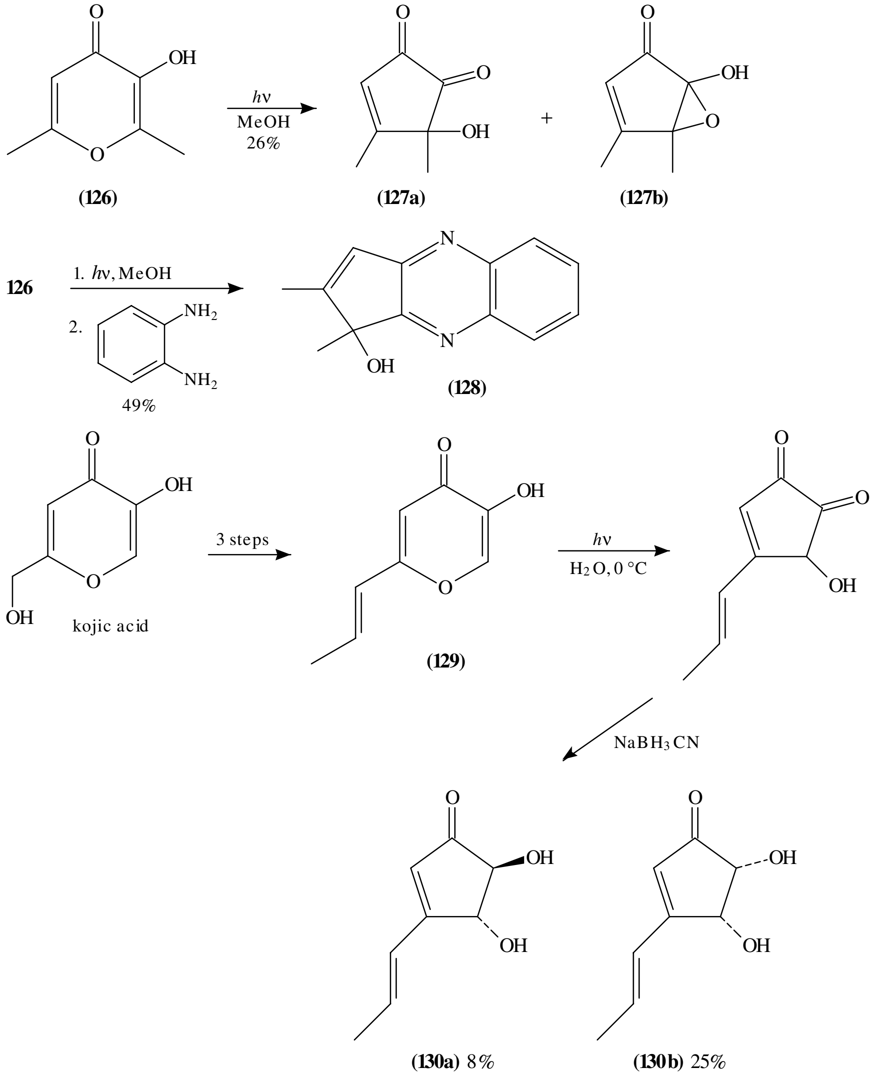
The analogous 2,6-cycloheptadien-1-ones display zwitterion-derived reactivity as well[52,53]. For example, the parent compound **113**, upon irradiation in either acetic acid or *t*-butanol, gave diastereomeric solvent adducts **114** and **115** (Scheme 28)[52a]. On the other hand, tetramethoxy derivatives **116** furnished rearranged products **117**, which are equivalent to the cyclopropyl ketone 1,4-shift products seen with cyclohexadienones[52b].



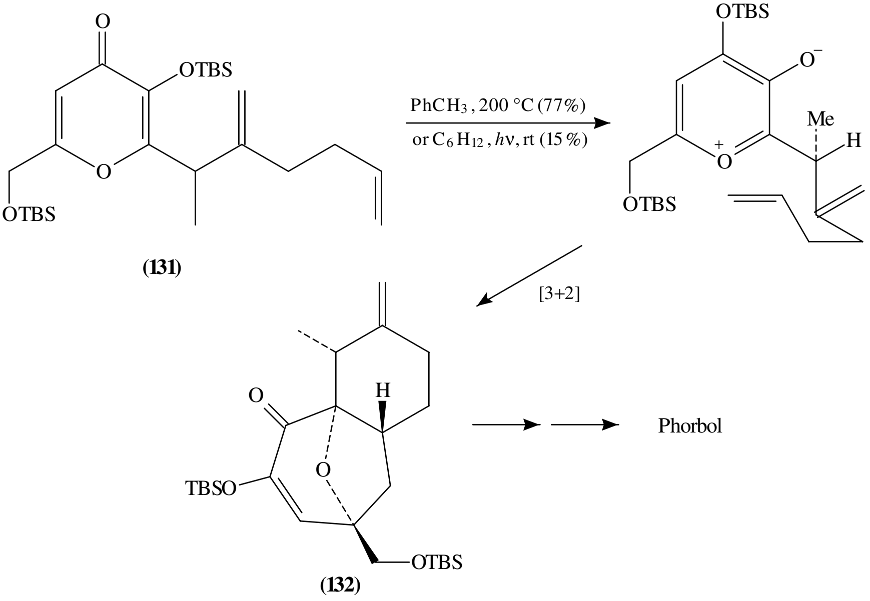
SCHEME 29

In addition to **117**, varying amounts of 7-norbornenones **118** were also isolated, apparently resulting from the 1,3-shift of **117**.

Pyran-4-ones bear an obvious structural similarity to the all-carbon cyclohexadienones discussed above. However, the original studies of their photochemical behavior revealed only dimerization processes to produce a cage product resulting from two successive head-to-tail [2 + 2]-photocycloadditions (Scheme 29)[54]. Much later, small amounts of substituted furfural **121** were observed during the irradiation of **119**[55a]. It was speculated that **121** could arise from bicyclic epoxide **120**, an intermediate analogous to those formed in cyclohexadienone photochemistry. Subsequent reports noted that further irradiation of



SCHEME 30

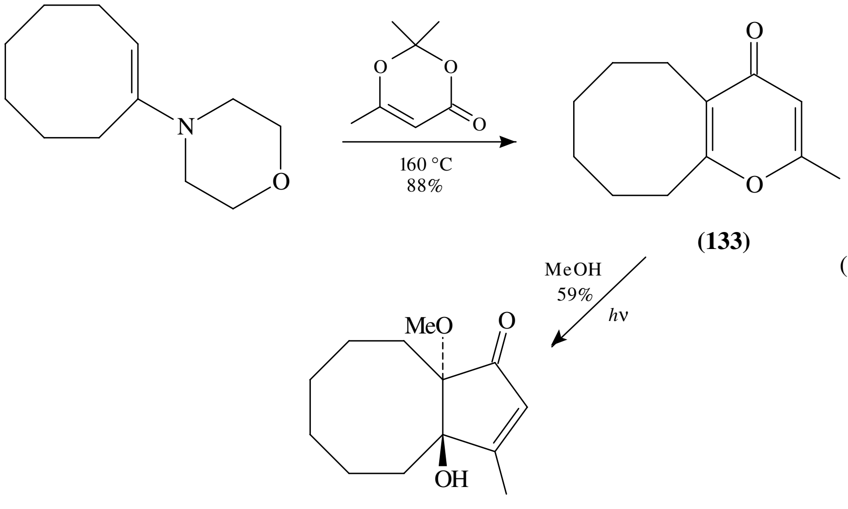


SCHEME 30. (*continued*)

120 led to 2-pyrone **122**, while exposure of **120** to acidic methanol furnished **121**[55b,c]. The photochemical behavior of 4-pyrones in dilute solutions of polar solvents has been examined in detail[56–58]. Rearrangement from 4- to 2-pyrones was found to be a major pathway, and the disposition of the ring substituents suggested the intermediacy of bicyclic zwitterion **123**. The isolation of solvent adducts **124** provided strong evidence for this intermediate. In addition, irradiation in the presence of excess furan led to photoadduct **125**, via a thermally allowed [4 + 3]-cycloaddition of the oxyallyl zwitterion and the diene[58]. Analogous rearrangement of 4-hydroxypyrylium ions to 2-hydroxypyrylium salts was also reported[59].

Substitution with a 3-hydroxy group permits an alternative rearrangement pathway for the zwitterion via deprotonation (Scheme 30). For example, 2,6-dimethyl-3-hydroxy-4-pyrone **126** was converted photochemically to a mixture of hydroxy dione **127a** and epoxy hemiketal **127b**[60a]. Irradiation in the presence of phenylenediamine allowed for an improved yield via *in situ* trapping of the dione to give **128**. A similar transformation was reported involving 3-hydroxy-6-propenyl-4-pyrone **129**, prepared in three steps from readily available kojic acid[60b]. *In situ* reduction gave both the natural product terrein **130a** and its diastereomer **130b**. Use of a 3-silyloxy substituent led to the intervention of an entirely different mechanism. Kojic acid derivative **131**, with a pendant olefin trap, underwent either photochemical or thermal silatropic shift to give a 4-silyloxy-3-oxidopyrylium salt. This intermediate underwent an intramolecular [3 + 2]-cycloaddition to give **132**, which was used in the total synthesis of phorbol[61].

A 2-step route to oxygenated bicyclo[n.3.0]alkanes via bicyclic 4-pyrones such as **133** has been reported (equation 2)[62]. Irradiation in hydroxylic solvents caused ring contraction to the zwitterion, followed by solvent incorporation to give fused bicyclic cyclopentenone **134**. Good regioselectivity in favor of solvent capture at the more substituted oxyallyl terminus was seen in differentially substituted examples, presumably due to increased charge density at that carbon. Attack by solvent was typically *anti* to the zwitterion epoxide, resulting in a *trans* ring-fusion.



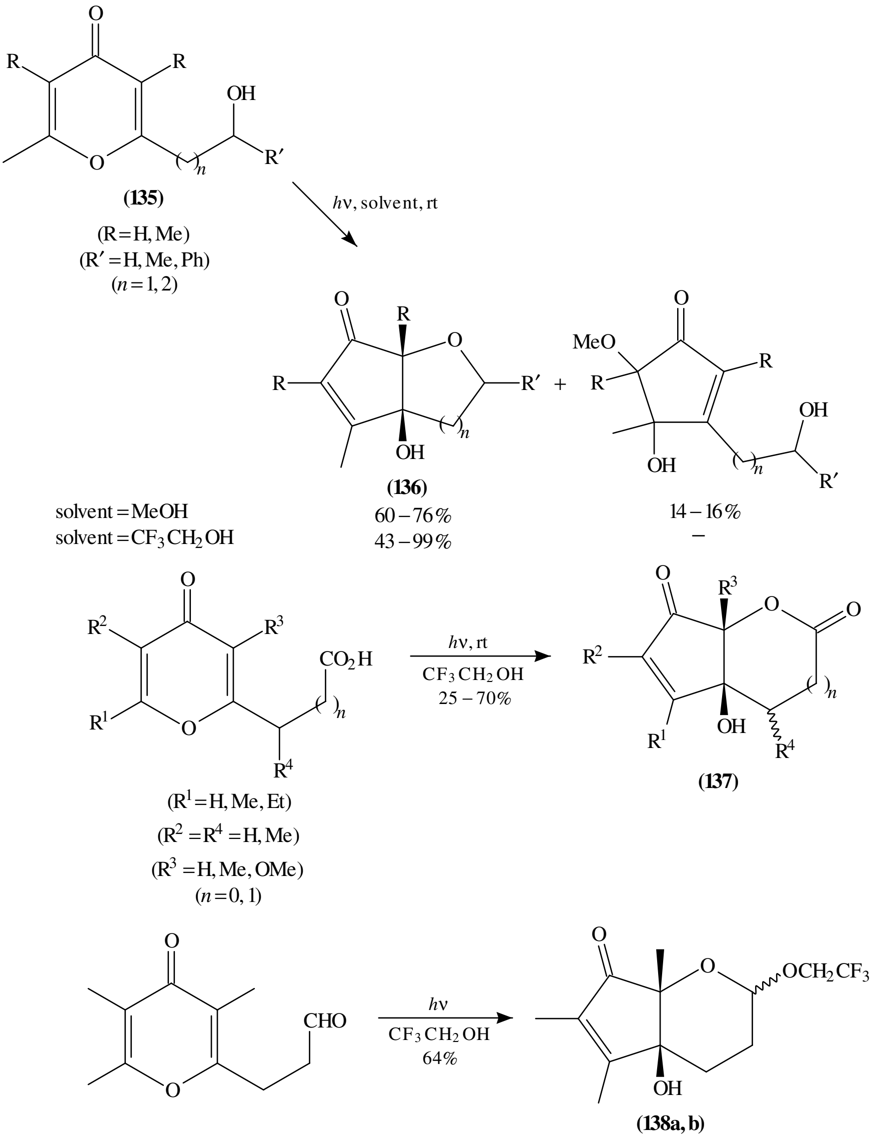
(133)

(134)

(2)

The efficiency of the nucleophilic trapping process could be improved by rendering it unimolecular, permitting a wider range of traps. A polar, protic solvent was necessary for efficient photochemical conversion, consistent with the intervention of a π,π^* excited state. This requirement permits a possible competition between the desired intramolecular reaction and intermolecular trapping. 2-Hydroxyalkyl-4-pyrones **135** furnished good yields of intramolecular trapping products **136** in methanol, and only minor amounts of the corresponding solvent adducts (Scheme 31)[63]. Solvent capture could be suppressed completely by use of the less nucleophilic trifluoroethanol. Pendant carboxylic acids were also used as internal traps, giving lactone-fused cyclopentenones **137**[64]. Prior proton transfer to generate a more reactive electrophile/nucleophile pair was deemed a likely possibility in this process. Preliminary studies indicate that a benzyl ether can intercept the zwitterion, with subsequent debenzylation, to give a bicyclic ether identical to that obtained from irradiation of the corresponding free alcohol[65]. Aldehydes were also found to trap through oxygen, giving epimeric bicyclic mixed acetals **138** after solvent addition to the resulting oxocarbenium ion[65].

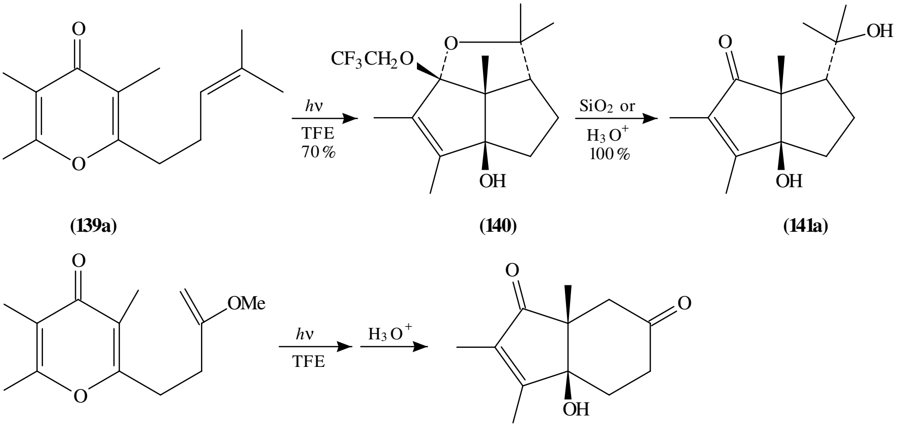
Neutral, π-rich carbon nucleophiles also served as effective internal traps[66]. Irradiation of **139a** in trifluoroethanol at room temperature led to rapid consumption of the starting 4-pyrone and formation of one principal new product, tricyclic mixed ketal **140** (Scheme 32). A second compound, determined to be hydrolysis product **141a**, was formed in trace quantities during chromatography, and could be obtained quantitatively from **140** by treatment with dilute acid. Notably, two new carbon–carbon bonds were formed and three new stereocenters were set with complete control in this process. By varying the olefin substitution pattern (e.g. **139b**), the cationic cyclization step could be switched from a 5-*exo* to a 6-*endo* mode. Substitution at C-3 had a pronounced effect on the stereoselectivity of the cyclization. In those cases bearing only hydrogen at C-3, a mixture of products was obtained, arising from unselective closure to a mixture of epimeric tertiary carbocations. On the other hand, complete diastereoselectivity in favor of an *endo*-oriented carbocation (the product of a compact transition state) was observed in



SCHEME 31

those cases with a nonhydrogen group at C-3. This may result from a destabilizing interaction in the extended transition state leading to the *exo*-disposed carbocation. Schultz and coworkers noted comparable diastereoselectivity in the 5-*exo* cationic cyclizations of 1,5-zwitterions[49c].

Intramolecular electrophilic aromatic substitution to give tricyclic products **142** is also a viable process, with trapping efficiency related to the electron density of the arene trap (equation 3)[67]. With a simple phenyl group pendant, rearrangement to the 2-pyrone was

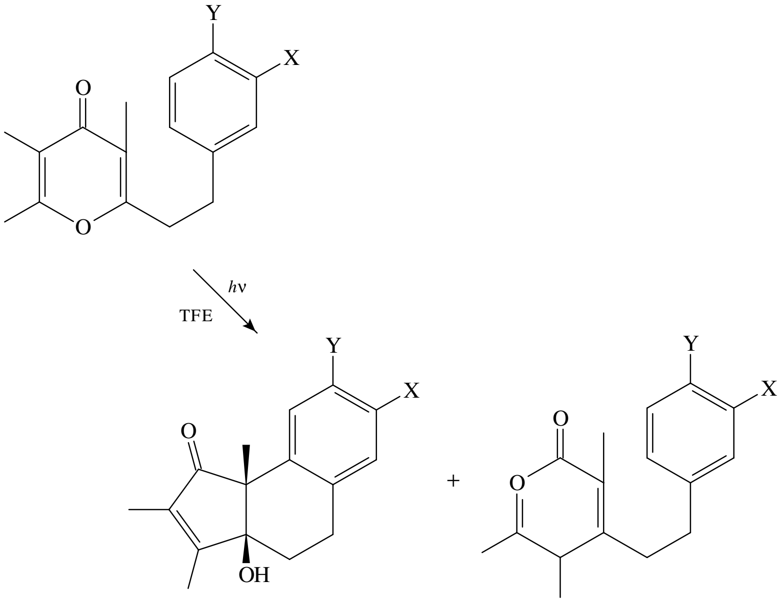


(139a) **(140)** **(141a)**

(139b) **(141b)** (61%)

SCHEME 32

the major pathway, and photocyclization was relatively minor. Additional alkoxy groups on the arene increased the efficiency of the cyclization step, and good yields of tricyclic trapping products were seen.



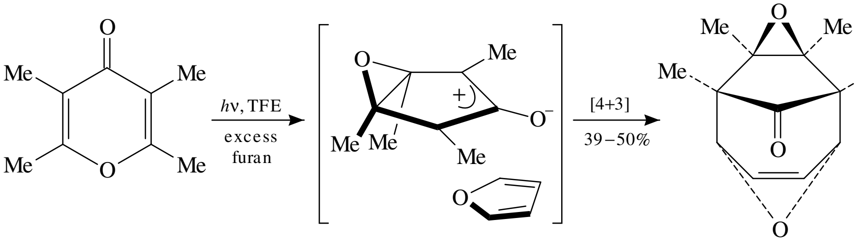
(3)

(142)

X = Y = H: 32% 51%

XY = OCH_2O: 75% –

As noted above, formation of a furan [4 + 3]-cycloadduct during irradiation of a 4-pyrone was advanced as evidence for the zwitterionic intermediate. This process can be moderately efficient (equation 4)[68], and can be envisioned as an approach to substituted cyclooctanoids. Besides the formation of three new carbon–carbon bonds, an additional attractive feature is the complete diastereoselectivity, arising from a compact [4 + 3]-cycloaddition transition state with approach from the face opposite the epoxide. However, the generality of the intermolecular reaction is limited, as competing [2 + 2]-photodimerization, solvent trapping and rearrangement often predominate[58].

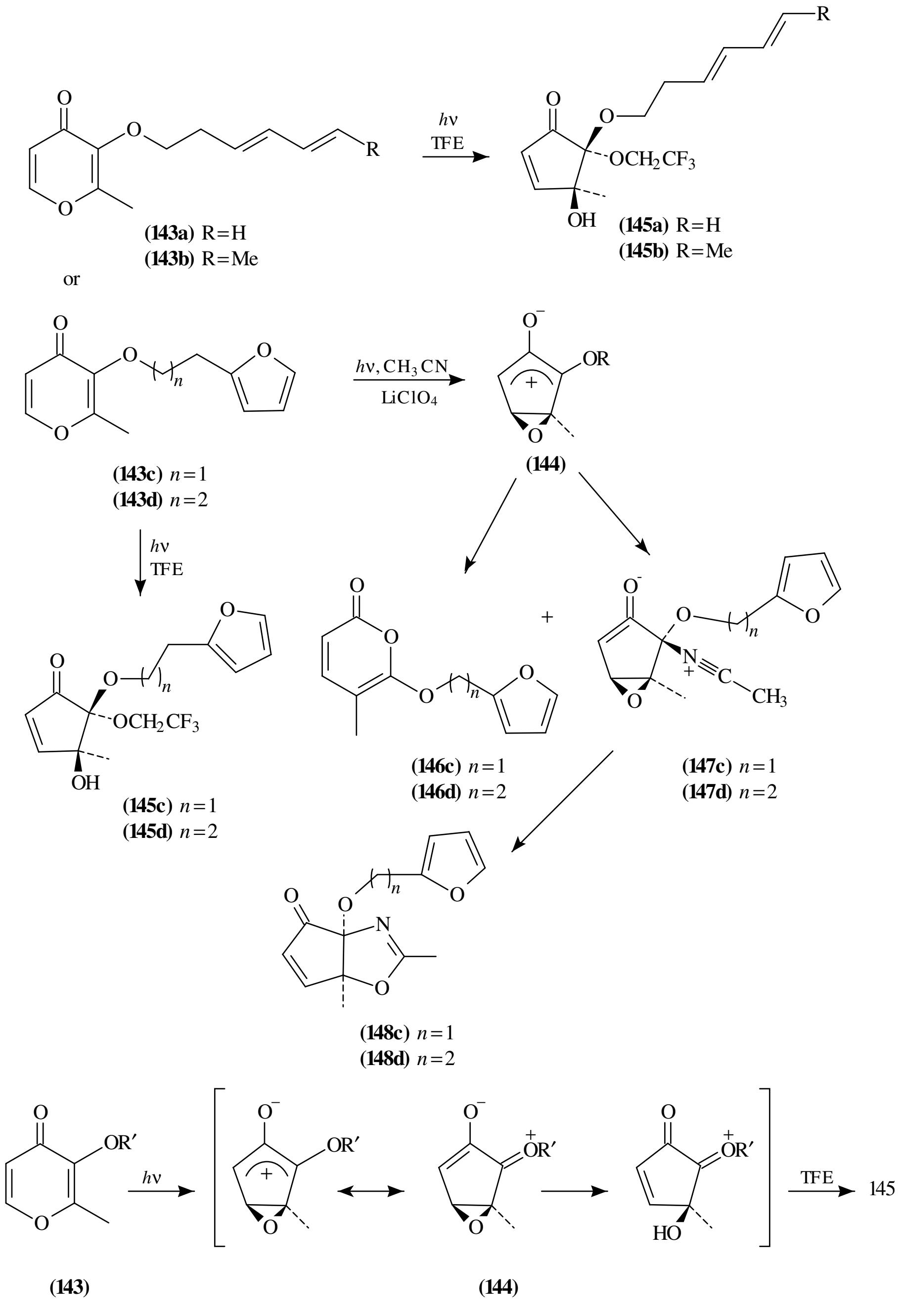


(4)

Irradiation of substrates **143** in trifluoroethanol led to their efficient consumption and formation in each case of a single new product, which surprisingly proved to be simple solvent adducts **145** rather than the expected intramolecular [4 + 3]-cycloadducts (Scheme 33)[68]. The unusually efficient capture by the relatively unreactive trifluoroethanol can be explained in terms of strongly polarized zwitterionic intermediates **144**, which undergo ionic processes in preference to the desired cycloadditions. Polar, aprotic solvent systems such as acetonitrile containing $LiClO_4$ were also examined, and in the case of **143c–d**, a mixture of 2-pyrones **146** and bicyclic oxazolines **148** was obtained[69]. The novel oxazoline products presumably arise from solvent capture of the zwitterion in a Ritter-type process, leading to nitrilium intermediates **147**. Subsequent epoxide opening would allow for attack of the alkoxide on the nitrilium to close the oxazoline ring.

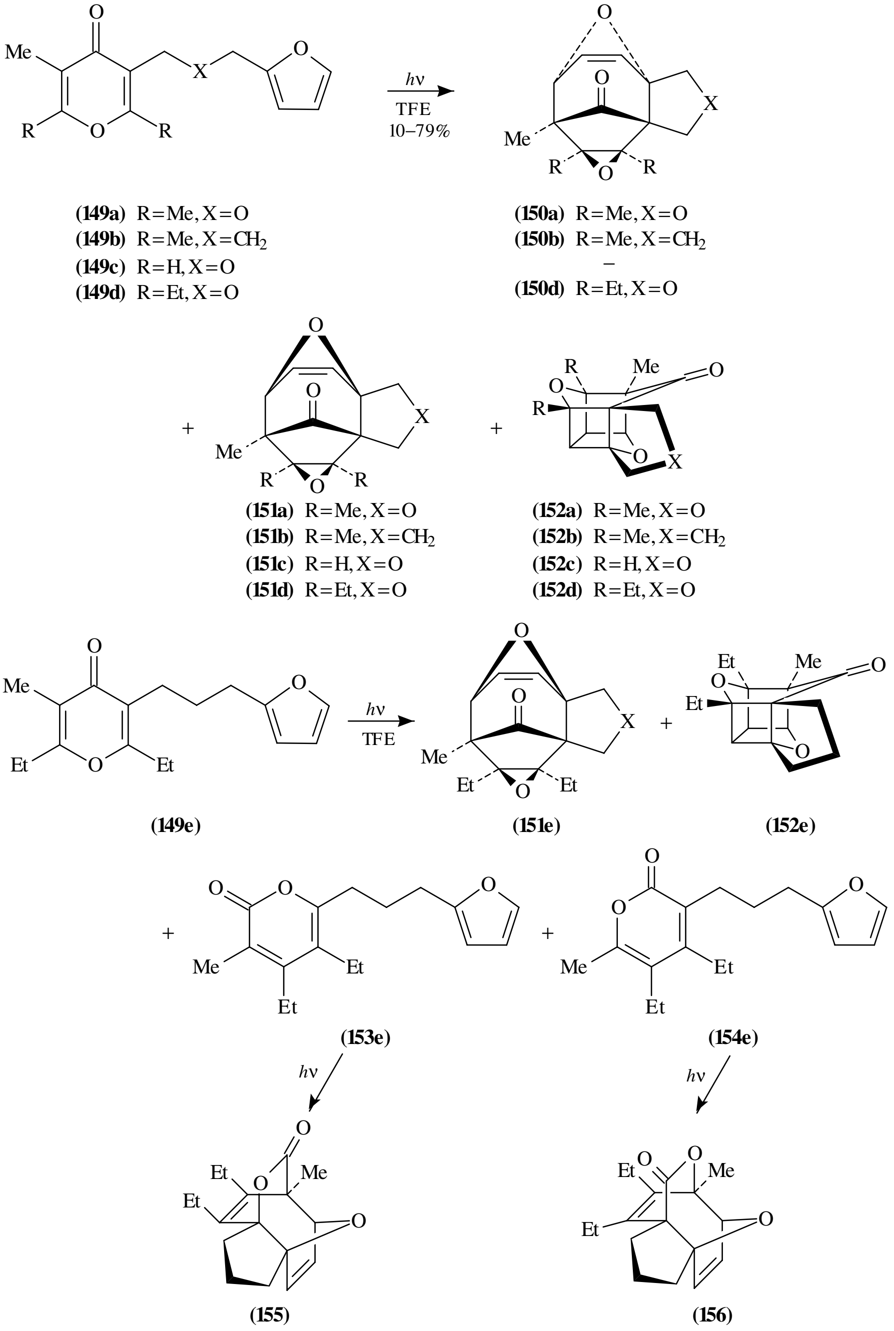
In contrast, substrates **149** all furnished [4 + 3]-cycloadducts **150** and **151** in yields ranging from 10–79% (Scheme 34)[68]. In all cases, exclusive approach of the furan from the zwitterion face opposite the epoxide ring was seen. In most cases, the *exo* diastereomer **151** was the major product or was formed to the exclusion of the *endo* diastereomer **150**. The contrasting diastereoselectivity seen in inter- and intramolecular cycloadditions may result from unfavorable nonbonding interactions in the *endo* transition state between the tether atoms and the alkyl groups at C-2 and C-5.

In some cases additional photoproducts were formed, including cage structure **152** (presumably arising from sequential intramolecular [2 + 2]-photocycloadditions in analogy to the previously discussed 4-pyrone dimers[54]). This is exemplified in Scheme 34 by the reaction of **149e**, leading to varying amounts of 2-pyrone rearrangement products **153e** and **154e**, and another side product[68]. The structure assigned was lactone bridged cyclooctadiene **155**, most likely formed via intramolecular [4 + 4]-photocycloaddition between the furan and 2-pyrone units of secondary photoproduct **153e**. This was confirmed by careful irradiation of **153e** and **154e** to give **155** and **156**, respectively, as the major photoproducts. A more detailed discussion of photochemical [4 + 4]-cycloaddition reactions of 2-pyrones and related diene systems is found elsewhere in this chapter.



(143a) R=H
(143b) R=Me
or
hν
TFE
(145a) R=H
(145b) R=Me
(143c) n=1
(143d) n=2
hν, CH3CN
LiClO4
(144)
hν
TFE
(145c) n=1
(145d) n=2
(146c) n=1
(146d) n=2
(147c) n=1
(147d) n=2
(148c) n=1
(148d) n=2
hν
TFE
145
(143)
(144)

SCHEME 33



(149a) R=Me, X=O
(149b) R=Me, X=CH_2
(149c) R=H, X=O
(149d) R=Et, X=O

(150a) R=Me, X=O
(150b) R=Me, X=CH_2
–
(150d) R=Et, X=O

(151a) R=Me, X=O
(151b) R=Me, X=CH_2
(151c) R=H, X=O
(151d) R=Et, X=O

(152a) R=Me, X=O
(152b) R=Me, X=CH_2
(152c) R=H, X=O
(152d) R=Et, X=O

(149e) **(151e)** **(152e)**

(153e) **(154e)**

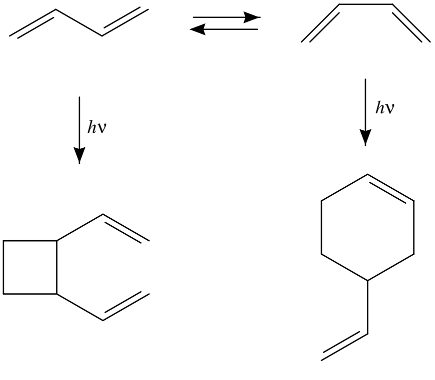
(155) **(156)**

SCHEME 34

III. PHOTOCYCLOADDITIONS INVOLVING DIENES AND POLYENES

A. [2 + 2]-Photodimerization of 1,3-Dienes

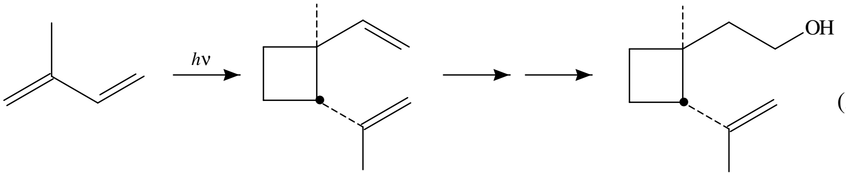
Sensitized irradiation of butadiene produces two significant photoproducts, the cyclobutane **157** as the major product and the minor cyclohexene isomer, **158** (Scheme 35)[70]. Based on extensive photophysical studies, **157** is thought to arise from excitation of the lower-energy s-*trans* ground state conformer, while **158** presumably arises primarily from the higher-energy s-*cis* ground state form. While this reaction has been well characterized, the photodimerization of other acyclic dienes often gives hopelessly complex mixtures of products, thereby limiting the synthetic utility of this process.



(157) **(158)**

SCHEME 35

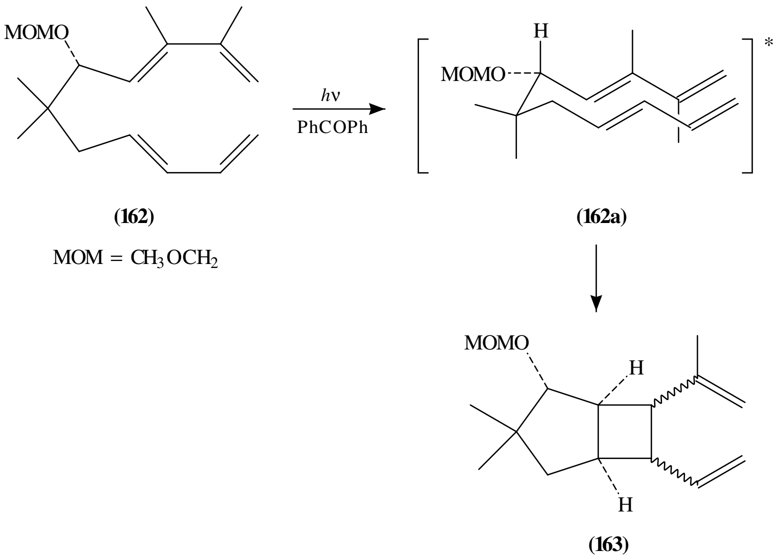
Though the triplet sensitized photolysis of isoprene **(159)** does, as noted above, produce a complex mixture of products, one of these adducts has been used in the context of complex molecule synthesis (equation 5)[71]. Cyclobutane **160**, which was formed in *ca* 20% yield by the benzophenone sensitized photolysis of **159**, could be easily transformed into fragrantolol, **161**, an isomer of grandisol isolated from the roots of the *Artemisia fragrans*, by simple hydroboration/oxidation of the less hindered double bond.



(5)

(159) **(160)** **(161)**

While the divinylcyclobutanes produced by the photodimerization of dienes would seem to possess considerable potential as synthons, the problems encountered by the often remarkably complex mixtures of regio- and stereoisomers produced in these reactions rendered these transformations unusable until recently. Wender and Correia have found an ingeneous solution to these problems by tethering the two reacting 1,3-diene moieties together, e.g. **162**, thereby eliminating most of the regio- and stereochemical issues which proved problematic in intermolecular diene photocycloadditions (Scheme 36)[72]. The initial [2 + 2] cycloadditon of bis(diene) **162** must afford adducts **163** in which the



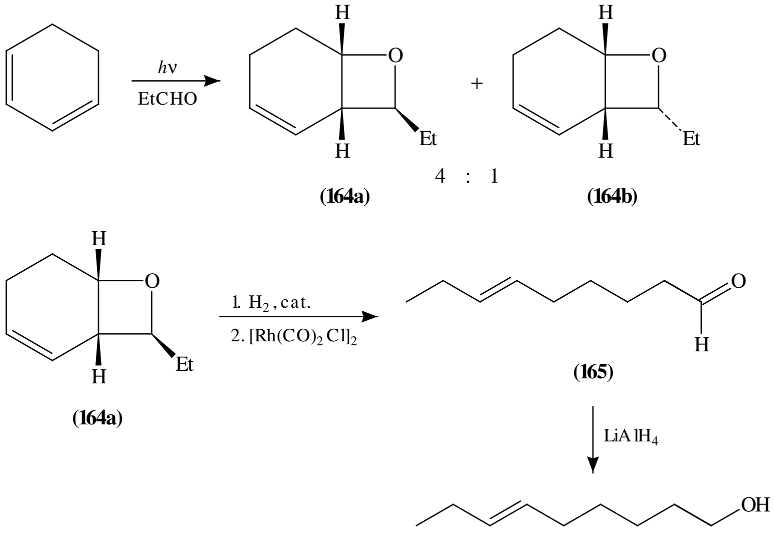
SCHEME 36

five- and four-membered rings in the adducts are *cis*-fused, as formation of the corresponding *trans*-fused products would be too energetically demanding. The regiochemistry of the photocycloaddition is also controlled by the tether. It is interesting to note that the protected alkoxy substituent on the tethering atoms in **162** profoundly affected the stereoinduction in the initial [2 + 2]-photocycloaddition; the high degree of stereocontrol exhibited during the formation of the three contiguous stereogenic centers in this adduct was rationalized in terms of this substituent adopting a pseudo-equatorial position in a reacting conformer such as **162a**. This approach was used as an entry into formal [4+4]-cycloadducts via subsequent ring-expansion of the divinylcyclobutanes (discussed below in Section III.C).

B. Paterno–Büchi Reactions Employing Conjugated Dienes

The [2+2]-photocycloaddition of carbonyl groups with olefins (Paterno–Büchi reaction) is one of the oldest known photochemical reactions and has become increasingly important for the synthesis of complex molecules. Existing reviews have summarized the mechanistic considerations and defined the scope and limitations of this photocycloaddition[73]. Although this reaction likely proceeds via initial excitation of the carbonyl compound and not the excited state of the diene, the many examples of this reaction in natural product synthesis justify inclusion in this chapter.

Synthetic application of Paterno–Büchi reaction of simple dienes with carbonyl compounds is rare[73]. While seemingly an extension of the photocycloaddition of olefins and carbonyl compounds, the reaction between dienes and carbonyls is often complicated by the fact that triplet excited states of carbonyl compounds are quenched by dienes, although the formation of oxetanes can be observed during these reactions[74]. Recall also that the photosensitized dimerization of diene triplet excited states is also a well known reaction (*vide infra*); these two observations would seem to naturally limit the synthetic potential of this process[75]. Kubota and coworkers found that irradiation of propanal in the presence of 1,3-cyclohexadiene produced oxetanes **164a** and **164b** in a 4:1 ratio (Scheme 37)[76].

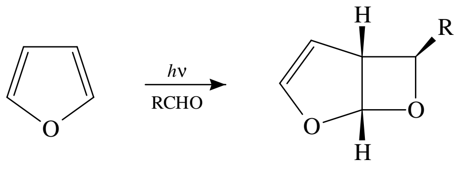


SCHEME 37

These adducts were thought to occur via attack of the first excited singlet state of propanal on the diene. Evidence from subsequent studies point to the fact that it is likely the excited singlet state of the aldehyde that is responsible for the Paterno–Büchi reaction with 1,3-dienes. This comes from a number of sources and includes evidence from a number of studies[73,77]. The synthesis of (*E*)-6-nonen-1-ol, a component of the sex pheromone of the Mediterranean fruit fly, applied this process as the first step[78]. Hydrogenation and metal catalyzed [2 + 2] cycloreversion gave **165**, which was then easily converted to the target by reduction (Scheme 37).

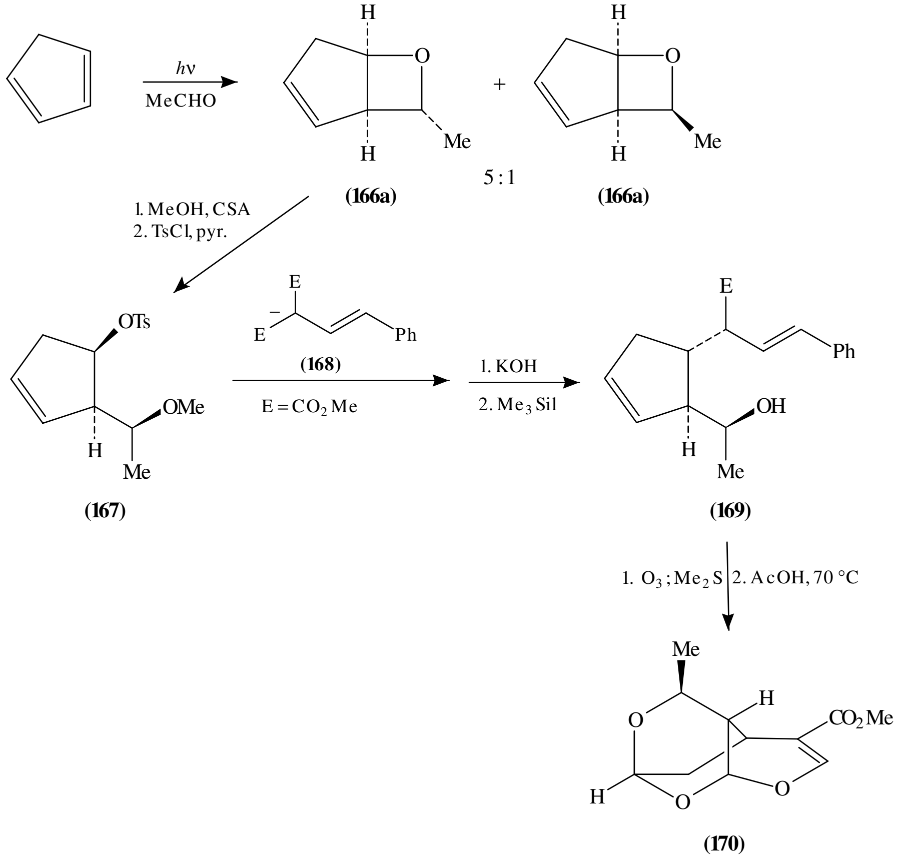
Hoye and Richardson have published an ingeneous synthesis of the tricyclic iridoid sarracenin **(170)** which relied on the Paterno–Büchi cycloaddition between acetaldehyde and cyclopentadiene as the intial step (Scheme 38)[79]. This reaction provided a 5:1 mixture of adducts **166a** and **166b**. The major adduct was opened with camphor-10-sulfonic acid (CSA) in methanol and the alcohol was tosylated to give **167**. Displacement with malonate **168** and decarboalkoxylation/demethylation steps gave **169**. Ozonolysis, reductive work-up and acid-catalyzed acetalization then furnished **170**.

The Paterno–Büchi photocycloaddition between carbonyl compounds and furans was first described in 1965 (equation 6)[80]. This report noted that only the head-to-head product **171** was formed, and that high *exo* face selectivity was exhibited. Subsequent to this and other early reports, this reaction has been systematically explored by several groups, owing largely to the various ways in which the 2,7-dioxabicyclo[3.2.0]hept-3-ene ring system can be exploited[73c,81].



(171)

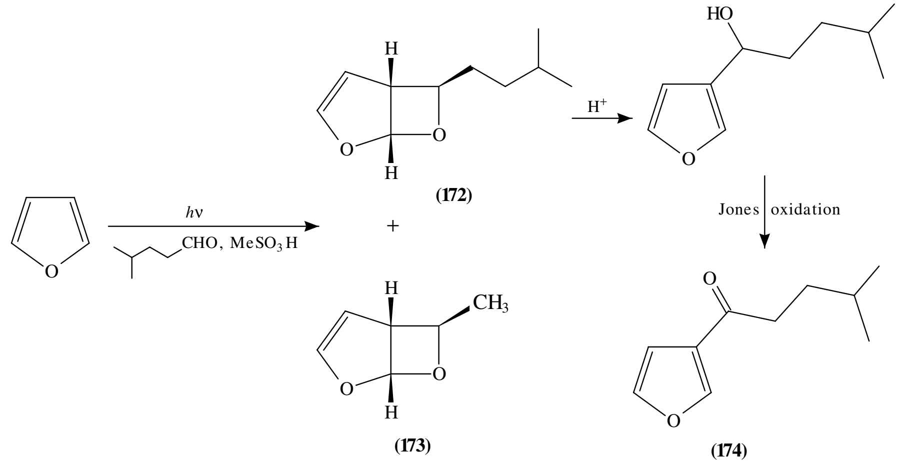
(6)



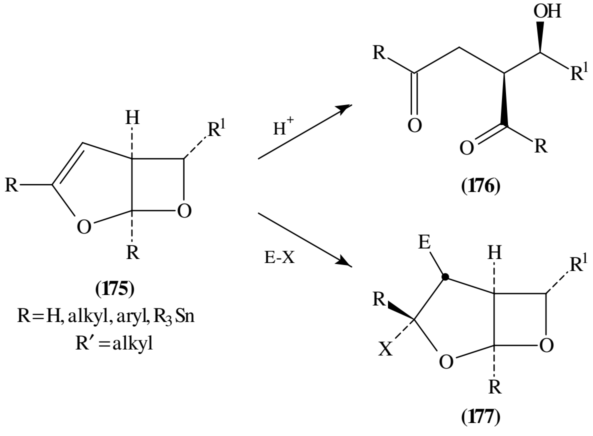
SCHEME 38

These cycloadducts, at their most elementary level, are excellent intermediates for the synthesis of 3-substituted furan derivatives. For example, Kawanisi and coworkers reported a synthesis of perillaketone **174** in which the critical step was a Paterno–Büchi photocycloaddition between furan and 4-methylpentanal in the presence of methanesulfonic acid (Scheme 39)[82]. This reaction furnished two initial photoadducts, **172** and **173**. The unexpected product **173** presumably arises from a Norrish Type II cleavage of 4-methylpentanal to give acetaldehyde, and subsequent cycloaddition with furan. The desired cycloadduct **172** was then converted uneventfully to **174** via acid-catalyzed aromatization and oxidation.

Schreiber and his coworkers have published extensively over the past decade on the use of this photocycloaddition for the synthesis of complex molecules[73c,81]. Schreiber was the first to recognize that the bicyclic adducts formed in these reactions could be unmasked under acidic conditions to afford *threo* aldol products of 1,4-dicarbonyl compounds (**175** to **176**) (Scheme 40). The *cis*-bicyclic system also offers excellent stereocontrol in the addition of various electrophilic reagents (E—X) to the enol ether of these photoadducts on its convex face (**175** to **177**). This strategy has been exploited in the synthesis of a variety of architecturally novel natural products.



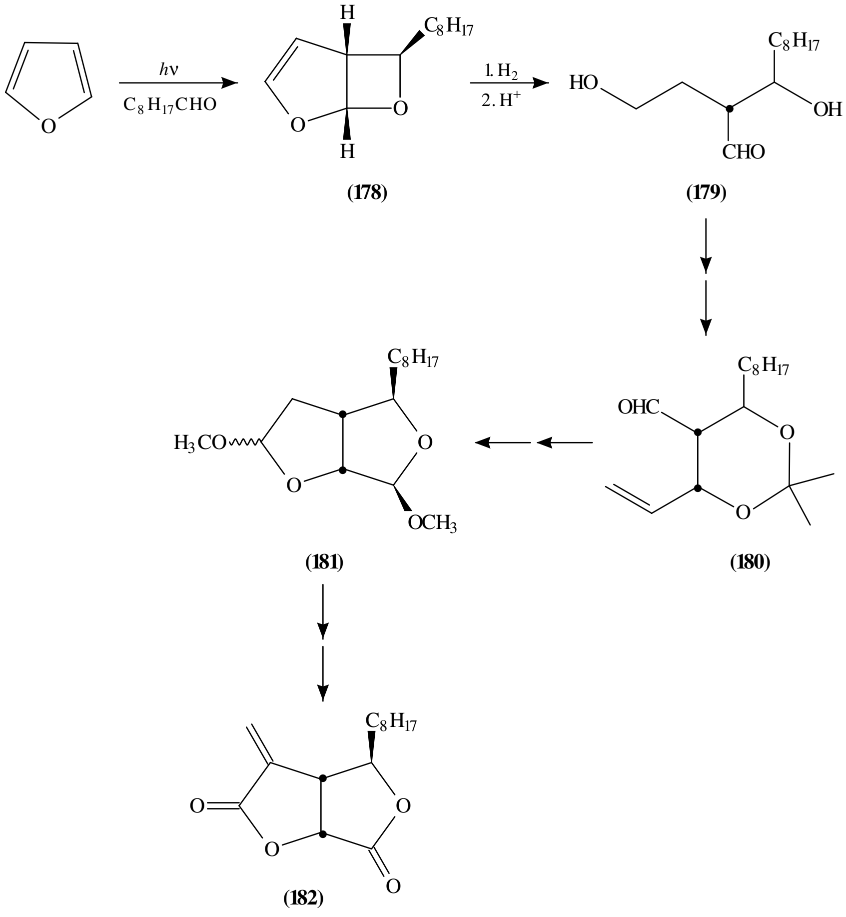
SCHEME 39



SCHEME 40

An application of this strategy to the synthesis of the antifungal metabolite (±)-avenaciolide **182** is shown in Scheme 41[83]. The photoadduct in this case, **178**, was hydrogenated and hydrolyzed to give **179**. Reaction of **179** with vinylmagnesium bromide and subsequent manipulation afforded aldehyde **180**, which could be transformed via ozonolysis, epimerization of the dialdehyde and acidification of the dialdehyde acetonide to protected bis(lactol) **181**. Oxidation and methylenation then afforded the desired target **182**.

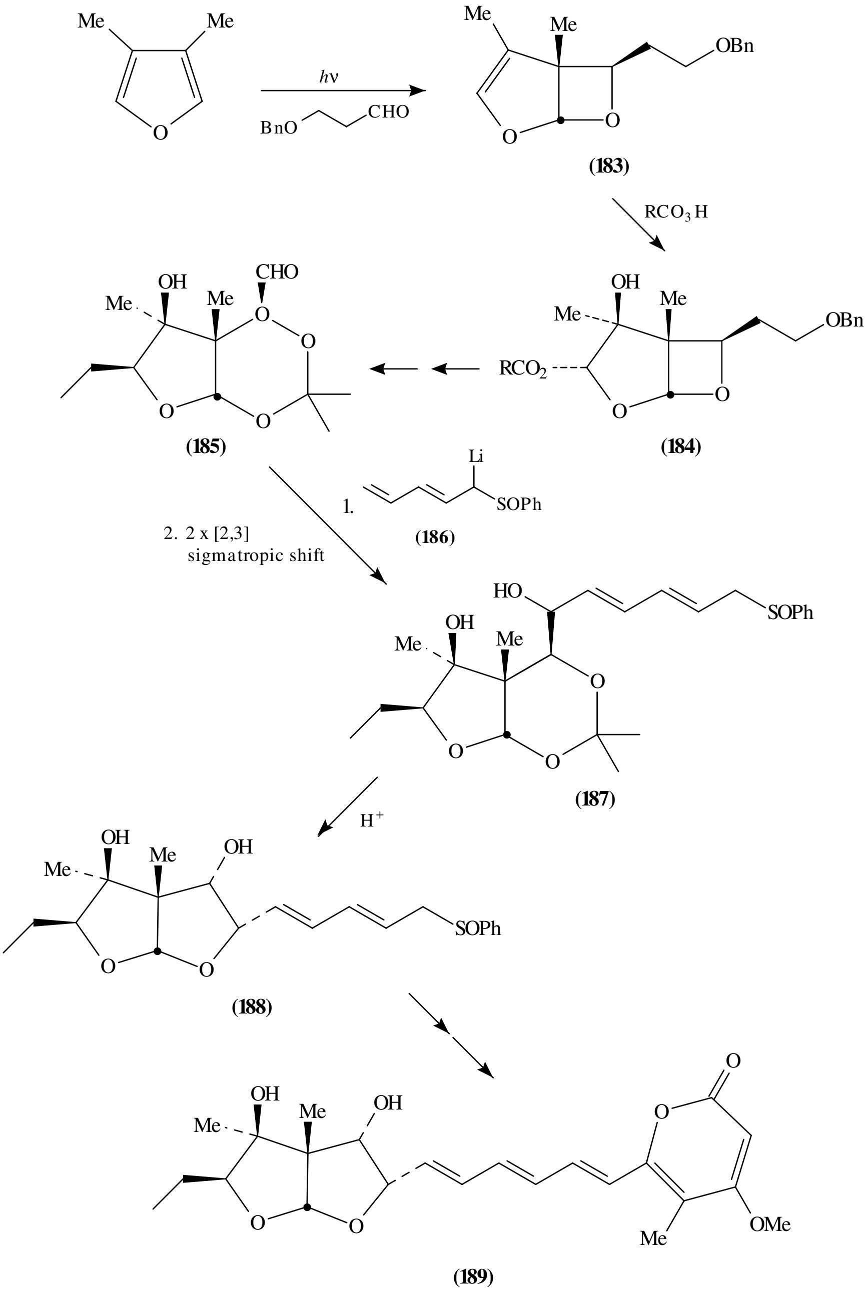
Efficient synthesis of the mycotoxin asteltoxin **189** was accomplished beginning with the cycloaddition between 3,4-dimethylfuran and 3-benzyloxypropanal, which furnished photoaldol **183** in 63% yield (Scheme 42)[84]. Epoxidation from the convex face of this adduct, with subsequent epoxide opening, afforded **184**, which was then elaborated through a series of steps to **185**. The side chain was introduced via lithiosulfoxide **186** to furnish, after double sigmatropic rearrangement, **187**. Hydrolysis of this afforded **188**, which was oxidized and elaborated to **189** in two steps.



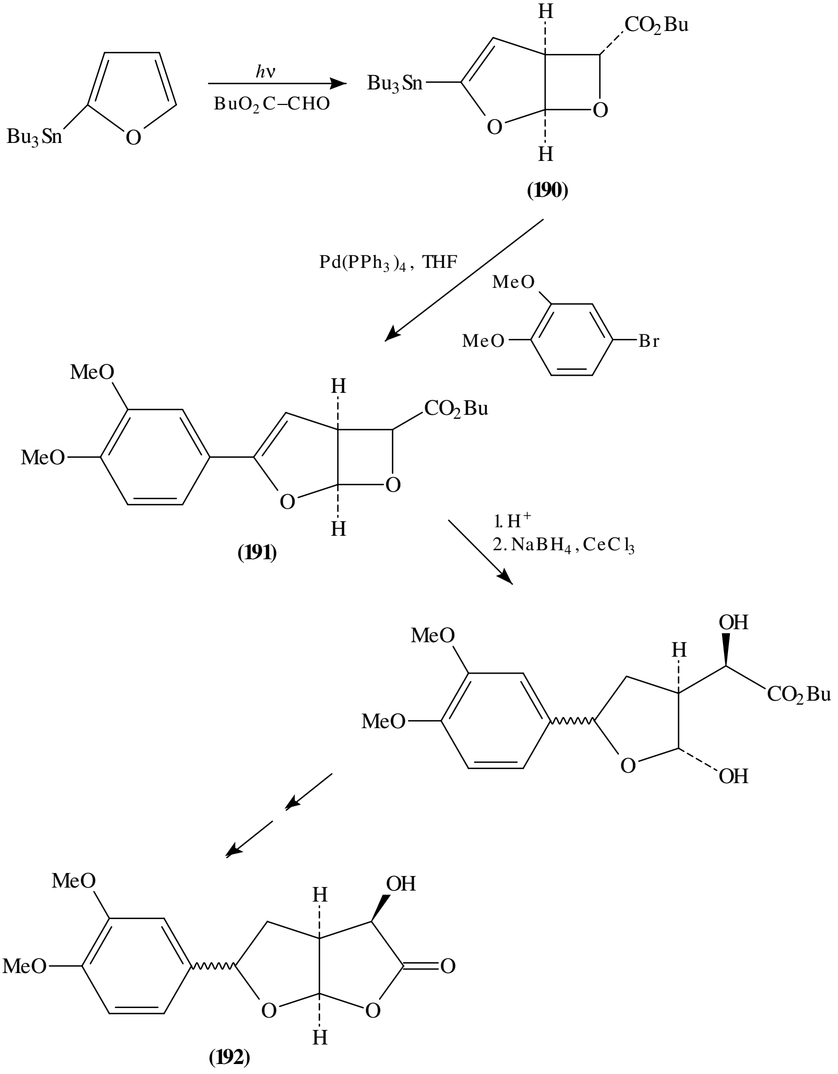
SCHEME 41

Schreiber and coworkers also have described an interesting variation on the furan-carbonyl photcycloaddition using silyl and stannyl furan derivatives[85]. These compounds have been developed to circumvent the lack of regioselectivity generally encountered when unsymmetrical furans are used in this photocycloaddition. This idea is nicely illustrated in the synthesis of **192**, which was designed to be a hybrid of ginkolide and kadsureneone, natural products which are both highly active PAF (platelet activating factor) antagonists (Scheme 43)[86]. Irradiation of 2-tributylstannylfuran and *n*-butyl glyoxylate gave adduct **190** as the sole photoproduct in 35% yield. Stille coupling of **190** with veratryl bromide afforded **191**, which could be elaborated to the target structure **192** in a series of steps. Note that in this strategy the main group element functions to both direct the photocycloaddition and allow introduction of a substituent via a transition metal catalyzed coupling reaction.

Hoveyda has also studied the intramolecular variant of the furan-carbonyl photocycloaddition[87]. Several examples of this reaction, each of which proceeds in modest yield, are shown in Scheme 44. However, given the ease of synthesis of the starting materials and the complexity of the adducts produced in these photocycloadditions, these

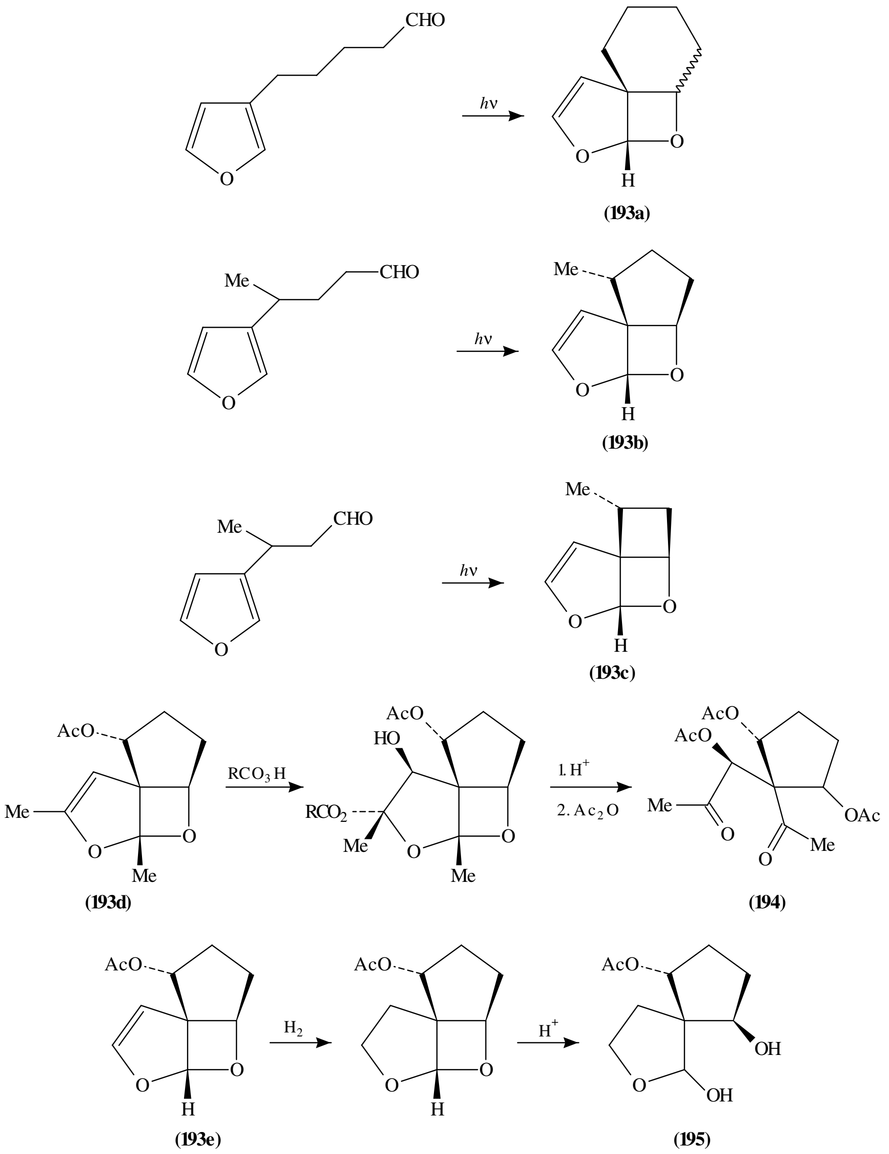

Me
Me
hν
BnO
CHO
Me
Me
OBn
O
O
(183)
RCO₃H
OH
Me
Me
OBn
RCO₂
O
O
(184)
OH
CHO
Me
Me
O
O
O
O
(185)
1.
Li
SOPh
(186)
2. 2 x [2,3]
sigmatropic shift
HO
SOPh
OH
Me
Me
O
O
O
(187)
H⁺
OH
Me
OH
Me
SOPh
O
O
(188)
O
OH
Me
OH
Me
O
O
O
OMe
Me
(189)

SCHEME 42



SCHEME 43

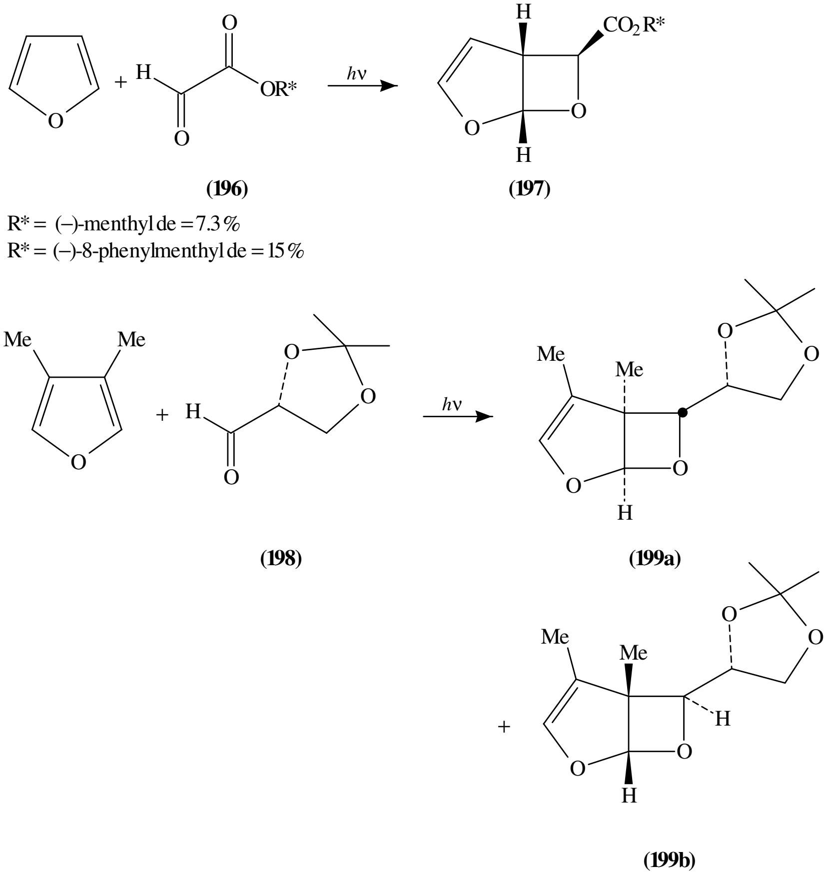
reactions certainly would seem to hold great promise in complex molecule synthesis. It was noted that the oxetane photoadducts produced in these reactions are much more difficult to manipulate and functionalize than their counterparts produced in the intermolecular photocycloaddition. For example, acidic hydrolysis of **193b** resulted in retro-[2 + 2]-photocycloaddition rather than the ring opening typically observed in the intermolecular photoadducts. Methods have been developed to circumvent these problems. Epoxidation of **193d** and hydrolysis afforded the dione **194**. Also, hydrogenation of the enol ether double bond in **193e** and subsequent hydrolysis gave the spirocycle **195**, again demonstrating the potential of this strategy for the rapid assembly of complex molecular architectures. It is also impressive to note that even highly strained systems (e.g. **193c**) can be produced



SCHEME 44

with good efficiency. A systematic study of the stereoinduction of substituents on the tether has also been conducted and the reader is referred elsewhere for a more detailed description[73c].

Zamojski and coworkers have explored the use of the furan-carbonyl photocycloaddition in asymmetric synthesis, with somewhat limited success[88]. Irradiation of chiral glyoxylate derivative **196** [R* = (*R*)(−)-menthyl and (*R*)(−)-8-phenylmenthyl] afforded adducts **197** with low selectivity (7.3% and 15% ee, respectively, after saponification of the ester; Scheme 45). This may be due to a lack of *endo* or *exo* selectivity during the photocycloaddition, or to a bad ratio of s-*cis* and s-*trans* conformers. Schreiber and Satake also noted low selectivity in the reaction of the protected glyceraldehyde derivative **198** with dimethylfuran as a 1.2:1 mixture of the diastereomeric acetonides **199a** and **199b** was produced[84b]; each of these was only *ca* 50% ee, indicating that this aldehyde may be labile toward racemization under the reaction conditions. Other attempts to react furans with conformationally restricted chiral, nonracemic ketones have met with somewhat better results, but this is still an area that is in development[84b].



(196) **(197)**

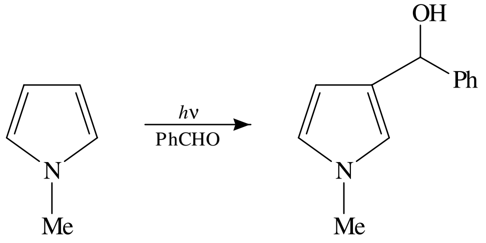
R* = (−)-menthyl de = 7.3%
R* = (−)-8-phenylmenthyl de = 15%

(198) **(199a)**

(199b)

SCHEME 45

Other aromatic heterocycles undergo Paterno–Büchi reaction with carbonyl compounds, although these reactions have seldom been applied to organic synthesis. For example, thiophene reacts cleanly with benzaldehyde to afford a single *exo* product in 63% yield[87]. Pyrroles also react with aldehydes and ketones; however, as a result of the lability of the presumed initial cycloadducts, the only products isolated, even with the rigorous exclusion of acid, are the 3-hydroxyalkylpyrroles **200** (equation 7)[89].

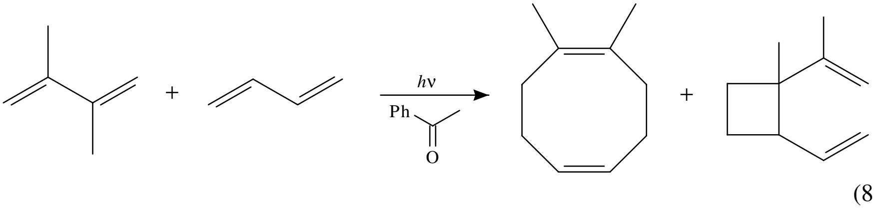


(200)

(7)

C. [4 + 4]-Photocycloadditions

Photodimerization of simple 1,3-dienes in a $4\pi + 4\pi$ cycloaddition process is typically an inefficient process[90]. This is not surprising, given the highly ordered transition state for [4+4]-cycloadditions, and the predominance of the unreactive s-*trans* conformation[70]. As a result, as noted above [2+2]-cycloadducts are often the major product, accompanied by varying amounts of vinylcyclohexenes and cyclooctadienes. Crossed photocycloadditions employing 1,3-dienes with substituents at the 2- or 3-positions can furnish greater amounts of cyclooctadiene products (equation 8)[91]. This presumably results from a perturbation of the diene conformational equilibration to provide a higher proportion of the s-*cis* conformer.

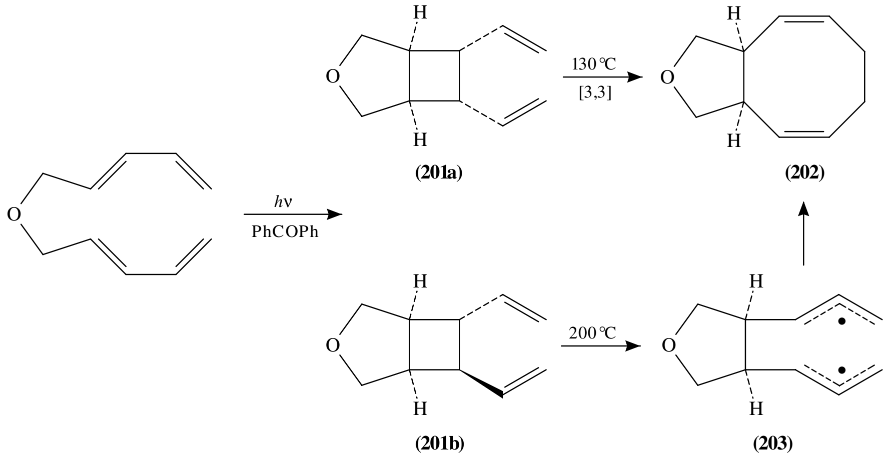


15%   58%

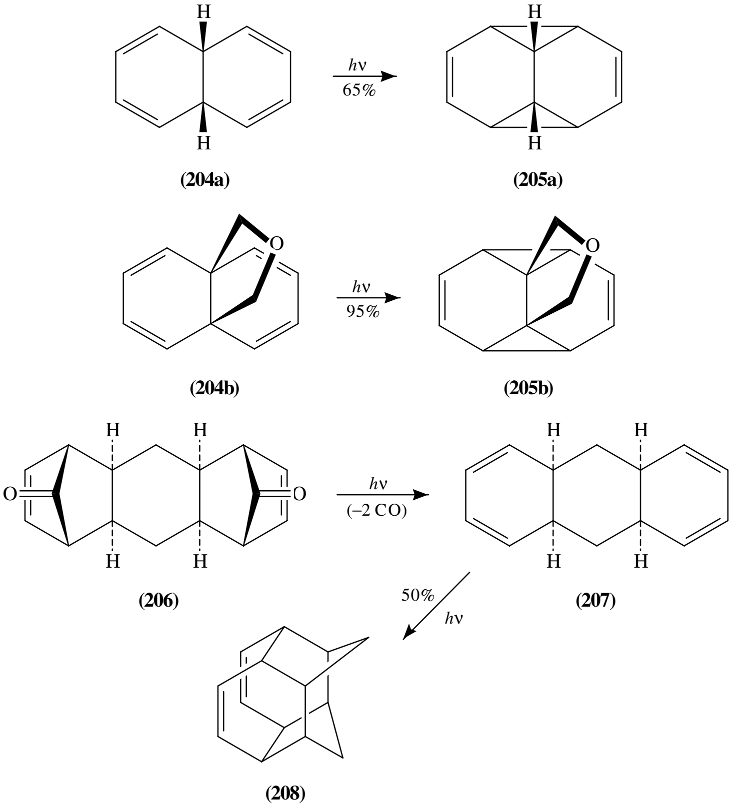
(8)

As noted previously in Section III.A, the [2 + 2]-cycloadducts formed from 1,3-diene dimerization are divinylcyclobutanes, and thus can potentially serve as precursors to cyclooctadienes via [3,3]-sigmatropic shift. This approach has been exploited by Wender and Correia (Scheme 46)[72]. Typically, the two diene units were joined by a three-atom tether, improving the efficiency of the photocycloaddition and leading to the generation of a bicyclo[3.2.0]heptane skeleton upon irradiation. Only the *cis* diastereomer **201a** can undergo the subsequent pericyclic process. However, at higher temperatures, the *trans* isomer **201b** also underwent conversion to the desired cyclooctadiene **202**, presumably via biradical intermediate. Mattay and coworkers have reported a similar tetraene to divinylcyclobutene process, using Cu(I) salts to preorganize the substrates in a reactive conformation[92].

There are a few exceptions to the generalizations made above regarding the periselectivity of 1,3-diene dimerization. These involve systems in which various structural constraints act to impede the typically favored [2 + 2]-cycloaddition process or enhance the [4 + 4]-cycloaddition. For example, *cis*-9,10-dihydronaphthalene **204a** furnished tetracyclic product **205a** in good yield (Scheme 47)[93]. Similarly, propellane **204b** underwent conversion to **205b** in nearly quantitative yield[94]. More recently, Srikrishna and Sunderbabu showed that hexahydroanthracene **207**, generated *in situ* from **206** via



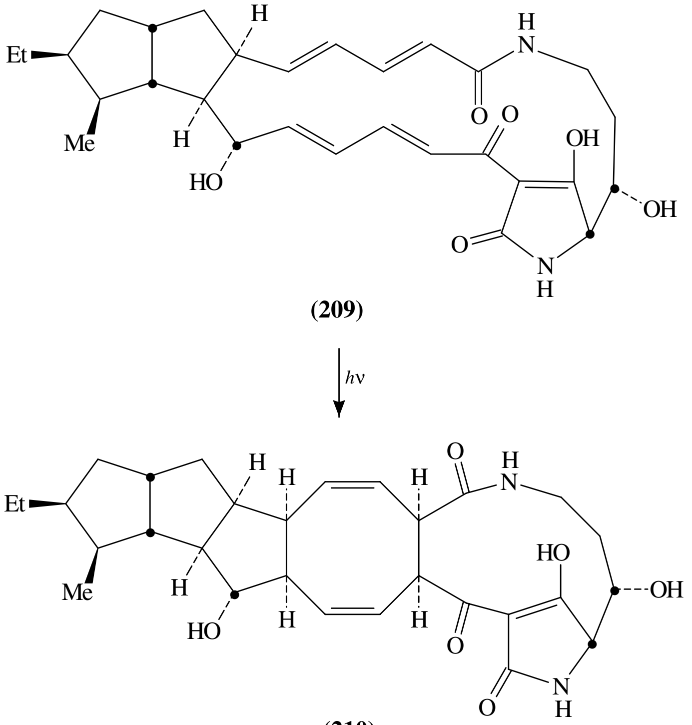
SCHEME 46



SCHEME 47

photochemical decarbonylation, suffered [4 + 4]-cycloaddition to give pentacyclic adduct **208** (Scheme 47)[95].

Another unique example was observed for the recently isolated marine natural product, alteramide A **(209)**, isolated from a symbiotic bacteria (*Alteromonas* sp.) found on the sponge *Halichondria okadai*[96]. It was found that the tetraene core of this compound underwent intramolecular [4 + 4]-photocycloaddition upon exposure to sunlight (equation 9). Deliberate irradiation led to a quantitative conversion to cyclooctadiene **210**.



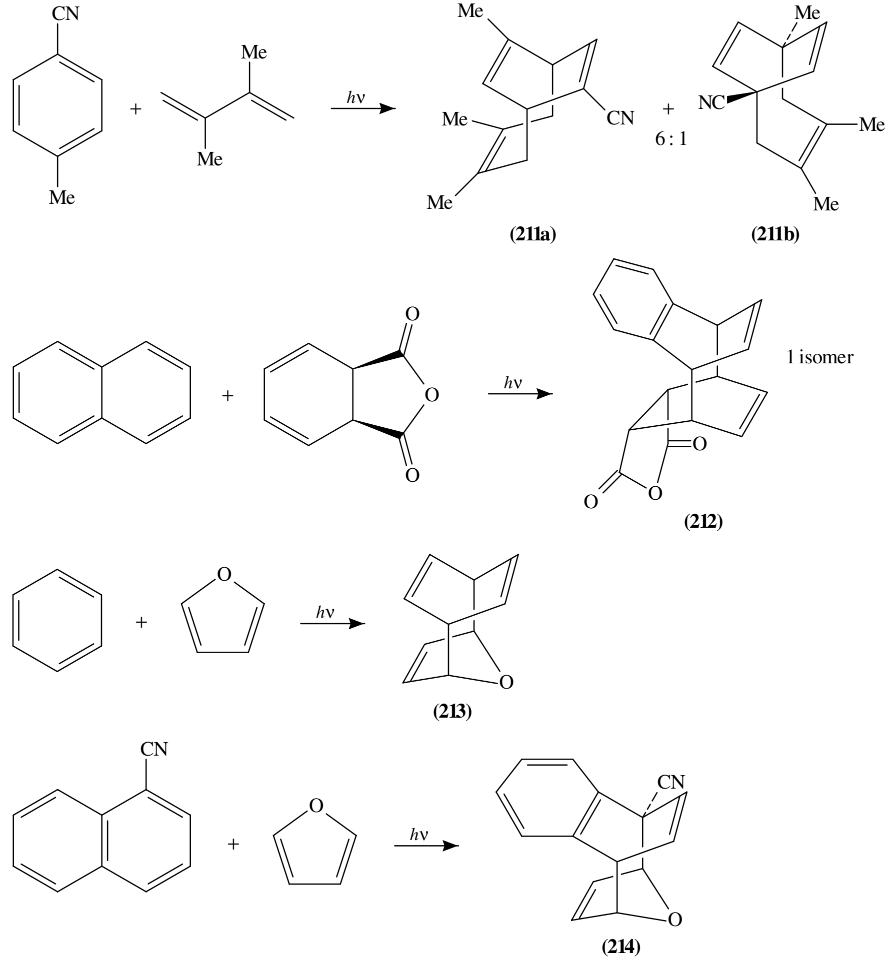
(209)

(9)

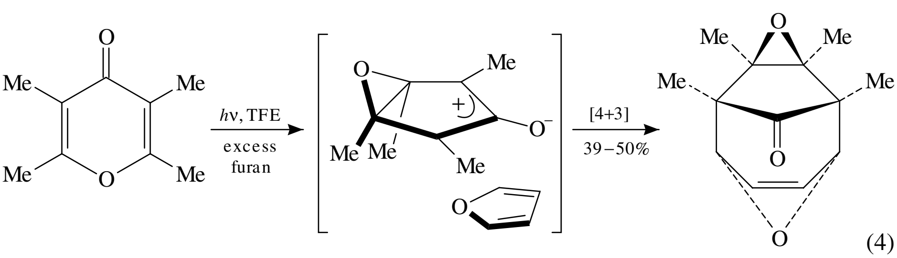
(210)

The literature of mechanistic aromatic photochemistry has produced a number of examples of [4 + 4]-photocycloadditions. The photodimerization of anthracene and its derivatives is one of the earliest known photochemical reactions of any type[97]. More recently, naphthalenes[98], 2-pyridones[99] and 2-aminopyridinium salts[100] have all been shown to undergo analogous head-to-tail [4 + 4]-photodimerization. Moreover, crossed [4+4]-photocycloaddition products can be obtained in some cases[101]. Acyclic 1,3-dienes, cyclohexadienes and furan can form [4 + 4]-cycloadducts **211–214** with a variety of aromatic partners (Scheme 48).

A common feature of these reactions is the incorporation of one or both of the reacting dienes within a ring, thereby ensuring that they exist in a reactive conformation. This strategy has been further explored by Sieburth and Chen, employing 2-pyridones as the diene units. These studies showed that mixed head-to-tail 2-pyridone dimers can be efficiently formed when the two heterocycles are joined by a three- or four-carbon chain, giving highly functionalized cyclooctadienes such as **215** bridged by two lactam units (equation 10)[102].

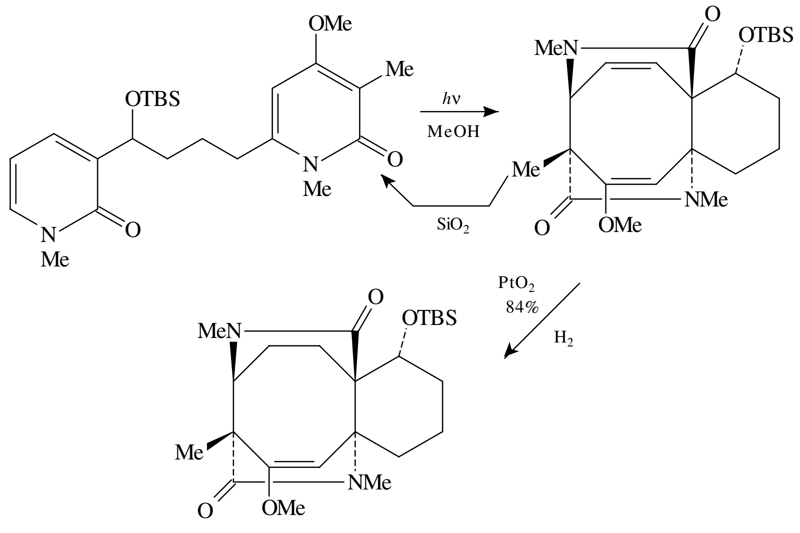


SCHEME 48



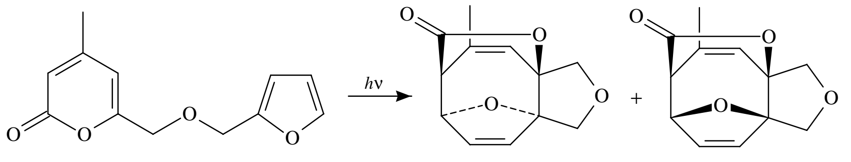
(4)

Further mechanistic work has revealed interesting solvent effects on diastereoselectivity[103]. A method for enriching isomer ratios in favor of the '*trans*' or *exo* diastereomer via a photo/thermal equilibration have also been reported. As a demonstration of its applicability to natural product targets containing the cyclooctane ring, the pyridone photodimerization process was employed as the key step in the construction of a taxane B-C ring synthon **216** (equation 11)[104].



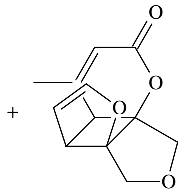
(11)

(216)

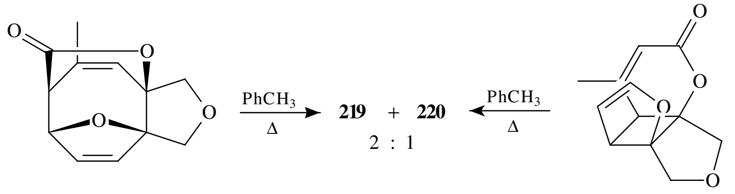


(217) **(218)** **(219)**

solvent	overall yield	ratio 218:219:220
$PhCH_3$	15%	1:1:1
H_2O	59%	2.1:2.3:1.0
aq. LiCl	86%	3.9:2.1:1.0
$Et_2O/LiClO_4$	56%	1.0:5.7:trace
acetone	60%	1:1:15



(220)

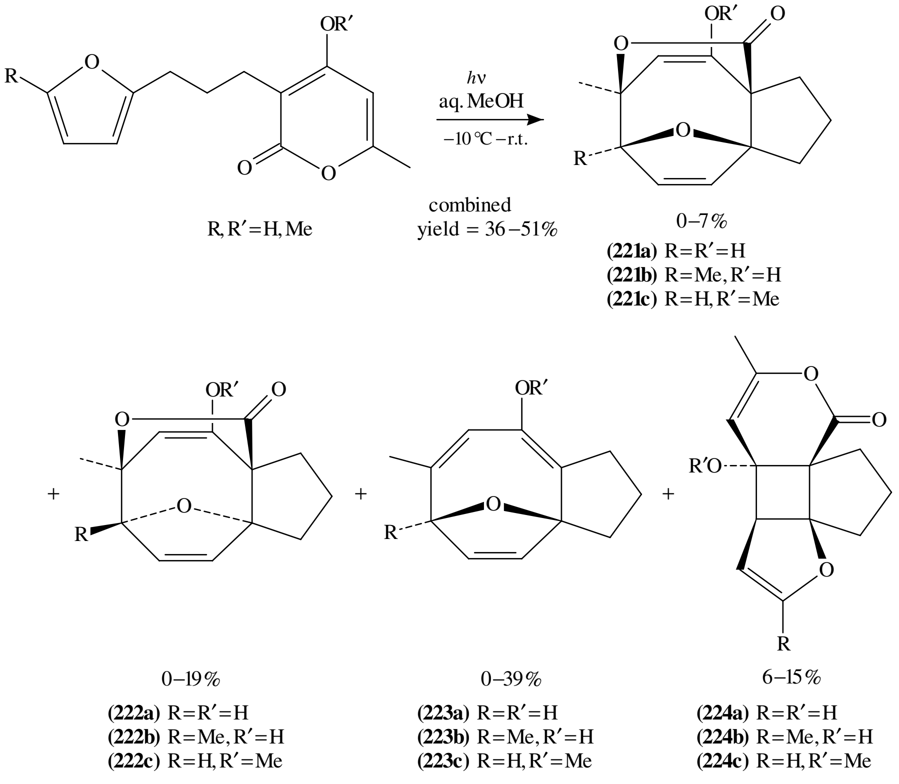


(219) **(220)**

SCHEME 49

West and coworkers have reported a similar approach to functionalized cyclooctanoids via the analogous [4 + 4]-photocycloaddition chemistry of 2-pyrones[105]. Rather than a pyrone–pyrone dimerization process[106], this chemistry entails a crossed [4 + 4]-cycloaddition between a 2-pyrone chromophore and a spectator diene, typically a furan. For example, unsymmetrical ether **217** gave varying amounts of [4 + 4]- and [2 + 2]-cycloadducts **218**, **219** and **220**, depending upon conditions (Scheme 49). The best conversion to [4 + 4]-adducts was obtained by irradiation in the highly organized medium aqueous LiCl. The stereochemistry of *exo* and *endo* diastereomers **218** and **219** was rigorously assigned by heating either **219** or **220** in toluene to give identical ratios of both compounds, presumably through equilibration via [3,3]-shifts. It was also found that extended irradiation led to a disappearance of **220**, and this was shown to involve photocycloreversion to starting material and subsequent conversion to the photochemically inert [4+4]-adducts. This isomerization process bears close resemblance to the photo/thermal equilibration noted by Sieburth and Lin[103b]. Related substrates gave similar results.

Substrates in which the furan was tethered at C-3 have also been examined[107]. These cases typically possessed ring-oxygenation at C-4, and the nature of this substituent proved to be important (Scheme 50). Examples with a free hydroxyl or a methyl ether at this position led to low yields of cycloadducts **221–224** and substantial amounts of polar by-products, possibly via competing solvent trapping pathways which ultimately lead to



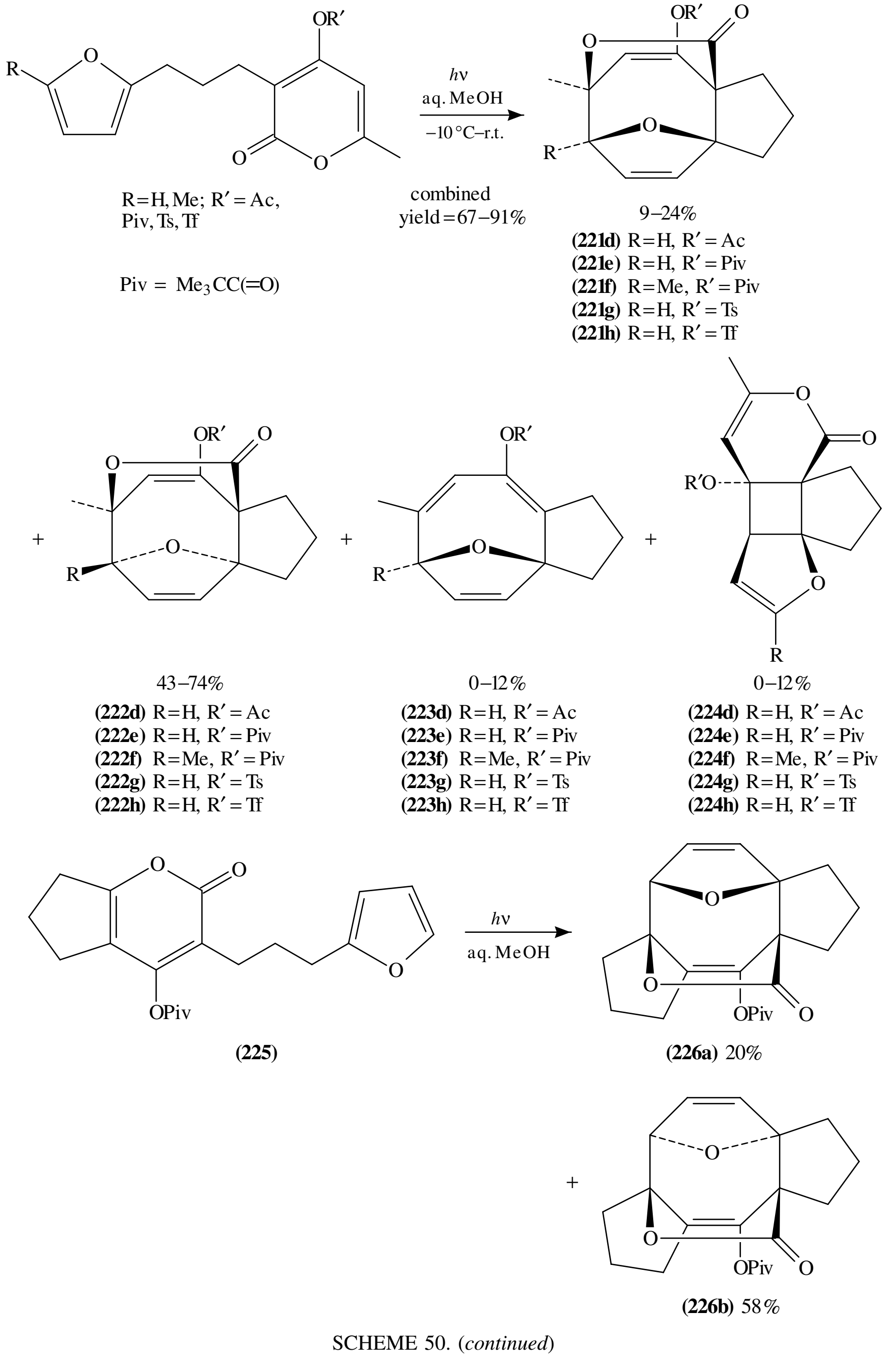
(221a) R=R′=H
(221b) R=Me, R′=H
(221c) R=H, R′=Me

(222a) R=R′=H
(222b) R=Me, R′=H
(222c) R=H, R′=Me

(223a) R=R′=H
(223b) R=Me, R′=H
(223c) R=H, R′=Me

(224a) R=R′=H
(224b) R=Me, R′=H
(224c) R=H, R′=Me

SCHEME 50



R = H, Me; R′ = Ac, Piv, Ts, Tf

Piv = $Me_3CC(=O)$

combined yield = 67–91%

9–24%

(221d) R = H, R′ = Ac
(221e) R = H, R′ = Piv
(221f) R = Me, R′ = Piv
(221g) R = H, R′ = Ts
(221h) R = H, R′ = Tf

43–74%

(222d) R = H, R′ = Ac
(222e) R = H, R′ = Piv
(222f) R = Me, R′ = Piv
(222g) R = H, R′ = Ts
(222h) R = H, R′ = Tf

0–12%

(223d) R = H, R′ = Ac
(223e) R = H, R′ = Piv
(223f) R = Me, R′ = Piv
(223g) R = H, R′ = Ts
(223h) R = H, R′ = Tf

0–12%

(224d) R = H, R′ = Ac
(224e) R = H, R′ = Piv
(224f) R = Me, R′ = Piv
(224g) R = H, R′ = Ts
(224h) R = H, R′ = Tf

(225)

(226a) 20%

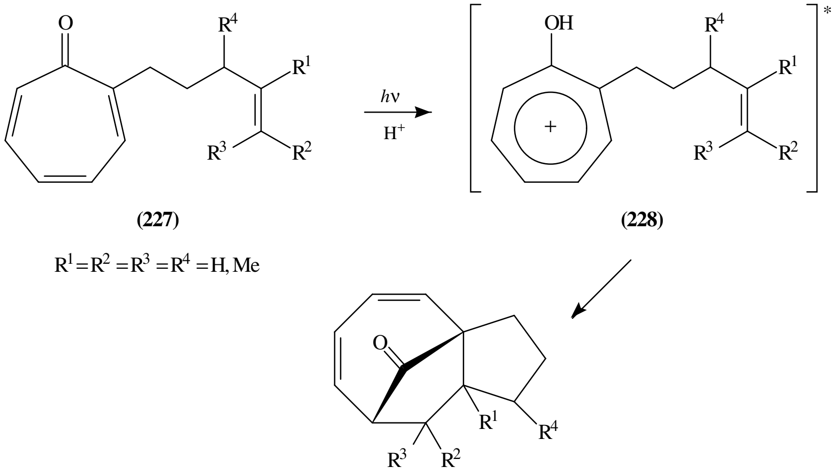
(226b) 58%

SCHEME 50. (*continued*)

acyclic carboxylic acid derivatives[13,14,108]. In contrast, carboxylate- or sulfonate-capped examples underwent efficient conversion to [4 + 4]-cycloadducts **221** and **222**. Significant amounts of trienes **223** were also observed in certain cases. This product seems to arise from *in situ* decarboxylation of **221** and/or **222**, and the extent of its formation is sensitive to both ring substitution and solvent polarity. The potential applicability of 2-pyrone [4 + 4]-photocycloaddition chemistry to complex targets was demonstrated in the conversion of **225** to adducts **226a** and **226b** in good yield and in a 1:3 ratio (Scheme 50). These products contain the 5-8-5 tricyclic core found in natural products of the fusicoccane and ophiobolane classes.

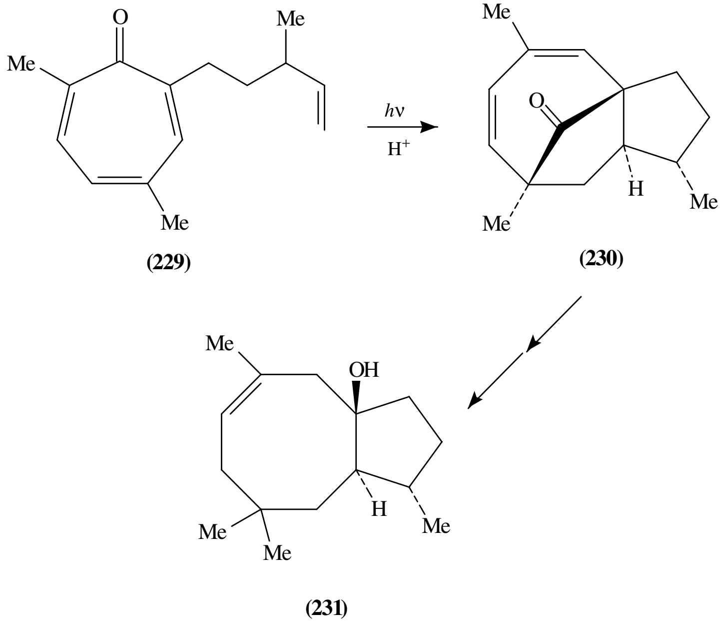
D. Other Higher-order Photocycloadditions

Tropone and its derivatives undergo an extensive and complex set of photochemical reactions[109], and it is only recently that the photochemistry of tropones has been efficiently utilized in natural products synthesis. Feldman and coworkers found that the complex photochemistry of tropones could be avoided by irradiating alkene tethered tropones (e.g. **227**) under acidic conditions and proceeding from the excited state of the corresponding hydroxytropylium ion **228** (Scheme 51)[110]. This critical observation has made the intramolecular [6 + 2]-photocycloaddition of alkene tethered tropones a useful synthetic tool. Though moderate yields of cycloadducts were observed in these reactions, these concerns are attenuated by the ease of preparation of the required substrates and the high degree of complexity change associated with this cycloaddition. Detailed considerations of both the mechanism and stereochemical consequences associated with this cycloaddition are given in the original papers. It is proposed that this photocycloaddition proceeds via an exciplex between the photoexcited tropylium ion and the tethered olefin. The stereochemistry and substitution inherent in this transient presumably determines the product distribution.

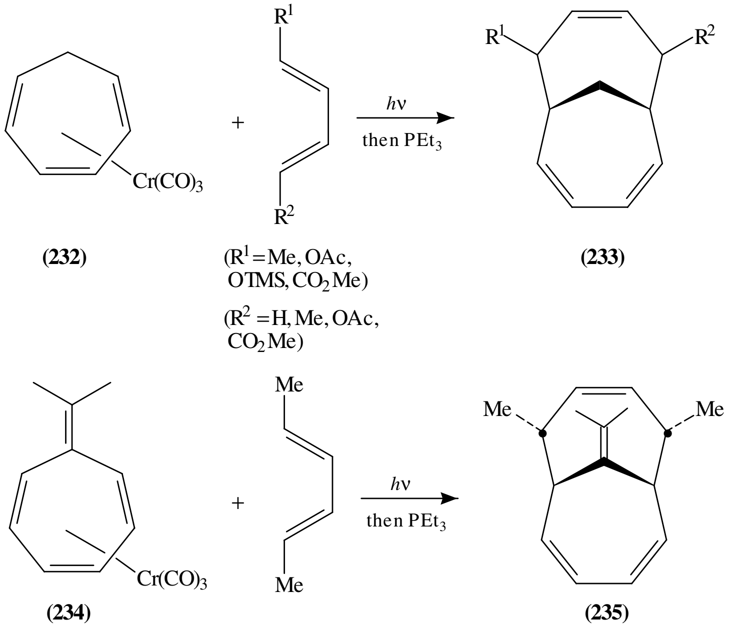


SCHEME 51

The power of this tropylium ion cycloaddition strategy for the synthesis of complex molecules can be seen in synthesis of dactylol **231** by Feldman and coworkers (Scheme 52)[111]. Irradiation of **229** (prepared from 4-methyltropone in two steps) afforded



SCHEME 52



SCHEME 53

230 in 41% yield. This intermediate could be elaborated to dactylol in another four steps via a regioselective cleavage of the one-carbon ketone bridge. This approach is clearly applicable to the bicyclo[6.3.0]undecane skeleton found in many cyclooctanoid natural products. However, the multiple bicyclic systems present in tricyclic adducts such as **230** should permit the use of this chemistry for a wide variety of targets.

In a similar vein, several groups have demonstrated that irradiation of metal complexes (generally chromium complexes) of cyclic polyenes in the presence of alkenes or dienes affords higher-order cycloadducts (either [6 + 2] or [6 + 4] cycloadditions, respectively) in good yields[112−120]. While not a 'traditional photochemical' process involving the polyene chromophore, the synthetic appeal and generality of these reactions argues for their inclusion in this chapter. The mechanism of these reactions, albeit complex, can be envisioned to entail initial photochemical loss of CO from the metal center; complexation of the alkene or diene in the vacant coordination site on the metal then initiates C−C bond formation and eventual cycloadduct formation.

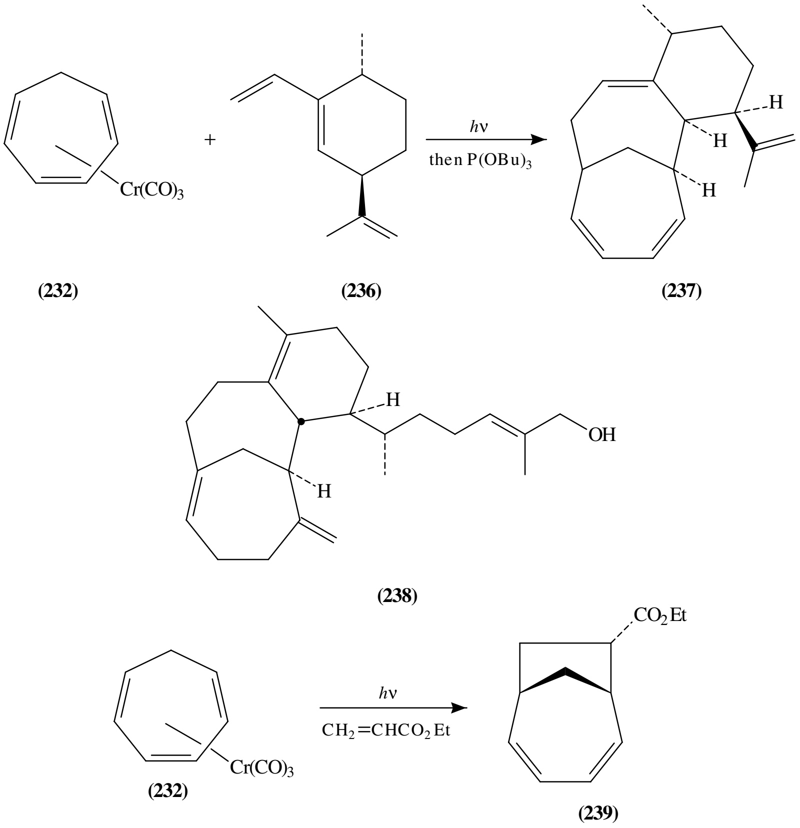
The potential of this technology in complex molecule synthesis is quite high. For example, in early exploratory studies, Kreiter's group found that irradiation of chromium complex **232** in the presence of dienes afforded the cycloadducts **233** in excellent yields following decomplexation of the metal (Scheme 53)[113a,b]. While not specifically delineated in this work, these cycloadditions provide the *endo* adducts exclusively, providing further evidence of the metal acting as a template in the reactions. The same group also found that irradiation of the chromium complex of heptafulvene **234** in the presence of a variety of dienes afforded high yields of the *endo* adducts **235**[113c]. Again, photochemically initiated loss of CO appears crucial to the initiation of this cycloaddition.

Rigby has quite elegantly expanded the scope and generality of these cycloadditions for the construction of complex systems, showing that both [6 + 4]- and [6 + 2]-photocycloadditions using these types of metal complexes provide rapid, efficient entry into a variety of structurally interesting skeleta[114]. For example, irradiation of **232** in the presence of diene **236** [derived from (*R*,*R*)-dihydrocarvone] afforded [6 + 4]-photoadduct **237** (Scheme 54). Tricyclic adduct **237** can be viewed as a model for the unusual sesterterpene cerorubenol I **(238)**[115]. The [6 + 2]-photocycloaddition of electron-deficient alkenes with these chromium complexes also proceeds well. This is illustrated by the reaction of **232** with ethyl acrylate, which furnished cycloadduct **239** in good yields following removal of the metal[116].

Intramolecular variants of this [6 + 4]-photocycloaddition efficiently produce very complex polycyclic materials (Scheme 55)[117]. Irradiation of **240** in hexanes followed by decomplexation of the metal with trimethyl phosphite **(241)** afforded the cycloadduct **242** in 85% yield. The corresponding tropone derivative gives the analogous [6 + 4]-cycloadduct in slightly lower yields. The ease of substrate construction coupled with the highly complex nature of these adducts portends great things for this strategy in complex molecule synthesis. The related intramolecular [6 + 2]-cycloaddition (**243** to **244**) was also reported in this paper. It is interesting to note that, in contrast to the intermolecular [6 + 2]-cycloadditions, the unactivated olefin reacted smoothly to furnish the cycloadduct in an intramolecular sense.

Rigby and coworkers have elegantly demonstrated the utility of these [6 + 4]-photocycloadditions in complex molecule construction in a recent paper which detailed the use of [6 + 4]-cycloadduct **245** as a common intermediate for ingenane **(246)** and phorbol **(247)** fragments (Scheme 56)[118]. It was also found that cycloadduct **248** could be efficiently converted to **249**, which has the generalized taxol ring skeleton, through a Lewis acid catalyzed rearrangement process.

The use of metal complexed heterocyclic polyenes in these cycloadditions has also proven useful, as both the 1,1-dioxythiepine and azepine derivatives **250** and **253** took part in [6 + 4]- and [6 + 2]-photocycloadditions, respectively, to afford good yields of the

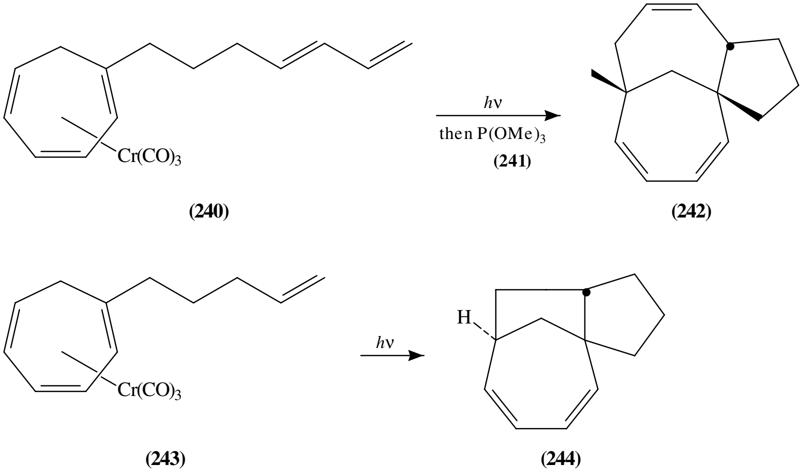


(232) **(236)** **(237)**

(238)

(232) **(239)**

SCHEME 54

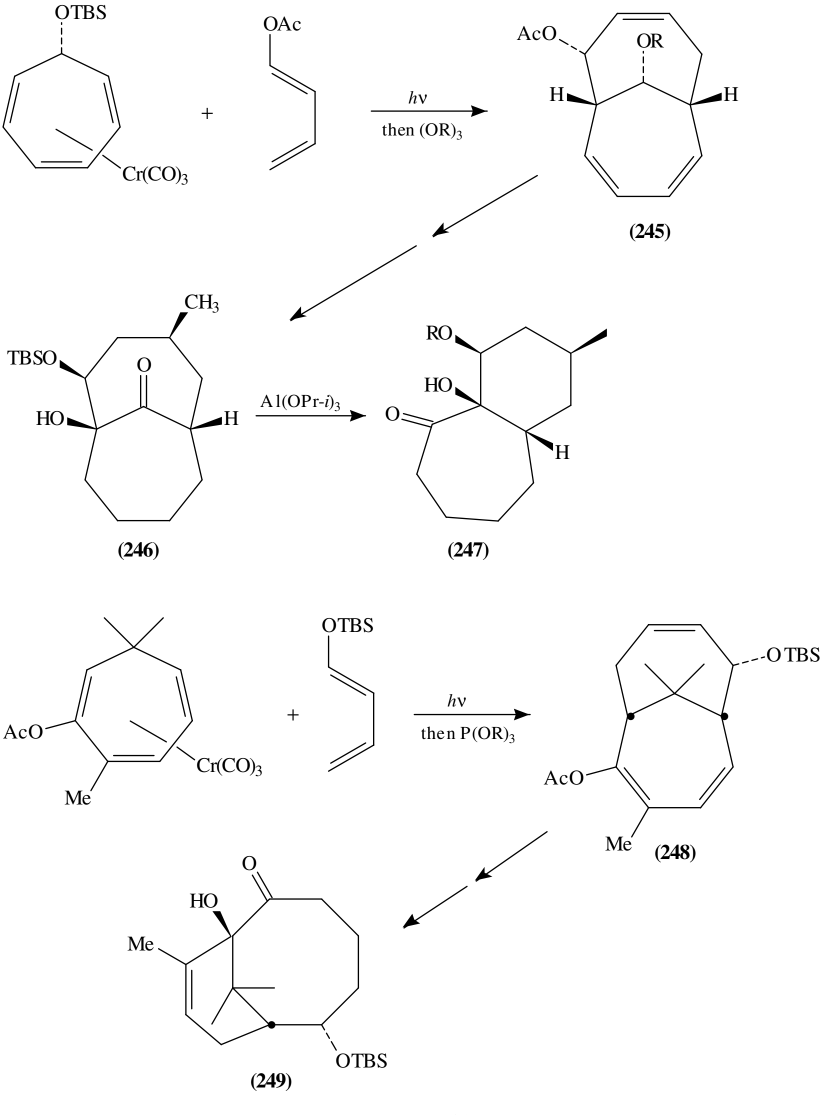


(241)

(240) **(242)**

(243) **(244)**

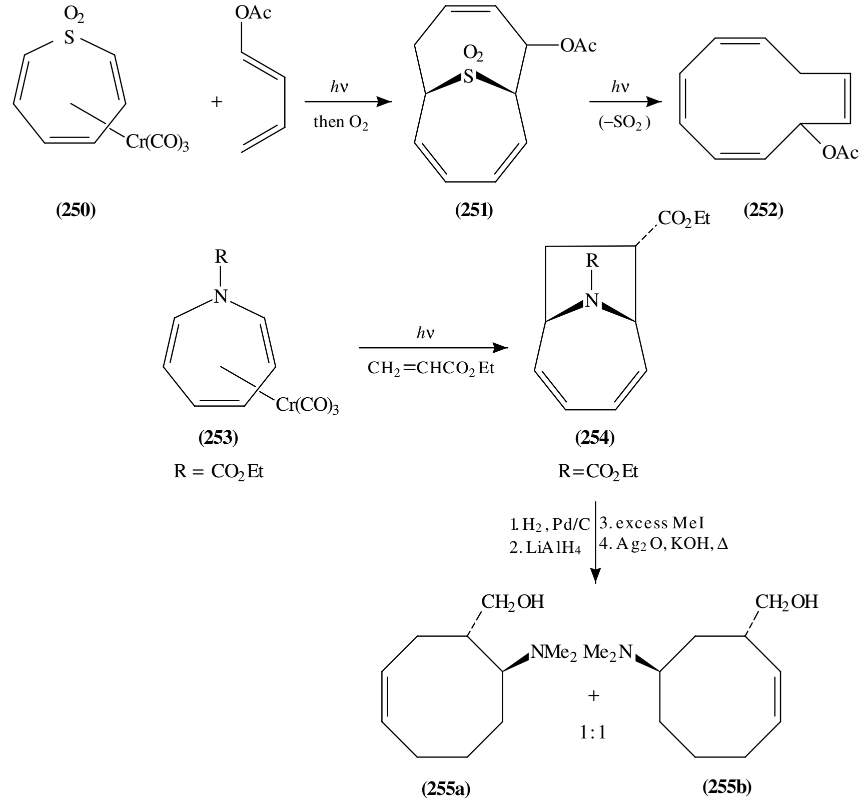
SCHEME 55



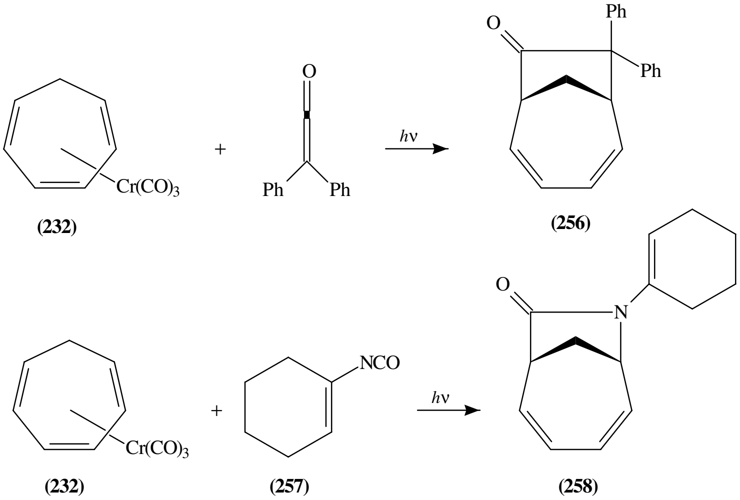
SCHEME 56

cycloadducts **251** and **254** (Scheme 57)[119]. These could be elaborated easily to cyclodecatetraene **252** or isomeric cyclooctenes **255a** and **255b**.

Ketenes and isocyanates also undergo facile [6 + 2]-photocycloaddition with metal complexed cyclic polyenes. Irradiation of **232** in the presence of diphenylketene gave **256** in good yield (Scheme 58)[120]. This should be contrasted with the normal behavior of ketenes toward alkenes, which typically involves [2 + 2]-cycloaddition. Isocyanates such as **257** work as well. The adducts are produced in high yields and have considerable potential in synthesis.



SCHEME 57



SCHEME 58

IV. CONCLUDING REMARKS

It is apparent from the quantity of material included in this chapter that there is an extensive body of work concerning the utilization of diene and polyene photochemistry in a synthetic setting. The unique behavior of the excited chromophores permits the application of powerful new methods for the construction of complex molecules. Unusual photochemical rearrangements and photocycloaddition pathways often lead to substantial increases in molecular complexity, allowing such processes to serve as key strategic steps in target oriented syntheses.

In light of the voluminous amounts of work already accomplished, one may well wonder what remains to be accomplished. In fact, there is much to do in the area of synthetic photochemistry in general, and with synthetic diene and polyene photochemistry in particular. First, many of the powerful transformations described above have not yet been used in total synthetic routes which adequately exploit the new connectivity that is produced. Furthermore, while asymmetric versions exist for many commonly employed reactions, this remains to be explored for most of the photochemical transformations covered in this chapter. In an era which increasingly emphasizes the importance of optically pure target molecules[121], this is clearly an area of emerging importance for synthetic photochemistry. Finally, with a greater understanding of the complex set of factors which control the photochemical reactivity of these systems will come new opportunities to take advantage of predictable photochemical behavior in new media, such as intact biological systems (for controlled formation or release of small, bioactive molecules) or the solid state (for the controlled modification of the structure or properties of 'designer solids'). Given this list of goals, it seems likely that the future will witness the increasing use of these fascinating processes in many new settings.

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CHAPTER 8

Radiation chemistry of dienes and polyenes

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I. INTRODUCTION

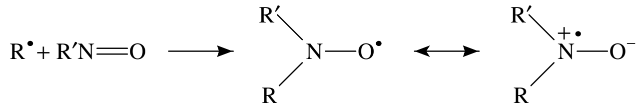
Radiation chemistry is the study of the chemical effects produced in a system by the absorption of ionizing radiation. This definition includes the chemical effects due to radiation from radioactive sources, high-energy charged particles and short-wavelength (less than about 400 Å) electromagnetic radiation from accelerators[1]. The principal characteristic of high-energy radiation is that it causes ionization in all materials. This makes a distinction between radiation chemistry and photochemistry[2,3]. Photochemistry deals with longer-wavelength electromagnetic radiation which have lower energy (less than about 30 eV). This relatively low energy leads in many cases only to the excitation of the molecules and does not produce ions. Usually, the energy of the particles and photons applied in radiation chemistry is much higher. The whole energy is not absorbed by a single molecule, as in photochemistry, but rather distributed over several molecules, along the track of the ionizing particle or photon. The high-energy photons and particles are not selective and may ionize, excite or dissociate any molecule lying in their path, while in photochemistry only some compounds may interact with the radiation, in accordance with the energy of the photons.

The high-energy photons or particles lose energy in successive events and produce ions and primary electrons, which in turn form several secondary electrons with lower energies[4]. The chemical effects of ionizing radiation occur almost exclusively through the secondary electrons, most of which have less than 100 eV. These electrons will cause ionization and excitation of the surrounding molecules and will lose energy until they reach thermal energies. In many solvents these thermal electrons polarize the solvent molecules and are bound in a stable quantum state to them; these electrons are called *solvated* electrons. On the average, half of the absorbed energy is spent on ionization while the other half leads to excited molecules.

The study of radiation chemistry might be divided, from the experimental point of view, into two parts. The first is the study of unstable intermediates which have short lifetimes and thus cannot be studied by the usual methods of chemistry. The second part is the study of the final products of the radiolysis which are measured by common chemical techniques.

One way to make the short-lived intermediates amenable to study is to increase their lifetime, usually by irradiation in the solid state and/or at very low temperatures. Then, the intermediates can be detected at the end of the irradiation by ESR or optical absorption spectroscopy. The ESR study of radicals in the solid state is done on single crystals, polycrystalline samples or frozen aqueous solution. In case of polycrystalline samples or frozen aqueous solution the identification of the radicals from the ESR spectra is difficult in many cases and, for better identification, the ESR experiment should be conducted on irradiated single crystals. Later, the method of spin trapping, developed for the liquid phase[5], was extended to polycrystalline solids. In this technique the polycrystalline solids are γ-irradiated and subsequently dissolved in a solution containing the spin trap.

An important method of making the lifetime longer in the liquid phase is by adding compounds which, upon addition of radicals, produce long-lived radicals; this method is called *spin trapping*[5]. In this method a diamagnetic spin-trap is used to convert radicals, which are short-lived, into long-lived radicals. For example, using nitroso compounds (as, e.g., *t*-nirosobutane, *t*-NB) the short-lived radicals form long-lived nitroxide radicals (the spin-adduct) according to equation 1[5]. Several spin traps were used[6].



$$R^{\bullet} + R'N{=}O \longrightarrow R'RN{-}O^{\bullet} \longleftrightarrow R'R\overset{+\bullet}{N}{-}O^{-} \qquad (1)$$

More common in the liquid phase is pulse radiolysis[7,8]. In this technique, electron accelerators which can deliver intense pulses of electrons lasting a very short time (ns up to μs) are used. Each single pulse can produce concentrations of intermediates which are high enough to be studied by various methods, such as light absorption spectroscopy or electrical conductivity.

The yields of radiolysis products are always expressed by the G value, which is defined as the number of particles (molecules, radicals, ions) produced or consumed per 100 eV of energy absorbed in the system, or the number of tenths of micromoles produced by 1 joule, i.e. the absorption of 1 joule leads to formation of 1×10^{-7} mole if $G = 1$ or to 0.6 μmole if $G = 6$.

The units for the absorbed energy (dose) are the rad, defined by 1 rad = 100 erg g^{-1} = 6.243×10^{13} eV g^{-1}, and the gray (Gy) defined by 1 Gy = 100 rad.

When radiolysing a solution, the radiation interacts mainly with solvent molecules, since the solution consists mainly of the latter and the radiation interacts with the molecules unselectively. Consequently, the radiation chemistry of a solution is the combination of the production of initial intermediates from the solvent, which will be the same as in pure solvents, and the reaction of those intermediates with the solute.

II. RADIOLYSIS OF AQUEOUS SOLUTIONS OF DIENES

Ionizing radiations (α, β and γ) react unselectively with all molecules and hence in the case of solutions they react mainly with the solvent. The changes induced in the solute due to radiolysis are consequences of the reactions of the solute with the intermediates formed by the radiolysis of the solvent. Radiolysis of water leads to formation of stable molecules H_2 and H_2O_2, which mostly do not take part in further reactions, and to very reactive radicals: the hydrated electron e_{aq}^-, hydrogen atom $H^\bullet$ and the hydroxyl radical $OH^\bullet$ (equation 2). The first two radicals are reductants while the third one is an oxidant. However there are some reactions in which H atom reacts similarly to OH radical rather than to e_{aq}^-, as e.g. abstraction of an hydrogen atom from alcohols, addition to a benzene ring or to an olefinic double bond, etc.

$$\begin{aligned} &H_2O \longrightarrow H_2O^+ + e^- + H_2O^* \\ &H_2O^+(+nH_2O) \longrightarrow {}^\bullet OH + H^+ \\ &e^-(+nH_2O) \longrightarrow e_{aq}^- \\ &H_2O^* \longrightarrow H^\bullet + {}^\bullet OH \end{aligned} \qquad (2)$$

In neutral water the radiation chemical yields G are 2.7×10^{-7} mol J^{-1} for the hydrated electron, 2.8×10^{-7} mol J^{-1} for the ${}^\bullet OH^\cdot$ radical and 6×10^{-8} mol J^{-1} for the H atom. These values vary slightly with the solute concentration, due to increased reaction with the solute in the radiation spurs. In order to study the reaction of one radical without interference of the others, scavengers have to be added to the system. The best scavengers are those which will convert the unwanted radical to the studied one. This can be done with e_{aq}^-, which can be converted to ${}^\bullet OH$ or to $H^\bullet$ by the addition of N_2O or H^+, respectively (equations 3 and 4).

$$e_{aq}^- + N_2O \longrightarrow N_2 + OH^- + {}^\bullet OH \quad (k = 9 \times 10^9\ M^{-1}\,s^{-1}) \qquad (3)$$

$$e_{aq}^- + H^+ \longrightarrow H^\bullet \quad (k = 2.3 \times 10^9\ M^{-1}\,s^{-1}) \qquad (4)$$

The reaction of H atoms can be studied in acidic solution if the OH radicals are scavenged by *t*-butyl alcohol, in a very fast reaction, while hydrogen atoms react only very slowly with this alcohol (equations 5 and 6). The radical produced in equation 5 is relatively unreactive and does not interfere with the study of the reaction of H atoms with the solute.

$${}^\bullet OH + (CH_3)_3COH \longrightarrow H_2O + {}^\bullet CH_2C(CH_3)_2OH \quad (k = 5 \times 10^8\ M^{-1}\,s^{-1}) \quad (5)$$

$$H^\bullet + (CH_3)_3COH \longrightarrow H_2 + {}^\bullet CH_2C(CH_3)_2OH \quad (k = 1.7 \times 10^5\ M^{-1}\,s^{-1}) \quad (6)$$

Another method to remove OH radicals and preserving H atoms is by addition of CD_3OH[9,10]. However, due to the high cost of CD_3OH this method was not used after the effect of *t*-butyl alcohol was found.

Hydrated electrons are obtained as predominant radicals by removing the OH radicals with *t*-butyl alcohol. The removal of both H and OH radicals is accomplished by isopropanol (equations 7 and 8).

$$\mathrm{H^\bullet + (CH_3)_2CHOH \longrightarrow H_2 + (CH_3)_2C^\bullet OH} \quad (k = 7.4 \times 10^7\ \mathrm{M^{-1}\,s^{-1}}) \tag{7}$$

$$\mathrm{^\bullet OH + (CH_3)_2CHOH \longrightarrow H_2O + (CH_3)_2C^\bullet OH\ (86\%) + (CH_3)_2CHO\ (1\%)}$$
$$\mathrm{+\ ^\bullet CH_2CH(OH)CH_3\ (13\%)} \quad (k = 1.9 \times 10^9\ \mathrm{M^{-1}\,s^{-1}}) \tag{8}$$

A. The Reaction of $e_{aq}{}^-$ with Dienes

A large difference in the reactivity toward hydrated electrons was found between unconjugated and conjugated dienes. Unconjugated dienes, like 1,4-cyclohexadiene[10], react very slowly with hydrated electrons ($<10^6$ $\mathrm{M^{-1}\,s^{-1}}$) similarly to a mono double-bond compound, like cyclohexene. On the other hand, compounds with conjugated double bonds react very fast with hydrated electrons. Hart and coworkers[11] found that $e_{aq}{}^-$ reacts with butadiene with a rate constant of 8×10^9 $\mathrm{M^{-1}\,s^{-1}}$, and Michael and Hart[10] found that 1,3-cyclohexadiene reacts with a rate constant of 1×10^9 $\mathrm{M^{-1}\,s^{-1}}$. They did not try to explain the quite large difference between butadiene and 1,3-cyclohexadiene.

B. The Reaction of $H^\bullet$ Atoms with Dienes

Michael and Hart[10] found that H atoms react quite rapidly with alkenes (3×10^9 $\mathrm{M^{-1}\,s^{-1}}$ with cyclohexene) and there is not much change for dienes. 1,4-Cyclohexadiene reacts with hydrogen (4.7×10^9 $\mathrm{M^{-1}\,s^{-1}}$) slightly (*ca* 60%) faster than cyclohexene. The increase of less than two-fold indicates that the hydrogen atom reacts not only by addition to the double bonds, but also by abstraction of the allylic hydrogens (the concentration of double bonds is twofold in 1,4-cyclohexadiene while the number of allylic hydrogens is the same). The reaction of H atoms with 1,3-hexadiene ($k = 9.8 \times 10^9$ $\mathrm{M^{-1}\,s^{-1}}$) is twice as fast as that with 1,4-hexadiene, indicating that H atoms are mainly added to the conjugated double-bond system. It should be mentioned that later studies on the reaction of H atoms with simple alkenes found higher rate constants, e.g. 7.0×10^9 for 1-butene, 1.0×10^{10} for 2-methylpropene and 5.2×10^9 $\mathrm{M^{-1}\,s^{-1}}$ for cyclohexene[12].

C. The Reaction of $^\bullet$OH Radicals

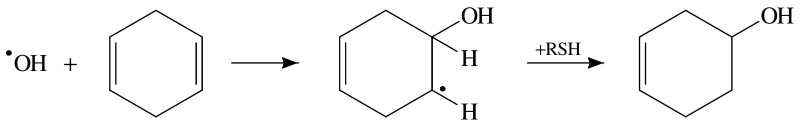
OH radicals react very fast (almost in a diffusion-controlled rate) with simple alkenes ($k = 7.0 \times 10^9$ for 1-butene or cyclopentene and 8.8×10^9 $\mathrm{M^{-1}\,s^{-1}}$ for cyclohexene) and there is almost no change for 1,3- or 1,4-cyclohexadiene. Cycloheptatriene reacts very fast with all the three radicals formed in the radiolysis of water: $k = 6 \times 10^9$ with $e_{aq}{}^-$, 8×10^9 with H atoms and 1×10^{10} $\mathrm{M^{-1}\,s^{-1}}$ with hydroxyl radicals[13].

D. Absorption Spectra of Intermediates

Michael and Hart[10] found that the reaction of OH radicals (formed by pulse radiolysis of aqueous solutions saturated with N_2O) with 1,3- and 1,4-cyclohexadienes leads to formation of an intermediate absorbing at 310 nm. In the case of 1,4-cyclohexadiene, another band at $\lambda \leqslant 240$ nm was also found. In this system there are both $^\bullet$H atoms and $^\bullet$OH radicals, however the yield of the OH radicals is 10 times higher than that of the $H^\bullet$ atoms. Michael and Hart[10] assumed that the band at 310 nm is due to $C_6H_7{}^\bullet$

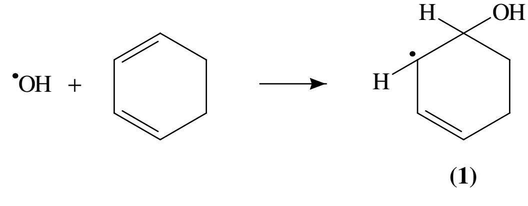
radical formed by $^{\bullet}$OH radical abstracting an hydrogen atom from either 1,4- or 1,3-cyclohexadiene. The proof for this assignment is that the same spectrum was obtained by the reaction of H atoms with benzene, where addition of the H atom to the benzene ring forms the $C_6H_7{}^{\bullet}$ radical. Using the molar absorption of the $C_6H_7{}^{\bullet}$ radical formed in the latter reaction (3300 $M^{-1}\,cm^{-1}$) and the absorption measured with the cyclohexadienes, it can be calculated that $^{\bullet}$OH abstracts hydrogen from the cyclohexadienes only partially, while the other fraction of radicals probably adds to the double bonds. They calculated that 45% of the $^{\bullet}$OH radicals abstract hydrogen from 1,4-C_6H_8, while 30% abstract hydrogen from the 1,3-isomer. The lower percentage in the case of the 1,3-isomer agrees with a higher tendency of addition to conjugated double bonds. Since $H^{\bullet}$ atoms react unusually fast with these compounds, they assumed that the $H^{\bullet}$ atoms add exclusively and do not abstract hydrogen atoms.

Von Sonntag and coworkers[14] repeated Michael and Hart's study of the reaction of $^{\bullet}$OH radical with 1,3- and 1,4-cyclohexadienes and extended it. They found that in the case of 1,4-cyclohexadiene, 50% of the $^{\bullet}$OH radicals abstract an hydrogen atom, while only about 25% of the $^{\bullet}$OH radicals abstract an hydrogen atom from 1,3-cyclohexadiene. The remaining $^{\bullet}$OH radicals probably add to the double bond. The addition to the double bond was confirmed by final products analysis in the case of the 1,4-isomer. When N_2O-saturated aqueous solution of 1,4-cyclohexadiene (10^{-2} M) together with lower (10^{-4} M) concentration of the thiol (1,4-dithiothreitol) was γ-radiolysed, it was found that 4-hydroxycyclohexene was produced with a yield of 0.29 $\mu mol\,J^{-1}$, i.e. a yield of 50% of the OH radicals (equation 9).



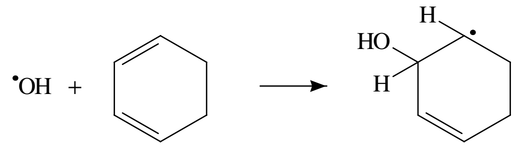
(9)

The 1,3-cyclohexadiene could not be prepared with higher purity than 98% and hence the analysis based on the final products is less meaningful. The yield of 3- and 4-hydroxycyclohexenes show that only 31% (0.18 $\mu mol\,J^{-1}$/0.58 $\mu mol\,J^{-1}$) of the OH radicals add to the double bonds. There is no information about the missing 44% (100% − 25% − 31%). Von Sonntag and coworkers suggested that the yield of hydroxycyclohexenes is not indicative of the OH addition to the double bonds due to non-quantitative reaction of the allylic radical **1** (equation 10) with RSH. Since, in the case of 1,4-cyclohexadiene, they found complete material balance, they concluded that the alkylic radical formed in reaction reacts quantitatively with the thiolic compound. Thus, radical **2** formed in reaction (11) will react quantitatively with RSH. The inefficiency of the reduction of the allylic radical by the thiol is probably due to the weak allylic C−H bond which leads to a six orders of magnitude lower rate constant for the RSH+ allylic radical reaction compared with the RSH+ alkyl radical reaction[15]. If all the material imbalance is due to incomplete reduction of the allylic radical, its formation is the main path of reaction of $^{\bullet}$OH with 1,3-cyclohexadiene.



(10)

(1)



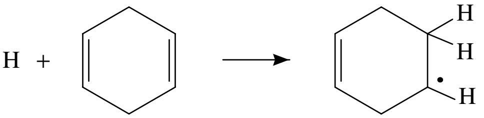
(11)

(2)

The pK_a of the $^•$OH radical is 11.9. The basic form is $O^{-•}$, which predominates at pH $\geqslant$ 12. Von Sonntag and coworkers[14] found that the absorption at 310 nm of pulse radiolysis of pH = 13 N_2O saturated solution of 1,4- or 1,3-cyclohexadiene indicates that $O^{-•}$ anion radical only abstracts hydrogen atoms but does not add to the double bond.

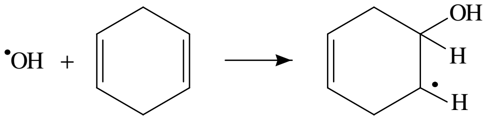
$H^•$ atom can both abstract hydrogen atoms and add to the double bonds. However it was found that the predominant reaction is the addition to the double bond. From the absorption of the cyclohexadienyl radical (formed by H abstraction) in acidic solution containing *t*-butanol (to scavenge the $^•$OH radicals) it was concluded[14] that only 22% and 7% of the H atoms abstract hydrogen from 1,4- and 1,3-cyclohexadiene, respectively.

Pulse radiolysis of N_2O-saturated aqueous solution of 1,4-cyclohexadiene leads to formation of three radicals, two by addition of either $^•$OH or H atoms to give the cyclohexenyl radicals **3** and **4** (equation 12 and 13) and one by abstraction of H atoms (equation 14). The last one, the cyclohexadienyl radical, can exist in two mesomeric forms (**5a** and **5b**). Fessenden and Schuler[16] found that the spin density of the cyclohexadienyl radical was highest at the central atom, i.e. form **5a** is the predominant one.



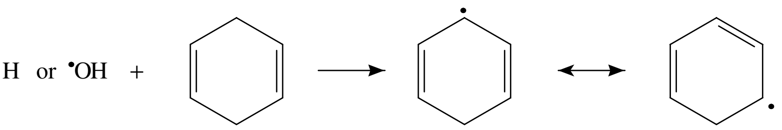
(12)

(3)



(13)

(4)

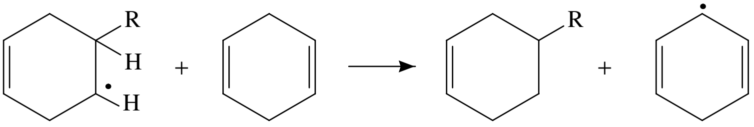


(14)

(5a) **(5b)**

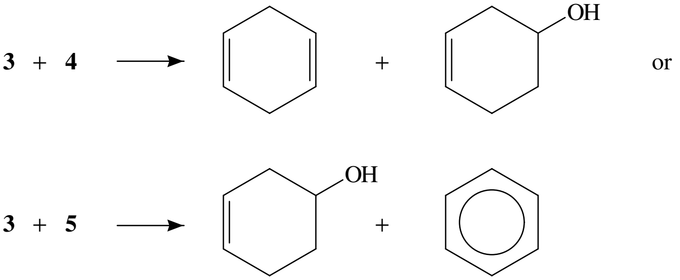
The cyclohexadienyl radicals decay by second-order kinetics, as proven by the absorption decay, with almost diffusion-controlled rate ($2k = 2.8 \times 10^9\ M^{-1}\,s^{-1}$). The cyclohexyl radicals **3** and **4** decay both in pseudo-first-order bimolecular reaction with the 1,4-cyclohexadiene to give the cyclohexadienyl radical **5** and cyclohexene (or its hydroxy derivative) (equation 15) and in a second order bimolecular reaction of two radicals. The cyclohexene (or its hydroxy derivative) can be formed also in a reaction of radical **3** or

4 with another radical by disproportionation (equation 16).



(15)

(**3**) R = H or (**4**) R = OH (**5**)



(16)

The fact that 4-hydroxycyclohexene can be formed both by a reaction in which two radicals disappear[16] and in a reaction which does not consume radicals complicates the calculation of the yield of radicals in the γ-radiolysis (continuous radiolysis) of N_2O-saturated aqueous solution of 1,4-cyclohexadiene. Von Sonntag and coworkers[14] wrote that the yield of radical **4** is 0.31 $\mu mol\,J^{-1}$. From their data it must be concluded that 4-hydroxycyclohexene (yield of 0.25 $\mu mol\,J^{-1}$) is formed solely by reaction 15, neglecting its formation by disproportionation (reaction 16). However, they found a yield of 0.085 $\mu mol\,J^{-1}$ benzene which can be formed only by disproportionation. Since in pulse radiolysis it was found that the yield of radical **4** is 0.29 $\mu mol\,J^{-1}$, and since its yield in dimers is 0.06 $\mu mol\,J^{-1}$ (2×0.02 for dimer **4–4** and 0.02 for 'dimer' **4–5**), it can be concluded that a maximum 0.23 $\mu mol\,J^{-1}$ of 4-hydroxycyclohexene was formed by reaction 15 and 0.02 $\mu mol\,J^{-1}$ of it came from disproportionation.

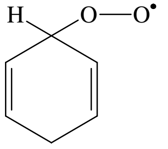
The 0.23 $\mu mol\,J^{-1}$ of reaction 15 increases the yield of radical **5** from 0.29 in pulse radiolysis to 0.52 $\mu mol\,J^{-1}$ in γ-radiolysis. Summing up all the yields of radical **5** gives $2 \times (0.085 + 0.056 + 0.067 + 0.021) + 0.02 = 0.48$. In this calculation we assume that benzene is formed solely from **5** + **5** disproportionation and none from reaction 16. In order to obtain closer agreement between the pulse and continuous radiolysis yields, less than 0.23 $\mu mol\,J^{-1}$ should be formed in reaction 15.

Three types of dimers could be formed by dimerization of the mesomeric radical **5**, i.e. **5a–5a**, **5b–5b** and **5a–5b**. From the yields of the various dimers the equilibrium concentration (the fractional spin density of the two mesomeric forms) can be calculated. (A typographical error in Reference 15 gave two dimers as **5b–5b**). The ratio of the equilibrium concentration can be calculated by

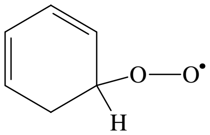
$$\mathbf{5a}/\mathbf{5b} = \sqrt{(\mathbf{5a}-\mathbf{5a})/(\mathbf{5b}-\mathbf{5b})} = 1.63 \text{ or } \mathbf{5a}/\mathbf{5b} = 2(\mathbf{5a}-\mathbf{5a})/(\mathbf{5a}-\mathbf{5b}) = 1.67$$

If the product ratios indicate the contribution of hybrid forms **5a** and **5b**, 62% of radicals **5** exist in the **5a** form.

Von Sonntag and coworkers[17] extended this study to the radiolysis of an aqueous solution of 1,4-cyclohexadiene saturated with N_2O:O_2 (4:1) mixture. Due to the higher solubility of N_2O in water all the hydrated electrons react with N_2O to give $^\bullet OH$ radicals, as in N_2O-saturated solution. However, the concentration of oxygen is sufficient to convert the radicals formed from cyclohexadiene to peroxyl radical, before reacting between themselves. O_2 can react also with H atom to produce $HO_2^{\bullet}$. The rate constant for $H^{\bullet} + O_2 \rightarrow HO_2^{\bullet}$ is four times higher than that for $H^{\bullet}+$ cyclohexadiene (2×10^{10} vs $4.7 \times 10^{9}\ M^{-1}\,s^{-1}$). If the concentration of 1,4-cyclohexadiene is considerably higher than that of $O_2 (2.4 \times 10^{-4}$ M), the hydrogen atoms will react preferentially with the cyclohexadiene. The absorption of radical **5** at 310 nm decays faster and, in first-order kinetics, in the presence of oxygen. Using N_2O/O_2 mixtures with at least 80% N_2O showed that the pseudo-first-order rate constant of the decay of the 310-nm maximum is linearly dependent on the oxygen concentration. The slope of this dependence yields the rate constant for $\mathbf{5} + O_2 \rightarrow$ peroxyl radical as $k = 1.2 \times 10^{9}\ M^{-1}\,s^{-1}$. Two isomers of cyclohexadienylperoxyl radicals **6a** and **6b** can be formed, by reaction at the two termini of the cyclohexadienyl radical (**5a** ↔ **5b**).



(6a)



(6b)

Most peroxyl radicals are oxidants[18], however the peroxyl radicals formed from the reaction of O_2 with the radicals induced by $H^{\bullet}/^{\bullet}OH$ reacting with 1,4-cyclohexadiene are reductants, as was proven by reduction in pulse radiolysis of tetranitromethane (TNM) to yield the strongly absorbing nitroform anion $C(NO_2)_3^{-}$[17]. The build-up of the nitroform anion has two distinctive steps. The major step is a very fast build up with $G = 1.7 \times 10^{-7}\ mol\,J^{-1}$. The second step has a lower yield ($0.4 \times 10^{-7}\ mol\,J^{-1}$) and is about 50 times slower. Only the origin of the first step was studied. Its rate was found to be linearly dependent on the concentration of TNM for low concentration and to reach a plateau at higher concentration. The rate at the plateau was found to be equal to the rate of formation of the peroxyl radical. For high concentration (0.5 mM) of TNM the rate of formation of the nitroform anion depends on O_2 concentration up to 40% O_2, where it reaches a plateau. This plateau can be either due to the rate constant of unimolecular decay of the cyclohexadienyl radical (equation 17), or due to the rate of the deprotonation of $HO_2^{\bullet}$ (equation 18).

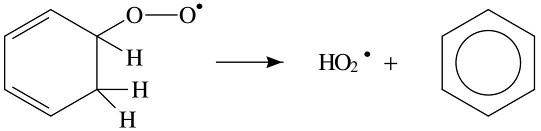
$$C_6H_7O_2 \longrightarrow C_6H_6 + HO_2^{\bullet} \tag{17}$$

$$HO_2^{\bullet} \longrightarrow H^{+} + O_2^{-\bullet} \tag{18}$$

It is known that $HO_2^{\bullet}$ reacts with TNM too slowly to be responsible for the fast build-up, and the build-up must be due to

$$C(NO_2)_4 + O_2^{-} \longrightarrow C(NO_2)_3^{-\bullet} + NO_2 + O_2$$

Using basic pH leads to higher plateau rate constants, indicating that the rate-determining step is reaction 18. Reaction 17 must be at least as fast as the rate of O_2 addition in the highest O_2 concentration used, $k_{17} \geqslant 8 \times 10^{5}\ s^{-1}$, which is the limit of the instrument measurement. The *G* of benzene in pulse radiolysis was found to be equal to that of the nitroform anion ($1.6 \times 10^{-7}\ mol\,J^{-1}$) as can be expected from reactions 17–19. Since the yield of the cyclohexadienylperoxyl radical is $2.9 \times 10^{-7}\ mol\,J^{-1}$ it means that only a fraction (*ca* 60%) of the cyclohexadienylperoxyl radicals eliminates $HO_2^{\bullet}$. The $HO_2^{\bullet}$ elimination occurs by H-transfer of the allylic hydrogen to the oxygen atom carrying the odd electron. It can be expected that the rate for this reaction will depend on the distance between these two atoms. Von Sonntag and coworkers[19] estimated that the H−O distance for the 1,3-cyclohexadiene isomer is 1.4–2.2 Å whereas for the 1,4-cyclohexadiene isomer it is 3.5–4.2 Å. Thus, they concluded that only the 1,3-isomer eliminates $HO_2^{\bullet}$ (at least fast enough) to give benzene (equation 19).



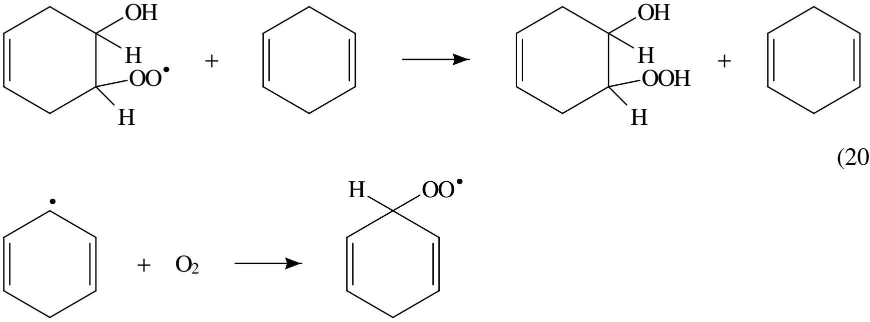
(6b)

(19)

This conclusion is supported by results of detailed study on the decay of hydroxyhexadienylperoxyl radicals, formed by addition of $^{\bullet}OH$ to benzene, followed by addition of dioxygen molecule. It was found that in the high dose rate of pulse radiolysis, hydroquinone is the major product whereas catechol was not observed, indicating that only the 1,3-isomer loses $HO_2^{\bullet}$ and hence does not lead to dihydroxybenzene. The observation that the yield of O_2^{-} is 60% of the yield of the cyclohexadienyl radicals indicates that when dioxygen molecules react with the cyclohexadienyl radical, the radical is 60% trapped in the mesomeric form of **5b**, whereas the results from the final products of dimerization in γ-radiolysis show that 60% react in the form **5a**.

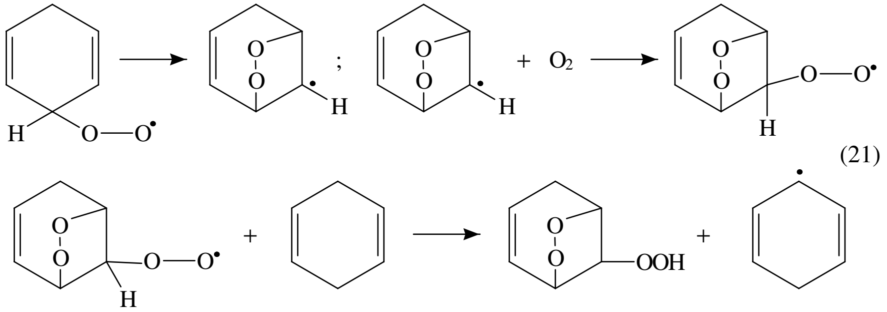
E. Final Products in the Continuous γ-Radiolysis of 1,4-Cyclohexadiene

In the γ-radiolysis of N_2O/O_2 saturated aqueous solution of 1,4-cyclohexadiene (CHD) (10 mM), the major final products are benzene with a radiolytic yield of 2.8×10^{-7} mol J^{-1} (higher than the yield for electron beam pulse radiolysis, where it is 1.6×10^{-7}) and 6-hydroxycyclohex-3-enyl hydroperoxide with the same radiolytic yield (1.5×10^{-7} and 1.3×10^{-7} mol J^{-1}) for the *trans* and *cis* isomers. The other major products are hydrogen peroxide (yield = 2.3×10^{-7} mol J^{-1}), formaldehyde (0.7×10^{-7}), acetaldehyde (0.44×10^{-7}) and cyclohexene endoperoxidic hydroperoxide (0.4×10^{-7}), lactic acid (0.32×10^{-7}) and cyclohex-3-enyl hydroperoxide (0.3×10^{-7} mol J^{-1}). The total oxygen uptake is 7.5×10^{-7} mol J^{-1}. The high oxygen uptake, which is higher than the yield of the radical, is due to some of the radicals reacting consecutively with two molecules of oxygen in the route to produce the hyperoxides, by abstracting hydrogen atom from the cyclohexadiene (CHD), producing another radical which reacts with oxygen (equation 20).



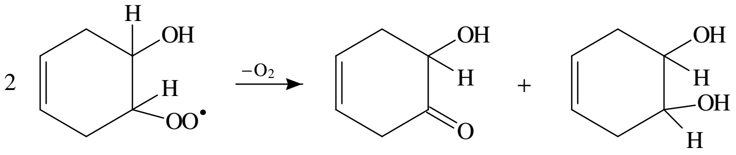
(20)

The peroxyl radical formed in this reaction, as well as by $^\bullet$OH and H$^\bullet$ hydrogen abstraction from CHD, can react with another oxygen molecule after intramolecular addition of the peroxyl radical to the double bond to give an endoperoxidic radical (equation 21).



(21)

In the case of low CHD concentration, The abstraction of hydrogen from CHD can be replaced, by reaction with O_2^- and H^+ to give O_2, due to the relatively high concentration of O_2^-. In order to remove O_2^- von Sonntag and coworkers[17] added superoxide dismutase. It was found that for low concentration of CHD and in the presence of superoxide dismutase, the yield of benzene is the same as in pulse radiolysis. In these conditions the oxygen uptake is only 0.56 μmol J^{-1}, equal to the yields of the initially formed OH radicals. The yield of the hydroperoxides is very low (0.6×10^{-7} compared to 3.5×10^{-7} mol J^{-1} in the high CHD concentration). In solutions containing superoxide dismutase the yield of the hydroperoxide is an increasing function of the CHD concentration in the range studied (0.5–10 mM). The yield of benzene in pulse radiolysis, or in γ-radiolysis of low CHD concentration with superoxide dismutase, represents the primary yield of 1,3-cyclohexadiene peroxyl radical, which eliminates $HO_2^\bullet$ to give benzene. The peroxyl radicals formed from the OH-adduct of CHD disproportionate bimolecularly to 6-hydroxycyclohex-3-en-1-one and 4,5-dihydroxycyclohexene (equation 22).



(22)

cis + *trans*

The yields of 6-hydroxycyclohex-3-en-1-one and 4,5-dihydroxycyclohexene are about equal (0.13 and 0.11 μmol s^{-1}, respectively), in accordance with this mechanism. Their yields account for more that 80% of their precursor — the peroxyl radical of the OH adduct ($G = 0.29$ μmol J^{-1}). Both the *cis* and *trans* isomers of 4,5-dihydroxycyclohexene are formed with the latter being predominant (*ca* 64%).

III. RADIOLYSIS IN NON-AQUEOUS SOLVENTS

We saw previously that hydrated electrons react very rapidly with the conjugated 1,3-butadiene ($k = 8 \times 10^9$ M^{-1} s^{-1}). In less polar solvents the attachment of an electron to 1,3-butadiene (with adiabatic electron affinity of -0.62 eV[20]) will be slower. The rate of attachment for non-polar solvents can be increased by increasing the pressure or decreasing the temperature[21,22]. Shida and Hamill[23] γ-irradiated methyltetrahydrofuran glass containing 1,3-butadiene or several homologs at 77 K. They found that the electrons are attached to the 1,3-butadiene, as can be seen by suppression of the solvent-trapped electron band and formation of new bands at 388 and 570 nm. These bands are formed also in other conjugated dienes: isoprene, *cis*-1,3-pentadiene, 2,4-hexadiene, 2,3-dimethyl-1,3-butadiene, 1,3-cyclohexadiene and 1,3-cyclooctadiene. The addition of non-conjugated dienes such as 1,4-cyclohexadiene and 1,5-hexadiene did not decrease significantly the solvent-trapped electron absorption (at 1000–1500 nm), indicating that the electrons are not attached to non-conjugated dienes. The formation of the conjugated diene anion is suppressed by the addition of efficient electron scavengers.

Shida and Hamill[23] found that the positive and negative molecular ions of 1,3-butadiene and its homologs have similar absorption spectra. Band maxima of the anions are not sensitive to substituent alkyl groups, whereas those of the cations are red-shifted as the number of substituent methyl groups increases. In alcoholic matrices the butadiene anions abstract the alcoholic proton to form an allylic radical (equation 23), as was proven by ESR spectroscopy.

$$(\mathrm{CH_2{=}CH{-}CH{=}CH_2})^{-\bullet} + \mathrm{ROH} \longrightarrow \mathrm{CH_2{=}CHC^{\bullet}HCH_3} + \mathrm{RO^-} \qquad (23)$$

The ESR spectrum obtained for irradiated methanol solution of 1,3-butadiene or *cis*-1,3-pentadiene is similar to that of irradiated methanol solution of allyl chloride, in which case it is known that the electron leads to reductive dehalogenation (equation 24).

$$\mathrm{CH_2{=}CHCH_2Cl} + \mathrm{e^-} \longrightarrow \mathrm{CH_2{=}CHC^{\bullet}H_2} + \mathrm{Cl^-} \qquad (24)$$

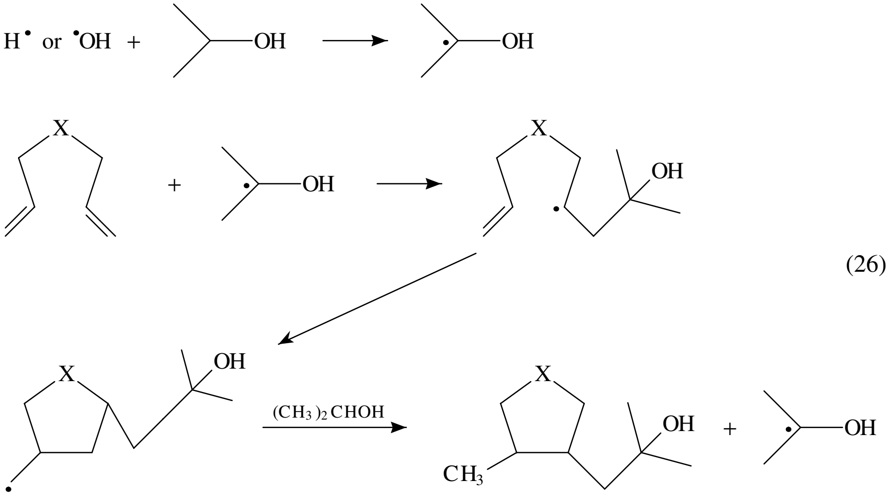
Holroyd and coworkers[24] studied the attachment of excess electrons to 1,3-butadiene in *n*-hexane solution, and the detachment of an electron from the butadiene anion. It was found that the equilibrium constant K for equation 25 increases rapidly with pressure and decreases with increasing temperature, as was found earlier for other molecules with negative electron affinities in non-polar solvents[21]. At $-7\,^{\circ}\mathrm{C}$ attachment is observed at 1 bar. At high pressure it was found that the rate of the attachment is diffusion-controlled. Freeman and coworkers[25] measured the free-ion yields in several liquid hydrocarbons, three of which were cyclic dienes, as a function of temperature. At room temperature they measured free-ion yields of 7.5 $\mathrm{nmol\,J^{-1}}$ and 23 $\mathrm{nmol\,J^{-1}}$ for 1,3- and 1,4-cyclohexadiene, respectively. They attributed the lower yield in the case of the conjugated diene to anion formation. It should be pointed out that the yield is even lower in the case of the bicyclic non-conjugated diene, bicyclo[2.2.1]heptadiene where the yield is 5.3 $\mathrm{nmol\,J^{-1}}$. This is ascribed to a through-space conjugation.

$$\mathrm{e^-} + \text{1,3-butadiene} \underset{\mathrm{k_d}}{\overset{\mathrm{k_a}}{\rightleftharpoons}} (\text{1,3-butadiene})^- \quad K = k_a/k_d \qquad (25)$$

Gamma radiolysis at 77 K of glassy alkanes leads to materials that emit weakly in the visible range on warming, thermoluminescence (TL). Brocklehurst and Robinson[26] studied the radiolysis of glassy 3-methylpentane (MP) and its solutions of olefins. MP alone emits on warming at 430 nm with a broad band, with a G value of 10^{-3}. MP solution of conjugated dienes (1,3-pentadiene and 2,4-hexadiene) give a very strong ($G = 0.05$–0.5) TL broad peak at 490 nm, similar to that found for aromatic solutes (naphthalene and toluene)[27]. This yield shows that both the efficiency of formation and the luminescence quantum yield of the emitter are high. Solution of mono olefins or of non-conjugated dienes give much lower yield with G values of 0.001 to 0.05.

These findings were explained by formation of a luminescent precursor-X, which is formed with very low yield in pure MP, but with higher yield in conjugated dienes solutions. The intermediate, X, was tentatively ascribed to twisted excited states although the possibility of emission by free radicals was not excluded. The assignment of the emitter in solution of butadiene derivatives was studied in detail recently[28]. The authors used glasses (at 77 K) of 2:1 mixtures of methylcyclohexane and isopentane, which were 2 and 10 mM in 10 various butadiene derivatives. After irradiation at 77 K (with doses of 375 or 750 Gy), the thermoluminescence spectra (TL) were measured. The solvent itself gave an emission band in TL at 450 nm. The maximum intensity is about 10 times weaker than that of the dienes, although it is broader, so that the integrated intensity is not much lower. The diene solution TL is at 480–520 nm. Both the width of the spectra (full width half maximum *ca* 85 nm) and the glow peaks were narrower than that of the solvent itself. It was found that the TL spectra were changed only very little with the substitution of the dienes, leading to the conclusion that the luminescence is due to excited states of the parent compound and to radicals formed by abstraction or addition of a hydrogen atom, similar to earlier conclusions for aromatic solutes[26,29].

Shevlin and coworkers[30] studied the radiolysis-induced addition of the α-hydroxy isopropyl radical to substituted 1,6-heptadienes and analogs containing a heteroatom. The radical was generated by γ-irradiation of propanol solutions of various 1,6-heptadienes. It was found that the adduct to the double bond decomposed to give a compound containing a five-membered ring (equation 26).



(26)

X = O, CH_2, CHCOOH, $C(COOH)_2$, NH, NCH_3 $N(CH_2CH{=}CH_2)$, $N(CH_3)_2{}^+Cl^-$

Bobrowski and Das published a series of papers on the transients in the pulse radiolysis of retinyl polyenes[31–37], due to their importance in a variety of biomolecular processes. They studied[32] the kinetics and mechanisms of protonation reaction. The protons were released by pulse radiolysis, on a nanosecond time scale, of 2-propanol air-saturated solutions containing, in addition to the retinyl polyenes, also 0.5 M acetone and 0.2 M CCl_4. Within less than 300 ns, the electron beam pulse results in formation of HCl. The protonated products of retinyl polyenes were found to absorb optically with λ_{max} at the range of 475–585 nm and were measured by this absorption. They found that the protonation rate constants of polyene's Schiff bases depend on the polyene chain length and geometry. The rate constants are close to the value for diffusion control. As the polyene chain length is increased, a slight increasing trend was observed for the protonation rate constants. They found that the protonation rate constant for all-*trans* retinal is smaller by more than two orders of magnitude than that for its Schiff base, in accordance with the lower basicity of a carbonyl oxygen relative to that of imino nitrogen.

Bobrowski and Das[33] studied the transient absorption phenomena observed in pulse radiolysis of several retinyl polyenes at submillimolar concentrations in acetone, *n*-hexane and 1,2-dichloroethane under conditions favourable for radical cation formation. The polyene radical cations are unreactive toward oxygen and are characterized by intense absorption with maxima at 575–635 nm. The peak of the absorption band was found to be almost independent of the functional group (aldehyde, alcohol, Schiff base ester, carboxylic acid). In acetone, the cations decay predominantly by first-order kinetics with half life times of 4–11 μs. The bimolecular rate constant for quenching of the radical cations by water, triethylamine and bromide ion in acetone are in the ranges $(0.8\text{–}2) \times 10^5$, $(0.3\text{–}2) \times 10^8$ and $(3 - 5) \times 10^{10}$ $M^{-1}\,s^{-1}$, respectively.

Bobrowski and Das[35] found that pulse radiolysis of O_2-saturated acetone solution of high concentration (1–10 mM) of all-*trans* retinal, retinoic acid and methyl retinoate give rise to a fast transient absorption process, which is suggested to be due to formation of a dimer cation radical, by association of the original cation radical with the parent polyene. The dependence of the absorption rate of formation on the polyene concentration yields an equilibrium constant (K) of dimerization of 220–440 M^{-1}. For 1,2-dichloroethane solutions of all-*trans* retinal and retinoic acid, K values are larger almost by an order of magnitude. Using non-protic solvents they observed[37] transient species (life time 0.5–7 μs, $\lambda_{max} = 575\text{–}590$ nm) from all-*trans* retinal and retinyl methyl ether which were identified as the radical anions. In case of retinyl esters (acetate and palmitate), the radical anions lose instantaneously carboxylate anions to give retinylmethyl radical.

Many studies used radiation chemistry to produce the radical and radical cations and anions of various dienes in order to measure their properties. Extensive work was devoted to the radical cation of norbornadiene in order to solve the question whether it is identical with the cation radical of quadricyclane[38–44]. Desrosiers and Trifunac[45] produced radical cations of 1,4-cyclohexadiene by pulse radiolysis in several solvents and measured by time-resolved fluorescence-detected magnetic resonance the ESR spectra of the cation radical. The cation radical of 1,4-cyclohexadiene was produced by charge transfer from saturated hydrocarbon cations formed by radiolysis of the solvent. In a similar system[46], the radical cations of 1,3- and 1,4-cyclohexadiene were studied in a zeolite matrix and their isomerization reactions were studied. Dienyl radicals similar to many other kinds of radicals were formed by radiolysis inside an admantane matrix[47]. Korth and coworkers[48] used this method to create cyclooctatrienyl radicals by radiolysis of bicyclo[5.1.0]octa-2,5-diene in admantane-D_{16} matrix, or of bromocyclooctatriene in the same matrix. Williams and coworkers irradiated 1,5-hexadiene in $CFCl_3$ matrix to obtain the radical cation which was found to undergo cyclization to the cyclohexene radical cation[49,50] through the intermediate cyclohexane-1,4-diyl radical cation.

Land and coworkers[51] produced by pulse radiolysis of benzene solution, flushed with argon, of carotenoid polyenes, the radical anion and the radical cation of the polyenes. The formation of the radical anion (with absorption at λ_{max} 975 nm) was found to be prevented by saturating the solution with N_2O — an efficient electron scavenger. Kubozono and colleagues[52] irradiated low-temperature (70–130 K) solid solutions of 1,3,5-cycloheptatriene and 1,3-cycloheptadiene in perhalocarbons, in order to produce their radical cations (by losing one electron from the molecule) and measured their structure and dynamics by ESR. For the radical cation of 1,3,5-cycloheptatriene in CCl_3CF_3 they found that ring inversion occurs across the molecular plane. Above 90 K they found thermal deprotonation of this radical in CCl_2FCFCl_2. Takamuku and coworkers[53] produced the radical cations of 1,ω-bis(diarylethenyl)alkanes $Ar_2C{=}CH(CH_2)_nCH{=}CAr_2$ (Ar $=$ *p*-methoxyphenyl; $n = 2-4$), both by pulse radiolysis and by continuous γ-radiolysis, in 1,2-dichloroethane solution (pulse radiolysis) and in a butyl chloride matrix at 77 K (γ-radiolysis). They found that for $n = 3$, 4 the initially formed radical cations undergo intramolecular cyclization to form 1,4-distonic radical cations (i.e. radical cations in which the cationic and radical sites are separated) as can be proven by their reaction with oxygen.

Takemura and Shida[54] prepared the allene radical ion by γ-radiolysis of halocarbon solid solution of allene at low temperatures and showed that the radical cation has a lower D_2 structure than the precursor with a skew angle of 30–40°. Kubonzo and coworkers[55,56] produced by γ-radiolysis in a low-temperature halocarbon matrix several derivatives of the allene radical cation, i.e. the radical cations of 1,2-butadiene, 3-methyl-1,2-butadiene, 1,2-pentadiene and 2,4-dimethyl-2,3-pentadiene. They studied the structure by ESR spectroscopy, compared it with semiempirical MO calculations and discussed the structure and thermal conversion into neutral radical species. They later extended this study to the radical cations of butatriene and tetramethylbutatriene. By comparing the experimental hyperfine splittings of the ESR spectra with those calculated by semiempirical MO they found skew angles of 25° and 50°, respectively. In all these studies the degassed halocarbon (CCl_3CF_3, CCl_3F, CCl_2FCClF_2, CCl_2FCCl_2F) solid solutions of the diene/triene is irradiated by γ-rays from a ^{60}Co irradiator at 77 K. Fujisawa and coworkers[57] produced, by low-temperature γ-radiolysis, the radical cations of *cis*- and *trans*-1,3-pentadiene and showed that they isomerized to the radical cation of cyclopentene, similar to the findings of Williams and colleagues[49,50] for the 1,5-hexadiene in some matrices. Kubozono and coworkers[58] found that the radical cation of 2,5-dimethyl-1,5-hexadiene in CCl_3CF_3 also isomerized. However, Prasad and coworkers[59] did not find cyclization of the radical cation of 2,5-dimethyl-2,4-hexatriene and 2,7-dimethyl-2,4,6-octatriene in frozen matrices of either CCl_4 or CCl_3F. In low-concentration solution (1%) they obtained the monomeric radical cations, while using 5–10% solution of the polyene together with $AlCl_3$ leads to the formation of the dimeric radical cation.

Prasad and coworkers[60] studied the ESR spectra of cation radicals of dienes, trienes, tetraenes and pentaenes formed in $CFCl_3$ matrix by X-ray irradiation. The structures of the resulting cation radicals were deduced by comparing the experimental coupling constant to those derived from INDO calculation. The unpaired spin density decreases with increasing chain length.

Pulse radiolysis is used also for preparation of excited states of dienes and polyenes. This is done by irradiation of the diene/polyene in toluene solution. The radiolysis of toluene yield high concentration of molecules in the triplet excited state of the solute. Wilbrandt and coworkers[61] pulse-radiolysed 1 mM solution of all-*trans*-1,3,5-heptatriene in toluene solution and observed the absorption spectra of the triplet state of the heptatriene with a maximum at 315 nm. The same group[62] produced and measured the absorption spectra of several isomeric retinals in their lowest excited triplet state by pulse irradiation of their dilute solution in Ar-saturated benzene containing 10^{-2} M naphthalene. Nakabayashi and coworkers[63] prepared the lowest triplet states of 1,3-cyclohexadiene, 1,3-cycloheptatriene and several bicyclic dienes by pulse radiolysis of benzene solution of the cyclic dienes, and measured the triplet life time. Gorman and coworkers[64] produced the triplet state of cycloheptatriene by pulse radiolysis of its solution in toluene. They found that it has considerably longer life (6 ± 1 μs) than the acylic trienes (*ca* 300 ns).

Woodruff and coworkers[65] produced triplet states for several carotenoid pigments by pulse radiolysing benzene solution of the carotenoids with higher concentration of naphthalene. The initially produced excited states of benzenes (both singlet and triplet) are rapidly converted by energy transfer and intersystem crossing to the triplet state of naphthalene which transfers its energy to the carotenoid. Gust and colleagues[66] prepared in a similar way the triplet states of both polyenes and carotenoporphyrins by using either a benzene solution alone or with a biphenyl as a triplet donor.

IV. REACTIONS WITH DIENES STUDIED BY RADIOLYSIS

Many studies used radiation chemistry and mainly pulse radiolysis, in which a high-intensity pulse of electrons hit the sample, producing high concentration of radicals, to study the reaction of various radicals with several dienes. Nielsen and coworkers[67] used this method to study the rate constants of NO_3 with a series of 7 dienes (1,3-butadiene, isoprene, 2,3-dimethyl-1,3-butadiene, *cis*- and *trans*-1,3-pentadiene, all-*trans*-2,4-hexadiene and 1,3-cyclohexadiene) in the gaseous phase at 295 K and total pressure of 1 atmosphere. The concentrations of NO_3 radicals were measured spectrophotometrically and their temporal behaviour was recorded digitally. Addition of dienes to a gas mixture whose radiolysis leads to formation of NO_3 radicals (0.3% HNO_3 + 99.7% SF_6) accelerates the rate of the decay of NO_3 radicals, and this acceleration is used to derive the rate constant of NO_3 with dienes. Nielsen[68] studied the reaction of SH radicals with 1,3-butadiene in a similar method by pulse radiolysis of H_2S/Ar mixture. Umemoto and coworkers[69] studied in this way the rate constant of a ground-state atomic nitrogen with 1,3-butadiene. Perner and Franken[70] measured the rate constant for the reaction of SH with 1,3-butadiene, 1,4-cyclohexadiene and allene. Nahor and Neta[71] produced, by radiolysis of perfluorobutyl iodide in aerated methanol solutions, the perfluorobutyl radical which reacts subsequently with O_2 to form the perfluoroperoxyl radical. They found that the radical added to the double bond rather than even abstract the doubly allylic hydrogens. Reasonable correlation was found between the rate constants and the σ^* Taft substituent constants.

V. RADIOLYSIS OF BULK DIENES AND OLIGOENES

The yield of free ions in the radiolysis of dienes is very similar to those found for monoalkenes ($G = 4.0$–4.2)[72]. Freeman and coworkers[73] measured the yield of the free ions (G_{fi}) and the secondary electron penetration (b_{Gp}) in radiolysis of unsaturated hydrocarbons. Some of the data are given in Table 1. It can be seen that the yield of the free ions is considerably smaller for the dienes studied. Also, the secondary electron penetration is smaller for the dienes, all of them having a similar value (3.9–4.4 nm).

Ionizing radiation leads also to formation of excited molecules in the triplet state. Okazaki and coworkers[74] calculated the yield of the triplets and found that the yields for conjugated dienes are significantly higher than those of monoalkenes. The yield for 1,3-butadiene is 2.66, whereas the values for 1-butene, 2-butene and 2-methylpropene are 1.51, 1.55 and 1.54, respectively.

The yields of the final products in the radiolysis of liquid aliphatic diene hydrocarbons were studied by van der Heyde and Wagner[75] for 1,5-hexadiene and by Shellberg and coworkers[76] for 2,6-dimethyl-2,6-octadiene. The results are summarized in Table 2. For 1,5-hexadiene, higher yields were obtained for C_6, C_9 and C_{12} products. Also, C_3 products have slightly higher yield. The high yield of C_9 and C_3 products are due to a weaker C−C bond in the allylic position, especially since the rupture of the σ bond between carbon atoms 3 and 4 leads to formation of two allylic radicals. Shellberg and coworkers[76] deduced from their results a free radical mechanism for the formation of hydrogen and light hydrocarbons in the radiolysis of 2,6-dimethyl-2,6-octadiene. The high yield of C_5 products is probably due to larger rupture of the σ bond between carbons 4 and 5 due to simultaneous formation of two allylic radicals.

TABLE 1. Yield of free ions (G_{fi}) and the secondary electron penetration (b_{Gp}) for radiolysis of unsaturated hydrocarbons

Hydrocarbons	T (K)	G_{fi}	b_{Gp} (nm)
Monoalkenes			
1-Butene	293	0.093	5.4
trans-2-Butene	293	0.080	5.3
cis-2-Butene	293	0.23	7.4
Isobutene	293	0.25	7.4
2-Methyl-2-butene	292	0.26	8.0
2,3-Dimethyl-2-butene	293	0.44	10.1
1-Hexene	293	0.10	5.2
trans-2-Hexene	293	0.092	5.1
trans-3-Hexene	293	0.10	5.3
cis-3-Hexene	293	0.13	5.6
Cyclohexene	293	0.20	6.2
Dienes			
Propadiene	282	0.050	4.3
1,3-Butadiene	269	0.038	3.9
1,4-Pentadiene	293	0.067	4.4
1,5-Hexadiene	292	0.066	4.2
1,6-Heptadiene	292	0.066	4.2
1,7-Octadiene	292	0.065	4.1
Alkynes			
Propyne	260	0.17	4.8
2-Butyne	293	0.32	9.7
1-Hexyne	253	0.10	4.4
2-Hexyne	293	0.19	6.8
3-Hexyne	293	0.21	7.1

TABLE 2. Yields of final products from radiolysis of liquid aliphatic dienes (G, molecule/100 eV)

Hydrocarbons / Products	1,5-Hexadiene	2,6-Dimethylocta-2,6-diene
Hydrogen	0.45	0.80
Methane		0.052
C_2 products	0.06	0.07
C_3 products	0.09	0.023
C_4 products	0.06	0.050
C_5 products	0.02	0.068
C_6 products	0.41	
C_7 products	0.02	
C_8 products	0.02	
C_9 products	0.42	
C_{10} products	0.02	
C_{12} products	0.77	

The radiation chemistry of cyclic oligoenes was studied, and the radiolytic yields of the final products are summarized in Table 3, which shows that 1,4-cyclohexadiene differs from all others in its high yield of hydrogen, both in the gas phase and in the liquid phase. Cserep and Foldiak[84] attributed it to the presence of two doubly allylic CH_2 groups. In addition, the geometric orientation of the allylic hydrogens is favourable for hydrogen

TABLE 3. Radiolytic yields of the final products of the radiolysis of cyclic oligoenes

I. Liquid phase

Substrate / Product	1,3-cyclo hexadiene[77]	1,4-cyclo hexadiene[78]	cyclo heptatriene[80]	1,3-cyclo octadiene[77]	cycloocta tetraene[81]	1,5,9-cyclo dodecatriene[77]
Hydrogen	0.22	1.18, 0.94[a]	0.06	0.24[a]	0.02	0.44
Methane	0.0015		0.0014	0.01		
$C_2 + C_4$ products	0.0079	0.08	0.016	0.021	0.018	0.57
1,3,5-Hexatriene		2.3				
Benzene		2.9				
Toluene			0.5			

[a] Reference 79.

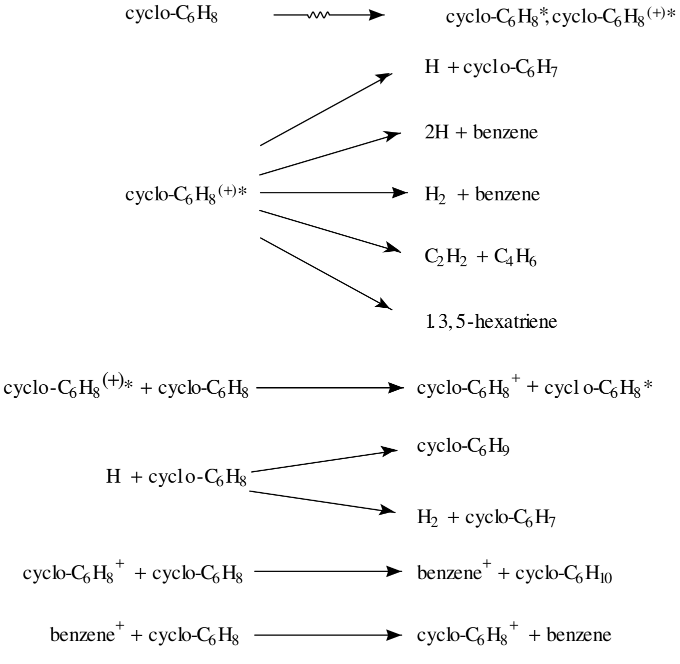
II. Gas phase

Substrate / Product	1,4-Cyclohexadiene[82]	Cycloheptatriene[83]
Hydrogen	1.95	0.50
Methane	trace	0.16
$C_2 + C_4$ products	1.25	1.52
Cyclopentadiene		0.29
Cyclohexene	14.0	
1,3-Cyclohexadiene	1.0	
1,3,5-Hexatriene	1.0	
Benzene	28.5	0.65

elimination. Two of the allylic hydrogens are perpendicular to the plane of the −CH=CH− group and are on the same side of the ring. However, Sakurai and coworkers[82] suggested a predominantly radical pathway for hydrogen formation in the gas-phase radiolysis of 1,4-cyclohexadiene, on the basis of the effect of NO on the yield of hydrogen. The geometric orientation is not important for the radical mechanism. While the yield of H_2 from radiolysis of cyclohexene is independent of dose up to 2000 $J\,g^{-1}$, the radiolytic yield of hydrogen from 1,4-cyclohexadiene decreases with increasing dose already from 300–400 $J\,g^{-1}$. This was ascribed to the effect of the other products, 1,3-cyclohexadiene, benzene and 1,3,5-hexatriene. Sakurai and coworkers[82] suggested Scheme 1 for the gas-phase radiolysis of 1,3-cyclohexadiene. In this scheme $C_3H_8{}^{(+)*}$ denotes an excited molecule or ion.

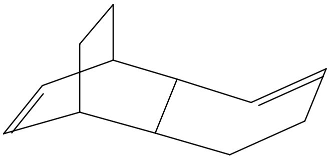
Okada and coworkers[78] studied the γ-radiolysis of 1,3- and 1,4-cyclohexadienes. From ESR studies and product determination they concluded that the main primary process for radiolysis of both isomers is the dissociation of allylic C−H bonds. The formed hydrogen atoms may add to double bonds or abstract other hydrogen atoms (mainly allylic ones). The ESR spectrum of the radiolysis product at 77 K showed the presence of the cyclohexadienyl radical in the case of 1,4-cyclohexadiene, whereas the main intermediate from 1,3-cyclohexadiene is the 2-cyclohexenyl radical[78,85], formed by addition of hydrogen atom to the parent molecule. This difference is in agreement with the higher reactivity to addition of radicals of the conjugated alkadienes.

Irradiation of mixtures of cyclohexene with 1,3-cyclohexadiene leads to high yield of dimers ($G = 6.3$)[86]. Schutte and Freeman[87] found that radiolysis of 1,3-cyclohexadiene dissolved in various solvents gives dimers mainly via cationic Diels-Alder addition,

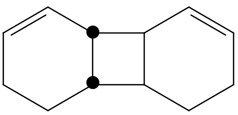


SCHEME 1

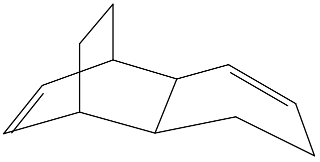
however another process is also involved, probably through a triplet excited state. Both processes are sensitized by benzene. Hammond and coworkers[88] postulated the formation of the four different dimers shown below from radiolysis of 1,3-cyclohexadiene, all of which are formed via the triplet state.



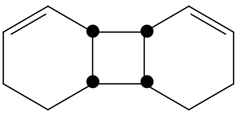
endo-Dicyclohexadiene



trans, cis, trans-Tricyclo [6.4.0.0]
dodeca-3, 11-diene



exo-Dicyclohexadiene



cis, cis, cis-Tricyclo [6.4.0.0]
dodeca-3, 11-diene

On the other hand, the 1,3,5-hexatriene was postulated to be formed from the singlet excited state. On the basis of electron-scavenging experiments it was concluded that the triplet state is probably largely due to neutralization, whereas the higher-energy singlet state is formed by primary excitation.

Cyclopentadiene behaves differently than the cyclohexadienes in that its radiolysis leads to high molecular weight polymer via a cationic mechanism[89], whereas such compounds are not formed in high yield from cyclohexadienes irradiated in the liquid phase.

The radiolysis of cycloheptatriene was studied in both the liquid and the gaseous phase. Increase of the pressure in the gas-phase radiolysis enhances the yields of acetylene and dimers and decreases those of benzene, toluene and cyclopentadiene. ESR studies[80] show similar signals to those obtained from benzene. The production of toluene in the radiolysis of cycloheptatriene was assumed to be via isomerization of excited heptatriene molecules, which were supposed also to lead to cyclopentadiene and acetylene, since their yields were almost unaffected by radical or ion scavengers. The energy of the precursor to cyclopentadiene and acetylene is probably higher than the energy of the precursor of toluene, since the yields of the two former compounds is pressure-independent. Since the yield of acetylene is higher than that of cyclopentadiene, it must be formed also by other processes, probably breaking the C_7 molecule into two C_2 and one C_3 molecules, or otherwise the cyclopentadiene is destroyed by a further reaction.

Shida and coworkers[81] found that cyclooctatetraene is even more radiation-resistant than benzene.

VI. RADIATION-INDUCED OLIGOMERIZATION AND POLYMERIZATION OF DIENES

Brown and white[90] studied the polymerization of several olefins and dienes in thiourea canal complexes, as molecular templates, for carrying out radiation-induced selective and stereospecific polymerization. High melting, crystalline, *trans*-1,4-addition polymers were obtained from 2,3-dimethylbutadiene, 2,3-dichlorobutadiene, 1,3-cyclohexadiene and cyclohexadiene monoxide. The yield and quality of the poly-*trans*-1,4-dimethylbutadiene obtained from a given dose of irradiation was virtually independent of temperature in the range $-78\,^{\circ}\mathrm{C}$ to $+30\,^{\circ}\mathrm{C}$ and of dose rate in the range 2.9 to $2.3 \times 10^5\ \mathrm{r\,s^{-1}}$. This behaviour is indicative of the absence of bimolecular interactions between growing chains, as would be expected for the polymerization of physically isolated sequences of monomers in canals. The lengths of the polymer obtained from carefully prepared dimethylbutadiene complexes were found to be 100–200 monomer units. Impurities, such as alkanes or cresols, reduce the molecular weight of the polymer.

White[91] used a 1,3-butadiene–urea canal complex to produce all-*trans*-1,4-polybutadiene. The complex is formed only at temperatures in the range $-55\,^{\circ}\mathrm{C}$ to $25\,^{\circ}\mathrm{C}$ and needs a small amount of methanol to be formed.

Alcock and coworkers[92] studied the polymerization of butadiene (as well as of monoolefins, acetylene and aromatic olefins) trapped within the tunnel clathrate system of tris(*O*-phenylenedioxy)cyclotriphosphazene, induced by ^{60}Co-γ-radiation. The host was used in order to find if the concatenation and orientation of the monomer molecules under the steric forces generated within the host crystal lattice will lead to stereospecific polymerization. The clathrate was prepared by addition of liquid butadiene to the pure host at low temperature. The irradiation was conducted at low temperatures. Irradiation of pure butadiene (unclathrated bulk monomer) leads to formation of a mixture of three addition products: 1,2-adduct, *cis*- and *trans*-1,4-adducts. In contrast, the radiation-induced polymerization within the tunnel system of the host yielded almost pure *trans*-1,4-polybutadiene. A small percentage of 1,2-addition product was observed, but no evidence for the formation of *cis*-1,4-adduct was found, confirming the earlier observation by Finter and Wegner[93]. The average molecular weight was about 5000, corresponding to 100 monomer units. This work was extended[94] to several dienes: 2,3-dimethylbutadiene, isoprene, *trans*-piperylene, *trans*-2-methyl-1,3-pentadiene, 4-methyl-1,3-pentadiene, chloroprene and 1,2-cyclohexadiene. Some mixtures of two dienes were also studied. It was found that for all these monomers, radiation-induced polymerization of the clathrate leads to *trans*-1,4-addition polymers. Radiation-induced polymerization of the monomers alone (without the host material) lead also to other reactions. Bulk polymerization (not constrained in clathrate) of 2,3-dimethylbutadiene yields a polymer that contained a mixture of both 1,4-*cis* and 1,4-*trans* sequences, in equal proportion. The molecular weight is about 3700 (45 monomer units). Similar results were obtained for ^{60}Co-radiation-induced polymerization at $-78\,^{\circ}$C and $25\,^{\circ}$C. The molecular weight of the polymer formed in the clathrate was 1000 (12 monomer units), all-1,4-*trans* addition for both $-78\,^{\circ}$C and $25\,^{\circ}$C irradiation. γ-Ray-induced polymerization of isoprene monomer in the bulk state yielded a high polymer that contained both 1,4-*cis* and 1,4-*trans* addition sequences, with higher proportion of the *trans* addition product. The molecular weight was 140,000 (2000 monomer units). Similar results were obtained at $25\,^{\circ}$C and $-78\,^{\circ}$C. Radiation-induced polymerization of clathrated isoprene yielded only 1,4-*trans*-polyisoprene with molecular weight of 24,000 (350 monomer units), at both $-78\,^{\circ}$C and $25\,^{\circ}$C irradiation. No noticeable post-polymerization effects could be detected (also for 2,3-dimethylbutadiene). For *trans*-piperylene, similar results to those of isoprene were found, except for the molecular weight. Bulk monomer radiative polymerization lead to molecular weight of 5700 (85 monomer units), whereas the polymerization of the clathrate yielded polymer with molecular weight of 13,000 (190 monomer units). In this case the clathrate leads to higher molecular weight, whereas for the previous monomers the opposite trend was observed.

Bulk polymerization of *trans*-2-methyl-1,3-pentadiene lead only to 1,4-*trans* addition polymer, however it allows randomization of the *trans* structure, leading to an atactic polymer. The polymerization of the clathrate of *trans*-2-methyl-1,3-pentadiene yielded an isotactic 1,4-*trans* addition polymer. The polymer formed from the bulk had a molecular weight of 20,000 (240 monomer units), and that formed from the clathrate had a molecular weight of 1000 (12 monomer units). Similar results were obtained for other dienes, and the results are summarized in Table 4. It can be concluded that polymerization of dienes in the clathrate lead exclusively to a 1,4-*trans* addition polymer, except in the case of 1,3-cyclohexadiene. For this monomer, although the polymer is formed entirely by 1,4-addition, the polymer formed is essentially atactic. In bulk polymerization, the polymerization proceeds in most cases through 1,4-addition (both *trans* and *cis*), but in the case of butadiene and 1,3-cyclohexadiene 1,2-additions were also observed. Actually, in the case of the bulk γ-induced polymerization of 1,3-cyclohexadiene the 1,2-addition process was favoured over the 1,4-addition process by a ratio of 4:3.

Ichikawa and coworkers[95,96] studied the polymerization and oligomerization of 2,3-dimethylbutadiene together with 2,3-dimethylbutane in thiourea clathrates. They found that the addition of 2,3-dimethylbutane to 2,3-dimethylbutadiene clathrates markedly lower the radiolytic yield of disappearance of monomers, G(-monomers), together with reducing the length of the formed polymer, as can be observed by the decrease of the melting point of the polymer, similar to the results of Brown and White[90]. An ESR study[97] showed that both monomer and polymer radicals of 2,3-dimethylbutadiene (DBE) are trapped in irradiated clathrate containing a mixture of 30% DBE and 70% 2,3-dimethylbutane (DBA). The ESR result suggests the formation of oligomer radicals of DBE. Ichikawa and coworkers[96] studied the formation of dimers of DBE by irradiation of thiourea clathrates containing mixtures of DBE and DBA. Three different dimers were formed — the linear dimer 2,3,6,7-tetramethyl-2,6-octadiene (**7**) and the two cyclic dimers 1,2,4-trimethyl-4-isopropylcyclohexene (**8**) and 1,2,4-trimethyl-4-isopropenylcyclohexene (**9**). (Note however, that **9** is not a dimer, since it contains two fewer hydrogens).

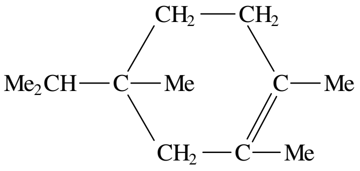
TABLE 4. Characteristics of the polymers obtained by ^{60}Co-radiation-induced polymerization of dienes

Monomer	Physical state	Stereochemistry	Molecular weight (kD)
Butadiene	bulk	1,4-*cis*, 1,4-*trans* and 1,2-	—
Butadiene	clathrated	1,4-*trans*	5.0
2,3-Dimethylbutadiene	bulk	1,4-*cis* and 1,4-*trans*	3.7
2,3-Dimethylbutadiene	clathrated	1,4-*trans*	1.0
Isoprene	bulk	1,4-*cis* and 1,4-*trans*	140
Isoprene	clathrated	1,4-*trans*	24
trans-Piperylene	bulk	1,4-*cis* and 1,4-*trans*	5.7
trans-Piperylene	clathrated	1,4-*trans*	83
trans-2-Methyl-1,3-pentadiene	bulk	atactic 1,4-*trans*	20
trans-2-Methyl-1,3-pentadiene	clathrated	isotactic 1,4-*trans*	1.0
4-Methyl-1,3-pentadiene	bulk	1,4-*trans*	38
4-Methyl-1,3-pentadiene	clathrated	1,4-*trans*	3.6
Chloroprene	bulk	1,4-*trans*	84
Chlotoprene	clathrated	1,4-*trans*	2.9
1,3-Cyclohexadiene	bulk	1,2- and 1,4-	4.5
1,3-Cyclohexadiene	clathrated	atactic 1,4-	6.7
Isoprene/2,3-dimethylbutadiene (1:1, V:V)	bulk	1,4-*cis* and 1,4-*trans*	50
Isoprene/2,3-dimethylbutadiene (1:1, V:V)	clathrated	1,4-*trans*	1.6
Isoprene/butadiene (1:1, M:M)[a]	bulk	1,2; 1,4-*cis* and 1,4-*trans*	3.0
Isoprene/butadiene (1:1, M:M)[a]	clathrated	1,4-*trans*	1.0
Isoprene/*trans*-piperylene (1:1, M:M)[a]	bulk	1,4-*cis* and 1,4-*trans*	3.9
Isoprene/*trans*-piperylene (1:1, M:M)[a]	clathrated	1,4-*trans*	4.0

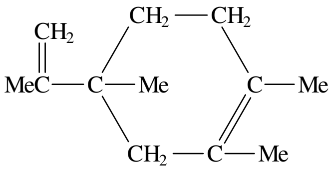
[a] M:M = monomer:monomer

$Me_2C{=}CMe-CH_2-CH_2-CMe{=}CMe_2$

(7)



(8)



(9)

The yields of each of the dimers reached maxima at about the same DBA content of 80% (DBA:DBE = 4:1). The total dimer yield reached 6% of the DBE at a dose of 3 MGy. At the same time the yield of the polymer is 11% and the unreacted DBE is 3%. Thus 80% of DBE is converted to trimers and higher oligomers.

Chapiro[98,99] irradiated liquid butadiene at 15 °C with γ-rays at a very low dose rate. The polymerization rate was very slow, 1×10^{-8} s^{-1}, at a dose rate of 0.023 rad s^{-1}. The product was a high-molecular-weight rubber. Anderson[100] used high-energy electrons to polymerize butadiene in the temperature range of $-195\,^{\circ}\mathrm{C}$ to $0\,^{\circ}\mathrm{C}$. Both the rates of the polymerization and the molecular weight of the polymer decreased with increasing temperature. The infrared spectrum of the polymer showed that the relative *cis*-1,4-, *trans*-1,4- and 1,2-double bonds were the same as with polybutadiene prepared with cationic initiators. The structure of the polymer did not change considerably with the polymerization temperature, indicating that the radiation-induced polymerization of butadiene occurs via a cationic mechanism, at least at the lower temperatures. However, in emulsion the cationic process was suppressed and the reaction proceeded mainly via a free radical mechanism.

Few experiments with poor reproducibility were done[101] on γ-ray-induced polymerization of butadiene adsorbed on carbon black.

Chapiro[102] polymerized liquid isoprene at 20 and $45\,^{\circ}\mathrm{C}$ by γ-ray irradiation. The rate was found to be temperature independent and to increase with the square root of the dose rate (in the range 0.5–9.7 $\mathrm{rad\,s^{-1}}$). Burlant and Green[103] polymerized isoprene at $-40\,^{\circ}\mathrm{C}$ with a higher dose rate (35 $\mathrm{rad\,s^{-1}}$) and obtained about 5.5 times higher rate of polymerization than Chapiro at 9.7 $\mathrm{rad\,s^{-1}}$, which suggests that the reaction has a negative activation energy, similar to butadiene. The negative activation energy together with the structure of the resulting polymer indicate that the polymerization, at least in part, is due to ionic processes.

VII. RADIATION CHEMISTRY OF POLYBUTADIENE AND POLYISOPRENE

Butadiene and isoprene have two double bonds, and they polymerize to polymers with one double bond per monomeric unit. Hence, these polymers have a high degree of unsaturation. Natural rubber is a linear *cis*-polyisoprene from 1,4-addition. The corresponding *trans* structure is that of gutta-percha. Synthetic polybutadienes and polyisoprenes and their copolymers usually contain numerous short-chain side branches, resulting from 1,2-additions during the polymerization. Polymers and copolymers of butadiene and isoprene as well as copolymers of butadiene with styrene (GR-S or Buna-S) and copolymers of butadiene with acrylonitrile (GR-N, Buna-N or Perbunan) have been found to cross-link under irradiation.

Golub[104] studied the radiolysis of high *cis*-polybutadiene. He found that the olefinic group concentration decreased with high yield [G(-double bond) $= 7.9$] together with a similar yield of conversion of the *cis* to the *trans* form ($G = 7.2$). Kuzminski and coworkers[105] reported earlier on a much higher radiolytic yield of double-bond disappearance [G(-double bond) *ca* 2000]. More extensive study was done by Parkinson and Sears[106]. They found that both *cis*-1,4-polybutadiene and *trans*-1,4-polybutadiene lose part of their olefinic groups after irradiation. In the *cis* specimens they found formation of olefinic groups in the *trans* form (the *cis* form absorbs at 740 and 3012 $\mathrm{cm^{-1}}$, whereas the *trans* olefinic form absorbs at 967 $\mathrm{cm^{-1}}$). In the high *trans*-1,4 polymer they found that an additional change is the destruction of the crystallinity. Since the degree of crystallinity influences the absorbance, it is difficult to measure accurately the radiation yields of loss of olefinic groups in *trans*-1,4 specimens. Using the absorptivities of crystalline and amorphous polymers they could set the upper and lower yields of double-bond destruction. At moderate doses the decrease of *cis*-vinylene groups follows a linear rather than a semilogarithmic plot, i.e. a zero-order rather than first-order decay as a function of dose. The formation of *trans*-vinylene groups in the radiolysis of *cis*-1,4-polybutadiene is a complex process, reaching a maximum when the concentration of the *cis*-vinylene groups has been reduced to less than one-third of its original value. They found G(-*cis*-vinylene groups) $= 15 \pm 1$ and G(-*trans*-vinylene groups) $= 16.5 \pm 5.5$. The activation energies for the yields are 3.7 ± 0.3 $\mathrm{kcal\,mol^{-1}}$. Although it seems that the loss of olefinic groups are the same for the *cis* and *trans* specimens, actually since for *cis*-poly-1,4-butadiene G is 6.8 for the formation of the *trans* vinylene groups, the total destruction of the olefinic groups is almost twice that in the case of *trans*-1,4-polybutadiene. Higher yields of destruction of olefinic groups were found for polymers with vinylic side chains (1,2-polybutadiene). In this case G(-vinylic groups) is 40 and the rate of disappearance decreased with increasing dose according to a first-order kinetics.

It is most reasonable that the loss of the olefinic groups leads to cross-linking. However, measurement of cross-linking[107,108] of polybutadienes shows yields of only $G = 3.6$. Golub[104] suggested that part of the destroyed olefins form cyclic structures as has been observed in irradiated polyethylenes[109,110].

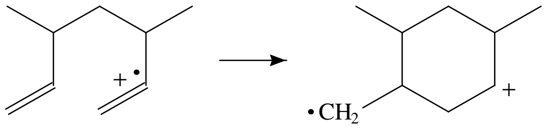
Other evidence for the wrong value of the very high yield of double-bond destruction can be found from the lower G(-double bond) found by Turner[111] and Turner and coworkers[112] in the case of irradiation of squalene and natural rubber.

Charlesby[113] studied the radiolysis of natural specimens (smoked sheets) under reactor irradiation. The swelling of the cross-linked gel was studied as a function of the radiation dose and the average molecular weight between cross-links M_c was determined from the Flory–Rehner equation[114]. The value of M_c was found to decrease linearly with radiation dose, indicating that the extent of cross-linking increased linearly with dose; G(cross-linking) was estimated to be approximately 2.0. Further studies by Charlesby and coworkers lead to G(cross-linking) of 1.5[115] for natural rubber and 1.05[116] for oriented rubber. The cross-linking yield of polybutadiene was found to be significantly higher than that of natural rubber; G(cross-linking) can be estimated to be approximately 3.5[115]. Much lower cross-linking yields were found for polybutadiene–styrene copolymer, where the cross-linking yields decrease with increasing styrene content in the polymer[117]. Kuzminski and coworkers[105] obtained approximately half of the cross-linking yield than the values reported by Charlesby's group. They found that the cross-linking yield increases monotonously with the temperature.

Turner and coworkers[111,118,119] used specially purified rubber samples and irradiated them in the absence of air. They found the yield of the physical cross-linking to decrease with the dose; the initial yield is $G = 3.5$. However, the yield of chemical cross-linking was found to be 1.3.

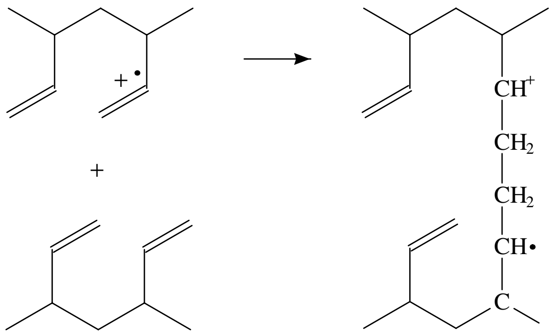
The effect of oxygen was studied extensively. An important post-irradiation oxidation of rubber was reported by Sears and Parkinson[120]. When oxygen is present, radiation-induced changes are often quite different (usually more severe) than under inert atmosphere (or in vaccum). The radiation-induced free radicals added to molecular oxygen dissolved within the material to produce peroxyl radicals[121]. A common phenomenon in radiation-induced oxidative degradation is the occurrence of heterogeneous oxidation[122,123]. This takes place when the rate at which oxygen is consumed within the polymer is higher than the rate at which it can be supplied from the surrounding atmosphere by diffusing into the material. Clough and Gillen[124] studied the γ-ray degradation of poly(butadiene-co-styrene) and poly(butadiene-co-acrylonitrile), SBR and Buna-n rubbers, respectively, in the presence of air. They found that the degradation of these materials is very heterogeneous through the sample thickness. There was a broad, paraboloid-shaped modulus profile through the sample interior, together with a dramatic change in modulus in the surface regions. They concluded by mechanistic studies that the radiation-induced degradation of these materials resulted from two different processes: (1) The standard free-radical-mediated radiation chemistry, which gave rise to oxidation involving O_2 dissolved in the polymer and which led to heterogeneous oxidation due to oxygen diffusion effects; and (2) ozone chemistry in the surface regions of the samples, which resulted from attack by O_3 generated by the action of ionizing radiation on the air atmosphere surrounding the samples.

Heusinger and coworkers[125–128] studied the radiation chemistry of 1,2-polybutadiene and 1,2- or 3,4-polyisoprene, in which there is a vinyl group in the side-chains rather than in the backbone of the polymer. Von Raven and Heusinger[125] studied the radiolytic changes in 1,2-polybutadiene. They found that the *G* value for double-bond conversion depends on the molecular weight, decreasing with decreasing molecular weight. The *G* values for cross-linking also decreased with decreasing molecular weight. The *G* value for double-bond conversion (20 to 200) is much higher than the *G* value for ion-pair formation (about 3), indicating that the disappearance of the double bonds is a chain reaction. The decrease of *G* with molecular weight is probably due to a larger effectivity of the chain-terminating step in viscous low molecular weight samples in comparison to the rubbery high molecular weight samples. *G* values for cross-linking is considerably smaller than *G* values for double-bond elimination, 7–12 vs 20–200, indicating that the double bonds disappear by other reactions than cross-linking, probably by cyclization. They proposed a mechanism for the double-bond conversion which involves intiation by a transformation of the primary radical ion in the vinyl group into a carbenium ion and a radical. Reaction of the carbenium ion with a vinyl group in the same chain leads to cyclization (equation 27) whereas reaction with a vinyl group in a neighbouring chain results in cross-linking (equation 28).



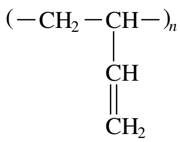
(27)

(10)



(28)

(11)

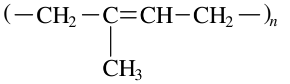


$$(-CH_2-\underset{\underset{\underset{CH_2}{\|}}{CH}}{\underset{|}{CH}}-)_n$$

1, 2-polybutadiene

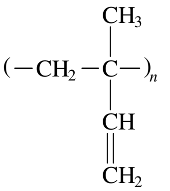
$(-CH_2-CH{=}CH-CH_2-)_n$

1, 4-polybutadiene



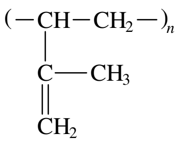
$$(-CH_2-\underset{\underset{CH_3}{|}}{C}{=}CH-CH_2-)_n$$

1, 4-polyisoprene



$$(-CH_2-\overset{\overset{CH_3}{|}}{\underset{\underset{\underset{\underset{CH_2}{\|}}{CH}}{|}}{C}}-)_n$$

1, 2-polyisoprene



$$(-\underset{\underset{\underset{\underset{CH_2}{\|}}{C-CH_3}}{|}}{CH}-CH_2-)_n$$

3, 4-polyisoprene

ESR studies at 77 K showed the presence of a five-line spectrum, corresponding to structure **11**. A spectrum corresponding to species **10** could not be found, probably due to its short life-time at 77 K. The carbenium ion and the radical in species **10** or **11** can start a chain reaction either via a cationic reaction or through a radical addition to a double bond. Von Raven and Heusinger suggested only cationic chain reaction. Comparison of the *G* values for elimination of the double bond with the *G* values for cross-linking shows that cyclization exceeds the formation of cross-links by a factor of about 10. It is interesting to note that these values of *G*(-double bond) and *G*(cross-linking) are much higher than those found for 1,4-polybutadiene, indicating that pendent vinyl groups in 1,2-polybutadiene are much more reactive than the vinylidene groups in the backbone of 1,4-polybutadiene. Von Raven and Heusinger studied the thermal degradation of irradiated and non-irradiated samples of 1,2-polybutadiene. In the non-irradiated samples, an important product is butadiene formed by depolymerization. However, for irradiated samples only very little butadiene was formed. Besides, the ratio of fragments with bicyclic rings (naphthalene, substituted naphthalene, dihydronaphthalene compounds) to fragments with monocyclic rings was found to be larger in irradiated than in non-irradiated samples. These results indicate that radiolysis of 1,2-polybutadiene leads to formation of condensed cyclohexane rings.

Katzer and Heusinger[127] studied the radiolysis of polyisoprenes with high content of 1,2- and 3,4-units. They found that *G*(-double bonds) is about 130 and *G*(cross-linking) is about 10. These values depend slightly on the molecular weight.

The *G* values are higher than the *G* values for initial species (*ca* 2.5), indicating a chain reaction. The much higher yield for the disappearance of a double bond indicates that cyclization occurs more frequently than cross-linking. Katzer and Heusinger concluded from the studies on the influence of dose rate, temperature and additives (air, anthracene and hydroquinone) that the chain proceeds via a cationic mechanism.

Kaufmann and Heusinger[128] studied the mechanism of radiolysis of 3,4-polyisoprene. They found $G(\text{cross-linking}) = 2$ and $G(\text{-double bonds}) = 120$. They found that *G*(-double bonds) depends on the dose rate exponentially with a coefficient of 0.9, and depends on the temperature with an activation energy of 11.7 kJ mol^{-1}. Addition of the radical scavenger, anthracene, markedly decreased the cross-linking while the conversion of double bonds did not change. Kaufmann and Heusinger suggested that the radiation-induced radical cation forms one cross-link by a radical reaction and, on the other hand, starts a cationic chain reaction leading to cyclization. Besides cross-linking, also chain scissions were found to occur to a small extent. The chain scissions are suggested to occur in the polymer containing a low content of the 1,4-units.

Zott and Heusinger[129] studied the radicals formed in γ-irradiation of 3,4-polyisoprene and 1,2-polybutadiene by ESR. In both polymers, alkyl and allyl radicals are formed. Alkyl radicals (shown as a septet spectra with 23 *G* hyperfine splitting for 3,4-polyisoprene and as a quintet of 27 *G* hyperfine splitting for 1,2-polybutadiene) are formed by a cross-linking reaction and are stable only at low temperatures. Allyl radicals (shown in the ESR spectra as a septet of 15–16 *G* hyperfine splitting) are formed by hydrogen abstraction from the main chain. They could be observed even at temperatures up to 0 °C. The irradiation of 1,2-polybutadiene or 3,4-polyisoprene adsorbed on silica gel leads to the same ESR spectra but with enhanced resolution. The enhanced resolution (lower line width) was explained as due to a reduction of the dipole–dipole interaction, which is achieved by the formation of a thin polymer layer. In the ESR spectrum of irradiated 3,4-polyisoprene they observed a singlet with a line width of 11*G*. The intensity of the singlet signal depends on the pre-treatment of the polymer and therefore on the physical structure of the polymer samples. The largest signal intensity was obtained for polymer samples prepared by dry-freezing and storing below the glass transition temperature (*ca* 0 °C). The singlet intensity for samples stored above the glass transition temperature before the γ-irradiation was either very low or not observable. The singlet is optically bleachable with near-infrared light ($\lambda > 800$ nm), but the ESR spectrum is not affected by illumination with visible light. The photobleaching with infrared light indicates that the ESR singlet is due to trapped electrons in the polymer. This conclusion is further supported by saturation of the ESR singlet amplitude with increasing microwave power at the power level of 0.06 mW. The saturation at relatively low power level indicates the presence of a weak interacting paramagnetic species such as trapped electrons. The addition of electron scavengers such as pyrene, anthracene and biphenyl had no influence on the singlet intensity, probably due to the trapping of the electrons in the crystalline parts of the polymer, since additives go only into amorphous regions.

Hesse and Heusinger[130] studied the ESR signal due to $\Delta m = 2$ transition of radical pairs in a number of γ-irradiated polymers including 1,2-polybutadiene (both atactic and isotactic) and 3,4-polyisoprene. It was found that the distance between the radicals in the pair is 0.53 ± 0.04 μm; $1.0 \pm 0.5\%$ of the radicals in 1,2-polybutadiene and 3,4-isoprene are arranged in pairs.

Sisman and Bopp[131], Charlesby[113], Turner[111] and Petrov and Karpov[132] studied the yield of total gas evolution from natural rubber, polybutadiene and various GR-S type copolymers subjected to ionizing radiation (reactor, ^{60}Co or electron accelerator). Most of the gas is $H_2 + CH_4$ (100% in the case of polybutadiene), however for some rubbers a small amount of $CO_2 + C_3H_6$ was found also. Turner[111] found that under bombardment with accelerated electrons, the evolution of hydrogen from purified natural rubber was linear with dose, up to 180 megarads, and corresponded to $G(H_2) = 0.64$. This radiolytic yield is noticeably smaller than those found in low-molecular-weight olefins.

Yamamoto and coworkers studied the effect of hydrogen atmosphere upon the radiation-induced gas evolution (light hydrocarbon molecules) from polyisoprene[133] and polybutadiene[134]. Samples were irradiated in hydrogen atmosphere from 0 to 1 MPa by ^{60}Co γ-rays up to 160 kGy at room temperature. The yield of the saturated hydrocarbons increased and the yield of the unsaturated hydrocarbons decreased with increasing hydrogen pressure. The following mechanism was suggested for radiolysis of polybutadiene in the presence of hydrogen. The main radical species formed on irradiation of 1,4-polybutadiene was found to be of an allylic type[135], either by C−H or C−C bond ruptures. The lighter hydrocarbons, methane and ethane, are supposed to be the product of chain end scission[136]. The reaction of the allylic radical formed by C−C scission with hydrogen atom (or with hydrogen molecule) increases the number of terminal CH_3 groups of the chain (equation 29).

$$-CH_2CH{=}CHCH_2^{\bullet} + H \longrightarrow -CH_2CH{=}CHCH_3 \qquad (29)$$

The reduction of evolution of ethylene in the presence of hydrogen was suggested to be due to the addition of the hydrogen to the ethylene formed by irradiation (equation 30).

$$CH_2{=}CH_2 + 2H \longrightarrow CH_3CH_3 \qquad (30)$$

This reaction decreases the ethylene yield while increasing the *G* of ethane.

The irradiated polybutadiene in atmosphere of hydrogen is hardly soluble in any solvent, indicating that the dominant reaction is cross-linking.

Smirnova and coworkers studied the influence of various types of ionizing radiations on the physiomechanical characteristics of a statistical polymer of butadiene and acrylonitrile[137]. Although the polymer is a statistical polymer, the nature of its thermomechanical curve indicates a block nature of the polymeric basis of the rubber; there is a statistically distributed admixture of polar (acrylonitrile) and non-polar (butadiene) blocks. In the case of irradiation (γ-rays of ^{60}Co, reactor neutrons or 100-MeV protons) in the presence of air, cross-linking was predominating in the polar blocks, whereas in the non-polar blocks, containing mainly chains with unsaturated bonds, destruction predominates. Whereas the results of irradiation in the presence of air are almost independent of the type of irradiation, the situation is substantially different for irradiation under vacuum. Under vacuum, the concentration of the internodal chains in the polar block is a maximum-type function of the dose for γ-radiation and protons, while it is a monotonous function for neutrons for the entire dose range (0.9 Mrad). In the non-polar block, γ-radiation and protons under vacuum do not change considerably the average concentration of internodal chains (ν), while neutrons at large doses increase sharply the intensity of cross-linking, just as in the polar blocks. Under air, protons, γ-rays and neutrons behave similarly, increasing ν slightly with the dose in the polar block, and decreasing it considerably in the non-polar blocks.

The total gas evolved from irradiation of the rubber is relatively small, due to the protective action of the π orbitals. The main gas liberated from the rubber is H_2. The amount of hydrogen evolved as a function of dose is a saturation-type curve. The amount is increasing in the order protons < gamma-rays < neutrons. The ratio hydrogen/hydrocarbon gases changes with the dose. The largest value of the ratio was found for reactor neutrons, probably due to a smaller number of double bonds formed in the polymer basis in the case of protons and γ-irradiation. In addition to hydrogen the following hydrocarbon gases were observed: C_2H_2, C_2H_4, C_3H_6 and C_4H_8. The authors suggested that the formation of unsaturated hydrocarbons is due to hydrogen transfer reactions in the main chain. The amount of hydrocarbons is largest for neutrons irradiation. The larger effect of the neutrons is suggested[138] to be due to neutron interaction creating defects in the polymer — cavities of molecular dimensions. Then, under a subsequent influence of radiation on the damaged structure, the chemical changes increased. In the irradiation of hydrogen-containing polymers by neutrons with an average energy of 2 MeV, the neutrons cause recoiling of protons, mainly of 1-MeV energy. Those protons mainly collide elastically with atoms of the chain backbone, leading through cascade processes with increased local density of energy liberation to the formation of structural defects. It was suggested that the displacement of atoms may occur by both scattering and track formation, which collectively displaces whole channels of atoms of the lattice. Bond ruptures promote the appearance of cross-links.

Basheer and Dole[139] studied the γ-irradiation of block and random copolymers of butadiene and styrene in comparison to the homopolymers polybutadiene and polystyrene. The following aspects were studied: formation of trapped electrons, contribution of ionic species to cross-linking and hydrogen gas evolution. They found that in block copolymers the yield of trapped electrons $G(e^-)$ increased linearly with increasing polystyrene content. In random copolymers they observed a deviation from linearity; $G(e^-)$ is smaller for random copolymers than for block copolymers (with the same styrene content). They found that 25–35% of the cross-linking is taking place by ionic reactions, whereas most of the cross-linking occurs by radical processes. The yield of hydrogen evolved on irradiation decreases with increasing styrene content. For block copolymers the decrease is linear, whereas for random copolymers a curved dependence was observed; $G(H_2)$ is higher for block copolymers than for random copolymers. The yields of cross-linking of the butadiene–styrene copolymer was studied for irradiation at 77 K and room temperature[140]. The measured yields were less than calculated from linear interpolation of the cross-linking yields of the homopolymers. This was attributed to energy transfer processes at the interface from polybutadiene segments to polystyrene, and to radiation resistance of polystyrene due to its aromatic nucleus.

VIII. RADIATION CHEMISTRY OF POLYALKYNES

Polyalkynes are polymers of conjugated double bonds. Yen and coworkers[141] studied the radiation stability of *trans*-polyacetylene. The radiation fields used were: (1) 1.6-MeV electrons with flux of 2×10^{11} electrons $\mathrm{cm}^{-2}\,\mathrm{s}^{-1}$ for 5000 s totalling 10^7 rad, (2) ^{60}Co-γ-ray totalling 10^5 rad. It was found that the radiation decreases only slightly the electrical resistance, from 3×10^4 ohm cm to 2.6×10^4 for 10^5 rad γ-rays and to 2×10^4 for 10^7 rad electrons. The solar absorbance and the thermal emissivity was not changed at all by the radiation. *cis*-Polyacetylene is a highly conductive (after doping) organic polymer which can be used as an electrode-active material in chemical batteries. A serious hindrance for the practical use of polyacetylene is the rapid degradation of the polymer during storage, due to conversion of the *cis*-polyacetylene to the *trans* form. As isomerization occurs, the elastic polymer film becomes brittle and loses partially its electromechanical activity. Tkachenko and coworkers[142] suggested using ^{60}Co γ-irradiation or an electron beam in order to form a number of cross-links in order to stabilize the polymer film, due to the limited mobility of the polymer chains. They found that irradiation under argon at a dose of 75–100 Mrad, regardless of the form of radiation (γ-rays, accelerated electrons), has little effect on the cyclic voltammetry curve, indicating that the film does not lose its electrochemical activity by the irradiation. However, the non-irradiated film suffers in a 3-month storage a 2–3-fold decrease in the conductivity (as evidenced by the decrease of the area under the anode and cathode curve in cyclic voltammetry), whereas the cyclic voltammetry curves of the irradiated films changes negligibly in 3–6 months storage. They found that 75 Mrad was optimal for the stabilization of thin films (*ca* 100 μm), whereas for thicker films (*ca* 350 μm) the optimum is 100 Mrad. They found that while in non-irradiated film, storage at 0 °C for 170 days leads to change in the content of the *cis* isomer from 97% to 66%, the same storage of the irradiated film changes the concentration of the *cis* isomer from 90.5% to 88%.

Nagels and Krikor[143] studied the effect of γ-irradiation on the electrical properties of *trans*-polyacetylene. They reported a marked decrease of the conductivity and a slight increase of the thermopower after γ-irradiation of 10 kGy (1 Mrad). Their study showed that no essential structural changes occur during irradiation.

Hola and coworkers[144–147] studied the ESR spectrum of non-irradiated and irradiated *trans*-polyacetylene. The spectrum displayed as a simple symmetrical line, as a result of reorientation of an isolated spin. They found[144] that irradiation leads first to a decrease in the relative spin concentration up to 0.33 kGy. Further irradiation increases the relative spin concentration up to 0.55 kGy. Above this dose the relative spin concentration decreases slightly again but the observed value is close to the initial one. They found that the line width of the ESR spectra was not changed with irradiation, indicating that the spin mobility remains unchanged. The observed minimum of spin concentration after 0.33 kGy could be due to a combination of the initial spins with the irradiation-initiated spins. The further increase of spin concentration is probably the result of those spins formed by the irradiation, but can be due also to oxidation and to the effect of impurities. This was studied[145] by high dose irradiation, up to doses of 3 MGy (300 Mrad), where they found that the relative spin concentration is approximately constant, independent of dose, up to 3000 kGy. The constant spin concentration indicates a high stability of the primary paramagnetic centres, in spite of the very high γ-doses. The previous results of initial decrease of the spin concentration were not found in this study. The authors suggest that the different results are due to the different methods used in the two studies. In the first study, the material was irradiated in one tube and then transferred to the ESR tube. In the second experiment the polyacetylene was sealed under inert atmosphere in the ESR tube and irradiated in this tube. Thus, the initial decrease of spin concentration in the first paper was suggested to be due to the presence of oxygen and other impurities. It was found[147] that the irradiation did not cause any changes, not only after the end of the irradiation but also after 17 months.

Masuda and coworkers[148–151] studied the radiation effects on high molecular weight polyacetylene with various substituents and hetero atoms. The molecular weights of polymers from disubstituted aliphatic acetylenes (2-octyne and 2-decyne) were remarkably reduced with irradiation in air, whereas no degradation occurred in radiolysis in vacuum[148]. The G values for chain scission in air were found to increase with dose and were 3.3–12.2 (for poly-2-octyne) in the dose range of 1–73 Mrad. The degraded polymers contain carbonyl and hydroxyl groups and are soluble in polar solvents such as methyl ethyl ketone and acetone. In contrast to the substituted aliphatic polyacetylene, polymers of 2-substituted phenyl acetylenes (1-phenyl-1-propyne and 1-chloro-2-phenylacetylene) degraded in air only slightly, even with radiation up to 40 Mrad. Whereas 40 Mrad changes M_n of poly-2-octyne from 8.4×10^4 to 2.5×10^3 and that of poly-2-decyne from 6.1×10^4 to 2.1×10^3, the change for poly(1-phenyl-1-propyne) was from 2.4×10^5 to 1.6×10^5 and for poly(1-butylacetylene) it is intermediate between the aliphatic and the aromatic substituted compounds as M_n is changed from 2.2×10^5 to 4.1×10^4. The degradation mechanism was suggested to involve H-atom addition to the triple bond, and reaction of the radical formed with oxygen to form peroxyl radical, followed by decomposition of the hydroperoxide to give a carbonyl compound and an alcohol, together with rupture of the backbone of the polymer. They suggested that the aromatic substituted polymers are stable since the resulting peroxyl radicals do not possess the ability of abstracting a hydrogen from the phenyl groups, due to higher bonding energy of aromatic hydrogens. However, while this explanation[148] may be plausible for poly(1-chloro-2-phenylacetylene), it is not possible for poly(1-phenyl-1-propyne), where the peroxyl radical can abstract the hydrogen of the methyl group as is done in poly(t-butylacetylene). The reason for the radiation stability of the aromatic substituted polymer is probably the reaction of H atoms with the aromatic ring rather than with the alkenic bond. Although the reaction of hydrogen atoms with olefinic double bonds ($k = 4 \times 10^9$ $M^{-1}\,s^{-1}$ for cyclohexene and 3×10^9 $M^{-1}\,s^{-1}$ for ethylene) is slightly faster than their reaction with benzene ($k = 9 \times 10^8$ $M^{-1}\,s^{-1}$)[152], geometric factors will enhance the reaction with the aromatic ring in the side chain rather than with the olefinic double bond in the backbone of the polymer. The higher C−H bond strength in the CH_3 groups of *t*-butyl than that of allylic CH_2 groups in the 2-octyne and 2-decyne might be the reason for the moderate degradation of poly(*t*-butylacetylene). The γ-radiolysis of poly(1-chloro-1-alkynes) $(-CCl{=}CR-)_n$ was studied for various alkyl groups (R) in the presence or absence of oxygen[149]. Irradiation of membranes of poly(1-chloro-1-hexyne) with 40 Mrad (2.2 Mrad h^{-1}, 40 °C) in air makes them brittle. Extraction of the irradiated polymer with chloroform in a Soxhlet extractor left no gel, indicating very little cross-linking. The irradiated polymer has molecular weight of no more than a few thousands. In contrast, about 14 wt% of the product from irradiation in vacuum was a blackish gel. For larger alkyl groups the percentage of the gel fraction increases. The gel fraction was always larger in vacuum than in air. Thus for poly(1-chloro-1-octyne) the gel fraction is 20% in air and above 50% in vacuum. For poly(1-chloro-1-decyne) the gel fraction is 45% in air and 97% in vaccum. The results suggest that oxygen induces degradation of the radiation-initiated radical. For poly(1-chloro-1-hexyne) in air it was found that G(scission) is 5.4, whereas G(cross-linking) is only 0.1; G(scission) was found to be independent of the molecular weight of the original polymer ($M_n = 10^5$ to 10^6). Besides reduction of the molecular weight, the irradiation increases the ratio M_ω/M_n, indicating a random degradation process. For copolymers of 1-chloro-1-hexyne/1-chloro-2-phenylacetylene it was found that G(scission) is a linear increasing function of the mol% of 1-chloro-1-hexyne. The radiation-induced cross-linking was studied for poly(1-chloro-1-decyne) in vacuum.

At 5 Mrad, 75% of the polymer gelled. The gel fraction increases with increasing dose; a black, strong, completely cross-linked membrane was formed at 40 Mrad; *G*(cross-linking) was found to be 1.1 and *G*(scission) was 0.18. The cross-linking leads to increase of the Young modulus and to a decrease of the elongation at break. Both properties changes monotonically with dose, due to decrease in the chain length between two cross-links. The chlorine content of all polymers was found to decrease on irradiation both in the presence of air and in vacuum, suggesting that the γ-irradiation ruptures the C−Cl bonds to form allylic radicals. The irradiation in air leads to formation of OH and C=O groups (as evidenced by the IR spectra), indicating a disproportionation of hydroperoxides.

Silicon-containing mono- and di-substituted polyacetylenes (e.g. $[-\text{CMe}{=}\text{C}(\text{SiMe}_3)]-_n$) undergo radiation-induced degradation in air with high yields of main-chain scission ($G > 1$). The yield of main-chain scission is usually larger for polymers having long alkyl groups — e.g. for $[\text{CH}{=}\text{C}{-}\text{CH}(n\text{-C}_3\text{H}_7)\text{SiMe}_2\text{C}_6\text{H}_{13} - n]_n$ $G = 2.3$ and for $(-\text{CMe}{=}\text{CSiEt}_3-)_n G$ is 1.9 compared with 1.2 for $(-\text{CMe}{=}\text{CSiMe}_3-)_n$. No polymer degradation was found for irradiation in vacuum. The polymers irradiated in air contained C=O and Si−O groups and were soluble in polar solvents, which do not dissolve the starting polymers.

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CHAPTER 9

Synthesis of conjugated dienes and polyenes

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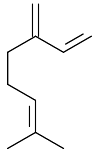
I. INTRODUCTION

Conjugated dienes and polyenes constitute an important functionality among organic compounds[1−10], discussed generally under the chemistry of alkenes. However, in recent years, they have emerged as a distinct class by themselves due to their increasing utility in organic synthesis and also due to their interesting physical properties. Dienes and polyene moieties are widely distributed among natural products[11]. Representative examples from natural products having diene and polyene moieties are gathered in Figure 1. Monoterpene, myrcene **(1)** and sesquiterpene β-farnesene **(2)** are among the simple examples of a 1,3-diene system present in nature. Retinal **(3)**, β-carotene **(4)** and lycopene **(5)** are representative conjugated polyenes from the carotenoid family, structures of which have been known for a long time[12]. Eicosinoids such as lipoxin A **(6)** are important intermediates in the biosynthetic chain between arachidonic acid and prostaglandins. Several insect pheromones, for example the alcohol dodeca-8,10-dienol **(7)**, have a diene or a polyene unit. However, isolation of several polyene macrolide antibiotics in recent years has added a new dimension to polyene chemistry. Amphoterecin B **(8)**, a 38-membered macrolide polyene, isolated from *Streptomycetes nodosus*, is a representative example from a growing number of similar antibiotics[13]. Linearmycin A 1 **(9)**, isolated recently from mycelial extract of streptomyces, sp.No. 30, is an antifungal C_{60} polyene antibiotic[14]. A C_2-symmetric anti-fungal marine natural product papuamine **(10)** is a representative example of nitrogen containing conjugated diene[15]. Dienes and polyenes have attracted a great deal of attention as they exhibit exceptional reactivity in cycloadditions and electrocyclic reactions. The most common use of dienes and polyenes is in Diels-Alder reactions (both inter- and intramolecular) and in thermal and photochemical reorganizations to furnish diverse carbo- and heterocyclic frameworks, which find application in synthesis of natural products and non-natural products[16]. Polyenes, due to their well defined architecture and delocalized π-system, are excellent substrates for energy and electron transfer. They are being explored (for example, the push-pull polyene **11**) as materials for non-linear optical applications, molecular electronics as well as photosynthesis mimics[17]. In view of such diverse applications and future potential, newer synthetic methods for assembling dienes and polyenes, under mild and efficient reaction conditions with regio- and stereocontrol, are being continually explored. Indeed, in the last few years, synthetic activity directed towards these substrates has witnessed explosive growth.

In this account, an overview of the methods employed for the synthesis of conjugated dienes and polyenes is presented. Dienes and polyenes with isolated double bonds are excluded, as they are accessed through methods usually employed for alkene synthesis[18]. Oligomerizations and polymerization reactions leading to polyenes are also not covered. Synthesis of 1,2-dienes, i.e. allenes, is excluded from the purview as there is a volume in the present series devoted to this functional group[19]. Synthesis of heterodienes, conjugated enol ethers, [n]-annulenes and related compounds are also not covered here. However, enynes, dienynes and enediynes syntheses have been included in a few cases in view of their emerging importance.



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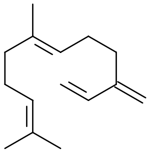

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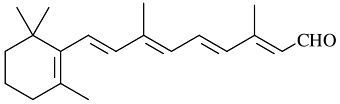

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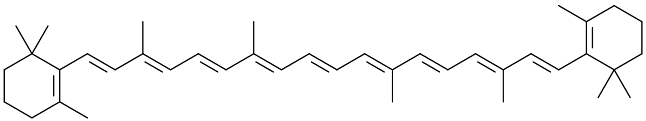

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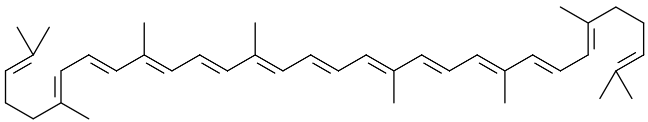

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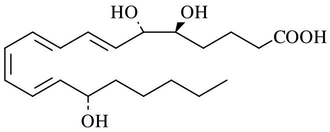

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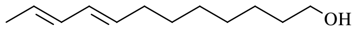
FIGURE 1



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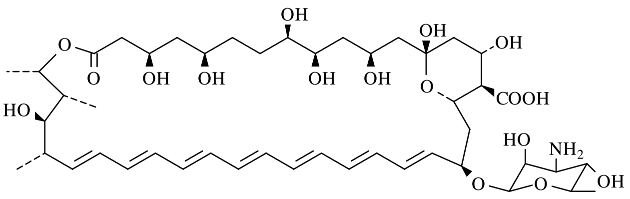

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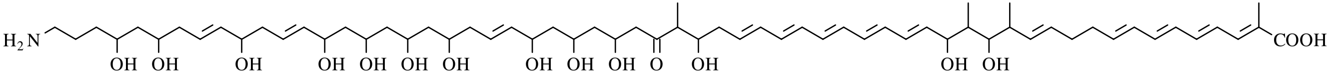

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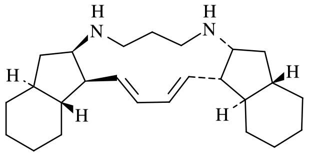

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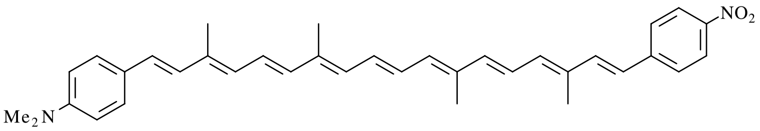


(11)

FIGURE 1. (*continued*)

The historical background to diene and polyene synthesis and literature up to 1964 has been reviewed in the earlier volume on alkenes of this series[1]. Literature up to the 70s has been reviewed exhaustively elsewhere[3] and some recent developments have been covered in *Comprehensive Organic Chemistry*[6], *Comprehensive Organic Synthesis*[8] and other monographs[4,5]. The present chapter provides a comprehensive overview with literature coverage up to mid-1995 and with emphasis on synthetic methods of preparative utility and general applicability. For the sake of convenience, various reactions leading to dienes and polyenes have been pooled together and presented under well known reaction types. Selected examples of commonly used methods, particularly of recent vintage, are gathered in the form of tables to illustrate the utility of the procedure involved. For the sake of convenience, the protecting groups have been abbreviated as 'P'.

II. ELIMINATION REACTIONS

A. General Aspects

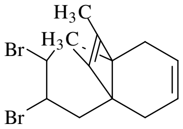
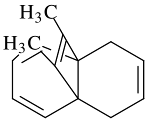
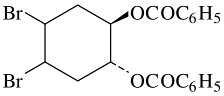
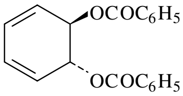
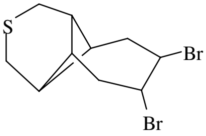
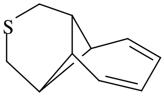
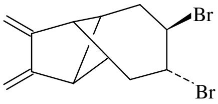
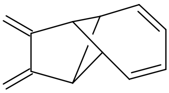
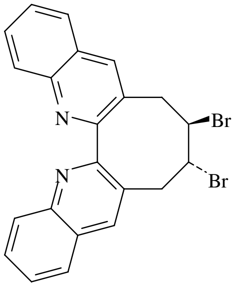
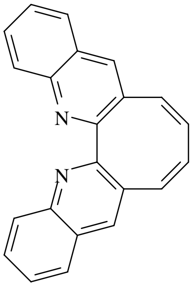
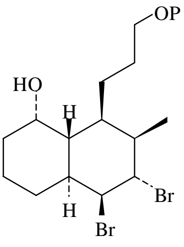
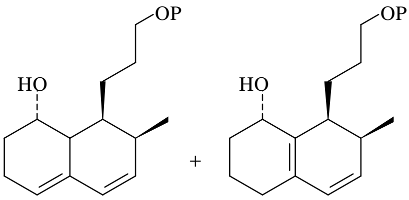
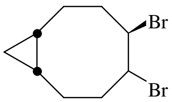
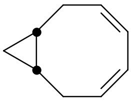
One of the simplest and classical methods for the generation of a diene moiety is through single or double elimination of appropriately functionalized alkane, alkene, allene or alkyne substrate[20]. The elimination reactions have been employed for the generation of both cyclic and acyclic dienes and polyenes. The eliminations could be either 1,2- or 1,4-. In some cases the elimination may involve rearrangements. A large number of leaving groups and reagents to facilitate the elimination process have been developed. In many of the classical elimination reactions, particularly those leading to the formation of acyclic dienes and polyenes, the reaction conditions employed are usually harsh, leading to low yields. However, more recent methods, such as palladium mediated allylic deacetylation reactions, work under milder conditions to result in products of high stereochemical purity[21]. In the following, different elimination reactions leading to the formation of dienes and polyenes with an emphasis on more recent developments is presented.

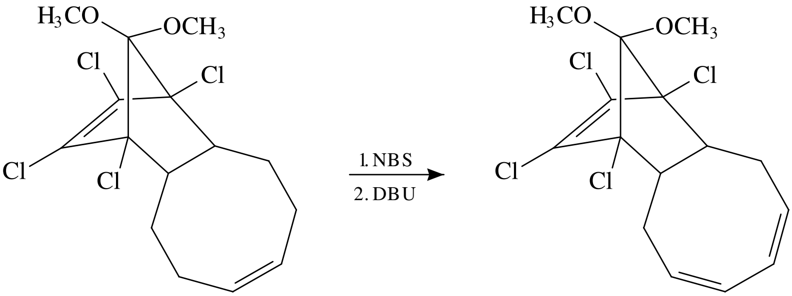
B. Dehydrohalogenations

Bromination of an olefin and double dehydrobromination of the resulting 1,2-dibromide is a classical method for the generation of 1,3-dienes (Table 1). Bromination of a double bond can be done with molecular bromine[22] or, more conveniently, with pyridinium bromide perbromide[23a]. A variety of bases has been employed for dehydrobromination. While potassium hydroxide and sodium methoxide have been used for a long time, lithium carbonate–lithium chloride in DMF or hexamethylphosphoric triamide (HMPA) works well in many cases[23a]. Double dehydrobromination with hindered bases such as potassium *t*-butoxide or diazabicyclononene (DBN) and diazabicycloundecene (DBU)[23e] give good results.

Monodehydrohalogenation of allylic halides is another classical method for diene synthesis[24]. This method is complementary to double dehydrohalogenation as both the 1,2-dihalides and allylic halides are readily accessed from alkenes. The commonly employed protocol for diene synthesis, particularly for cyclic 1,3-dienes, is through the allylic monobromination of the alkene with *N*-bromosuccinimide or related reagents followed by dehydrobromination with hindered bases such as DBN or DBU (equation 1)[25].

TABLE 1. Dienes through double dehydrobromination

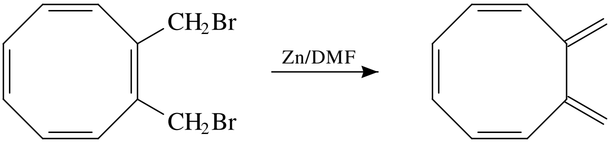
Substrate	Product	Reference
		23a
		23b
		23c
		23d
		23e
 P = t-BuMe$_2$Si		23f
		23g



(1)

C. Dehalogenations

Dehalogenation of 1,2- and 1,4-allylic dihalides offers another simple entry into dienes and polyenes[26] (Table 2). Dehalogenations, particularly debrominations, can be achieved by Zn/DMF (equation 2)[27], zinc amalgam[28a] or a combination of activated zinc/potassium iodide and iodine[28c]. The 1,4-dehalogenation method is particularly useful for the generation of orthoquinodimethanes from the corresponding 1,2-bisbromomethylbenzene derivatives[28c]. A high-yielding method for 1,4-elimination of 1,4-dibromo-2-enes to generate 1,3-dienes using a catalytic amount of sodium 2-thienyltellurolate has been reported[28d]. This method can also be used for 1,2-debromination to alkenes. Thus, a 1,2,3,4-tetrabromo compound has been converted to a diene in excellent yields under mild conditions (Table 2)[28d]. The *cis*- and *trans*-perfluoro-1,3,5-hexatrienes which show contrasting properties from those of the parent *cis*- and *trans*-1,3,5-hexatrienes have been synthesized by dehalogenation (Cl, Br) using zinc dust[28e].

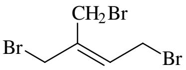
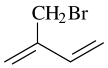
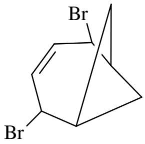
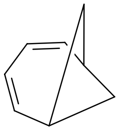
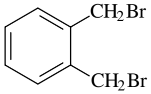
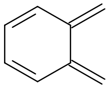
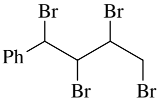
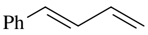
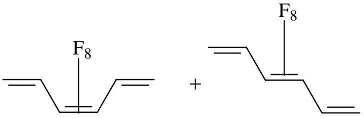


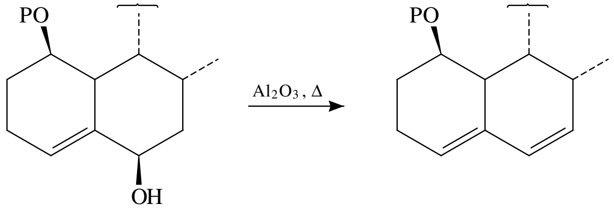
(2)

D. Dehydration and Related Reactions

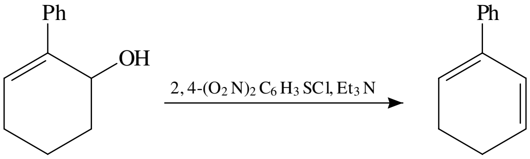
Dehydration of allylic alcohols, which are generated either by 1,2-reduction of α,β-unsaturated cabonyl compounds or by the nucleophilic addition of a vinyl group to a carbonyl compound, is a routinely employed method for the generation of 1,3-dienes and polyenes. Addition of vinyl- and polyenyl anions to a carbonyl group and subsequent dehydration will be discussed under a separate section. Allylic dehydrations can be performed by a variety of acidic reagents such as sulphuric acid, phosphoric acid, *p*-toluenesulphonic acid or Lewis acids such as $BF_3 \cdot Et_2O$, $SnCl_4$, metal oxides, metal salts as well as solid supports. Examples of diene synthesis through dehydration of allylic alcohols are well documented in the literature. However, three illustrative examples from recent literature employing alumina (equation 3)[29a,b], 2,4-dinitrobenzene sulphenyl chloride (equation 4)[29c] and methyltriphenoxyphosphonium iodide in HMPT (equation 5)[29d] as dehydrating agents are given here.

TABLE 2. Dienes through debromination

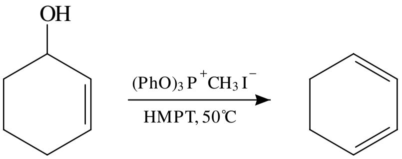
Substrate	Product	Reference
		28a
		28b
		28c
		28d
$BrCF_2CFClCF_2CFClCF_2Br$		28e



P = *t*-BuMe$_2$Si (3)

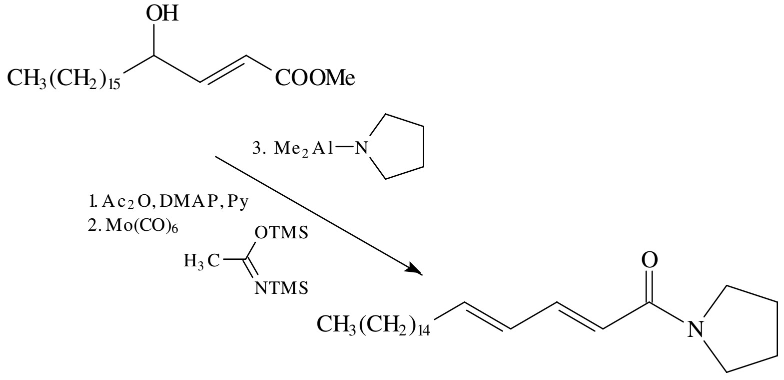


(4)



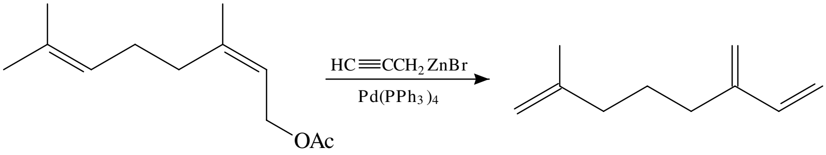
(5)

Allylic alcohols can be converted to dienes by a two-step method involving activation of the hydroxy group to a better leaving group and elimination[30]. These eliminations are commonly conducted in the presence of non-nucleophilic bases employing mesylate (OMs) or tosylate (OTs) derivatives (Table 3)[31]. Cyclic ene-1,4-diol mesylates can also be converted to dienes on treatment with sodium iodide in acetone[32]. Allylic acetates can also serve as precursors of dienes through elimination of acetic acid[33] as applied in the synthesis of the natural product trichonine (equation 6)[33a]. An interesting application is the transformation of neryl acetate to myrcene in quantitative yield in the presence of propargylzinc bromide and $Pd(PPh_3)_4$ catalyst (equation 7)[34]. Palladium catalysed 1,4-elimination in allylic carbonates also leads to dienes (equation 8)[35].

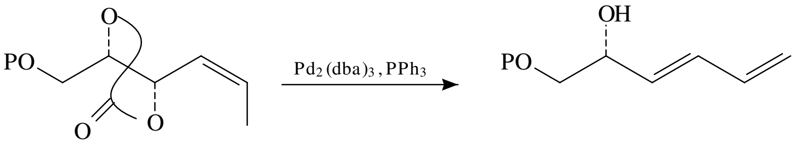


Trichonine

(6)



(7)



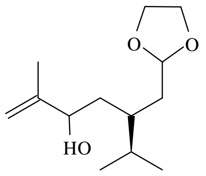
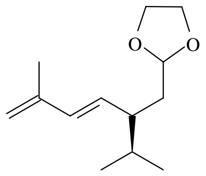
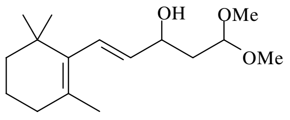
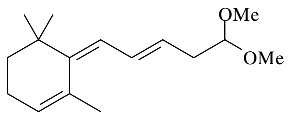
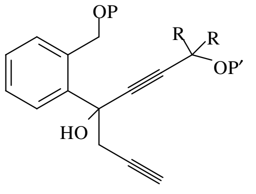
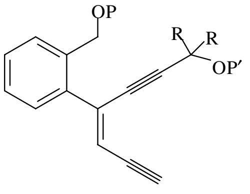
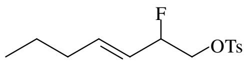
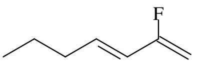
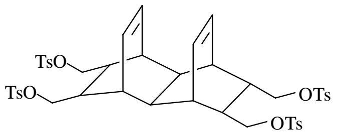
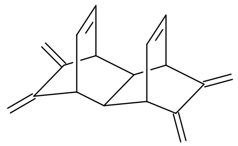
$P = p\text{-}MeOC_6H_4CH_2$

(8)

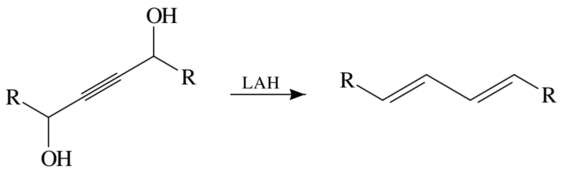
E. Reductive Deoxygenations

Reductive deoxygenation-rearrangement of 2-yne-1,4-diols to 1,3-dienes is a useful synthetic procedure since a large variety of ynediols are available in a few steps by sequential reaction at both ends of acetylene with aldehydes. Acetylenic 1,4-diols can be deoxygenated reductively by lithium aluminium hydride to form conjugated dienes of high stereoisomeric purity (equation 9)[36]. A modification to this procedure is the use of acetylenic 1,4-diol mono-THP derivative[37]. Allenic *tertiary* alcohols which are intermediates in the reaction can be separated and subjected to reductive elimination rearrangement

TABLE 3. Dienes via elimination of sulfonic acids

Substrate	Product	Reference
		31a
		31b
		31c
P = $Me_2CHMe_2CMe_2Si$;	P′ = P-$MeOC_6H_4CH_2$	
		31d
		31e

with LAH (equation 10)[38]. Some of the dienes and polyenes which have been synthesized following this procedure are given in Table 4[36,39].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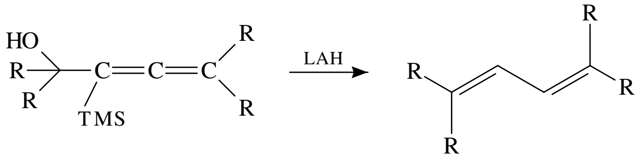
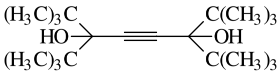
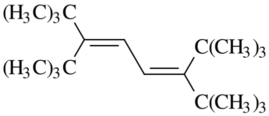
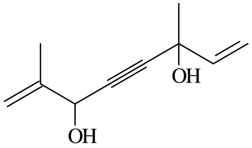
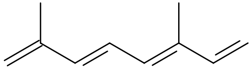
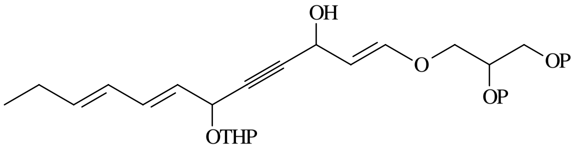
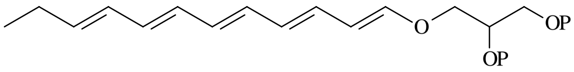
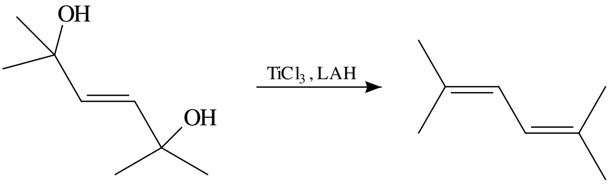

(10)

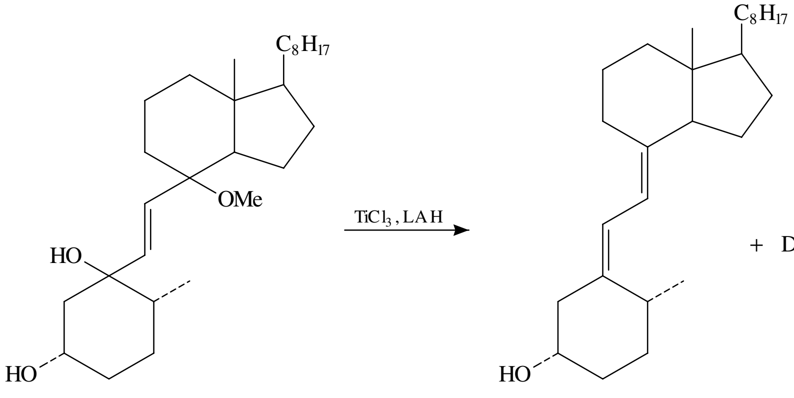
TABLE 4. Dienes and polyenes through reductive deoxygenations

Substrate	Product	Reference
		39a
	 Cosmene	36
 P = t-BuMe$_2$Si	 Fecapentaene derivative	39b

Walborsky and Wust found that allylic 1,4-diols or their dialkyl ethers can be reductively deoxygenated using low-valent titanium species generated *in situ* from titanium trichloride and LAH (equation 11)[40]. Reaction of both *E*- and *Z*-allylic 1,4-diols result in the formation of 1,3-dienes. It has been proposed that this reaction takes place on the titanium metal surface involving radical interemediates, like McMurry coupling reaction. Utilizing this procedure, a total synthesis of dihydrovitamin D3 (DHV3) and dihydrotachysterol (DHT3) has been devised (equation 12)[41]. A related reaction for the synthesis of conjugated all *trans*-trienes by reductive elimination of 1,6-dibenzoate-2,4-dienes (equation 13) using low-valent titanium species has been reported[42]. Under these conditions trienes are formed stereoselectively and in quantitative yield. This method was utilized for the synthesis of all *trans*-triene component of leukotriene B_4 (equation 14)[43]. As an alternative to low-valent titanium compounds, sodium amalgam has also been used as an electron transfer agent for stereospecific diene and triene synthesis[44]. Utilizing this procedure, stereospecific syntheses of *cis*- and *trans*-galbolenes have been reported (equation 15)[45].



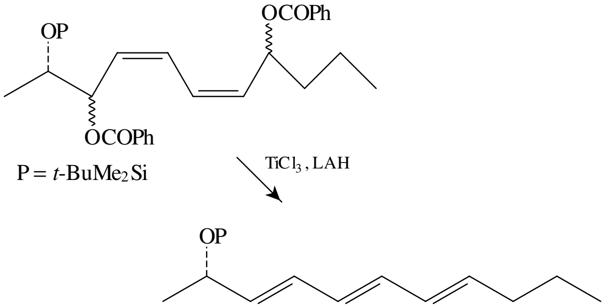
(11)



(12)

+ DHT 3

DHV 3



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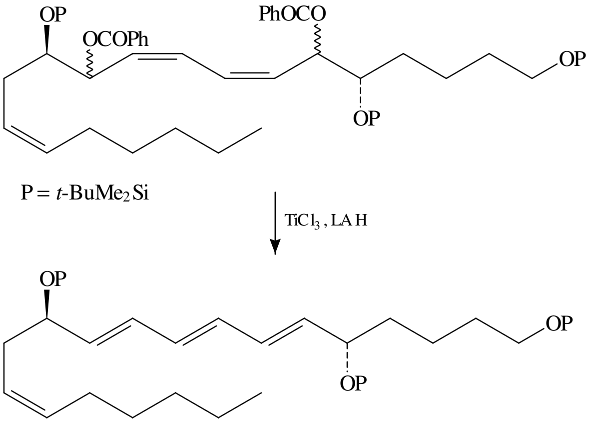

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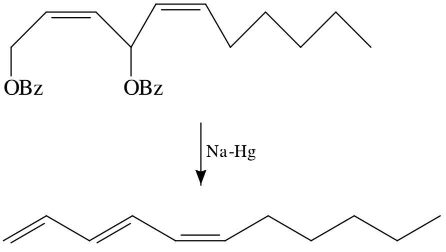
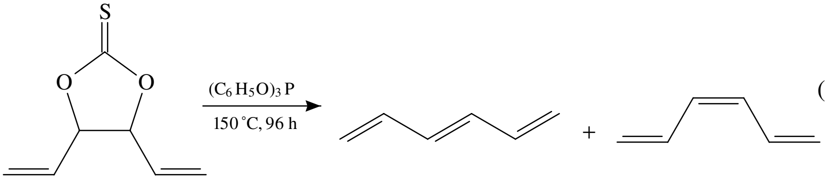


cis-Galbolene

(15)

Iodotrimethylsilane formed *in situ* from the reaction of chlorotrimethylsilane and sodium iodide, also effects the conversion of 2-ene-1,4-diols to 1,3-dienes (equation 16)[46]. Allylic thionocarbonates on heating with triphenylphosphite undergo deoxygenation (Corey–Winter reaction) to generate olefins[47]. This procedure has been used for making hexatrienes (equation 17)[47b].

(16)

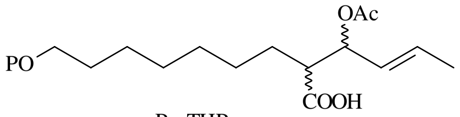
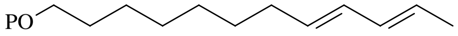
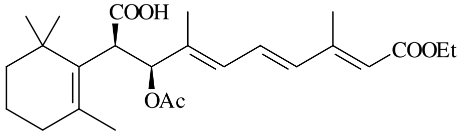
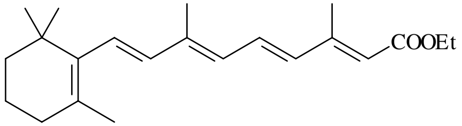


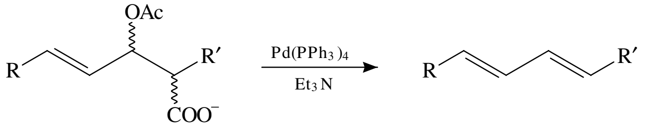
(17)

F. Decarboxylative Eliminations

Trost and coworkers have devised a stereocontrolled 1,3-diene synthesis employing a palladium-catalysed decarboxylative elimination procedure from allylic acetates carrying carboxylic acid functionality β- to the acetate group (equation 18)[48]. This decarboxylative elimination strategy has been applied to the synthesis of an insect pheromone, codlemone[48a] and the ethyl ester of vitamin A carboxylic acid (Table 5)[48b].

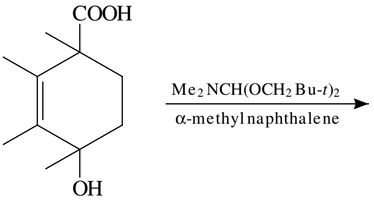
TABLE 5. Dienes and polyenes through decarboxylative elimination

Substrate	Product	Reference
 P = THP		48a
		48b



(18)

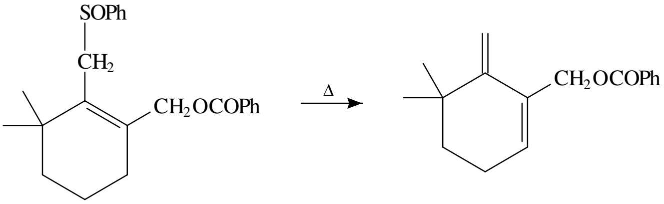
1,4-Decarboxylative elimination in 4-hydroxycyclohex-2-enecarboxylic acids with dimethylformamidedineopentylacetal has been shown to result in the formation of dienes in a regioselective manner under neutral conditions (equation 19)[49].



(19)

G. Elimination of Sulphoxides and Selenoxides

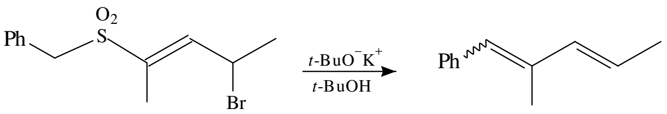
Sulphoxides and selenoxides undergo *syn* elimination under thermal conditions. A 1,4-elimination of sulphenic acid from an allyl sulphoxide leads to dienes (equation 20)[50]. Precursor sulphoxides are generated by oxidation of corresponding sulphides. This reaction, however, did not give good results when applied to more complicated systems[51].



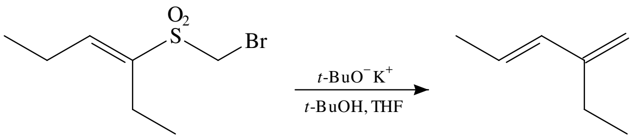
(20)

H. Ramberg–Backlund Reaction

The reaction of α-halosulphone with a base to give an olefin is known as Ramberg–Backlund reaction[52]. A vinylogous version of this rearrangement results in the formation of 1,3-dienes (equation 21)[53]. Another variation of this reaction is shown in equation 22[54]. These rearrangements proceed with moderate stereoselectivity.

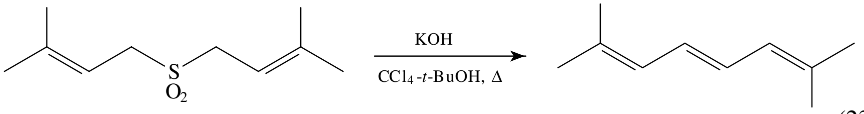


(21)

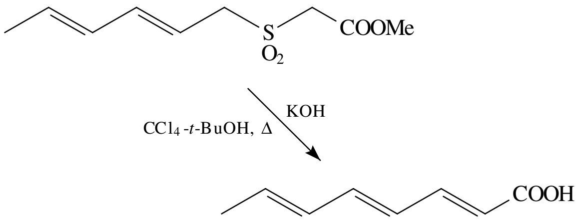


(22)

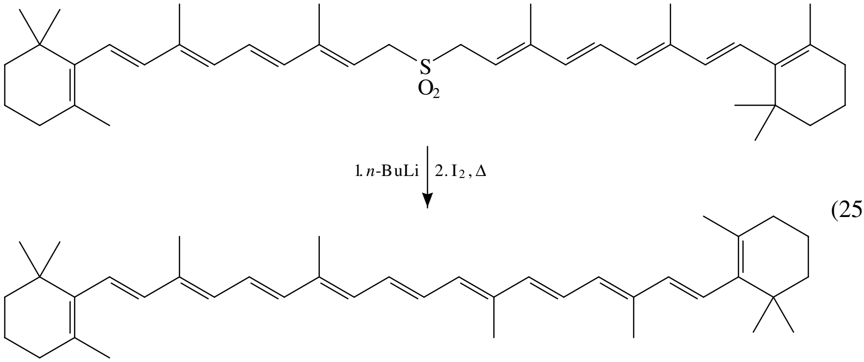
Bisallylic sulphones can be converted to trienes stereospecifically by treatment with potassium hydroxide in CCl_4–*t*-BuOH (equation 23)[55,56]. This method has been extended for the synthesis of trienoic acids by starting with dienyl β-sulphonyl esters (equation 24)[57]. β-Carotene has been prepared by treating the α,α'-dianion generated from starting sulphone with bromine or iodine followed by rearrangement (equation 25)[55]. Utilizing the Ramberg–Backlund reaction, an interesting cyclic enediyne has been made (equation 26)[58].



(23)

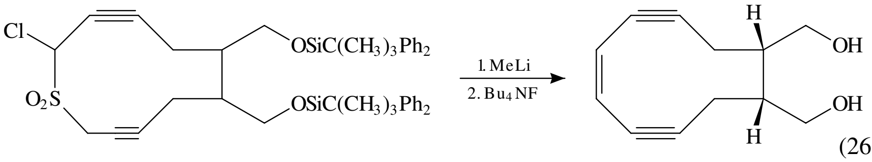


(24)



β-Carotene

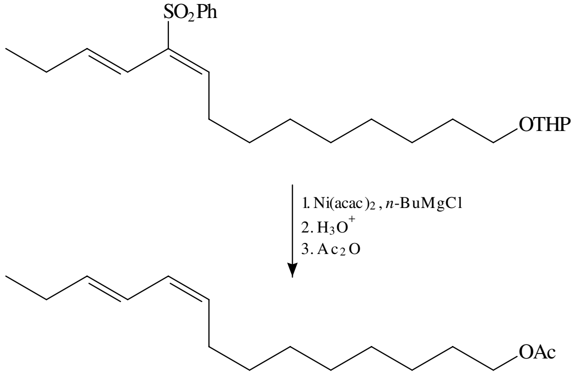
(25)



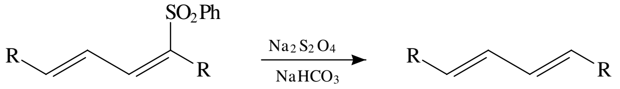
(26)

I. Reductive Desulphonylations

In general, reductive removal of a sulphonyl group from vinyl sulphones is not a stereospecific reaction. However, two methods, both developed by Julia, result in stereospecific products. The first one involves reaction of the vinyl sulphone with *n*-BuMgCl in the presence of a transition metal catalyst such as $Ni(acac)_2$. This method was used to synthesize a pheromone having a (*Z*,*E*)-diene (equation 27)[59]. Palladium catalysts can also be used for reductive desulphonylation reaction provided that appropriate ligands are used. The other method for vinyl sulphone hydrogenolysis is to treat it with sodium dithionite and sodium bicarbonate in aqueous DMF (equation 28)[60]. The mechanism of this reaction involves conjugate addition of HSO_2^- followed by the loss of sulphur dioxide and sulphinate moiety[61].



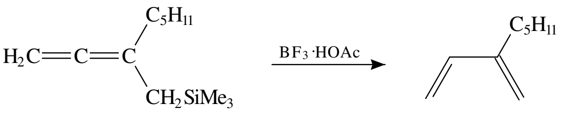
(27)



(28)

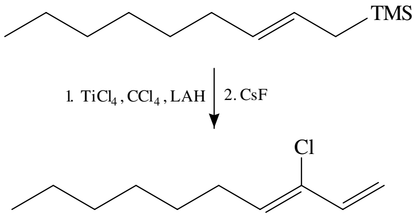
J. Elimination of Silyl Groups

Dienes can be obtained from silylallenes by protodesilylation using boron trifluoride–acetic acid complex (equation 29)[62]. Since silylallenes can be obtained by the reaction of propargyl acetate with cuprous reagent derived from chloromethyltrimethylsilane, this reaction sequence constitutes conversion of propargylic acetate to butadiene through one carbon homologation.



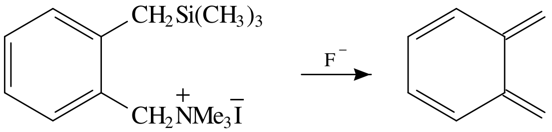
(29)

Allylic silanes react with dichlorocarbenes, generated from dechlorination of carbon tetrachloride with low valent titanium species, to furnish dichlorocyclopropanes, which in turn get desilylated with CsF in DMF to generate 3-chloro-1,3-butadienes (equation 30)[63].

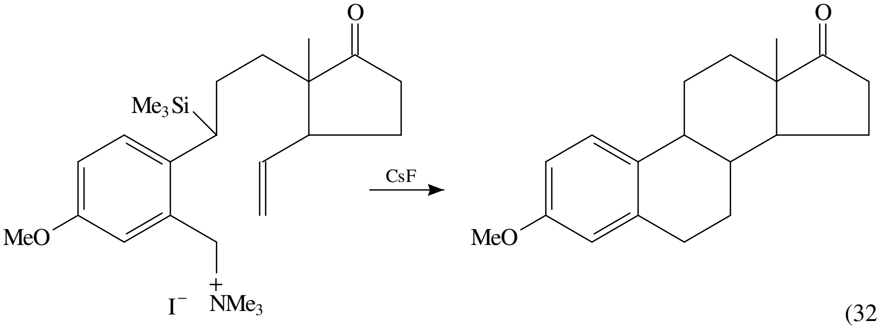


(30)

An efficient method for the generation of *o*-quinodimethanes via desilylation reaction involves treatment of a 2-[(trimethylsilylmethyl)benzyl]trimethylammonium iodide with fluoride ion (equation 31)[64]. This reaction was applied by Saegusa and coworkers for the synthesis of estrone in which an intramolecular Diels-Alder reaction of an *o*-quinodimethane, generated *in situ*, served as the key reaction (equation 32)[65].



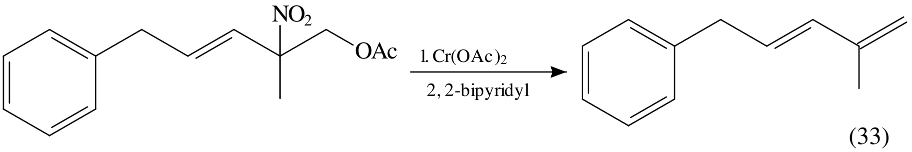
(31)



(32)

K. Reductive Elimination of Nitroacetates

Zard and coworkers have developed a synthesis of substituted dienes by reductive elimination of allylic nitroacetates (equation 33)[66]. Allylic nitroacetates can be prepared by condensation of nitromethane with the carbonyl compound followed by addition of formaldehyde and acetylation[67]. Reductive elimination can be carried out by employing either chromous acetate or samarium iodide.

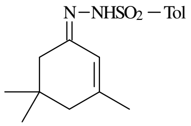
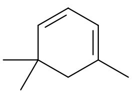
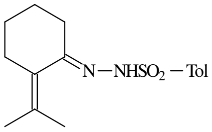
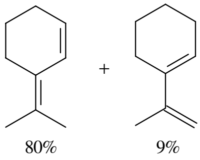
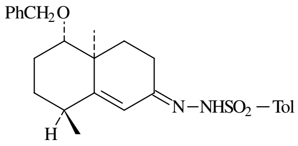
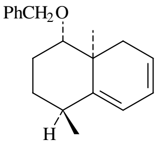


(33)

L. The Shapiro Reaction

Ketone *p*-toluenesulphonyl hydrazones can be converted to alkenes on treatment with strong bases such as alkyl lithium or lithium dialkylamides. This reaction is known as the Shapiro reaction[68]. When α,β-unsaturated ketones are the substrates, the products are dienes. This reaction is generally applied to the generation of dienes in cyclic systems where stereochemistry of the double bond is fixed. A few examples where dienes have been generated by the Shapiro reaction have been gathered in Table 6[69].

TABLE 6. Dienes through the Shapiro reaction

Substrate	Product	Reference
		69a
		69b
		69c

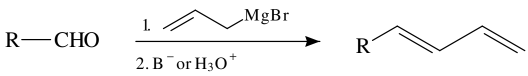
III. ADDITION-ELIMINATION REACTIONS

A. General Aspects

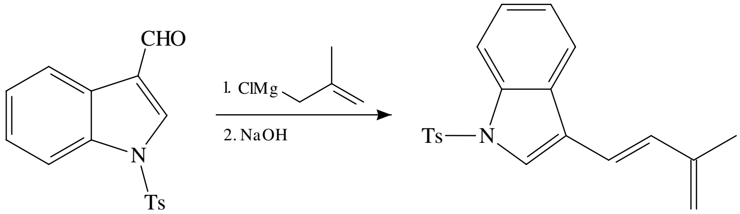
Nucleophilic additions to carbonyl groups lead to alcohols which on dehydration, furnish alkenes[70,71]. This two-step protocol has been extremely useful for diene and polyene synthesis with wide variation in the carbonyl substrate and the nucleophilic addendum. Diene synthesis using aldol-type condensation as well as phenyl sulphonyl carbanion (the Julia reaction) are also discussed in this section.

B. Allyl and Vinyl Organometallics

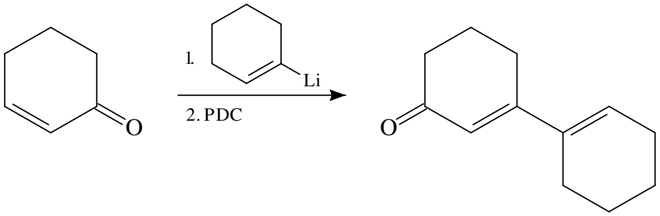
A simple two-step protocol for the generation of a terminal diene is to add allyl magnesium bromide to an aldehyde or a ketone and subsequent acid or base catalysed dehydration (equation 34)[72]. Cheng and coworkers used this sequence for the synthesis of some indole natural products (equation 35)[72a]. Regiospecific dienones can be prepared by 1,2-addition of vinyllithium to α,β-unsaturated carbonyl compounds and oxidative rearrangement of the resulting dienols with pyridinium dichromate (equation 36)[73].



(34)



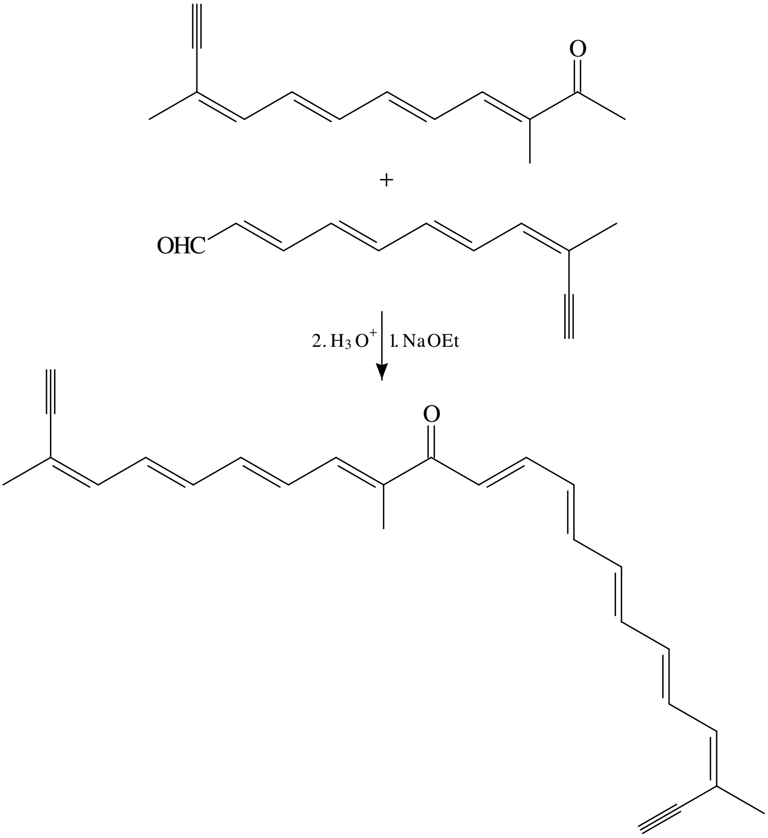
(35)



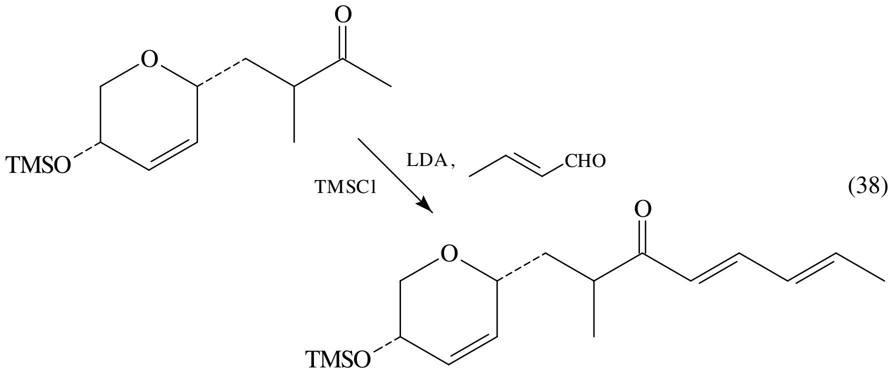
(36)

C. Aldol Condensation-dehydration (Knoevenagel Reaction)

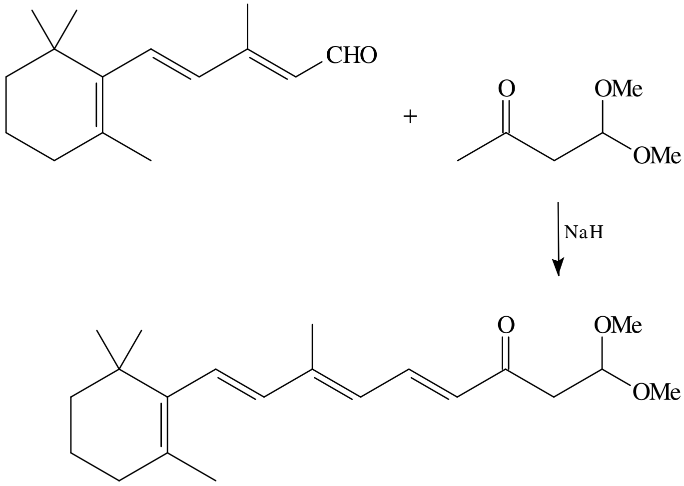
The nucleophilic addition of a carbanion to an aldehyde or a ketone having a conjugated double bond and the subsequent dehydration sequence (Knoevenagel reaction) is a popular method for generating dienes and polyenes (equation 37)[74]. This reaction takes place efficiently and stereoselectively, when LDA is used as a base in the presence of chlorotrimethylsilane (equation 38)[75]. Knoevenagel condensation was a key reaction during many classical carotenoid syntheses[76]. Recently, Seltzer and coworkers used the dimethyl acetal of acetylacetaldehyde for aldol condensation with a C_{15}-aldehyde, to generate the tetraenyl ketone acetal (equation 39)[77].



(37)

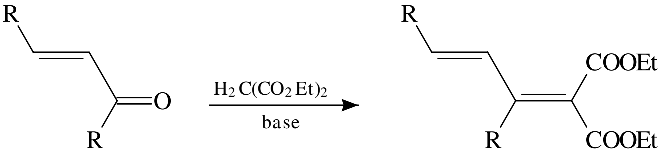


(38)

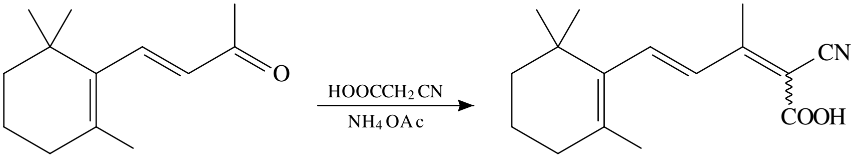


(39)

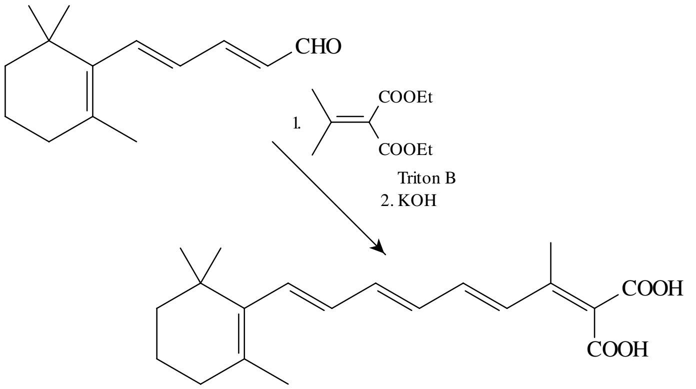
Knoevenagel condensation of diethyl malonate or related compounds with *α*,*β*-unsaturated aldehydes and ketones results in diene esters (equation 40)[78]. This condensation reaction has been used to extend the polyene chain length of vitamin A related compounds (equations 41[79] and 42[80]).



(40)

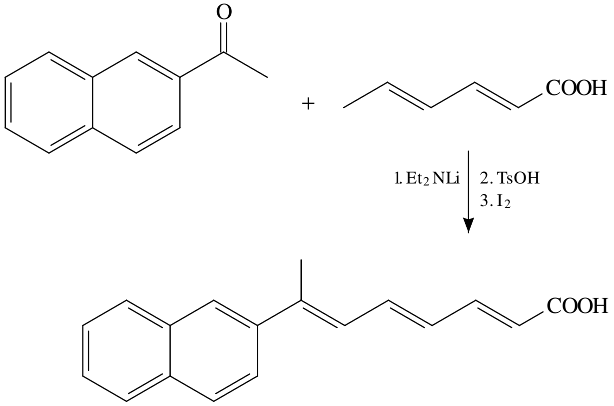


(41)

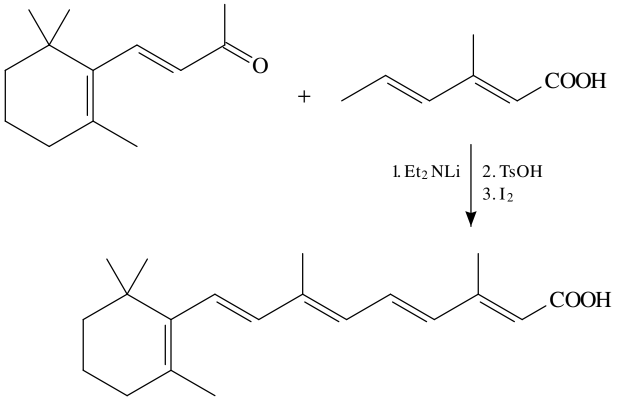


(42)

A convenient way of six-carbon homologation of aldehydes and ketones is the nucleophilic addition of the dianion generated from sorbic acid, (2*E*,4*E*)-hexa-2,4-dienoic acid and subsequent dehydration to form the corresponding trienoic acid (equation 43)[81]. The 3-methyl analogue of sorbic acid has been used in a similar fashion for a short synthesis of vitamin A carboxylic acid (equation 44)[82].



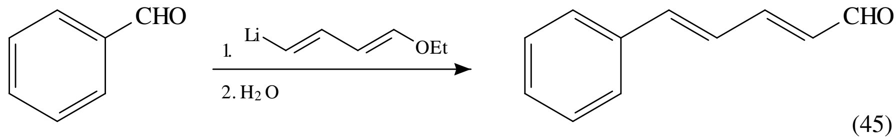
(43)



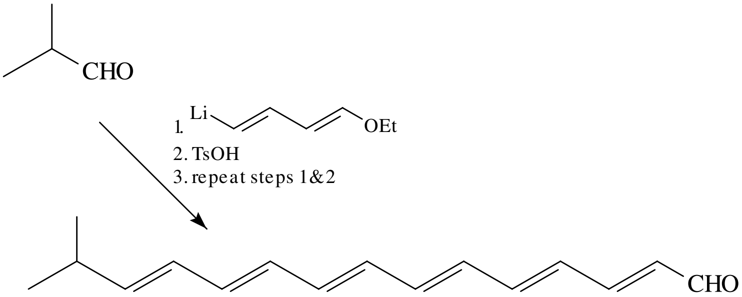
(44)

D. Wollenberg Method

Wollenberg introduced 4-lithio-butadienyl ethyl ether as a versatile reagent for four-carbon homologation of carbonyl compounds to the corresponding dienals (Table 7)[83]. This reagent, which is obtained *in situ* by transmetallation of 4-(tri-*n*-butylstannyl)butadienyl ethyl ether, adds to carbonyl compounds to generate intermediate alcohols which, on dehydration and hydrolysis of the enol ether, result in dienals (equation 45)[83a]. The advantage of this method is the generation of the aldehyde function at the end of the reaction so that it can be subjected to iterative Wollenberg reaction for polyene synthesis (equation 46)[83b]. Rychnovsky and coworkers found this methodology to be specially useful for the synthesis of polyene portions of macrolide antibiotics such as roflamycoin[83c] and roxaticin[83d] (Table 7).

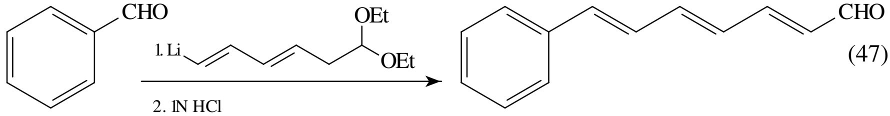


(45)



(46)

Duhamel and coworkers introduced a convenient isoprenylating reagent, 1-lithio-2-methyl-4-trimethylsiloxybutadiene, for five-carbon homologation of a carbonyl group[83g]. Utilizing this reagent, in a reiterative fashion, retinal was synthesized in good yields starting from β-ionylideneacetaldehyde[83g]. In a related study, Duhamel and coworkers developed the dimethy; acetal derivative of ω-lithiosorbaldehyde for six-carbon homologation[84] (equation 47) and 4-lithio-1-trimethylsiloxybutadiene for four-carbon homologation[85] (equation 48) of carbonyl compounds. Simultaneously, the same group also introduced C_7 reagents, 1-lithio-6-methoxy-4-methylhexatriene and 1-lithio-4-methyl-6-trimethylsiloxyhexatriene for a seven-carbon homologation of carbonyl compounds[83g]. These C_7 units were utilized for a short $C_{13} + C_7$ synthesis of retinal, starting from abundantly available β-ionone (equation 49). Extending further, 1-lithio-2,6-dimethyl-8-methoxyoctatetra-1,3,5,7-ene was introduced as C_{10} reagent for $C_{10} + C_{10}$ synthesis of vitamin A aldehyde, retinal (equation 50)[86,87].



(47)

TABLE 7. Dienes and polyenes through the Wollenberg method

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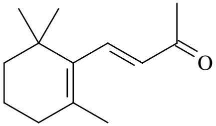
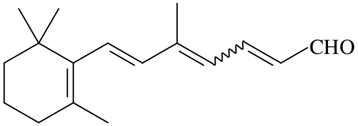
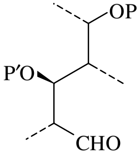
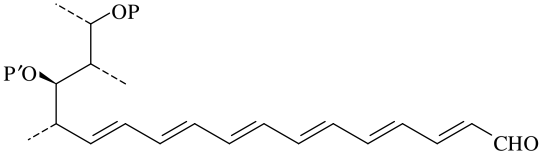
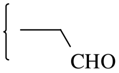
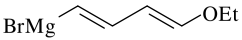
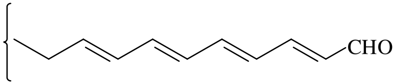
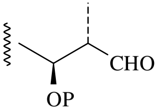
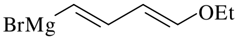
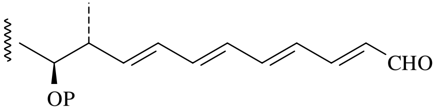
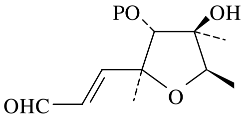
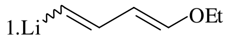
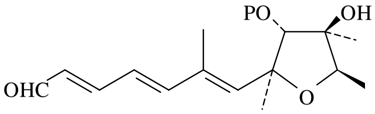
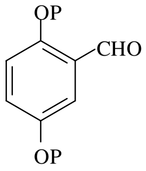
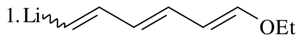
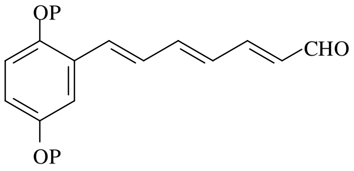
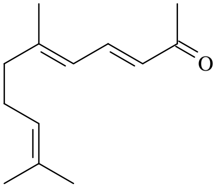
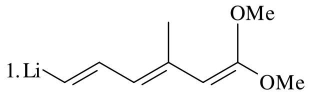
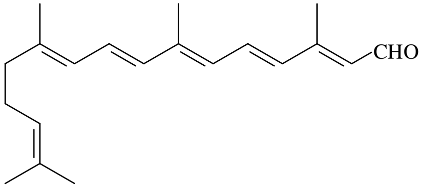
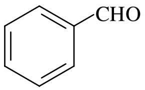
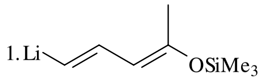
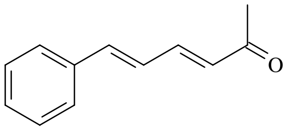
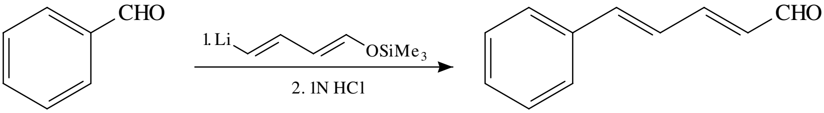
	1. LiCH=CH—CH=CH—OEt 2. TsOH		83a
 P = MeOCH$_2$;	1. LiCH=CH—CH=CH—OEt 2. TsOH 3. repeat steps 1 & 2 P′ = TBS	 (Amphotericoin B fragment)	83b
	1.  2. MsCl, Et$_3$N 3. repeat steps 1 & 2	 (Roflamycoin fragment)	83c
 P = 1,3-Benzodithiolan-2-yl	1.  2. MsCl, Et$_3$N 3. repeat steps 1 & 2	 (Roxaticin fragment)	83d

continued overleaf

TABLE 7. (*continued*)

Starting ketone	Reagents	Product	Reference
 P = $MeOCH_2$	 2. SiO_2		83e
	 2. 1N HCl P = t-$BuMe_2Si$		83f
	 2. 1N HCl		83g
	 2. H_3O^+		83h



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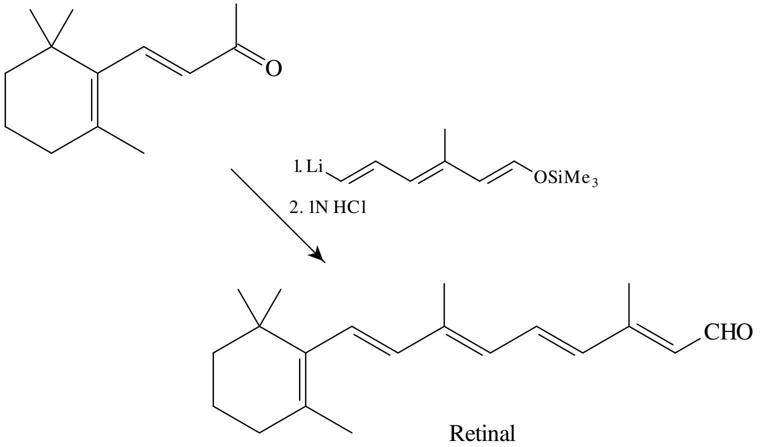
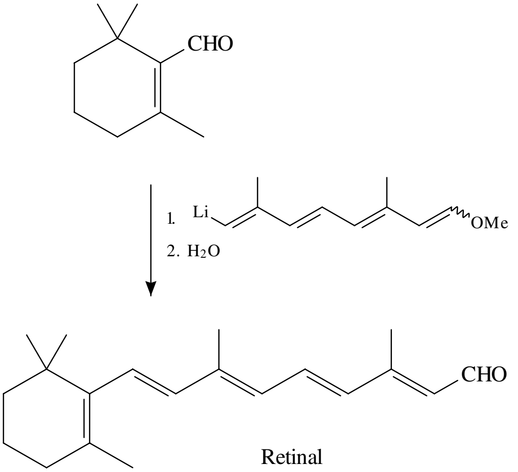
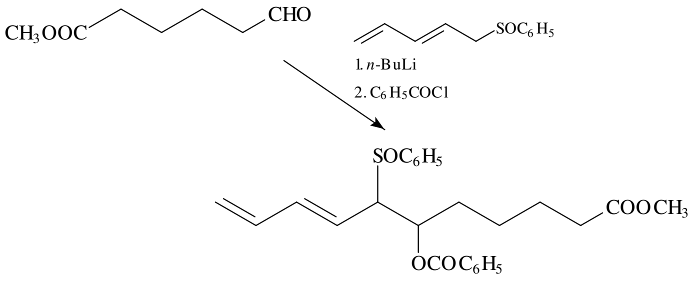


(49)

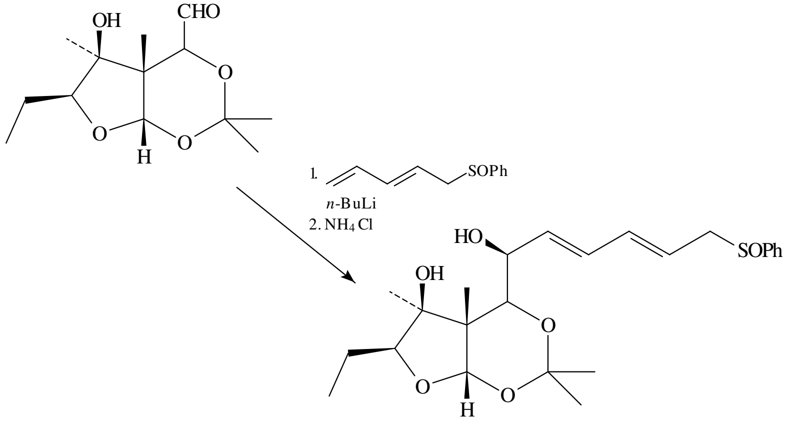


(50)

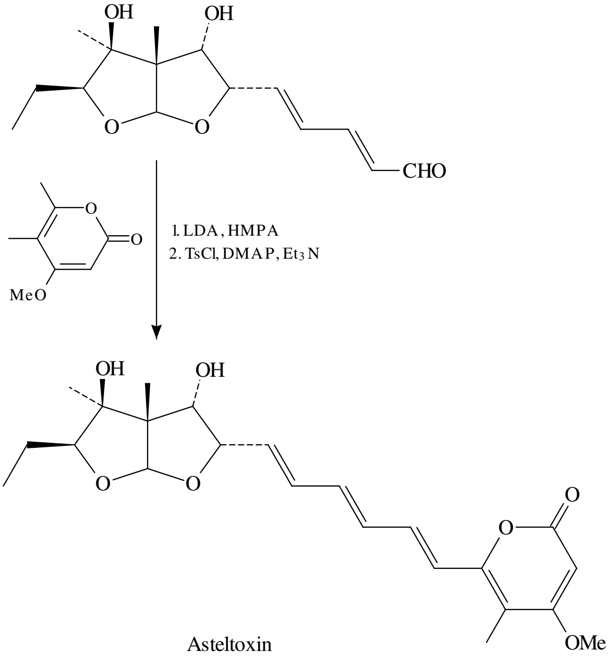
Corey and coworkers used the anion from *E*-1-phenylsulfinylmethyl-1,3-butadiene as an equivalent of the 4-formyl-(*E*,*E*)-1,3-butadienyl anion for the synthesis of 5-desoxyleukotriene D. Thus, the lithio derivative of pentadienyl sulphoxide reacts with methyl 5-formylpentanoate to result in the aldol, which on double [3.2]sigmatropic rearrangement furnishes diene product (equation 51)[88]. Conversion of phenyl sulphoxide to aldehyde was achieved through the Pummerer rearrangement-hydrolysis pathway. The dienal so formed was ready for Wittig reaction to generate the (*E*,*E*,*Z*)-triene moiety present in the target molecule. Schreiber and Satake also made use of lithiated pentadienyl sulphoxide as 4-formyl-(*E*,*E*)-1,3-butadienyl anion equivalent and subsequent Pummerer rearrangement, aldol condensation and dehydration led to the total synthesis of polyene antibiotic asteltoxin (equations 52 and 53)[89].



(51)



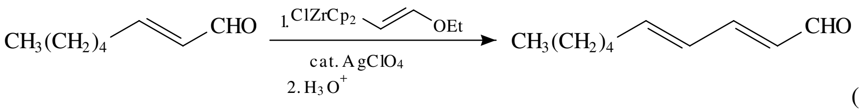
(52)



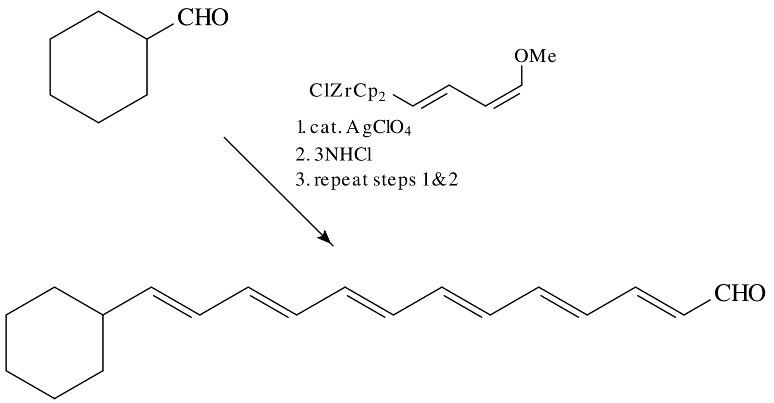
(53)

Asteltoxin

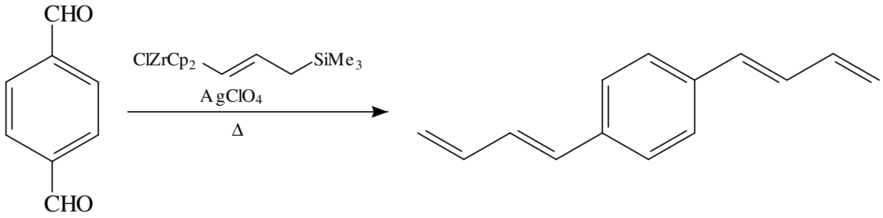
Alkenylzirconocene reagents add to carbonyl compounds in the presence of a catalytic amount of silver perchlorate to give allylic alcohols which, on dehydration, give dienes (equation 54)[90]. Since alkenylzirconocene intermediates are accessible readily from alkynes by reacting with Schwartz reagent [$Cp_2Zr(H)Cl$][91], this sequence is of immense practical importance. An application of this reaction in an iterative fashion for the preparation of polyenals is shown in equation 55[92]. Trimethylsilyl-1-propenylzirconocene chloride also adds to carbonyl compounds leading to allylic alcohols which, on Peterson-type elimination, give predominantly *E*,*E*-1,3-dienes (equation 56)[93].



(54)

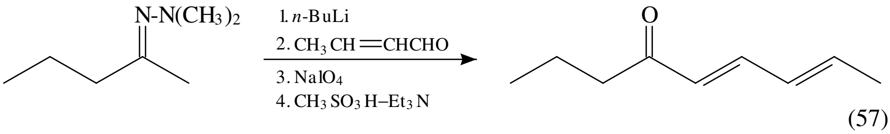


(55)



(56)

Crossed aldol condensation of an anion generated α- to a ketone equivalent with α,β-unsaturated aldehyde, dehydration and release of the ketone is an effective way of generation of dienones. Corey and Enders found that α-lithiated *N*,*N*-dimethylhydrazones undergo 1,2-addition to the aldehydes and ketones to form β-hydroxy derivatives. Sequential treatment of the intermediate with sodium periodate and methanesulphonyl chloride-triethylamine furnishes *E*,*E*-2,4-dienone derivative (equation 57)[94].

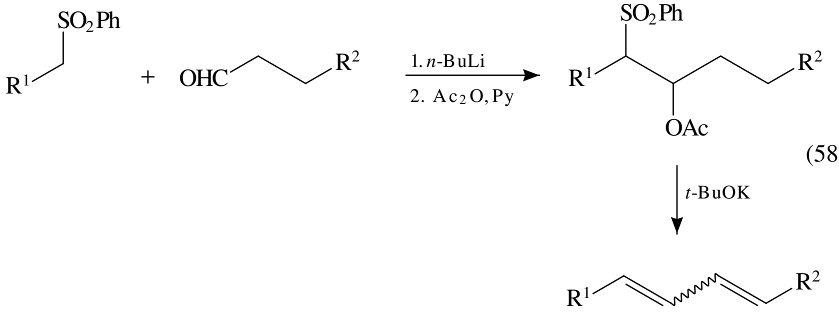


(57)

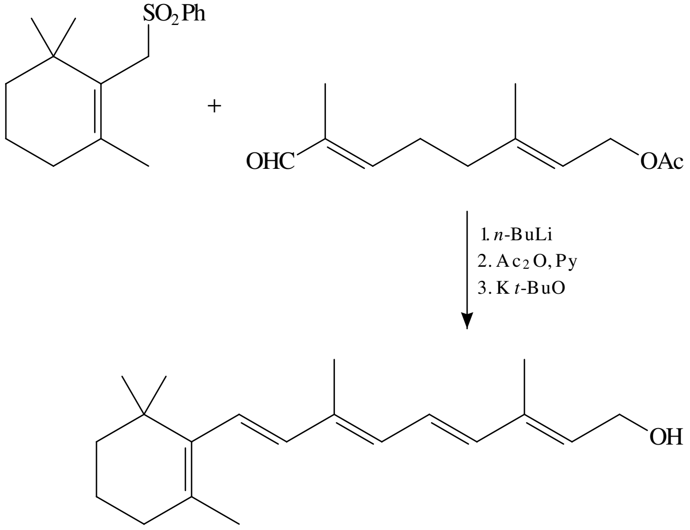
E. Sulphones (Julia and Related Reactions)

α-Sulphone carbanions add to aldehydes and ketones to generate β-hydroxy sulphones. Concomitant reductive removal of the hydroxy group and sulphenic acid results in alkene formation[95]. Since the alkene formation in this reaction (Julia reaction) is equilibrium controlled, E/Z selectivity is usually high, favouring the E-isomer. When one of the reacting partners, either the sulphone or the carbonyl compound, has a double bond already present, then the product is a diene. Julia coupling methodology has been used extensively for the generation of conjugated diene (Table 8)[96] and polyene (Table 9)[97] moieties.

Otera and coworkers developed an alternative procedure to the Julia method for generating dienes or alkynes in the same reaction by the double elimination of β-acetoxy or β-alkoxy sulphones with potassium t-butoxide (equation 58)[98,99]. The reaction pathway leading to the diene or an alkyne depends on the substrate structure and the reaction conditions. If an allylic hydrogen is present in the substrate then diene is formed; otherwise, the alkyne is the product of the reaction. This modified Julia methodology has been applied to the synthesis of vitamin A (equation 59)[100], alkaloids piperine (equation 60)[101] and trichonine (equation 61)[102].



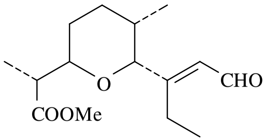
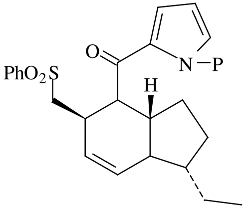
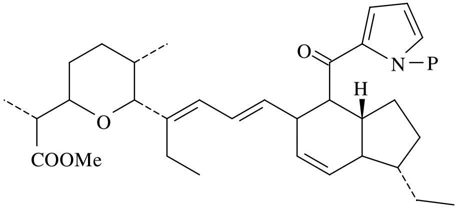
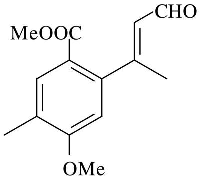
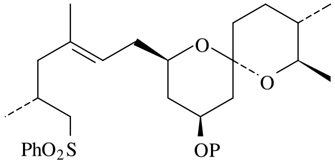
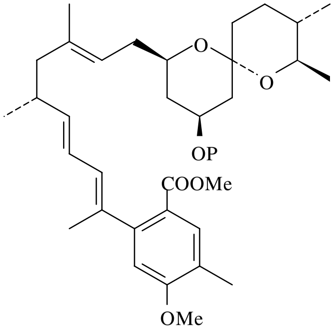
(58)



(59)

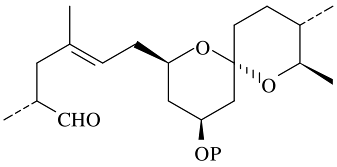
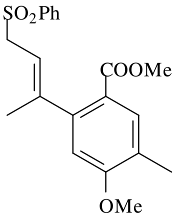
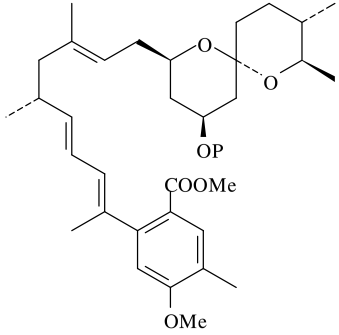
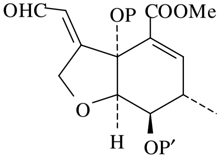
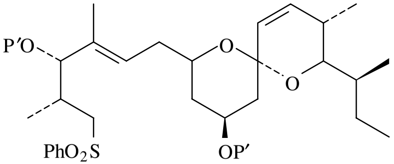
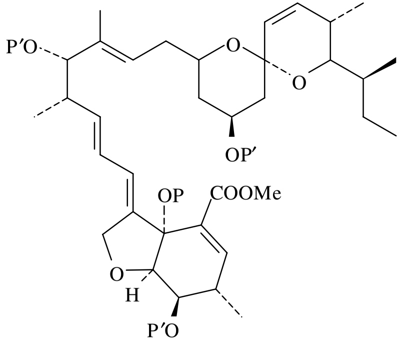
Retinol

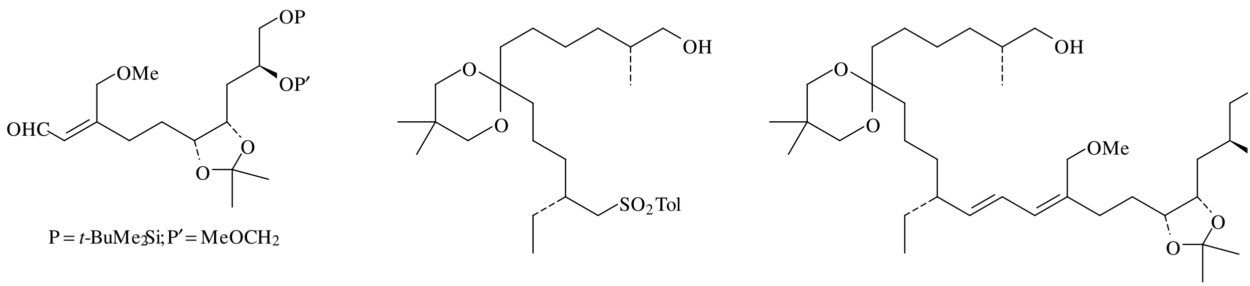
TABLE 8. Dienes through the Julia reaction

Aldehyde	Sulphone	Product	Reference
 P = Me$_3$SiCH$_2$CH$_2$O			96a
	 P = *t*-BuPh$_2$Si		96b

continued overleaf

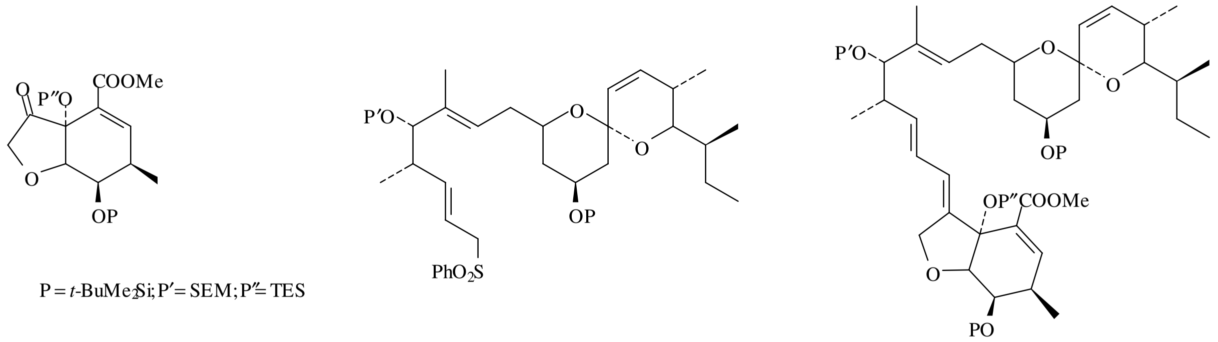
TABLE 8. (*continued*)

Aldehyde	Sulphone	Product	Reference
 P = *t*-BuMe$_2$Si			96c
 P = Me$_3$Si; P′ = *t*-BuMe$_2$Si			96d



P = *t*-BuMe$_2$Si; P′ = MeOCH$_2$

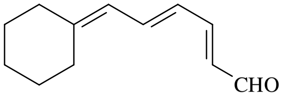
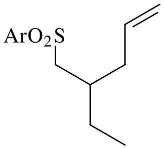
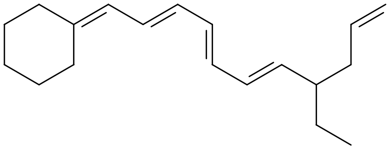
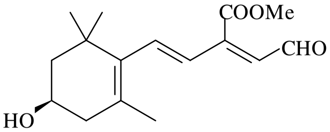
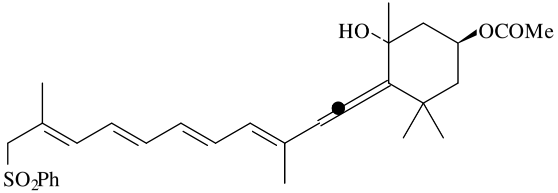
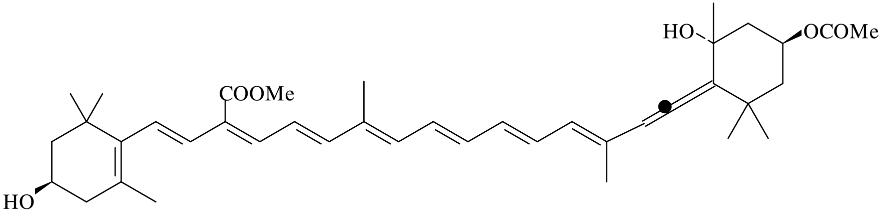
96e

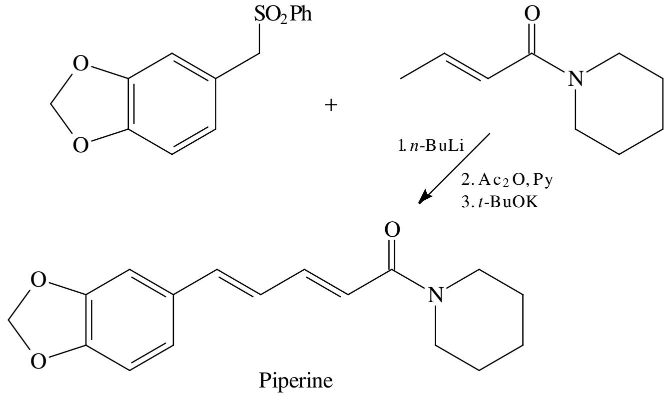


P = *t*-BuMe$_2$Si; P′ = SEM; P″ = TES

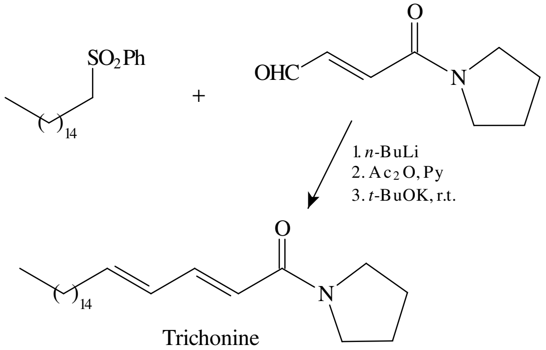
96f

TABLE 9. Polyenes through the Julia reaction

Aldehyde	Sulphone	Product	Reference
			97a
			
			97b

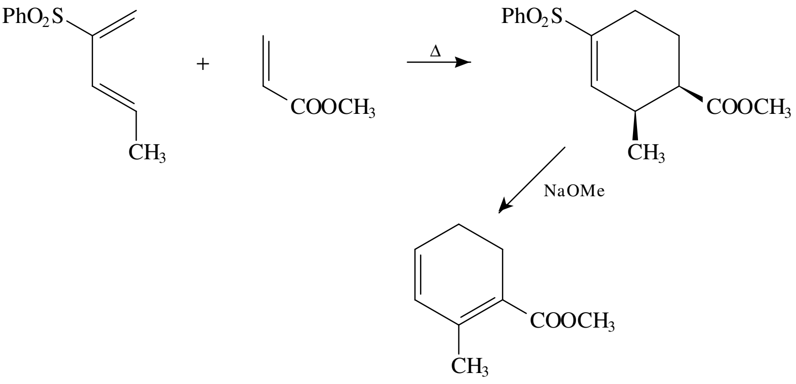


(60)

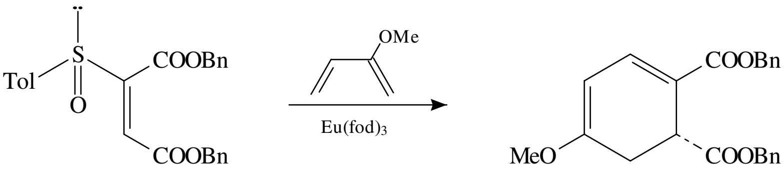


(61)

Backvall and Juntunen and Fuchs and Braish have developed (*E*)-2-phenylsuphonyl-1,3-dienes prepared under Julia conditions as versatile synthones for a variety of organic transformations[103]. These dienes undergo facile Diels–Alder reaction and subsequent 1,4-elimination of sulphinic acid by base to generate a new diene (equation 62)[103a]. An elegant extension of this method is to use chiral sulfinylmaleate which, on Diels–Alder reaction and elimination of the sulfinyl group, generates an optically active diene for further applications (equation 63)[104].

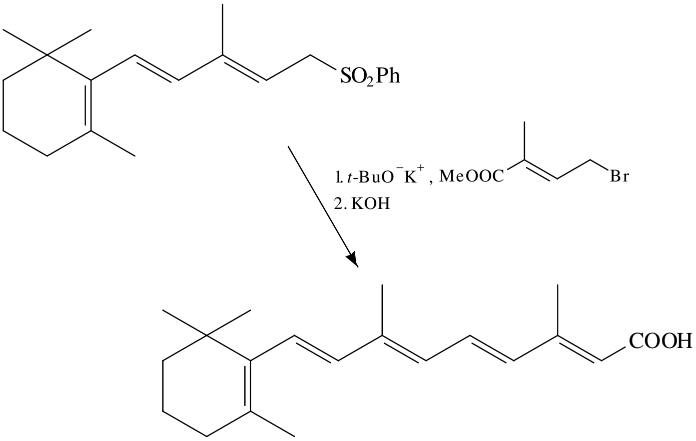


(62)

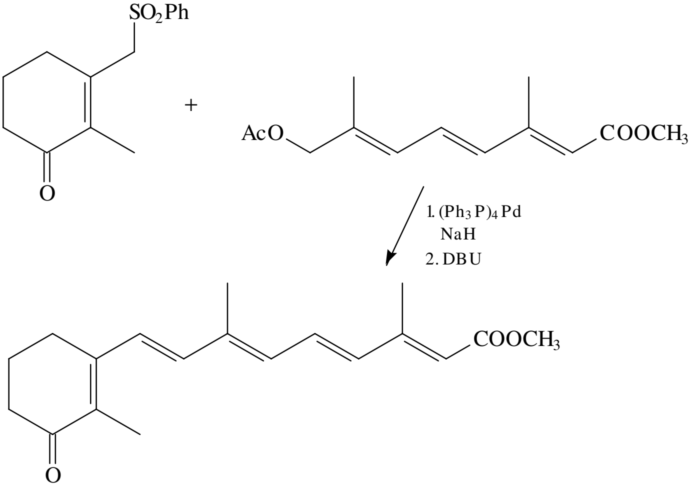


(63)

Allyl sulphones can be converted to dienes by alkylation and elimination of sulphinic acid under basic conditions (equation 64)[105]. Several vitamin A related polyenes have been synthesized following this two-step protocol (Table 10)[106]. The poor leaving-group ability of the arylsulphonyl group requires treatment with strong base for elimination. However, elimination of the allylsulphonyl group takes place readily under palladium catalysis (equation 65)[107]. Vinyl sulphones can be converted to dienes via Michael addition, alkylation with allyl halides and elimination of sulphinic acid sequence (equation 66)[108].



(64)



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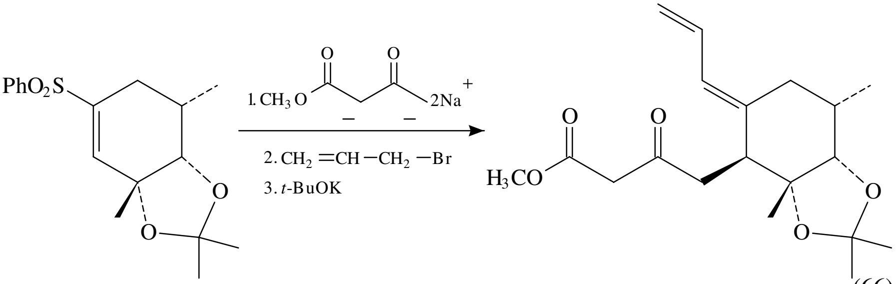
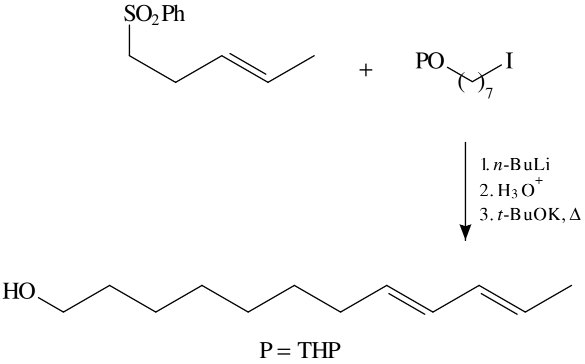


(66)

An alternative approach to the synthesis of 1,3-dienes is by elimination of benzenesulphinic acid from homoallylic sulphones under basic conditions. This method has been used for the synthesis of a pheromone constituent of the codling moth (equation 67)[109].



(67)

IV. CONCERTED REACTIONS

A. General Aspects

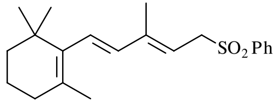
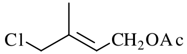
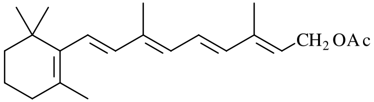
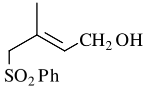
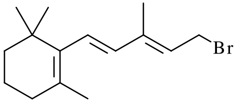
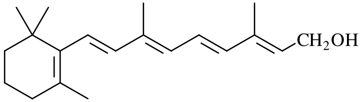
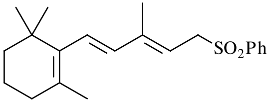
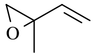
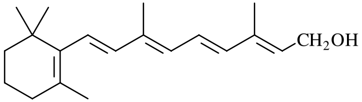
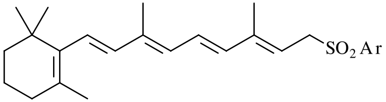
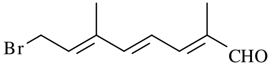
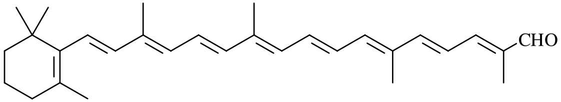
Symmetry-allowed concerted reactions such as retro Diels–Alder reactions and electrocyclic ring-opening reactions are popular methods for releasing the diene component for further manipulations[110]. As the reactions take place via symmetry-allowed processes[111], the diene products can be obtained with high stereochemical purity. Extrusion of molecules such as sulphur dioxide, nitrogen, oxygen and carbon dioxide from cyclic substrates is another commonly used methodology for the stereoselective generation of dienes.

B. Extrusion of Neutral Species

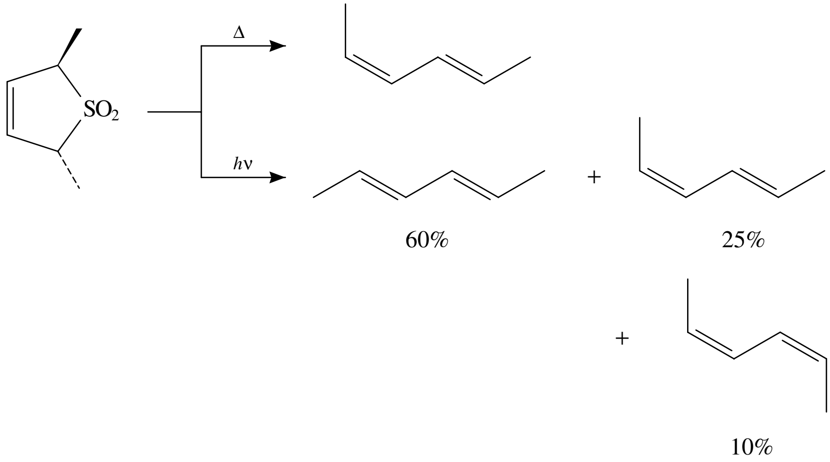
1. Sulphur dioxide

Extrusion of sulphur dioxide from cyclic systems leading to dienes has proved to be a synthetically useful reaction[112]. Thermolysis of *cis*- and *trans*-2,5-disubstituted sulpholenes, which can be readily obtained through regio- and stereoselective alkylation, proceeds in a stereospecific manner affording 1,3-dienes of high stereochemical purity, as predicted by symmetry rules (equations 68 and 69)[113]. On the other hand, a photochemical process is not completely stereospecific (equation 68)[114]. 2,5-Dialkylative cyclization

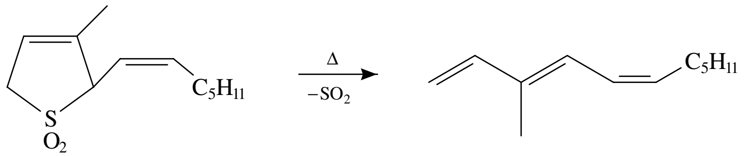
TABLE 10. Synthesis of vitamin A and related compounds through allyl sulphones

Allyl Sulphone	Electrophile	Product	Reference
			106a
			106b
			106c
 Ar: $C_6H_5OC_6H_4$			106d

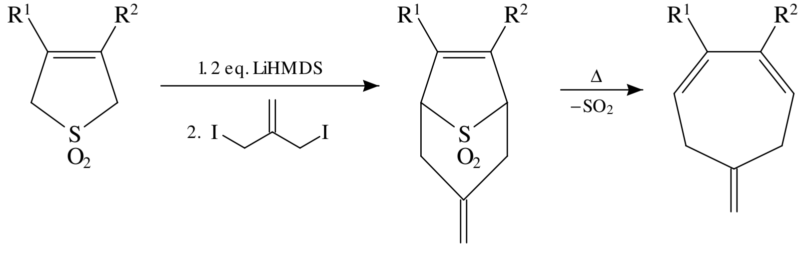
can be performed on 3-sulpholene with 3-chloro-2-(chloromethyl)propene and sulphur dioxide extrusion from the [3.2.1]bicyclic product results in a seven-membered cyclic diene (equation 70)[115]. Regioselective monoalkylation of sulpholene derivatives can be performed via their 2-stannyl or 2-manganese derivatives with vinyl iodides in the presence of a Pd^0 complex[116]. Sulphur dioxide extrusion from the products result in trienes with well-defined stereochemistry (equation 71).



(68)

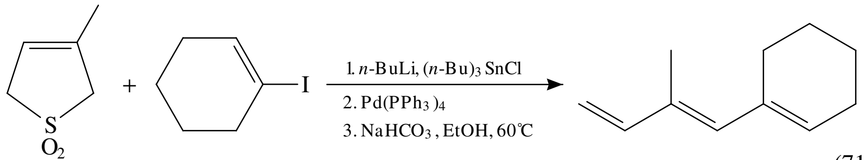


(69)



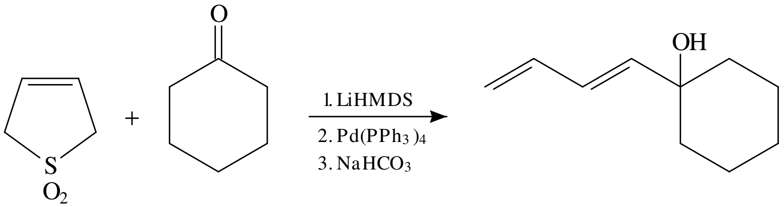
(70)

LiHMDS = lithium hexamethyldisilazide



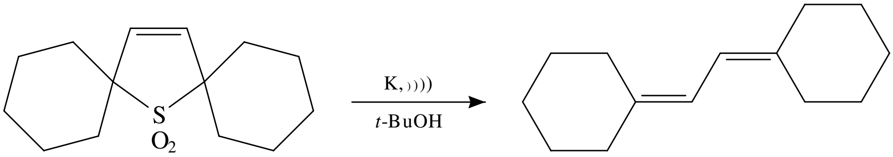
(71)

The carbanion generated from deprotonation of the α-carbon atom of sulpholene reacts with aldehydes and ketones to give alcohols. Sulphur dioxide extrusion from the products results in (E)-α-hydroxy-1,3-dienes (equation 72), or dehydration followed by thermal desulphonylation results in trienes[117]. Dienones can be obtained if the initial condensation is conducted with an aldehyde, followed by oxidation and sulphur dioxide removal[117].



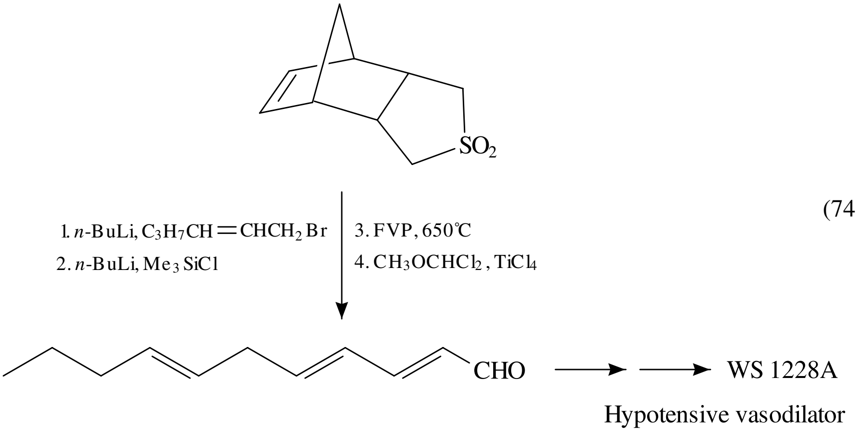
(72)

Even though sulphur dioxide extrusion from sulpholene derivatives is generally conducted either by heating in a non-polar solvent or in the presence of base[118], alternative reagents such as LAH[119], and finely dispersed potassium metal[120] are also used. Syntheses of some tetrasubstituted butadienes were achieved by treating the corresponding sulpholenes with ultrasonically dispersed potassium metal in the presence of water (equation 73)[120b].

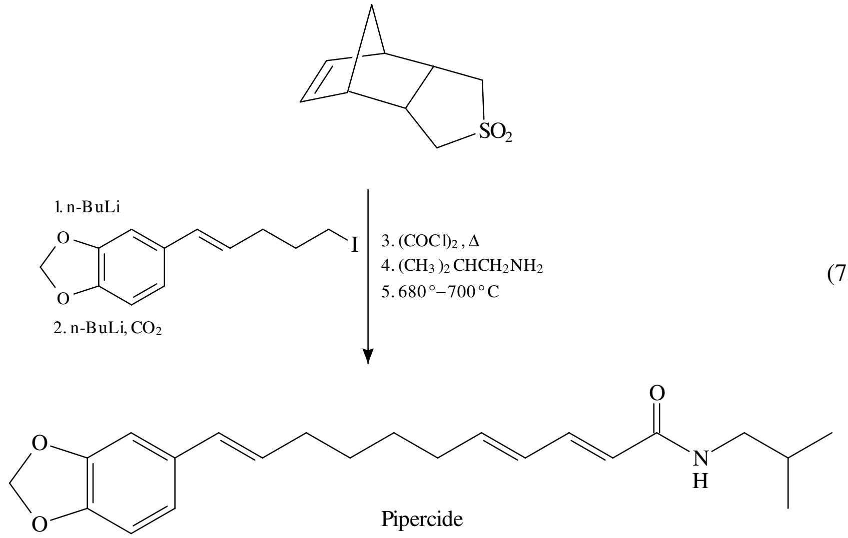


(73)

The Diels–Alder adduct of sulpholene and cyclopentadiene is a useful starting material for substituted diene synthesis[121]. The diene moiety is unmasked by retro-Diels–Alder reaction and sulphur dioxide extrusion under flash vacuum pyrolysis conditions (equations 74 and 75)[122,123].

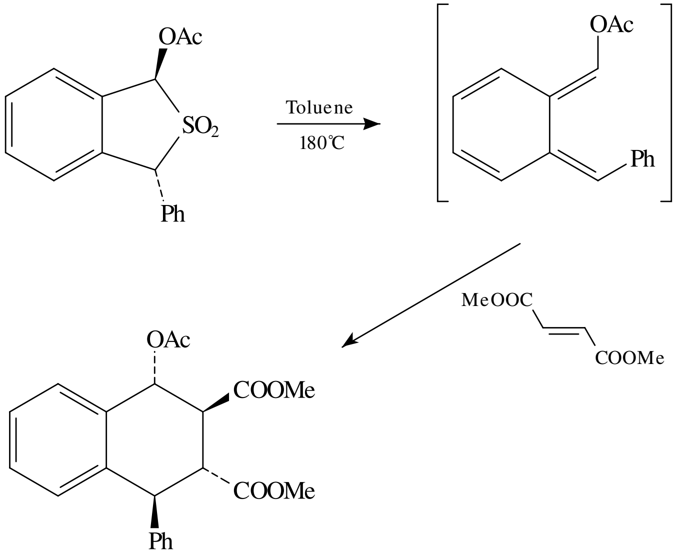


(74)

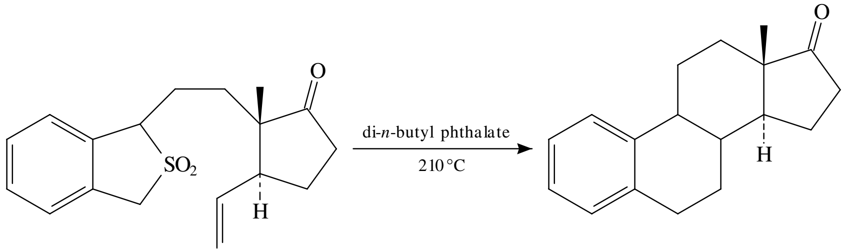


(75)

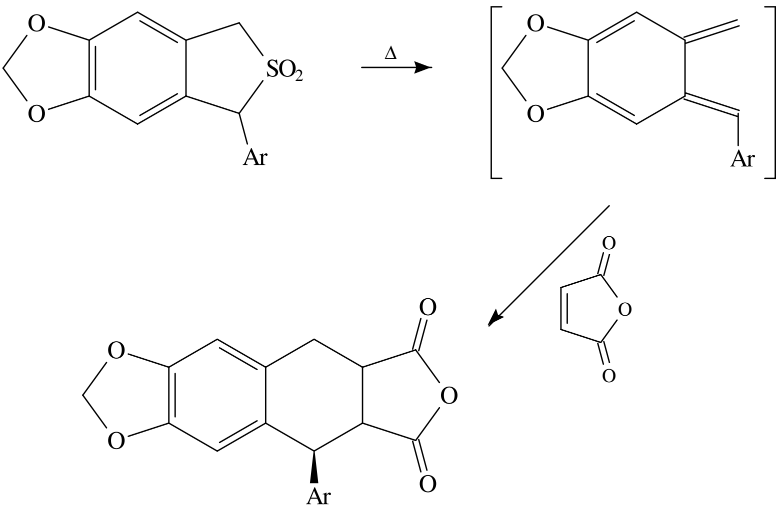
o-Quinodimethanes can be made *in situ* by sulphur dioxide extrusion from 1,3-dihydro-4,5-benzo[*c*]thiophene-2,2-dioxide derivatives (equation 76)[124,124j]. *o*-Quinodimethanes undergo facile intramolecular Diels–Alder reaction with an internal alkene to result in polycyclic compounds. An expedient synthesis of estrone derivative, an enantioselective synthesis of (+)-esterdiol and a short synthesis of a lignane: were achieved following this strategy (equations 77 and 78)[125,126]. Heteroaromatic *o*-quinodimethanes can be prepared *in situ* by sulphur dioxide extrusion from the appropriate sulpholene precursors which readily undergo Diels–Alder reactions (equation 79)[127].



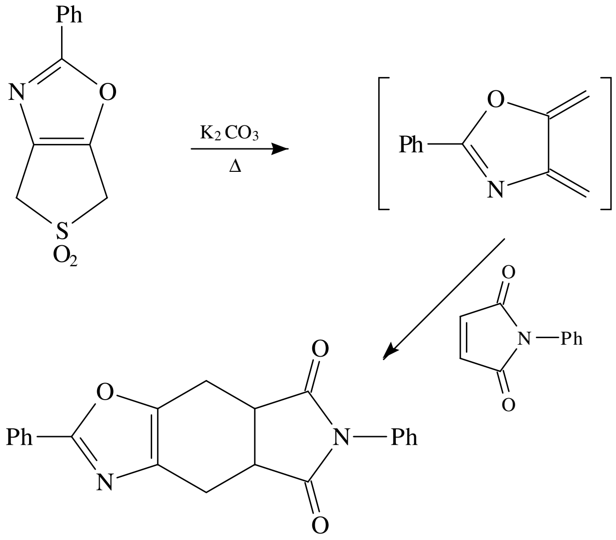
(76)



(77)



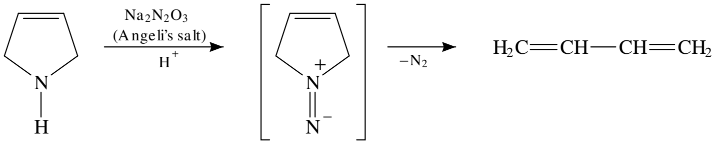
(78)



(79)

2. Nitrogen

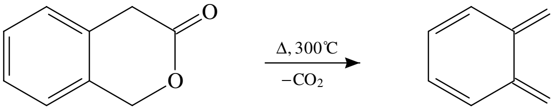
Butadiene can be obtained by thermal extrusion of a nitrogen molecule from a cyclic diazene (equation 80)[128]. However, this reaction has found only limited synthetic applications.



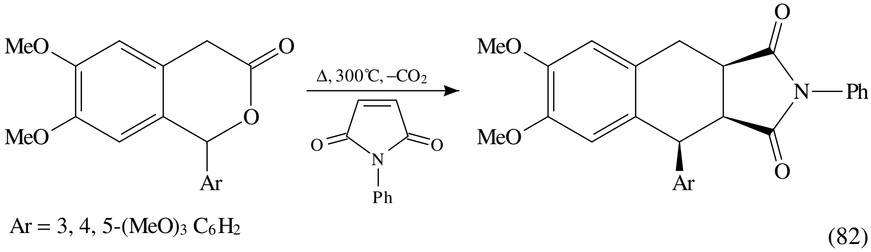
(80)

3. Carbon dioxide and carbon monoxide

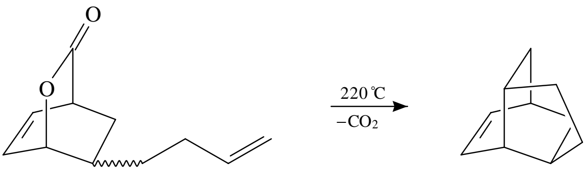
Isochromones lose carbon dioxide on heating via retro-Diels–Alder pathway to result in *o*-quinodimethanes (equation 81)[124i,129]. An isochromone route to podophyllotoxin derivative has been described (equation 82)[130]. Diels–Alder adducts of α-pyrone readily extrude carbon dioxide on thermal activation to furnish cyclohexadienes, which are useful substrates in tandem Diels–Alder reactions (equation 83)[131].



(81)

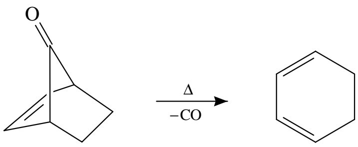


(82)



(83)

Photo- and thermal decarbonylation of cyclic unsaturated ketones leads to the formation of cyclic 1,3-dienes. Such decarbonylations are commonly observed in 7-ketonorbornenes and related bridged bicyclic systems to give cyclohexadienes (equation 84)[132].

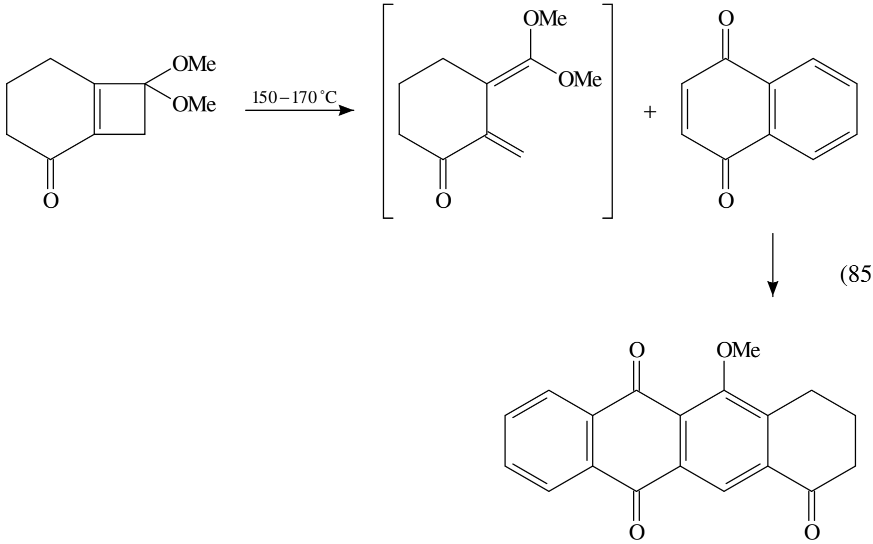


(84)

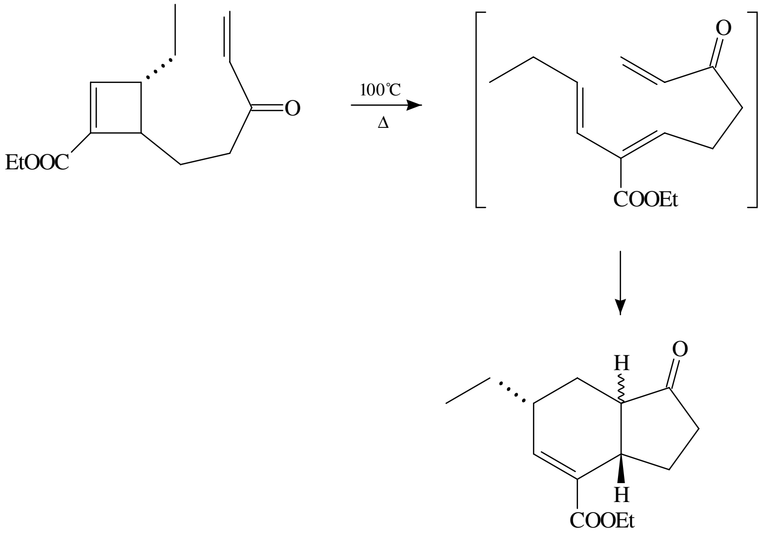
C. Ring Opening of Cyclobutenes

Cyclobutenes undergo facile, thermally induced conrotatory ring opening to generate 1,3-dienes[133]. Highly oxygenated butadienes are useful in Diels–Alder and hetero-Diels–Alder reactions. A number of such oxygenated 1,3-butadienes can be readily prepared from the corresponding cyclobutenes by thermal ring opening. Examples are given in Table 11.

1,3-Dienes generated in this fashion can be trapped with dienophiles, either intramolecularly or intermolecularly, and this strategy has been exploited for the synthesis of natural products (equations 85 and 86)[135,136].

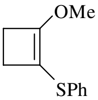
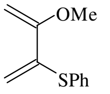
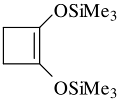
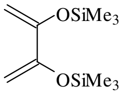
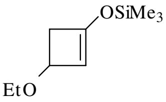
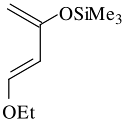
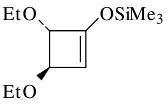
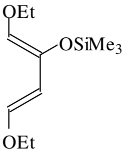
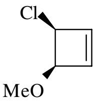
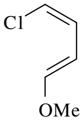
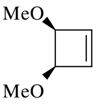
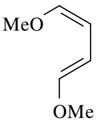
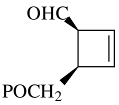
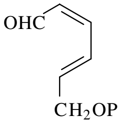
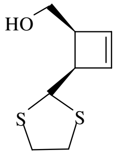
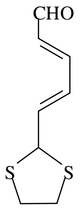
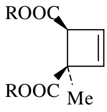
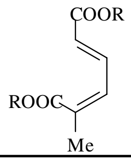


(85)



(86)

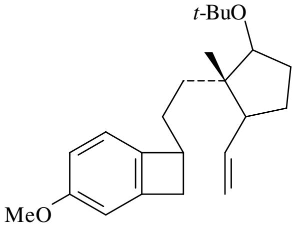
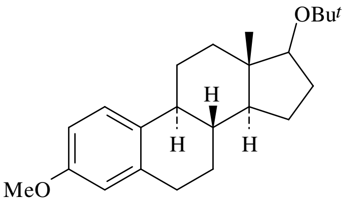
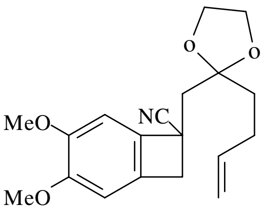
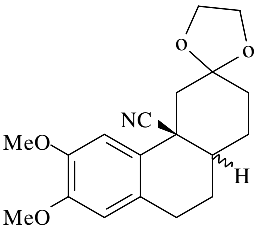
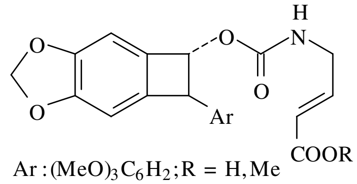
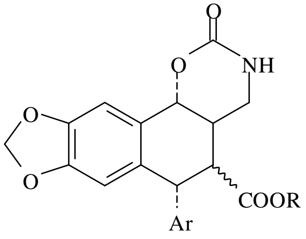
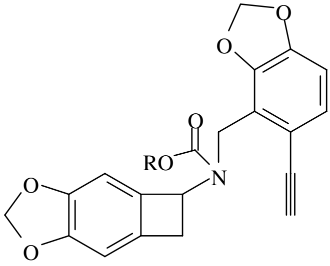
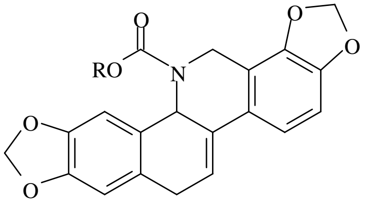
TABLE 11. Substituted butadienes through cyclobutene ring-opening reactions

Substrate	Condtions	Product	Reference
	$\xrightarrow{340\ ^\circ\mathrm{C}}$		134a
	$\xrightarrow{180\ ^\circ\mathrm{C}}$		134b
	$\xrightarrow{25\ ^\circ\mathrm{C}}$		134c
	$\xrightarrow{25\ ^\circ\mathrm{C}}$		134c
	$\xrightarrow{80\ ^\circ\mathrm{C}}$		134d
	$\xrightarrow{80\ ^\circ\mathrm{C}}$		134d
	$\xrightarrow{-78\ ^\circ\mathrm{C}}$ $\mathrm{P = 4\text{-}MeOC_6H_4CH_2}$		134e
	$\xrightarrow{\mathrm{PCC, RT}}$		134e
	$\xrightarrow{\Delta}$		134f

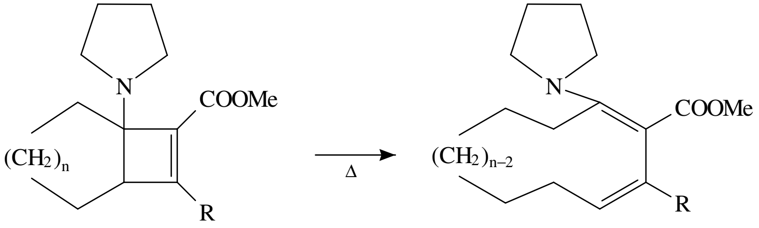
Several ingenious syntheses of natural products have been developed by exploiting benzcyclobutene ring opening to *o*-quinodimethane. Particularly, the intramolecular Diels–Alder strategy employing *o*-quinodimethane intermediates has been very effective for the construction of polycyclic structures. Selected examples are gathered in Table 12.

[*n*.2.0]Bicyclic butenes having a dialkylamino substituent on the bridge head carbon undergo facile ring opening to result in 2-carbon ring enlarged cyclic 1,3-dienes (equation 87)[138]. This approach has been utilized for the synthesis of several natural

TABLE 12. Polycycles through benzocyclobutene ring opening

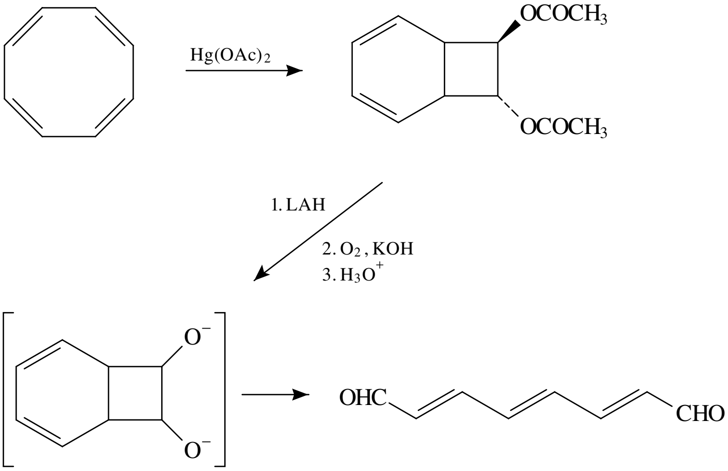
Substrate	Product	Reference
		137a
		137b
 Ar : $(MeO)_3C_6H_2$; R = H, Me		137c
 R = C_7H_7	 Chelidonine intermediate	137d

products which contain medium or large rings such as steganone[139], muscone[140] and velleral[141].



(87)

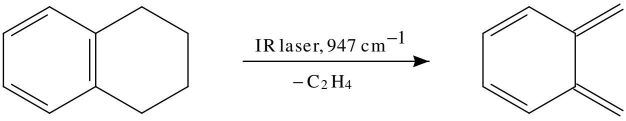
trans-7,8-Diacetoxy[4.2.0]octa-2,4-diene derived from cyclooctatetraene, on reduction with lithium aluminium hydride and oxidative ring opening of the cyclobutane ring, results in octa-2,4,6-triene-1,8-dial (equation 88)[142]. This synthon has been used for the construction of the heptaene portion of the macrolide antibiotic amphotericin B[143].



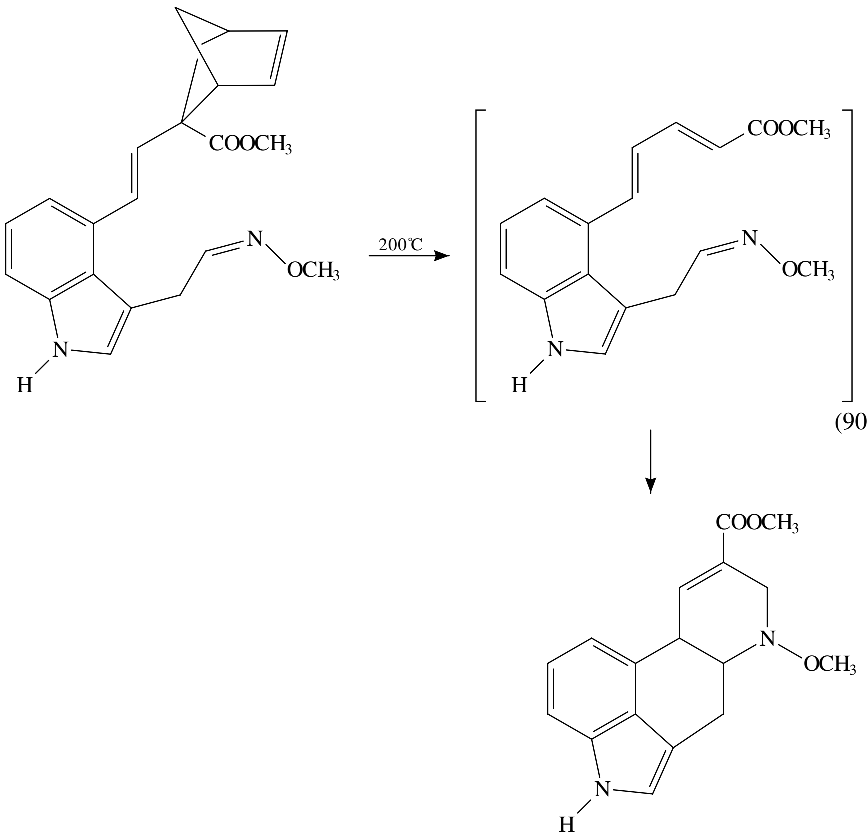
(88)

D. Retro-Diels–Alder Reactions

Retro-Diels–Alder reactions can be used to regenerate dienes or alkenes from 'Diels–Alder protected' cyclohexene derivatives under pyrolytic conditions[144]. Most of the synthetic utility of this reaction comes from releasing the alkene by diene-deprotection. However, tetralin undergoes cycloreversion via the retro-Diels–Alder pathway to generate *o*-quinodimethane under laser photolysis (equation 89)[145]. A precursor of lysergic acid has been obtained by deprotection of the conjugated double bond and intramolecular Diels Alder reaction (equation 90)[146].



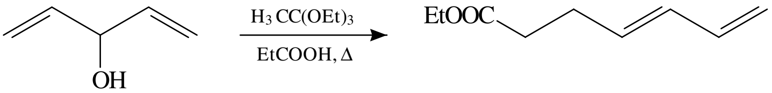
(89)



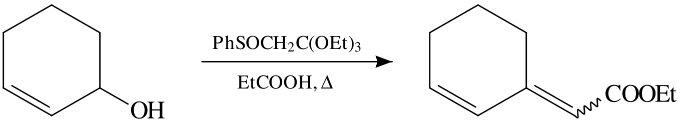
(90)

E. Orthoester Claisen Rearrangements

Allylic alcohols undergo symmetry-allowed orthoester Claisen rearrangement, when treated with trialkyl orthoacetate in the presence of an acid catalyst. When this reaction is applied to 2-butyne-1,4-diols, one of the products formed is a 1,3-diene[147]. 1,3-Dienes also result when this reaction is performed on bisallylic alcohols (equation 91)[148]. Regiospecific conversion of allylic alcohols to two-carbon extended dienoate esters, by performing an orthoester Claisen rearrangement with phenylsulfinyl orthoacetate, has been described (equation 92)[149].



(91)



(92)

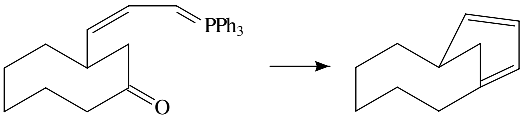
V. WITTIG AND RELATED REACTIONS

A. The Wittig Reaction

The Wittig reaction is a classical method for the transformation of a carbonyl group to an olefin[150]. The stereoselectivity of the olefin formation in the Wittig reaction depends highly on the ylide structure and the reaction conditions[151]. Generally, non-stabilized ylides give predominantly the Z-alkenes and stabilized ylides give higher selectivity of E-alkenes. The nature of the base also plays a role in stereoselectivity of olefins derived from unsaturated ylides[152]. Wittig carbonyl olefination is used extensively in olefin, diene and polyene synthesis and has found new areas of application in industrial practice. Application of the Wittig reaction for the synthesis of natural products, especially carotenoids, has been extensively reviewed[150c,153].

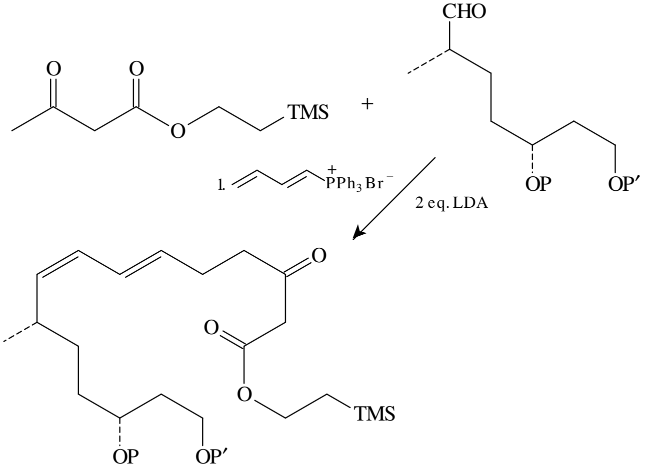
When one of the reacting partners of the Wittig reaction, i.e. the carbonyl compound or the ylide, has a double bond already present in it, the resulting product is a diene. Usually, when polyenes are synthesized following the Wittig method, a mixture of stereoisomers is formed. However, all *trans*-polyenes can be obtained by equilibrating the mixture with a catalytic amount of iodine, or under photolytic conditions. Examples of dienes and polyenes generated via a Wittig reaction are given in Tables 13 and 14, respectively.

The Wittig methodology can also be employed for diene synthesis in an intramolecular version. Propenylidinephosphoranes having a carbonyl group undergo intramolecular Wittig reactions to generate cyclic dienes (equation 93)[156].



(93)

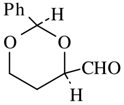
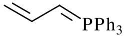
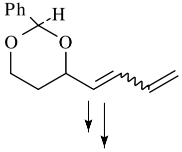
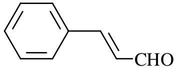
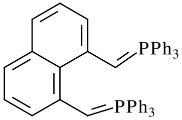
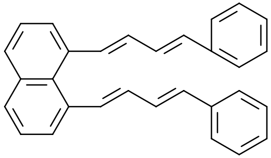
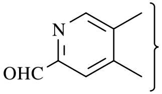
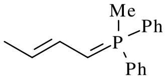
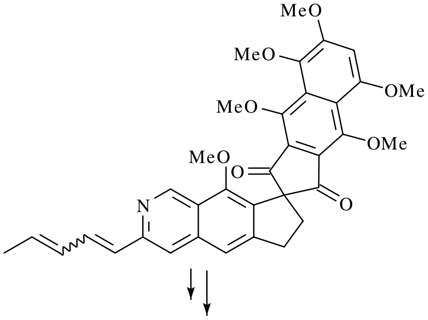
The butadienylphosphonium salt reacts with dianions on the end-carbon atom to result in an intermediate Wittig ylide, which undergoes normal olefination to generate (E,Z)-dienes of high stereoselectivity. This reaction is in effect a three-component coupling of a nucleophile, Wittig salt and an electrophile[157]. This strategy of three-component coupling was utilized for the diene construction of macrolide latrunculin A (equation 94)[158].

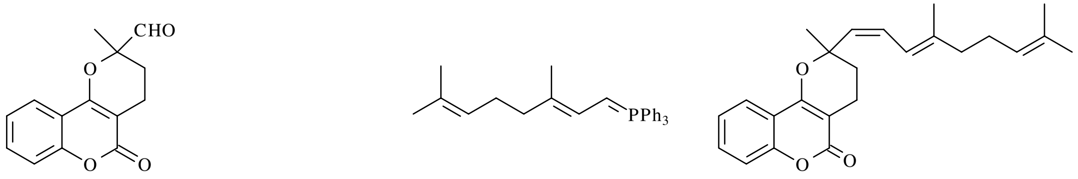


(94)

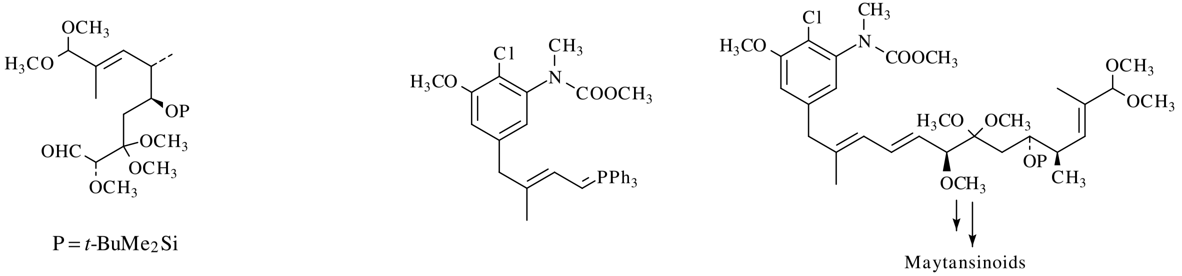
P = [2-(trimethylsilyl) ethoxy] methyl; P′ = t-BuMe$_2$Si

TABLE 13. Dienes through Wittig reaction

Carbonyl Compound	Wittig Yilide	Product	Reference
		 Swainsonine	154a
			154b
		 Fredericamycin	154c

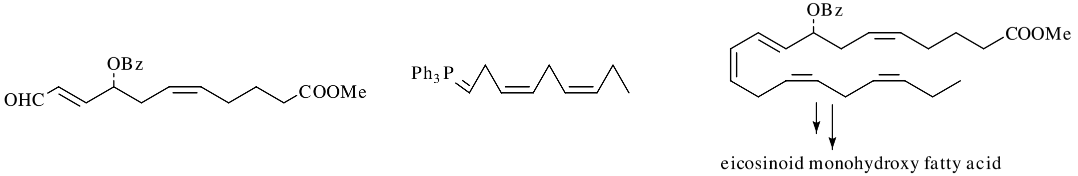


154d



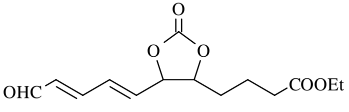
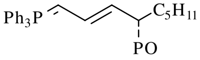
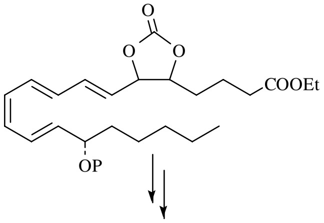
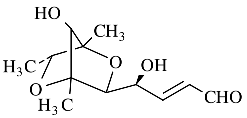
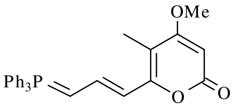
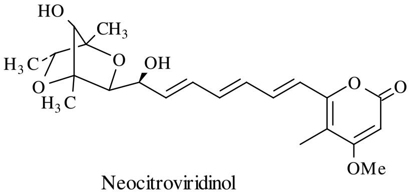
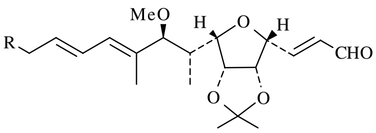
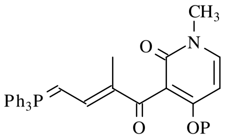
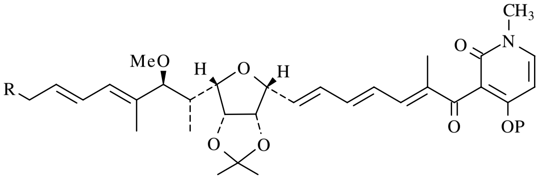
P = *t*-BuMe$_2$Si

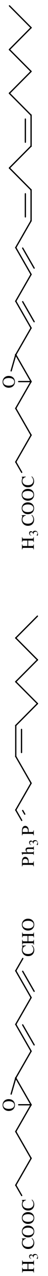
154e



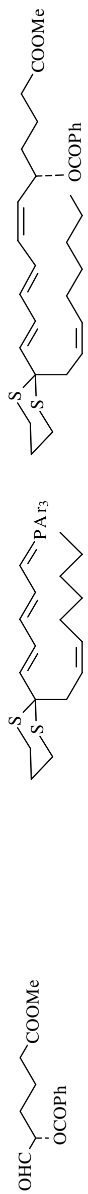
154f

TABLE 14. Polyene synthesis through the Wittig reaction

Ketone	Wittig ylide	Olefinic compound	Reference
 p = *t*-BuPh$_2$Si		 Lipoxin A	155a
		 Neocitroviridinol	155b
 R = NHCOOCH$_2$CCl$_3$; P = PhCH$_2$			155c

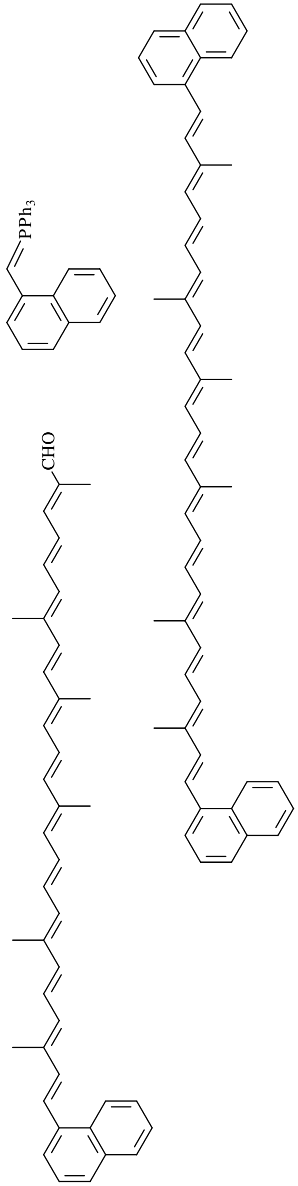


155d



Ar = p-Anisyl

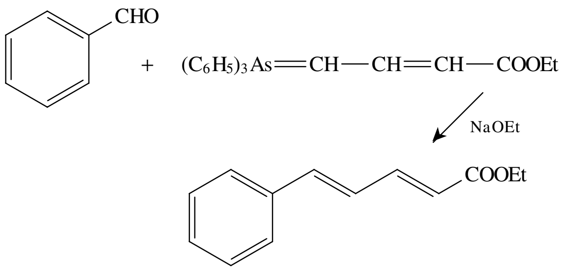
155e



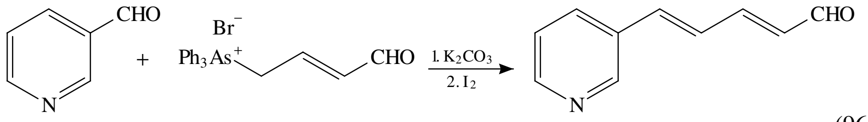
155f

B. Arsenic Ylides

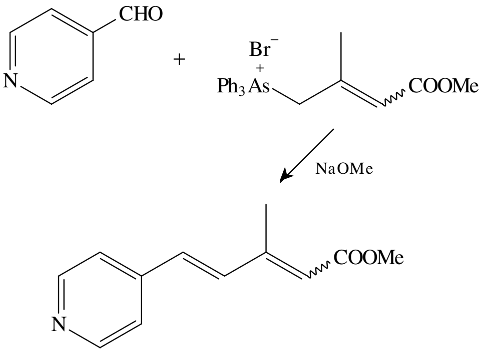
Stabilized arsenic ylides are more reactive than the corresponding phosphorus (Wittig) ylides[159]. In many cases where phosphorus ylides failed to react with carbonyl compounds, the corresponding arsenic ylides have been applied in the olefin forming reactions. Huang and coworkers developed the chemistry of arsenic ylides for the synthesis of dienes and polyenes[160]. Thus, 3-ethoxycarbonylallylidenetriphenylarsone reacts with a variety of aldehydes and ketones to afford diene esters (equation 95). This reagent reacts with aromatic aldehydes stereospecifically leading to the formation of *E*, *E*-products. Another reagent of high synthetic potential is formylallyltriphenylarsonium bromide[161]. This reagent reacts with aldehydes to give dienals, which can again be subjected to olefination in an iterative fashion (equation 96). In a similar manner, an isoprenoid arsone reagent, 3-methoxycarbonyl-2-methyl-2-propenylidenetriphenylarsorane, for appending isoprenoid unit to aldehydes, has been developed (equation 97)[161b]. Applications of arsenic ylides for the synthesis of dienes and polyenes are given in Table 15[160,161a,162].



(95)



(96)

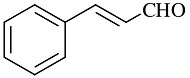
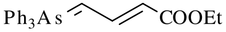
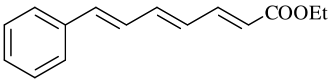
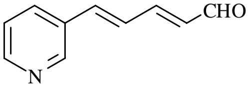
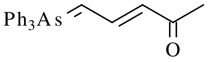
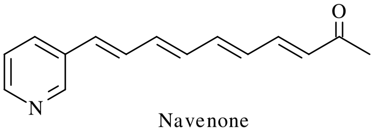
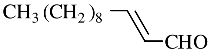
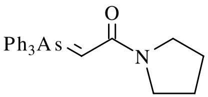
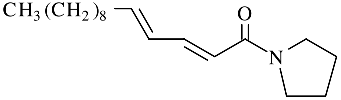


(97)

C. The Horner–Wadsworth–Emmons (HWE) Reaction

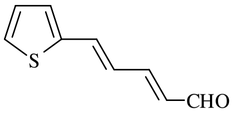
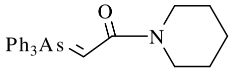
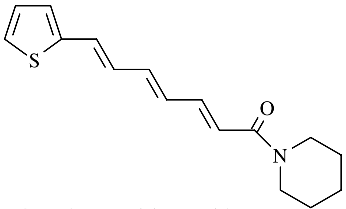
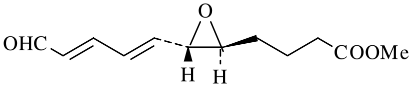
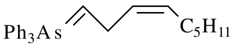
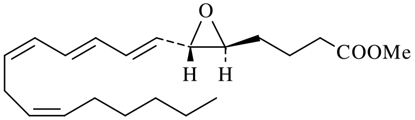
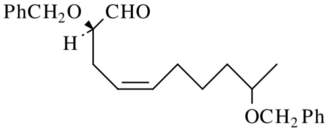
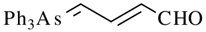
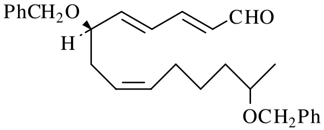
An important modification to the Wittig reaction is the use of stabilized phosphonate carbanions in olefin synthesis. This reaction, originally discovered by Horner but developed by Wadsworth and Emmons, is used extensively for transformation of a carbonyl

TABLE 15. Dienes and polyenes with arsenic ylides

Substrate	Arsenic ylide	Product	Reference
			160
		 Navenone	161a
		 Achillea amide	162a

continued overleaf

TABLE 15. (*continued*)

Substrate	Arsenium ylide	Product	Reference
		 Otanthus maritina amide	162a
		 Leukotriene A_4 (LTA_4) methylester	162b
			162c

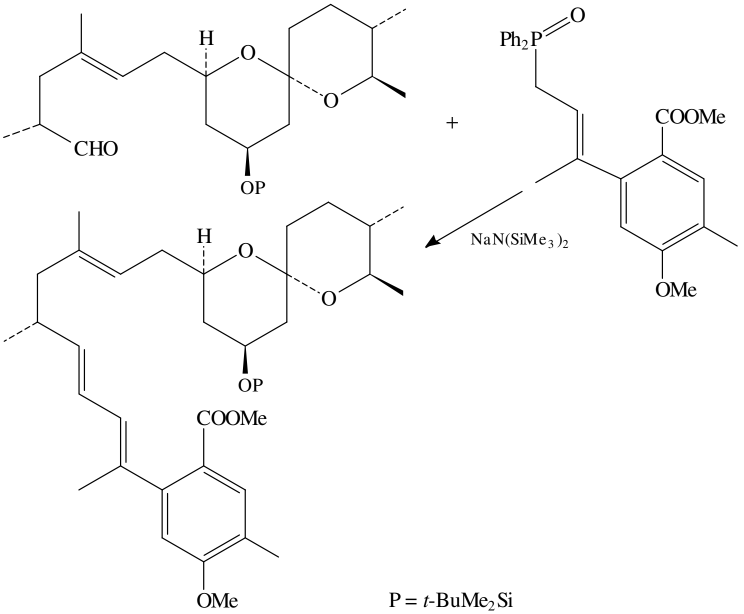
group to an olefin[163]. Phosphonate carbanions are more nucleophilic than the corresponding Wittig ylides, and therefore are more reactive towards carbonyl compounds, especially when the substituent on the phosphonate reagent is an electron-withdrawing group. When the substituent on the phosphonate reagent is an electron-withdrawing group such as an ester or ketone, the product in the olefination reaction is predominantly *E*.

HWE reaction has been used extensively for the synthesis of dienes and polyenes. Examples from recent literature are shown in Table 16 (dienes) and Table 17 (polyenes). HWE reaction also has been used for intramolecular cyclizations leading to polyene macrolides (Table 18).

D. The Wittig–Horner Reaction

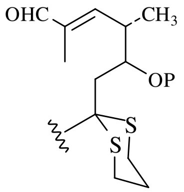
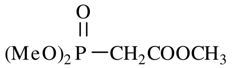
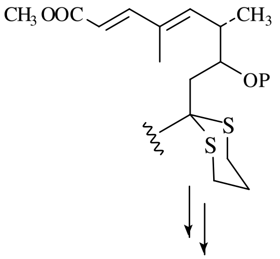
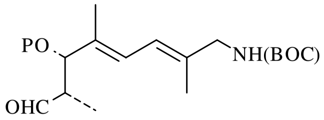
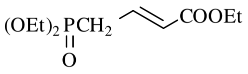
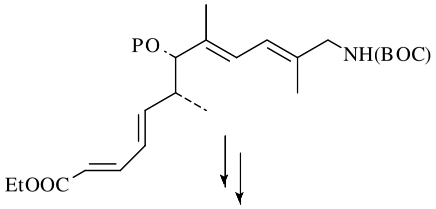
Another variation of the Wittig reaction is the Wittig–Horner reaction, in which the anion generated α- to phosphine oxide is used as a nucleophile to react with carbonyl compounds[167]. The intermediate formed in this reaction, β-hydroxyphosphine oxide, is isolable particularly when bases with lithium counterion are used for deprotonation. Since the β-hydroxyphosphine oxides are diastereomers, they can be separated and subjected to elimination to form the corresponding alkenes[168]. Since the elimination of phosphonate moiety is *syn*, stereospecific alkenes are obtained from the elimination step[169]. As expected, the generation of *erythro* and *threo* isomers is dependent on the solvent and the reaction conditions.

When one of the reacting partners in the Wittig–Horner reaction, either the phosphine oxide or the carbonyl compound, has a double bond, the product is a diene. The Wittig–Horner reaction was utilized by Smith and coworkers in the total synthesis of milbemycin (equation 98)[170]. They found that when sodium hexamethyldisilazide was employed as a base, the desired *E*-diene selectivity is high (85%). Some examples from the literature where the Wittig–Horner reaction has been utilized for the construction of *E*-double bonds present in dienes and polyenes are given in Table 19[171].



(98)

TABLE 16. Diene synthesis through HWE reaction

Starting aldehyde	Phosphonate	Product	Reference
 $P = MeOCH_2$	 $(MeO)_2\overset{\overset{O}{\parallel}}{P}-CH_2COOCH_3$	 Methylmaysenine	164a
 $P = t\text{-}BuMe_2Si$		 lejimalides	164b

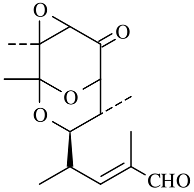
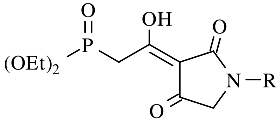
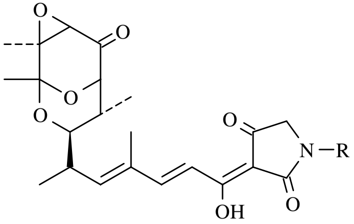
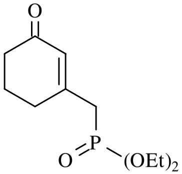
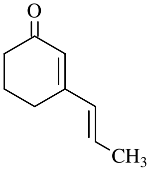
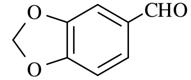
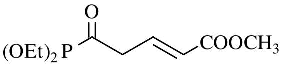
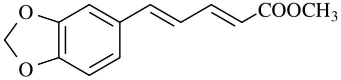
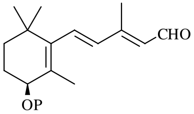
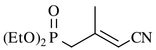
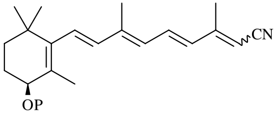
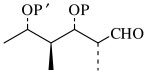
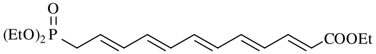
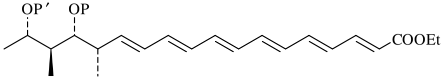
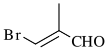
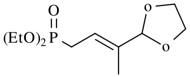
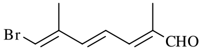
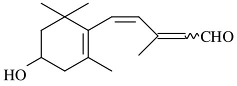
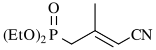
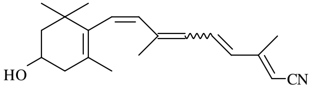
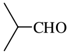
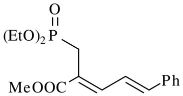
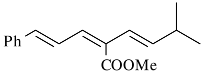
 R = $(MeO)_2C_6H_3CH_2$			164c
CH_3CHO			164d
			164e

TABLE 17. Polyene synthesis through HWE reaction

Aldehyde	Phosphonate	Product	Reference
 P = t-BuMe$_2$Si			165a
 P = t-BuMe$_2$Si; P′ = Et$_3$Si		 (Amphotericin fragment)	143
			86
			165b
			165c

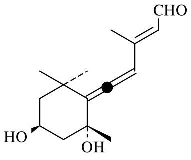
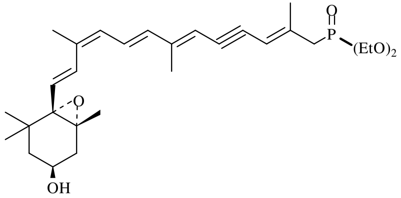
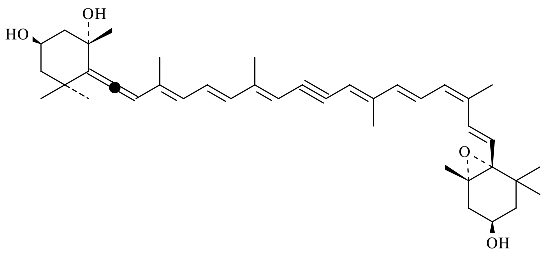
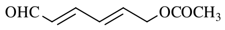
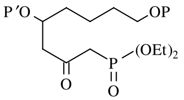
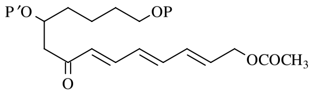
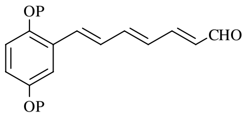
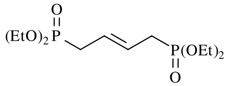
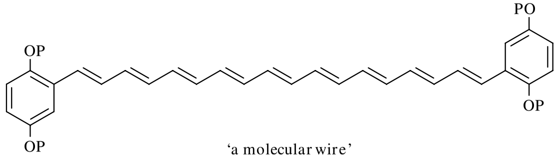
			165d
 P = PhCH$_2$; P′ = *t*-BuMe$_2$Si			165e
 P = *t*-BuMe$_2$Si		 ‘a molecular wire’	83f

TABLE 18. Intramolecular HWE reactions for macrocyclizations

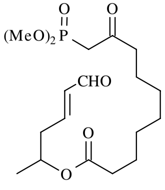
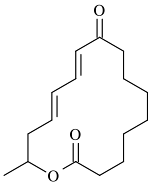
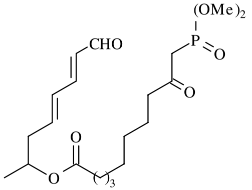
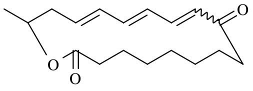
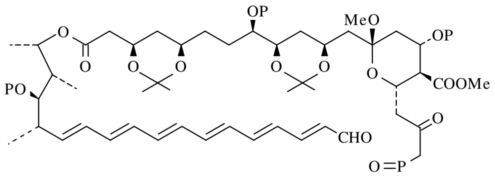
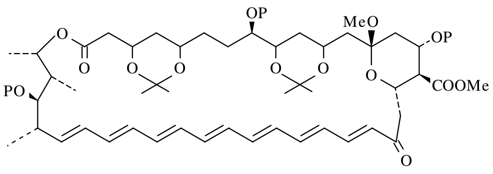
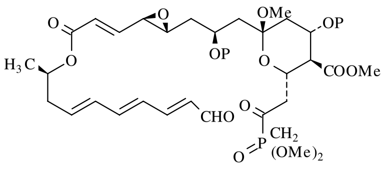
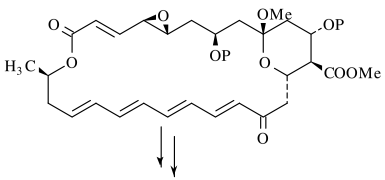
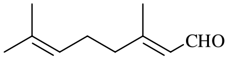
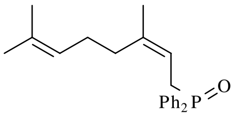
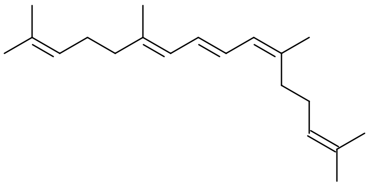
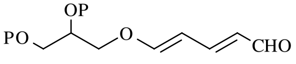
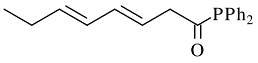
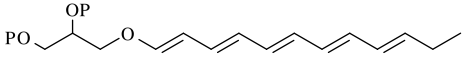
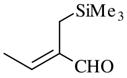
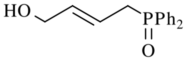
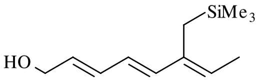
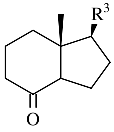
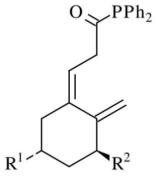
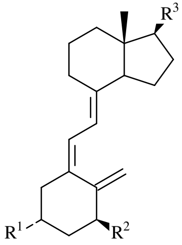
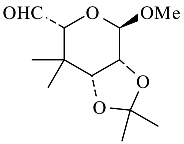
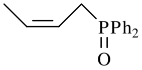
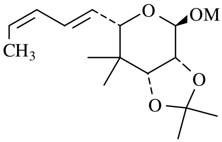
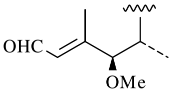
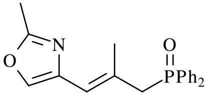
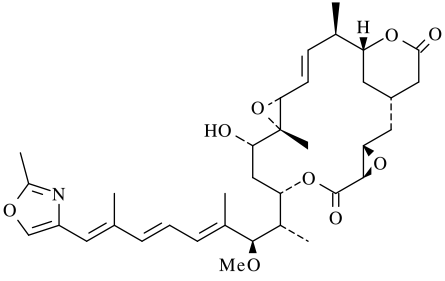
Substrate	Product	Reference
		166a
		166a
 P = *t*-BuMe$_2$Si		166b
 P = *t*-BuMe$_2$Si	 Pimarolide methylester	166c

TABLE 19. Dienes and polyenes through the Wittig–Horner reaction

Substrate	Phosphine oxide	Product	Reference
			171a
 $P = t\text{-}BuPh_2Si$			171b
			171c
			171d

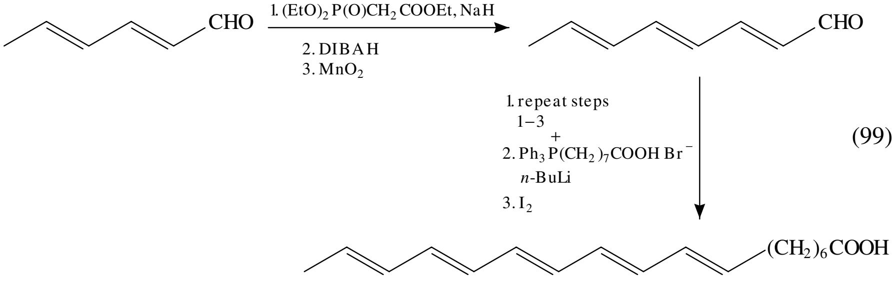
continued overleaf

TABLE 19. (*continued*)

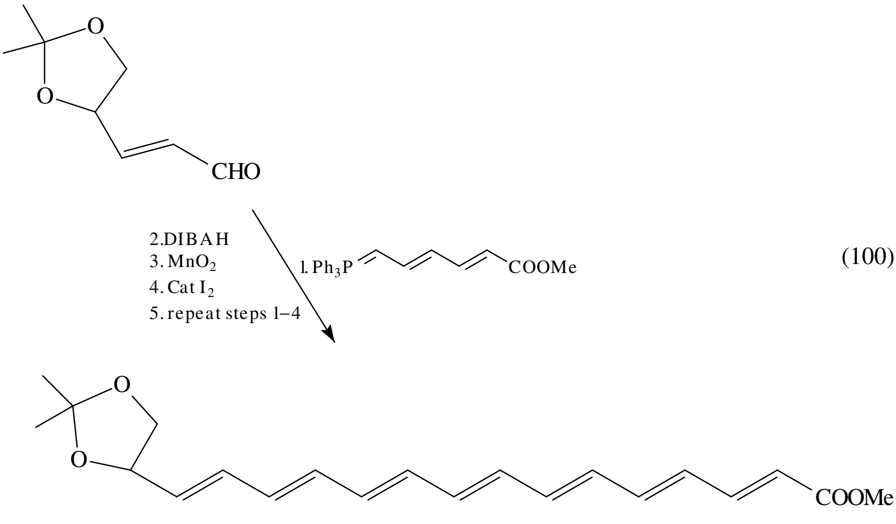
Substrate	Phosphine oxide	Product	Reference
			171e
		 Rhizoxin	171f

E. Iterative Wittig-type Reactions

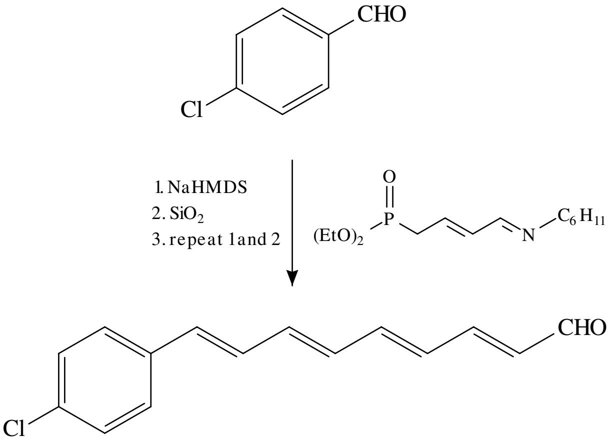
When the HWE reaction is performed with anylide having a functional group such as an ester or a masked aldehyde on the terminal carbon, the olefin generated can be set to perform another HWE reaction in an iterative fashion by generating the aldehyde group through simple chemical manipulations. This methodology is very popular for polyene synthesis. Various functionalized ylides for specific homologation of carbonyl compounds are available. For example, triethylphosphonoacetate is a two-carbon homologating agent. The ylide generated from this reagent reacts with aldehydes readily to give an *α*,*β*-unsaturated ester, which on reduction and controlled oxidation sequence generates *α*,*β*-unsaturated aldehyde which is ready for the HWE reaction again (equation 99)[172]. Similarly, a dienic ylide has been introduced for six-carbon homologation (equation 100)[173]. Polyenes having up to seven-conjugated double bonds have been prepared utilizing this iterative protocol[173c]. Four- and five-carbon bifunctional HWE ylides having an imine functionality have also been developed[174,175]. These synthons react with aldehydes and ketones in the presence of base, in Wittig fashion, and on work-up release aldehyde group (equation 101)[175]. The iterative HWE protocol has been used for the synthesis of the polyene portion of cyclophane-based trienic esters[176] and the natural product, roxaticin[177].



(99)



(100)

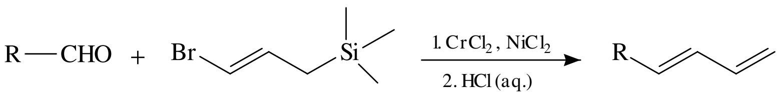


(101)

F. Peterson and Related Reactions

The Peterson olefination reaction involves the addition of an α-silyl substituted anion to an aldehyde or a ketone followed by the elimination of silylcarbinol either under acidic (*anti*-elimination) or basic (*syn*-elimination) conditions to furnish olefins[178]. Thus, Peterson olefination, just like Wittig and related reactions, is a method for regioselective conversion of a carbonyl compound to an olefin. Dienes and polyenes can be generated when the Peterson reaction is conducted using either an α,β-unsaturated carbonyl compound or unsaturated silyl derivatives as reaction partners (Table 20)[179].

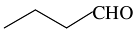
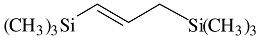
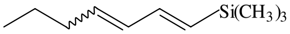
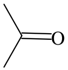
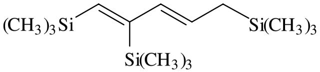
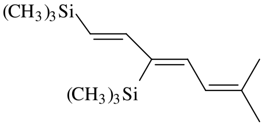
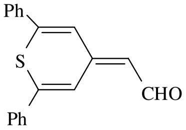
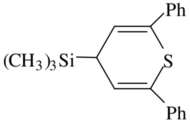
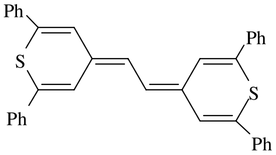
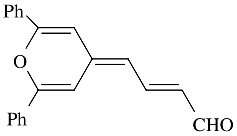
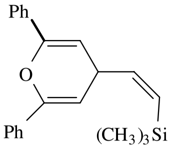
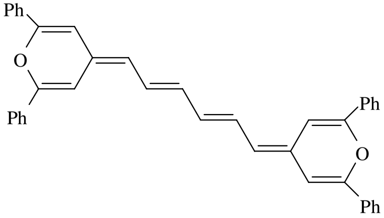
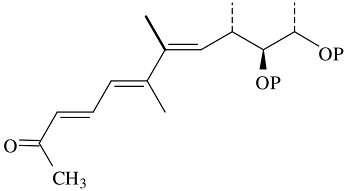
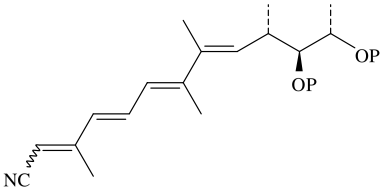
Several strategies closely related to the Peterson synthesis have been developed for diene and polyene generation. Angell, Parsons and coworkers reported a mild method for the diene installation on a carbonyl group using a γ-bromoallylsilane reagent in the presence of excess chromous chloride and a catalytic amount of nickel(II) chloride (equation 102)[180].

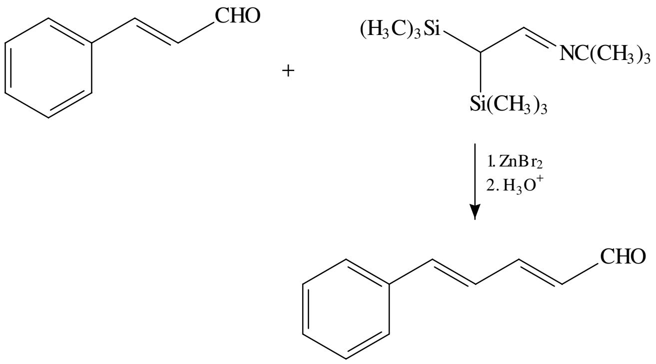


(102)

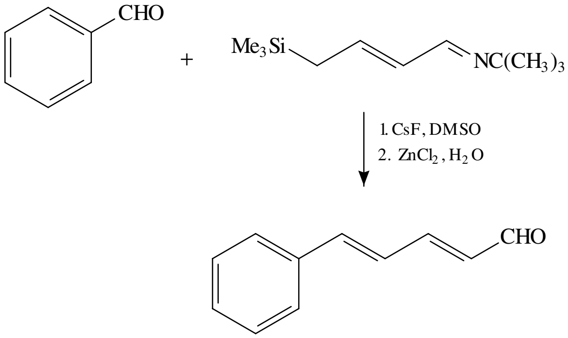
Bellassoued and Majidi introduced a two-carbon homologation reagent, α,α-bis(trimethylsilyl)-*N*-*tert*-butylacetaldimine, the anion of which reacts with an aldehyde in the presence of a catalytic amount of zinc bromide to afford two-carbon homologated α,β-unsaturated aldehyde (equation 103)[181]. This sequence in an iterative mode provides access to polyenes. A four-carbon homologation reagent has also been introduced by the same group[182]. Anion generated from trimethylsilylcrotanaldimine reacts with aldehydes smoothly in the presence of a catalytic amount of caesium fluoride to furnish a dienal (equation 104)[182]. Wang and coworkers have described the synthetic utility of γ-trimethylsilyl substituted allyl boranes for stereospecific generation of terminal 1,3-dienes (equation 105)[183]. Ring opening of epoxysilanes with alkenyl cuprate reagents in the presence of $BF_3 \cdot Et_2O$ affords β-hydroxysilanes which, on Peterson elimination, give stereospecific dienes[183].

TABLE 20. Dienes and polyenes through the Peterson reaction

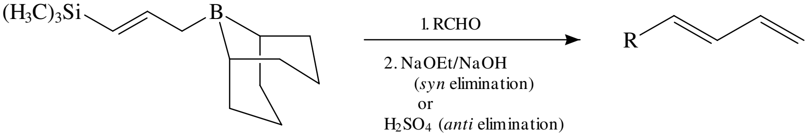
Substrate	Silane	Product	Reference
			179a
			179b
			179c
			179d
 P = *t*-BuMe$_2$Si	(CH$_3$)$_3$SiCH$_2$CN	 Calyculin fragment	179e



(103)



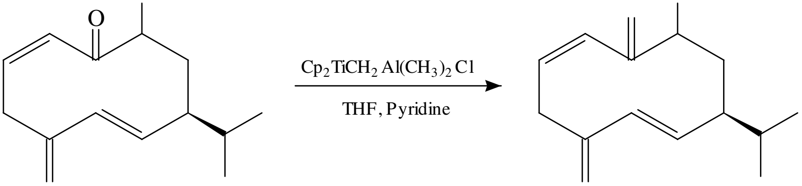
(104)



(105)

G. Organotitanium Reagents

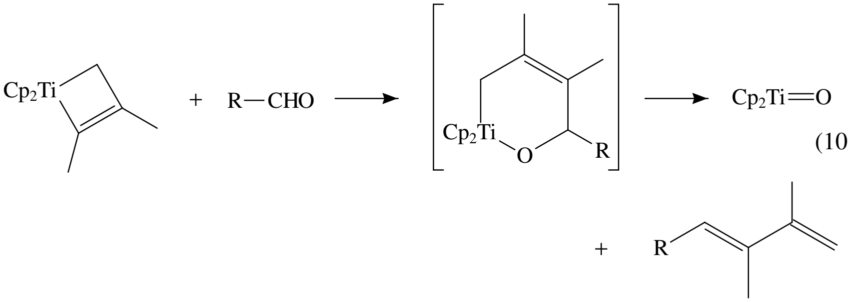
Tebbe's reagent, $Cp_2TiCH_2Al(CH_3)_2Cl$, converts carbonyl compounds to methylenes[184]. This reagent when applied to α,β-unsturated aldehydes and ketones generates dienes (equation 106)[184c]. Synthetic utility of the reagent for generation of dienes and polyenes is limited because of the difficulty in the preparation and incompatibility with other functional groups such as esters etc.



(106)

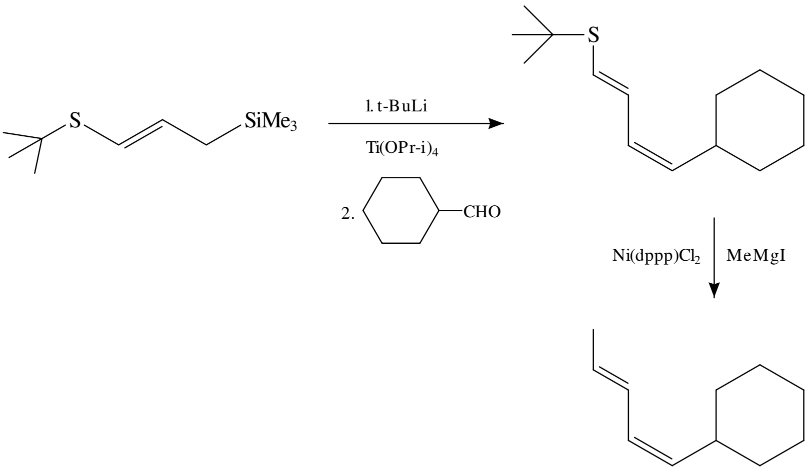
P = *t*-$BuMe_2Si$

Titanacyclobutenes, prepared readily from Tebbe reagent and alkynes, react with aldehydes and ketones to form insertion products which undergo facile retro-Diels-Alder reaction to afford substituted 1,3-dienes (equation 107)[185].



(107)

Organotitanium reagent generated from 1-*tert*-butylthio-3-trimethylsilyl-1-propene condenses with aldehydes to give 1-*tert*-butylthio-(E, Z)-1,3-alkadienes, via β-hydroxysilane intermediates[186]. The *tert*-butyl sulphide group on the diene can be replaced by an alkyl group by a cross-coupling reaction with a Grignard reagent in the presence of nickel catalyst (equation 108). The utility of this method was illustrated by an application to the synthesis of spilanthol, a naturally occurring insecticide[186].



(108)

VI. COUPLING REACTIONS

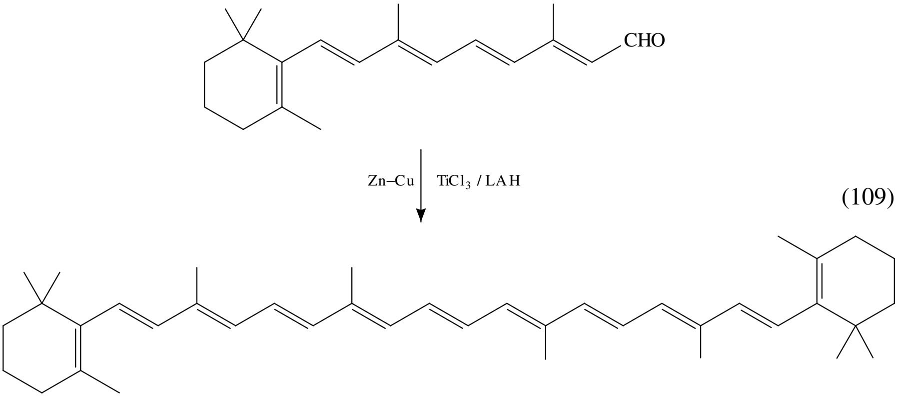
A. General Aspects

Though coupling reactions are among one of the earliest known C—C bond forming reactions, they have found only limited synthetic applications owing to lack of control and unsatisfactory yield. However, during the past two decades development in organometallic chemistry had a profound impact on revising the coupling process as an important synthetic reaction. Employing a variety of organometallic catalysts and intermediates it is now possible to carry out diverse coupling reactions in good yield, under mild conditions and with high stereocontrol.

B. Reductive Carbonyl Coupling Reactions

1. The McMurry coupling reaction

The McMurry reaction involving low-valent titanium species accomplishes coupling of two carbonyl groups to furnish alkenes[187]. The low-valent titanium species is generated either from $TiCl_3$/LAH[187a], $TiCl_3$/Mg[188] or $TiCl_4$/Zn–Cu[189]. When one or both carbonyl substrates carry one or more additional double bonds, dienes or polyenes result from this reaction (equation 109)[187a]. The McMurry coupling reaction is remarkably selective and a wide variety of functionalities are tolerated. This reaction can be carried out in both inter- and intramolecular modes to furnish a variety of dienes and polyenes. Synthesis of dienes and polyenes where McMurry coupling has been a key reaction is given in Table 21[190].



(109)

β - carotene

TABLE 21. Dienes and polyenes through McMurry coupling

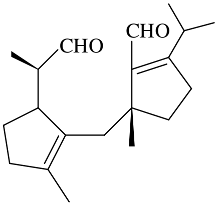
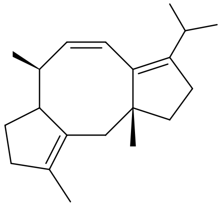
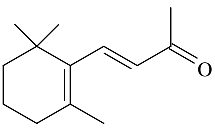
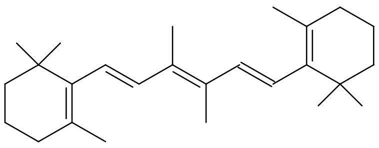
Substrate	Product	Reference
	 Fusicoccane type	190a
	 A minicarotene	190b

TABLE 21. (*continued*)

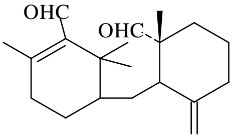
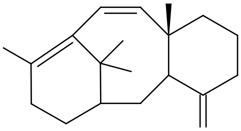
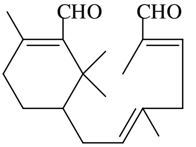
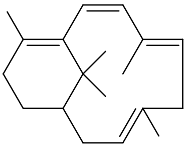
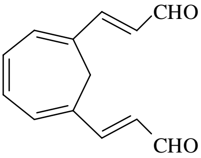
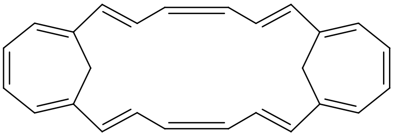
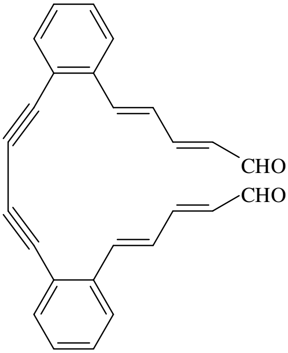
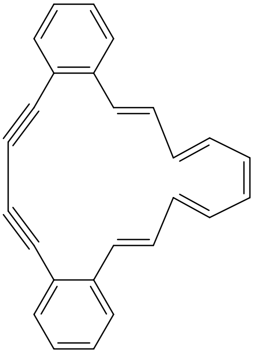
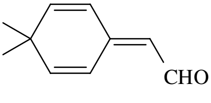
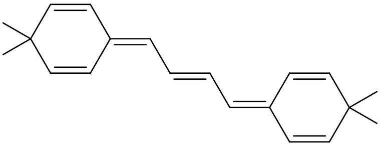
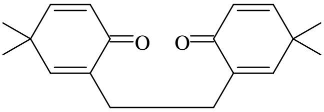
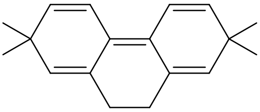
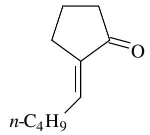
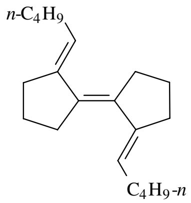
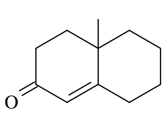
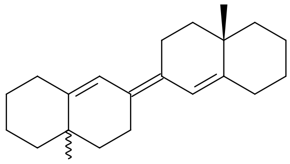
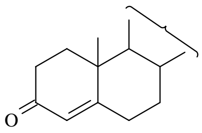
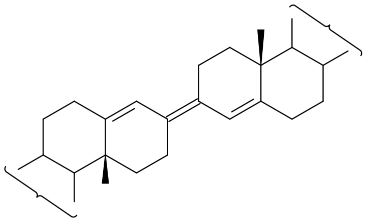
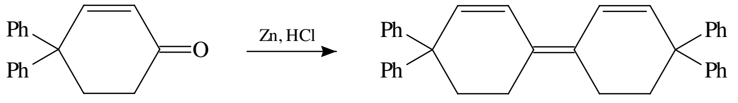
Substrate	Product	Reference
	 Taxane skeleton	190c
		190d
		190e
		190f
		190g
		190h

TABLE 22. Polyenes through reductive coupling with zinc

Substrate	Product	Reference
		193a
		193b
 Chlost-4-ene-3-one		193b

2. Organozinc intermediates

α,β-Unsaturated carbonyl compounds undergo a reductive coupling reaction to generate trienes on the surface of the reactive zinc metal (equation 110)[191]. Zn–HCl[191], Zn–Hg–HCl[192], Zn–TMSCl or Zn–1,2-bis(chlorodimethylsilyl)ethane[193] have been employed for carrying out this reaction (Table 22)[193]. When Zn–HCl is employed, coupled products as well as Clemmensen reduction products are formed.



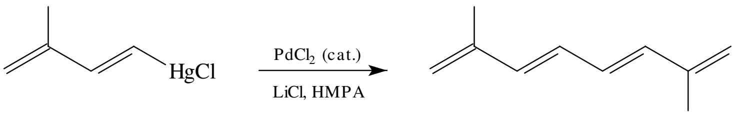
(110)

C. Homo-coupling Reactions

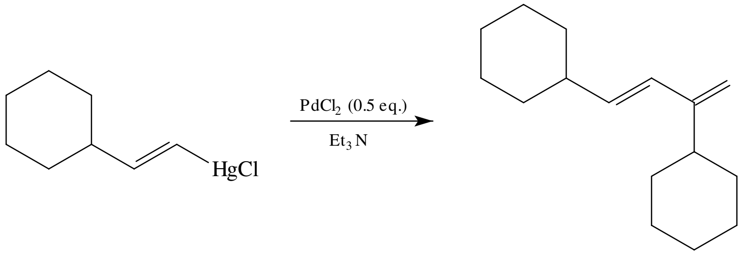
1. Organopalladium intermediates

1,3-Dienes can be obtained by direct coupling of alkenes with palladium acetate[194]. However, this reaction is seldom applied as a synthetic procedure, since the yields are low and side products due to oxidation of the double bond also contaminate the reaction.

Homo-coupling of vinylic mercurials occurs readily under palladium[195] or rhodium[196] catalysis, but with the stoichoimetric amount of a reagent (equation 111)[195]. Divinylpalladium intermediates may be involved in this reaction. This reaction is also of limited synthetic scope since organomercurials are usually prepared via vinylboranes, which themeselves are known to undergo coupling under palladium catalysis. Moreover, a stoichiometric amount of palladium has to be used to effect these reactions. However, surprisingly, when the reaction of trans-2-cyclohexylethenylmercuric chloride was carried out with 0.5 equivalent of palladium chloride, an unsymmetrical 'head-to-tail' coupling took place (equation 112)[197].

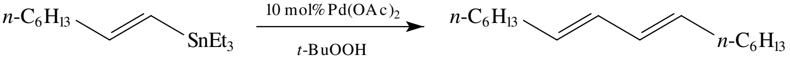


(111)

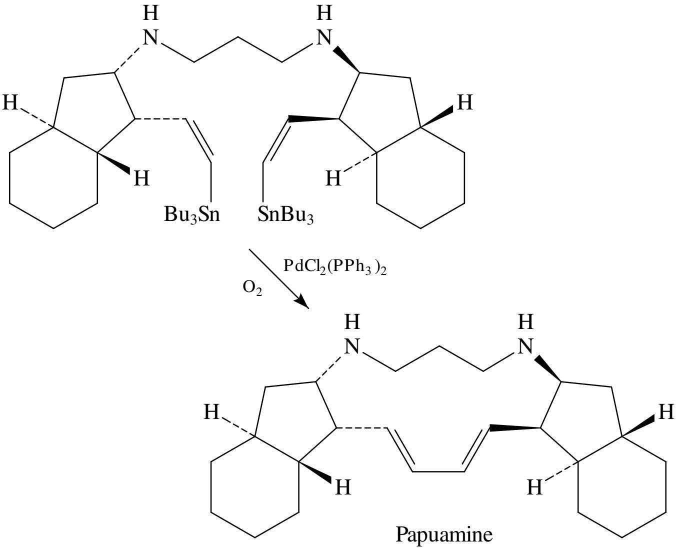


(112)

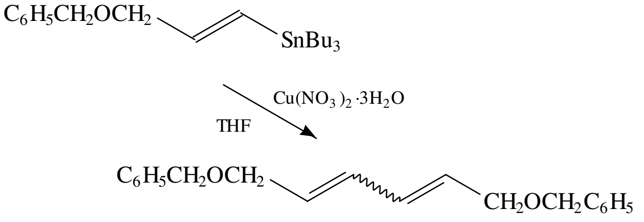
Vinyl stannanes also undergo oxidative homo-coupling under transition metal catalysis to result in dienes (equation 113)[198]. An intramolecular version of this method was employed for the macrocyclization-coupling reaction leading to the synthesis of papuamine (equation 114)[199]. Homo-coupling of vinylstannanes also takes place readily under the mediation of copper(II) nitrate to result in dienes in moderate to good yields (equation 115)[200]. This reaction is analogous to copper-mediated dimerization of terminal alkynes[201].



(113)



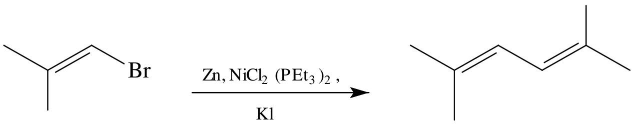
(114)



(115)

2. Organonickel intermediates

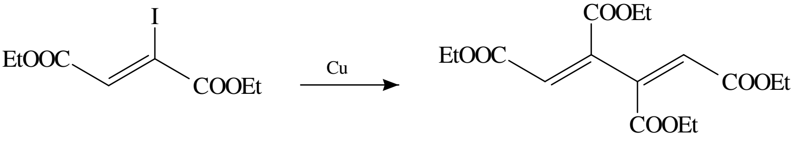
Direct homo-coupling of vinyl halides is a simple way of generating 1,3-dienes. This transformation can be achieved employing various transition metal catalysts such as nickel(0) reagent in the presence of phosphine ligand[202] or a nickel(0) reagent in the presence of potassium iodide and thiourea (equation 116)[203].



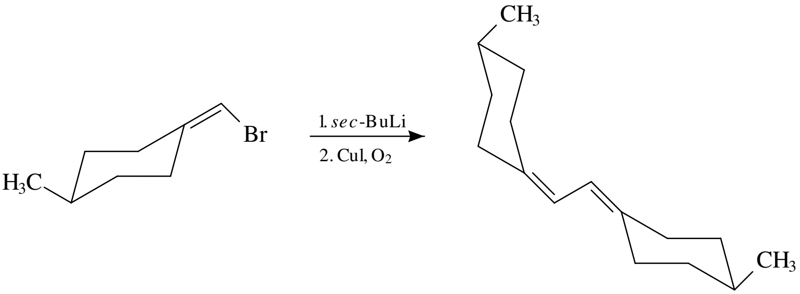
(116)

3. Organocopper intermediates

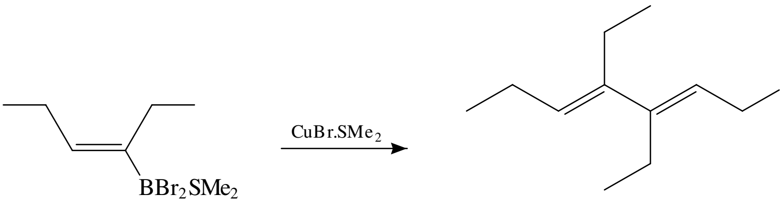
Vinyl halides, particularly vinyl iodides and bromides, dimerize readily in the presence of activated copper (equation 117)[204]. This reaction is analogous to classical Ullmann biphenyl synthesis. A general method for self-coupling of vinyl halides consists of conversion to the corresponding lithium divinyl cuprate followed by heating[205] or treatment with oxygen[206] (equation 118). Vinyl boranes and vinylzirconium derivatives in the presence of copper reagents undergo stereospecific dimerization to furnish (*E*,*E*)-1,3-butadiene or (*Z*,*Z*)-1,3-butadiene depending on the stereochemistry of the vinyl metal intermediate (equation 119)[207]. Alkenyl cuprates prepared by hydrocupration of terminal alkynes decompose to give (*E*,*E*)-1,3-dienes in good yields (equation 120)[201].



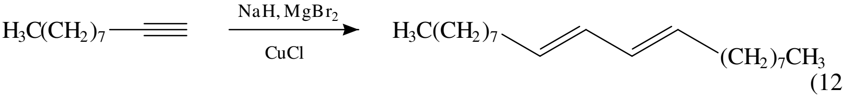
(117)



(118)



(119)

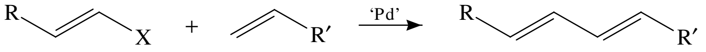


(120)

D. Cross-coupling Reactions

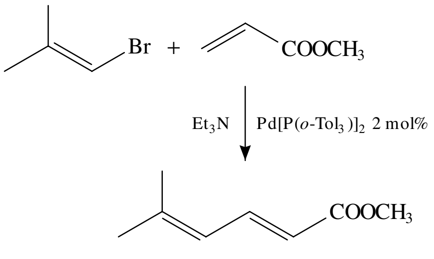
1. The Heck reaction

a. Alkene–alkene coupling. The palladium(0) catalysed arylation or alkenylation of alkenes is known as the Heck reaction[21,208] (equation 121) and has found extensive applications in synthesis (Table 23). Several variations of the Heck reaction have also been reported.



(121)

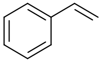
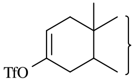
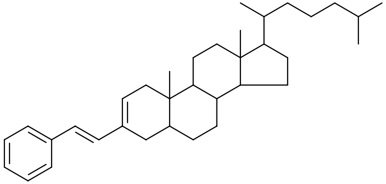
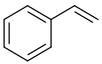
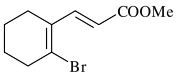
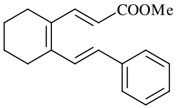
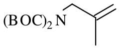
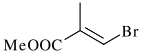
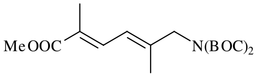
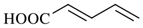
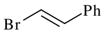
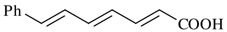
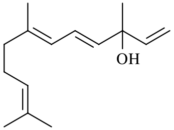
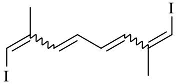
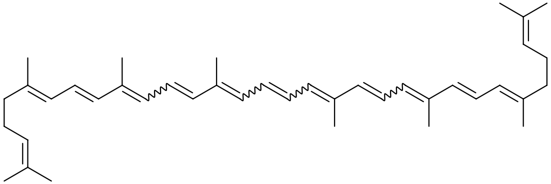
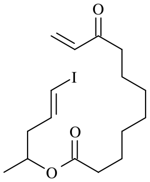
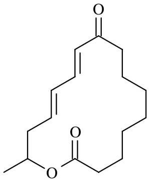
The reaction involves insertion of Pd(0) species in vinyl halides, generating reactive species which undergo *cis*-addition to alkenes to form a new carbon–carbon bond; subsequent *syn* elimination of the palladium species generates the diene. The regiochemistry of the addition of the organopalladium intermediate to the alkene appears to be sterically controlled, with the organic group acting as the largest part of the reagent and therefore adding to the least substituted carbon of the double bond. If an electron-withdrawing group is present on one of the carbons of the alkene, then the vinylic group adds exclusively to the other carbon (equation 122). A Heck reaction is generally conducted in aqueous acetonitrile[210] since water is found to accelerate the reaction. In many cases the reaction is also accelerated by the presence of silver(I)[211] or thallium(I) salts[212]. Recent reports indicate that Heck reactions can be carried out at room temperature either employing high pressure[213] or phase transfer catalysis[214].

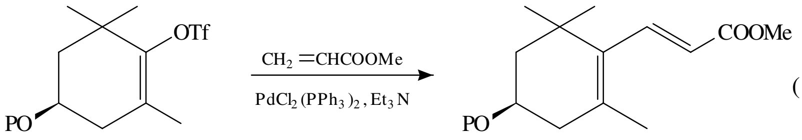


(122)

Alkenyl trifluoromethanesulphonates (enol triflates) undergo Heck coupling with alkenes efficiently (equation 123)[209a,215]. This reaction is a useful variation of the use of vinyl halides not only because they are easy to prepare from the corresponding carbonyl compounds, but also because yields are good, and the stereochemistry of the triflate is largely maintained.

TABLE 23. Dienes and polyenes through the Heck reaction

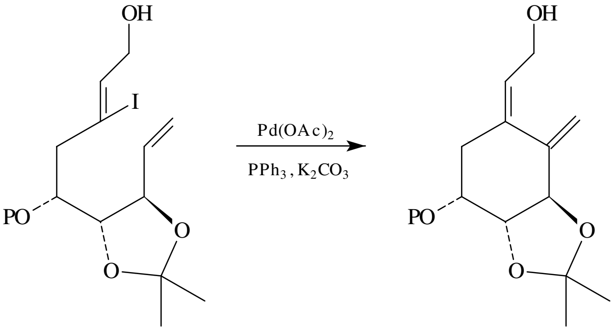
Substrate-1	Substrate-2	Product	Reference
			209a
			209b
			209c
			209d
			209e
			209f



(123)

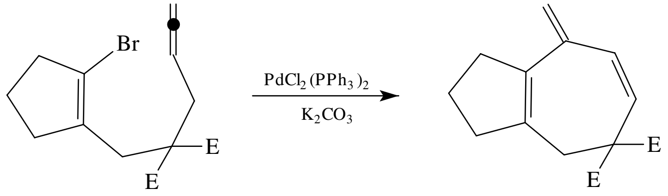
P = *t*-BuMe$_2$Si

Suitably positioned vinyl halide can undergo Heck-type intramolecular coupling to generate dienes (equations 124 and 125)[216,217]. When one of the reacting partners in the Heck reaction is a diene, trienes are obtained (equation 126)[218]. Heck coupling of allylic alcohols and alkenyl iodides has been employed for the synthesis of vitamin A and related compounds (equation 127)[219,220]. A similar double Heck reaction on a C_{10}-diiodide with a C_{15}-allylic alcohol leads to *β*-carotene as a mixture of isomers (equation 128)[209e].



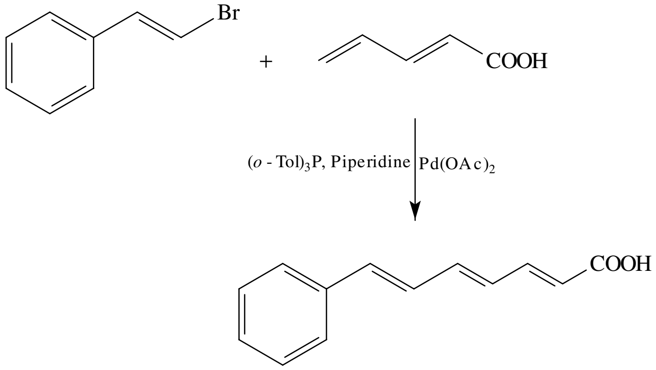
(124)

P = MeOCH$_2$

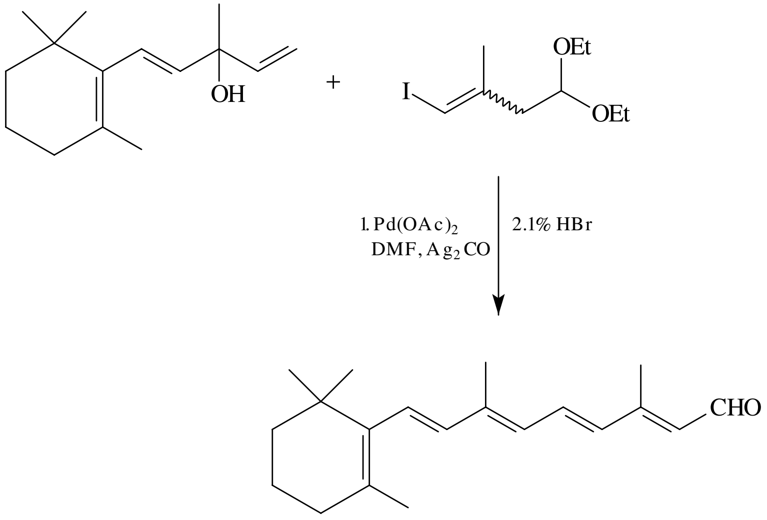


(125)

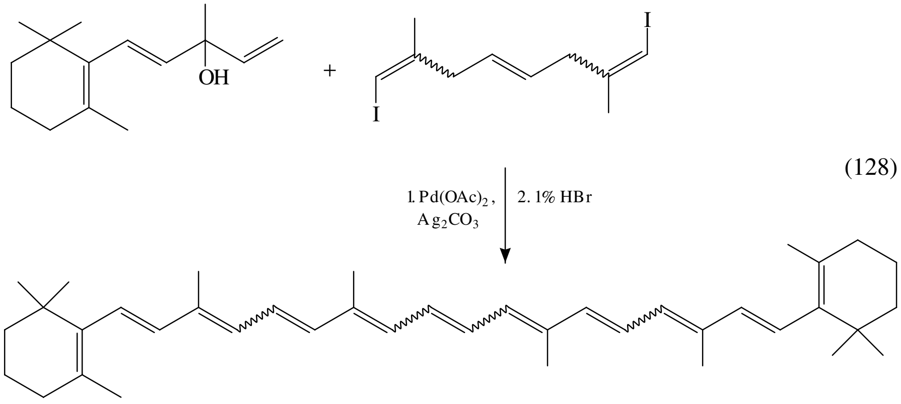
E = COOEt



(126)

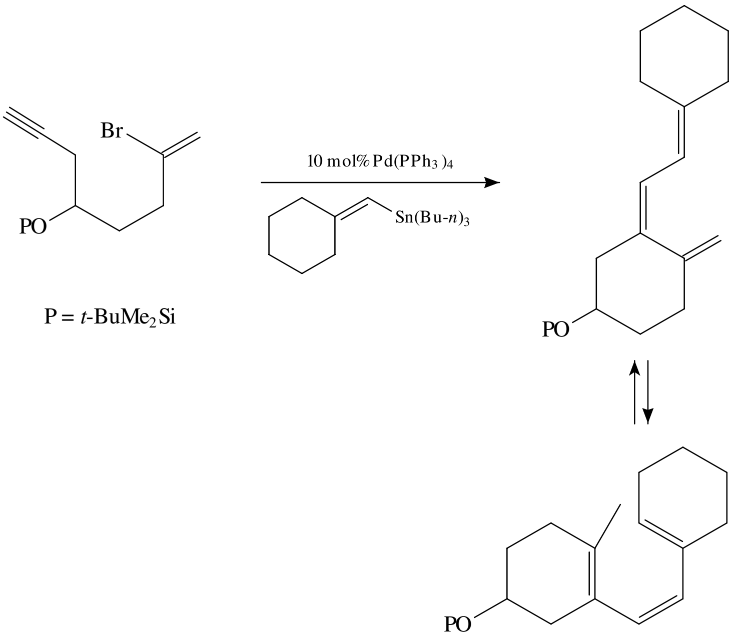


(127)

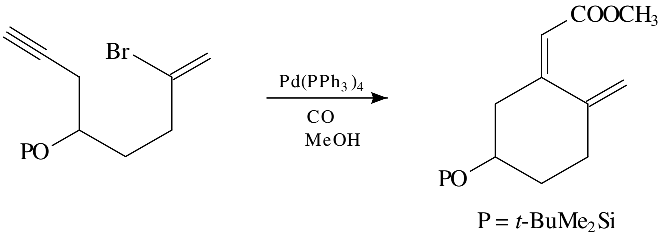


(128)

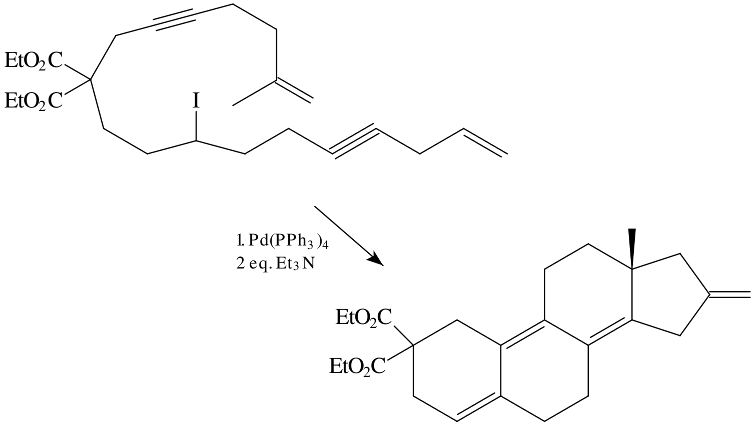
b. Alkene–alkyne reductive coupling. Intramolecular Heck coupling involving appropriately positioned alkenyl halide and an alkyne leads to a vinylpalladium intermediate which reacts with nucleophiles readily to furnish cyclic products[221]. This strategy was applied by Nuss and coworkers for the synthesis of triene unit of vitamin D_3 (equation 129)[222]. Alternatively, organopalladium intermediates can be carbometallated to yield diene ester, which is a suitable intermediate for vitamin D_3 synthesis (equation 130)[222]. Alkenyl palladium intermediates generated by intramolecular addition of haloalkane to a triple bond may also be captured by alkenes to form polycyclic compounds. An elegant example of intramolecular cascade cyclization is the synthesis of steroidal polyene generated from an acyclic precursor (equation 131)[223]. Two more examples of palladium-mediated cascade cyclizations and subsequent pericyclic reactions leading to the formation of polycyclic diene products are given in equations 132[224] and 133[225].


Br
PO
P = t-BuMe2Si
10 mol% Pd(PPh3)4
Sn(Bu-n)3
PO
PO

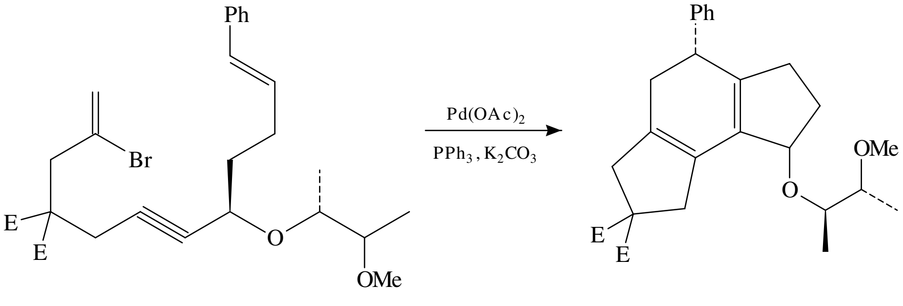
(129)


Br
PO
Pd(PPh3)4
CO
MeOH
COOCH3
PO
P = t-BuMe2Si

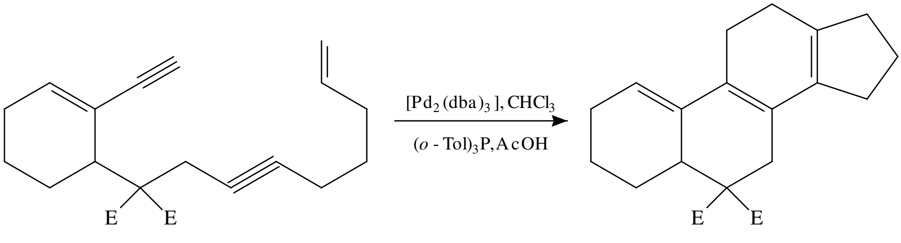
(130)


EtO2C
EtO2C
I
1. Pd(PPh3)4
2 eq. Et3N
EtO2C
EtO2C

(131)

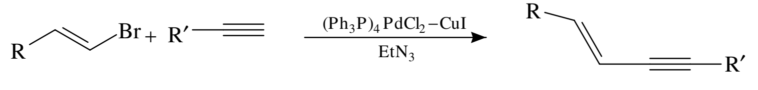


(132)

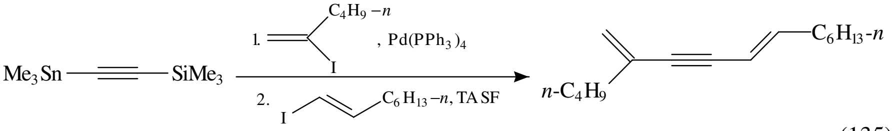


(133)

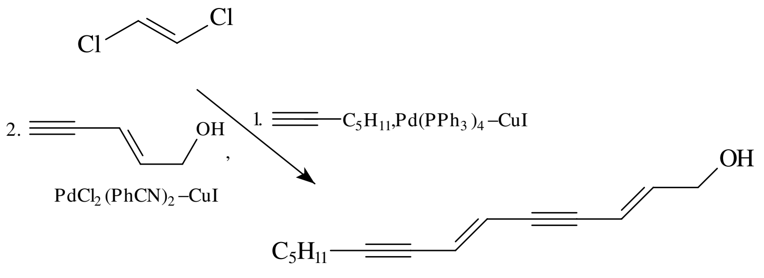
c. Alkene–alkyne oxidative coupling. Enynes and enediynes are important structural fragments present in several natural products, especially in enediyne antibiotics^{226}. Enynes can be prepared stereospecifically by coupling of alkynes with alkenyl halides in the presence of catalytic amount of palladium complex and copper(I) salt (equation 134)^{227,228,232}. Several alkynyl derivatives such as alkynylmagnesium bromides^{229}, alkynylzinc chloride^{230}, alkynylsilanes^{231} and alkynylstannanes (discussed under the Stille reaction) participate in this reaction effectively. Palladium-catalysed one-pot sequential cross-coupling of trimethylstannyl(trimethylsilyl)ethyne, first with one alkenyl iodide and then with another alkenyl iodide in the presence of newly added *tris*(diethylamino)sulphonium trimethyldifluorosilicate (TASF), affords conjugated dienynes (equation 135)^{231}. When either *E*- or *Z*-1,2-dihaloalkenes are used as substrates, enediynes result from the reaction (equation 136)^{233}. A few examples from recent literature on the synthesis of some enynes and enediynes are presented in Table 24^{234}.



(134)



(135)

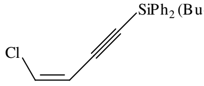
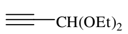
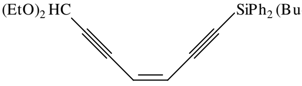
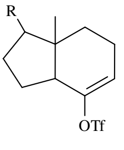
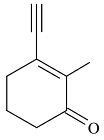
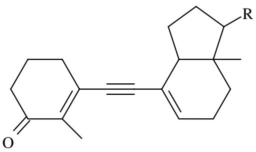
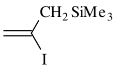
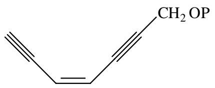
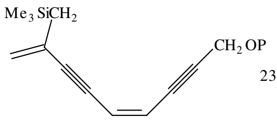
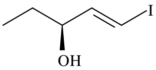
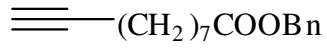
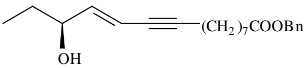


(136)

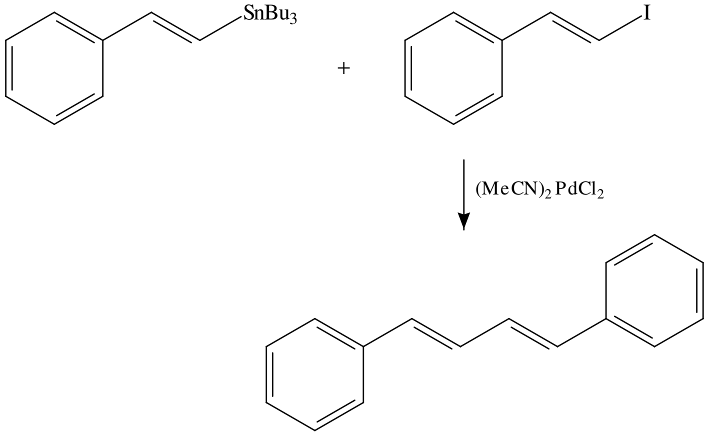
2. Stille coupling

a. Alkene–alkene coupling. The cross-coupling reaction of alkenyltin reagents with alkenyl electrophiles catalysed by palladium complexes to generate dienes of high stereoselectivity is known as Stille coupling (equation 137)[235]. When leaving group on the alkenyl electrophile is iodide (or iodonium salt)[236], triflate or a mesylate[237], the reaction works at room temperature, whereas with vinyl bromides, heating up to 100 °C is required. Vinylstannanes can be prepared by a variety of methods such as transmetallation of vinyllithium[238], vinylaluminium[239], vinylcuprate[240a] or reaction of vinyl halides with a tin cuprate[240b]. They can also be prepared by the stereospecific addition of a tin–metal bond across a carbon–carbon triple bond[241,242]. Palladium catalysts such as $Pd(PPh_3)_4$, $PdCl_2(MeCN)_2$, $PdCl_2(PPh_3)_2$ and $Pd_2(dba)_3$ are commonly employed. However, the presence of a palladium catalyst for this coupling is not always necessary. Piers and

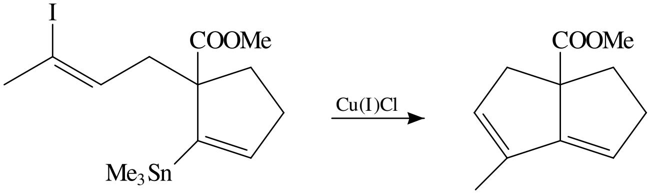
TABLE 24. Enynes through alkyne–alkene coupling

Alkene component	Alkyne component	Enediyne/dieneyne/eneyne	Reference
			234a
			234b
	 P = THP		234c
			233

Wong reported that stoichiometric amounts of copper(I) chloride alone can promote the intramolecular Stille coupling (equation 138)[243]. In fact, copper(I)-mediated reaction was cleaner and faster compared with that catalysed by Pd(0) species. Selected examples of intermolecular Stille coupling reactions leading to dienes (Table 25)[236a,242b,244], polyenes (Table 26)[245] and macrocyclizations (Table 27)[246] are given in the respective tables.

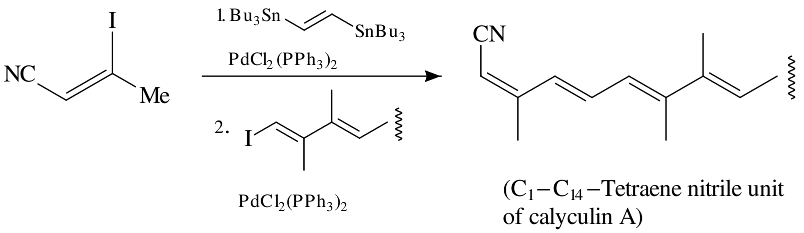


(137)



(138)

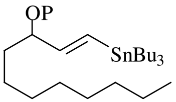
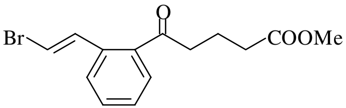
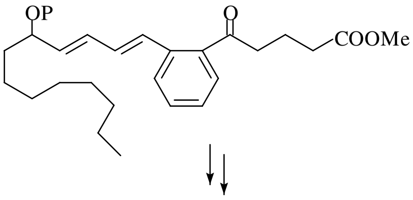
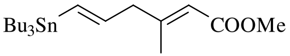
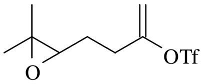
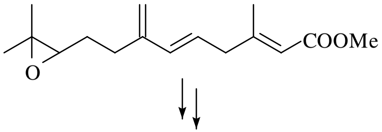
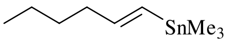
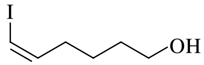
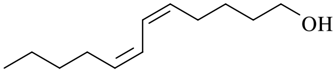
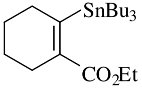
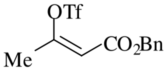
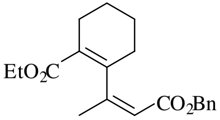
trans-1,2-Bis(tri-*n*-butylstannyl)ethylene, prepared from *trans*-dichloroethylene in a two-step process via tri-*n*-butylchloroethenylstannane[247], is a versatile substrate for double Stille coupling in a sequential manner. Barrett employed it to generate the required dienyl stannane in the first step and later employed it for further coupling with another alkenyl iodide during the synthesis of tetraene portion of calyculin A (equation 139)[248]. Extraordinary versatility of Stille coupling was demonstrated by Nicolaou and coworkers during the total synthesis of rapamycin. A double Stille coupling was employed for the macrocycle construction and the formation of a triene unit in the total synthesis of this polyene macrolide antibiotic (equation 140)[249].



(139)

(C_1–C_{14}–Tetraene nitrile unit of calyculin A)

TABLE 25. Synthesis of dienes through a Stille coupling reaction

Stannane	Vinyl halide/triflate	Product	Reference
 P = THP		 (benzoleukotriene B_3)	244a
		 (C_{16} Juvenile hormone)	244b
			236a
			244c

continued overleaf

TABLE 25. (*continued*)

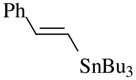
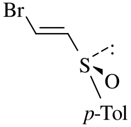
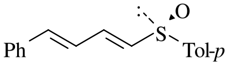
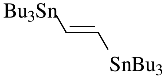
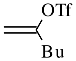
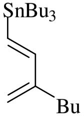
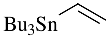
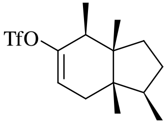
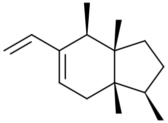
Stannane	Vinylhalide/triflate	Product	Reference
			244d
			242b
			244e

TABLE 26. Synthesis of polyenes through Stille coupling

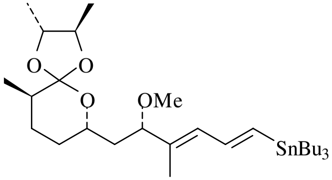
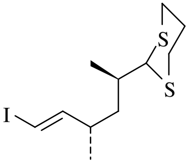
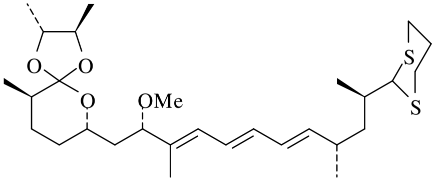
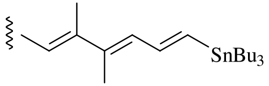
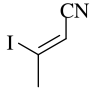
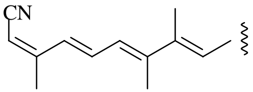
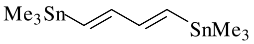
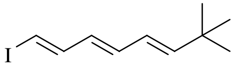
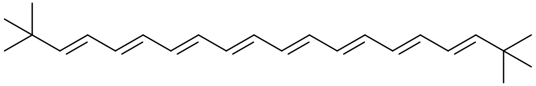
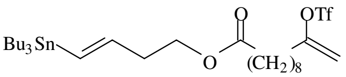
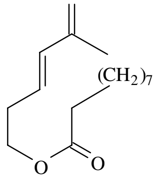
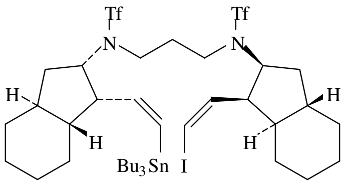
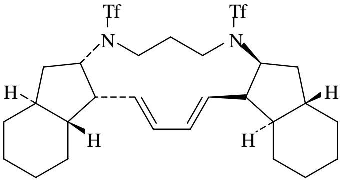
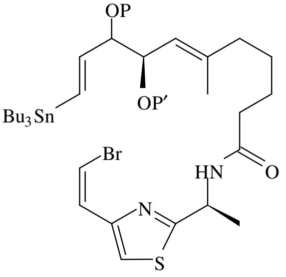
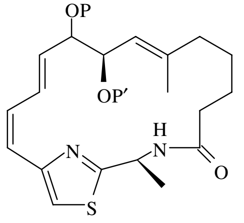
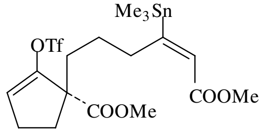
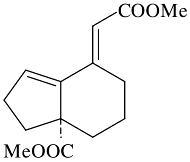
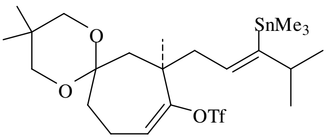
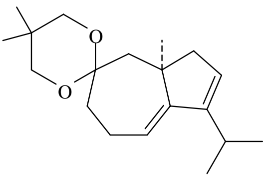
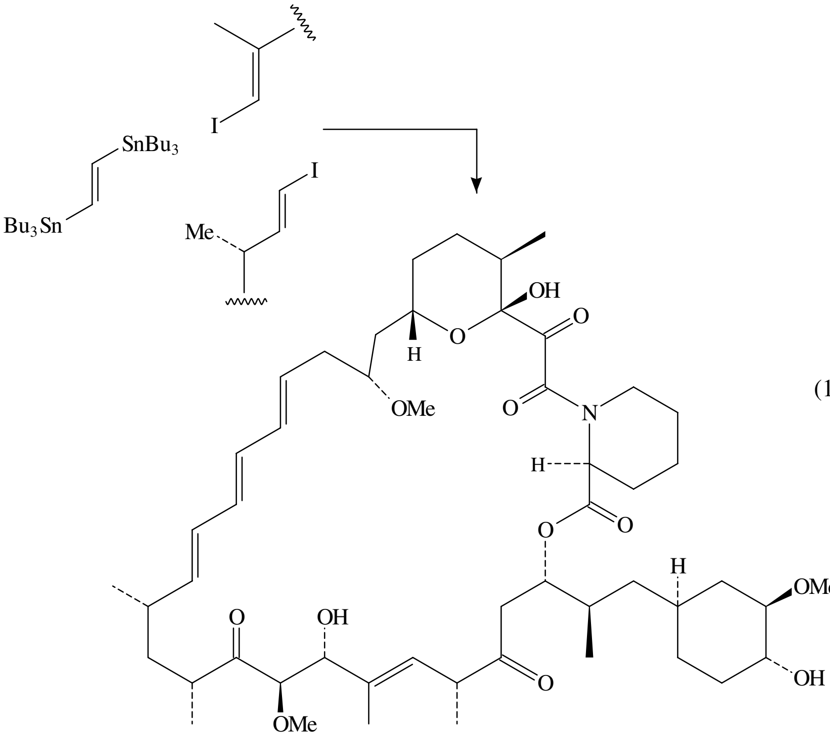
Stannane	Alkenyl iodide	Product	Reference
		 (rapamycin fragment)	245a
		 (calyculin A fragment)	245b
			245c

TABLE 27. Intramolecular cyclizations through Stille coupling

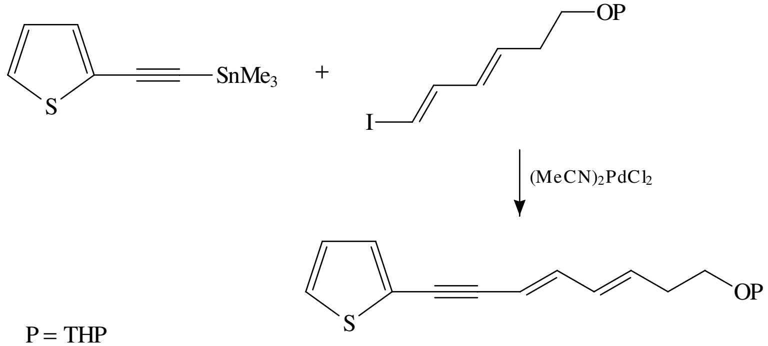
Substrate	Product	Reference
		246a
	 Papuamine	246b
	 P = t-BuMe$_2$Si; P′ = MeOCH$_2$	246c
		246d
		246e



(140)

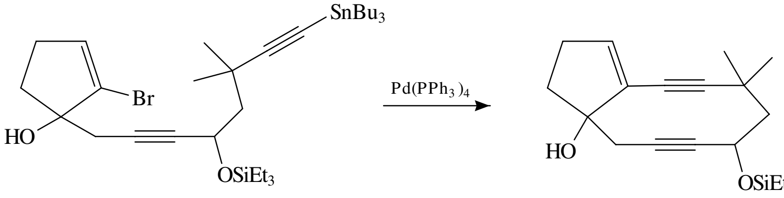
Rapamycin

b. Alkene–alkyne coupling. Alkynyl tin compounds couple with vinyl iodides or vinyl bromides under palladium catalysis to result in conjugated enynes stereospecifically[250]. This reaction has been employed for the enyne formation leading to the synthesis of a tetrahydropyranyl derivative of a natural insecticide, (3*E*,5*E*)-8-(2-thienyl)-3,5-octadien-7-yn-1-ol (equation 141)[250]. An intramolecular version of this reaction generates a 10-membered ring analogue of the chromophore of the antitumer antibiotic neocarzinostatin (equation 142)[251].



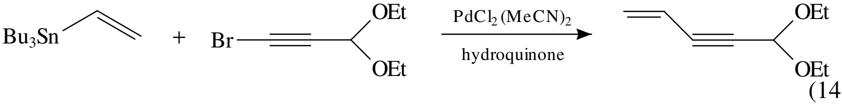
(141)

P = THP

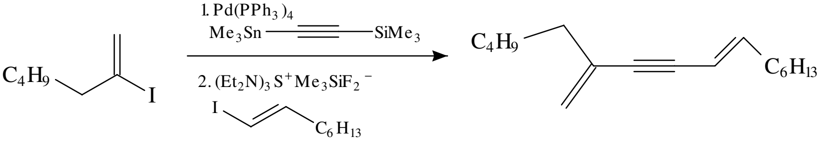


(142)

Bromoalkynes also couple with vinylstannanes readily to result in enynes. Synthesis of protected enynals via cross-coupling of vinylstannanes with 1-bromoalkynes in the presence of a catalytic amount of Pd(II) has been reported (equation 143)[252]. Hiyama and coworkers extended the Stille methodology for sequential three-component coupling of trimethylstannyl(trimethylsilyl)acetylene with a vinyl iodide in the first step and cross-coupling of the intermediate trimethylsilylethyne with another alkenyl iodide in the presence of tris(diethylamino)sulphonium trimethyldifluorosilicate in the second step to generate a dienyne (equation 144)[253]. Both steps occur under palladium catalysis, in one-pot, to result in stereodefined 1,5-dien-3-ynes.



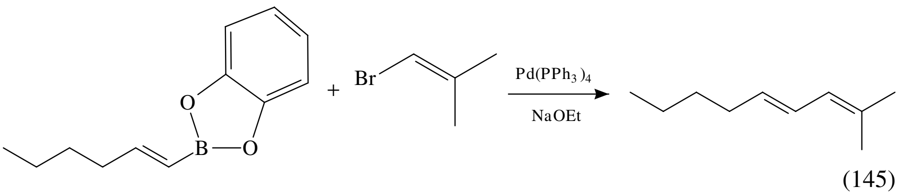
(143)



(144)

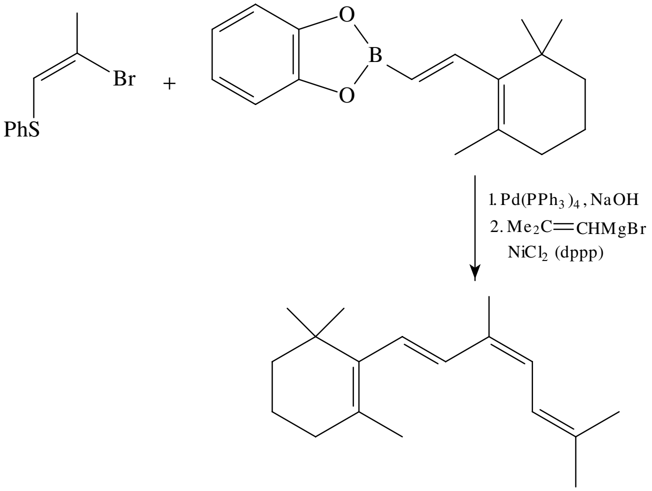
3. Suzuki coupling and related reactions

Coupling of 1-alkenyldiorganoboranes, prepared readily by hydroboration of terminal alkynes, with bromo- or iodo-alkenes in the presence of a catalytic amount of palladium(0) complex and a base, is known as Suzuki coupling (equation 145)[254]. Stereoselectivity in this reaction is very high and the yields are good. Stereochemistry of both the coupling partners, viz. organoborane and vinyl halide, are retained in the reaction. Since, both E–[255] and Z-vinylboranes[256] can be prepared stereoselectively from 1-alkynes, this coupling reaction is of immense synthetic value (Table 28)[257]. Vinylboranes can be prepared by *syn* addition of either catecholborane or disiamylborane across terminal alkynes. The presence of an equivalent of a base such as TlOH, Ag$_2$O or even Na$_2$CO$_3$ is a must for this reaction, since the base assists in the formation of organoborates, thereby increasing the acidity of the α-carbon atom[254a,258].



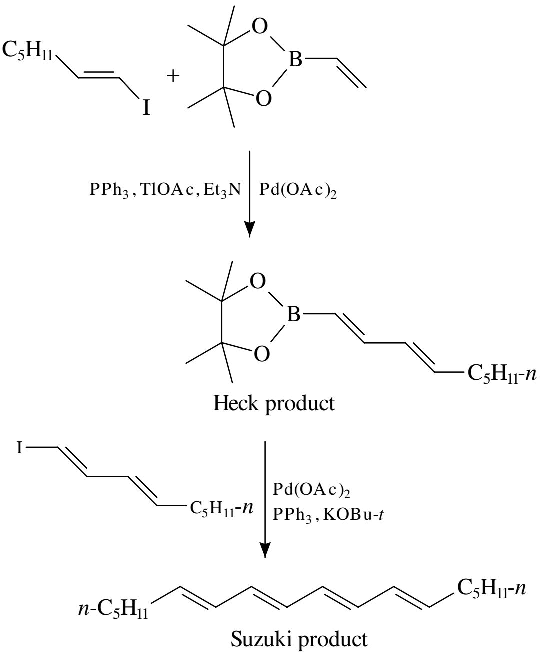
(145)

Stereo- and regioselective synthesis of trienes and tetraenes has been reported by palladium-catalysed coupling of (*E*)- or (*Z*)-1-alkenyl boronates with (*E*)- or (*Z*)-2-bromo-1-phenylthio-1-alkenes followed by treatment with a Grignard reagent in the presence of a nickel catalyst (equation 146)[259].



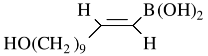
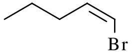
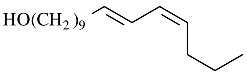
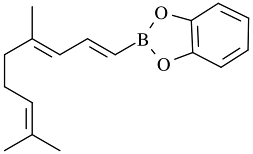
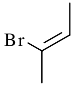
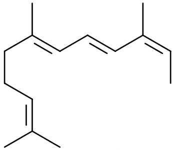
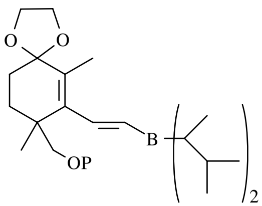
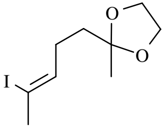
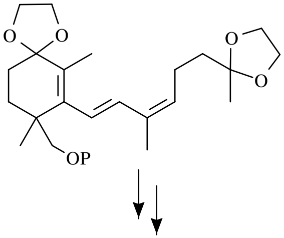
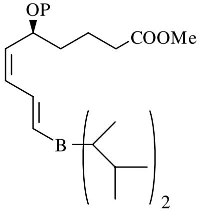
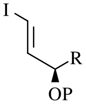
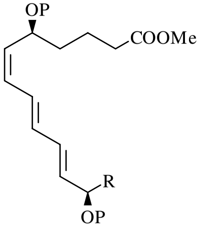
(146)

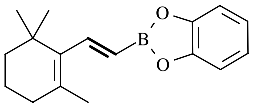
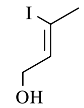
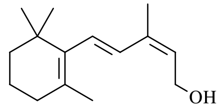
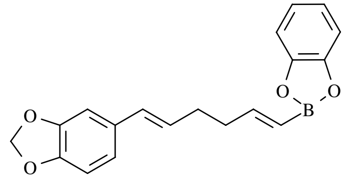
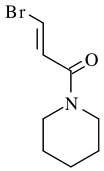
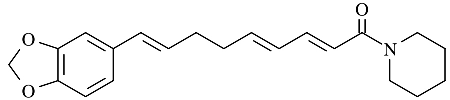
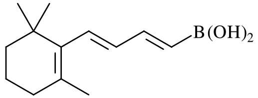
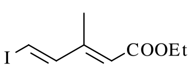
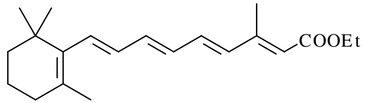
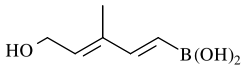
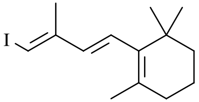
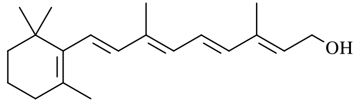
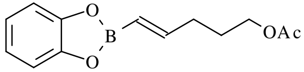
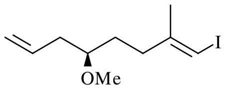
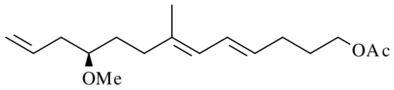
Stewart and Whiting have reported a useful application of sequential Heck and Suzuki coupling reactions of a vinylborane pinacol ester with palladium catalysis to generate a tetraene (equation 147)[260].



(147)

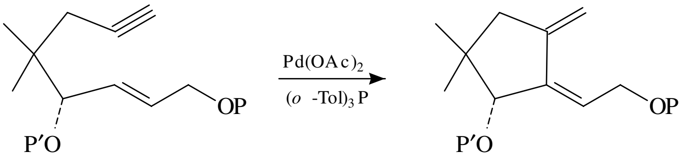
TABLE 28. Dienes and polyenes through Suzuki coupling

Substrate	Alkenyl halide	Product	Reference
		 Bombykol	257a
		 Allofarnesene	257b
	 P = PhCH$_2$	 Trisporol B	257c
	 P = TBDMS		257d

			257e
			257f
			257g
			257h
		 Curacin A intermediate	257i

4. Trost alkene–alkyne cyclizations

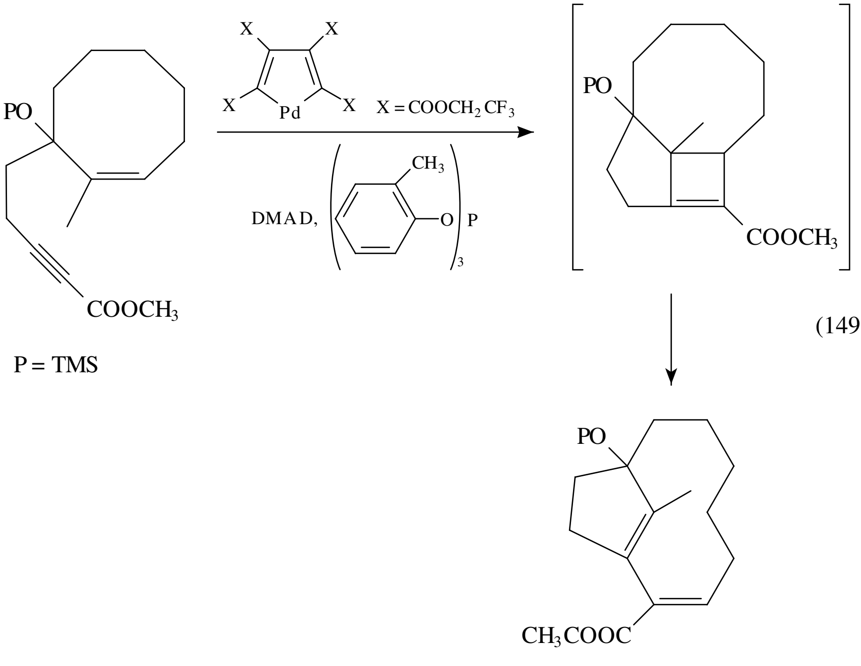
Trost and coworkers extended the synthetic utility of palladium-catalysed intramolecular reactions by finding that suitably positioned alkene–alkyne groups present in an acyclic molecule readily cyclize in the presence of acetic acid to result in cyclic 1,3-dienes[261]. The mechanism of this reaction is markedly different from that of the Heck reaction. The hydridopalladium intermediate, generated by oxidative addition of acetic acid to the Pd(0) catalyst, adds to the carbon–carbon triple bond regio- and stereoselectively to form an organopalladium intermediate. Palladium metal also coordinates with the alkenyl group. The next step is the formation of a carbon–carbon bond to result in the cyclic intermediate. Depending on the substrate, loss of a specific β-proton takes place with the regeneration of catalyst and release of the diene product. Thus, the overall process is a type of Alder-ene reaction (equation 148). Trost utilized the product shown in equation 148 for the synthesis of isolactarane-type sesquiterpenoid sterepolide[261b,262] and merulidial[263].



(148)

P = t-BuMe$_2$Si ; P′ = 4-MeOC$_6$H$_4$CH$_2$

Palladocyclopentadiene reagent promotes [2 + 2]-cycloaddition of suitably positioned enynes to form cyclobutenes which undergo symmetry allowed ring opening to form 1,3-dienes with a bridgehead double bond (equation 149)[264].

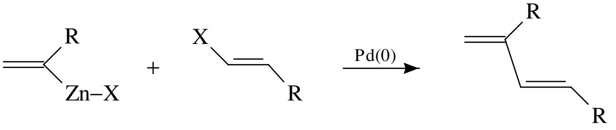


(149)

P = TMS

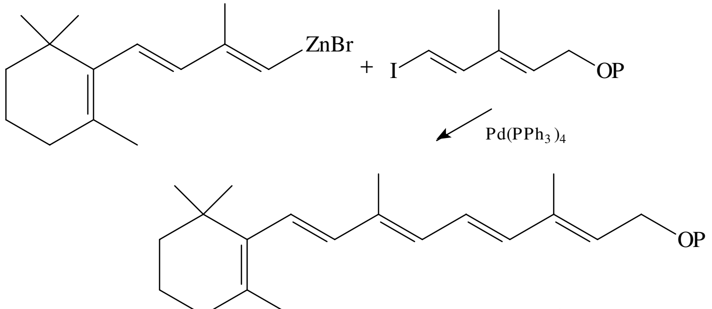
5. Alkenyl zinc intermediates

The alkenylzinc intermediates, prepared by transmetallation of vinyllithium derivatives with zinc halide, couple with alkenyl halides in the presence of a catalytic amount of a palladium reagent, in a process reminiscent of the Heck reaction, leading to dienes stereospecifically (equation 150)[265]. In fact, this type of coupling is among the best known methods for stereospecific generation of dienes. Following this method an efficient synthesis of a vitamin A derivative via C_{14}-alkenyl zinc coupling with C_6-vinyl iodide in the presence of a catalytic palladium(0) species has been described (equation 151)[266]. This method is also an effective way of coupling α-lithio enol ethers with alkenyl halides to furnish 2-alkoxy-1,3-dienes (equation 152)[267].



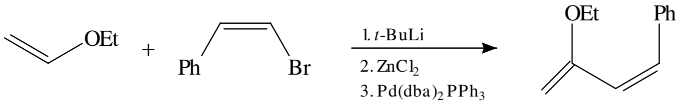
(150)

R = SEt, $SiMe_3$, OEt ; R′ = H, alkyl



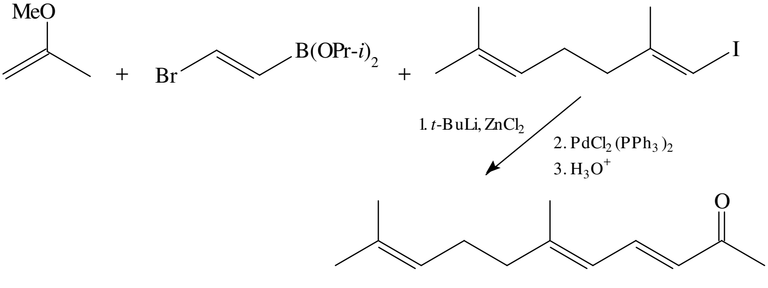
(151)

P = t-BuMe$_2$Si



(152)

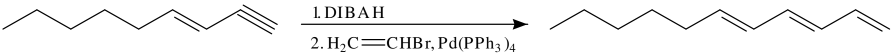
Suzuki and coworkers described a one-pot, stepwise, palladium-catalysed three-component stereospecific cross-coupling of (*E*)-(2-bromoethenyl)diisopropylboron, a vinyl ether and a vinyl iodide. The first coupling is with the organozinc species generated from the vinyl ether and is followed by coupling with vinyl halide to generate (*E*,*E*)-dienone (equation 153)[268].



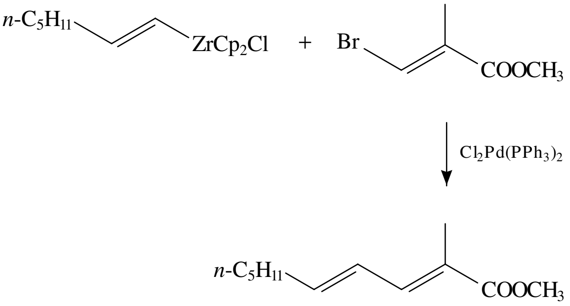
(153)

6. Alkenylalanes and alkenylzirconium intermediates

Similar to the reactions of alkenylboranes, alkenylalanes and alkenylzirconium intermediates undergo facile coupling with vinyl bromides or iodides in the presence of palladium(0) catalyst to generate dienes of high stereochemical purity (equations 154 and 155)[269]. Since alkenylalanes and alkenylzirconium species are prepared from alkynes, this reaction constitutes a method for generation of dienes from alkynes with alkenyl halides. The presence of a stoichiometric amount of zinc chloride in the reaction medium promotes the coupling process. The advantage of the alkenylzirconium method is that many sensitive functional groups such as carbonyl, ester or acetal present on the vinyl halide partner are tolerated.



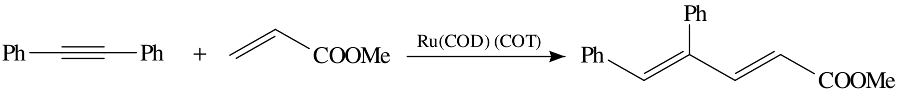
(154)



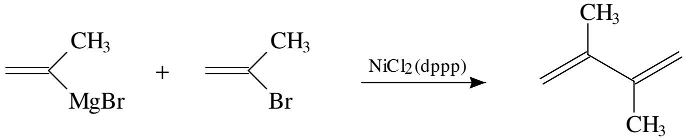
(155)

7. Ruthenium and nickel catalysed coupling reactions

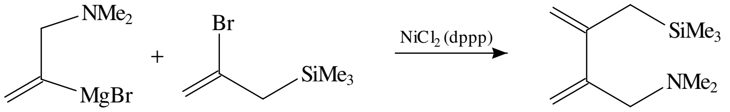
Acetylenic compounds couple with alkenes to furnish stereoselective dienes under ruthenium complex catalysis (equation 156)[270]. Direct coupling of vinyl Grignard reagents with vinyl halides to furnish dienes takes place in the presence of nickel catalysts such as $NiCl_2(PPh_3)_2$ and $NiCl_2(dppp)$ (equation 157)[271]. Even though regioselectivity and yields in the reaction are high, it is seldom applied in the synthesis since vinyl Grignard reagents do not tolerate many functional groups. Hosomi and coworkers used this method to prepare 2-dimethylaminomethyl-3-trimethylsilylmethyl-1,3-butadiene, a useful precursor for tandem Diels-Alder reaction (equation 158)[272]. Vinyl Grignard reagent reacts with alkenyl sulphides in the presence of a catalytic amount of $NiCl_2(dppe)$ to give dienes in good yields (equation 159)[273].



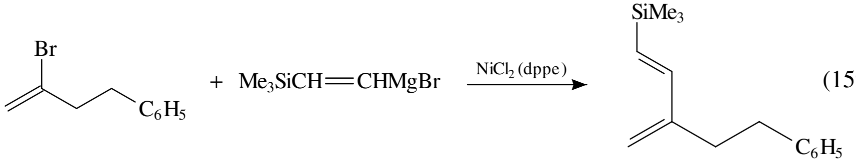
(156)



(157)



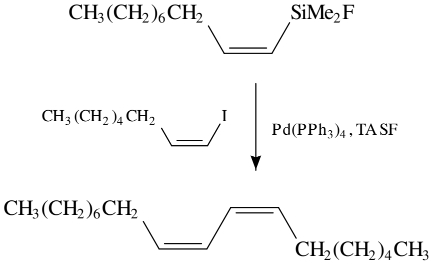
(158)



(159)

8. Alkenylsilanes

Alkenylfluorosilanes readily couple with alkenyl iodides in the presence of a palladium(0) catalyst and TASF to form dienes of high stereospecificity (equation 160)[274]. Since the alkenylsilane preparation and coupling reaction are conducted under neutral conditions, without the involvement of strong reducing agents, this coupling reaction has wide applicability.



(160)

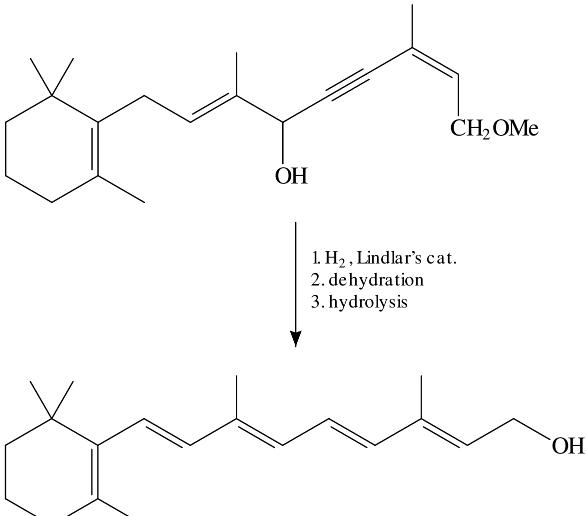
TASF : $(Me_2N)_3S(Me_3SiF_2)$

VII. FROM ALKYNES

A. Reduction of Enynes

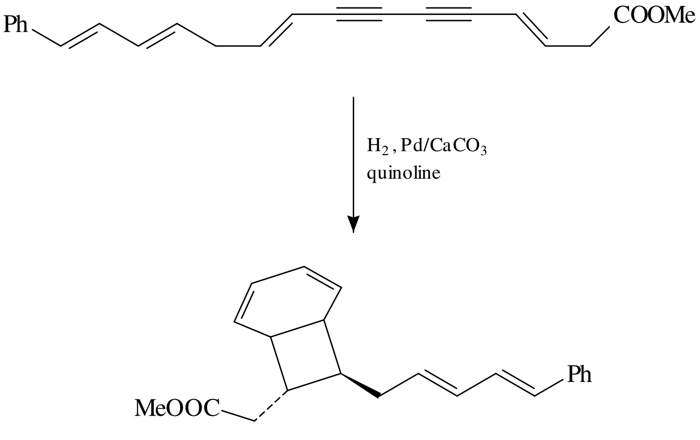
The reduction of conjugated acetylenic compounds to dienes and polyenes is a simple, straight forward method for their generation. A variety of compounds having conjugated or non-conjugated enyne functionality can be generated easily by making use of the acidity of the acetylenic hydrogen. Partial reduction of a carbon–carbon triple bond to a *Z*-double bond can be accomplished by selective hydrogenation[275]. Catalysts prepared from palladium are most commonly used, but additives such as quinoline, pyridine or ethylenediamine, which partially poison the catalyst, and adsorbent materials such as a polymer matrix, $CaCO_3$, $Pb(OAc)_2$, $BaSO_4$ and $SrCO_3$ have a profound effect on selectivity. Lindlar's catalyst (palladium deposited on $CaCO_3$–PbO) in the presence of quinoline is the generally used catalyst for the controlled hydrogenation of enynes to dienes[276]. An interlamellar montmorillonite–diphenylphosphinepalladium(II) complex for the partial hydrogenation of enynes to dienes has been developed as an alternative to the Lindlar catalyst[276c]. The advantage with this semihydrogenation procedure is that the reagents and reaction conditions tolerate a variety of reducible functional groups such as a carbon–carbon double bond, carbonyl, nitrile etc.

Industrial synthesis of vitamin A (Hoffman-La-Roche) goes through partial hydrogenation of an enyne (equation 161)[277]. A number of syntheses of pheromones, where the reduction of an enyne to a diene is the key step, have been devised. A few selected examples are given in Table 29[278]. During the total synthesis of endiandric acids, Nicolaou employed hydrogenation of a polyenyne intermediate with a Lindlar catalyst to generate an intermediate which underwent symmetry-allowed cyclizations to result in the natural product (equation 162)[279].



Vitamin A

(161)

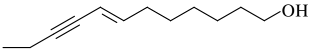
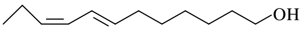
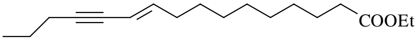
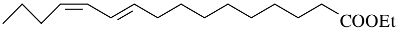
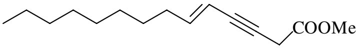
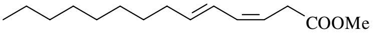


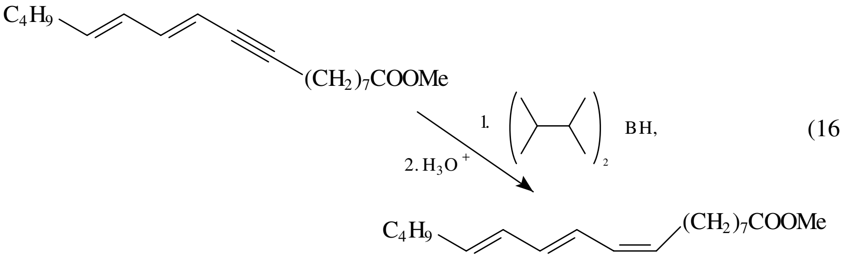
(162)

Endiandric acid D methyl ester

A hydroboration–protonolysis procedure for the conversion of conjugated enynes to dienes is far superior to partial hydrogenation over Lindlar's catalyst, in terms of stereoselectivity and yields[280]. Ratovelomanana and Linstrumelle reported the synthesis of methyl α-eleostearate (equation 163) and methyl punicate by employing this strategy[280].

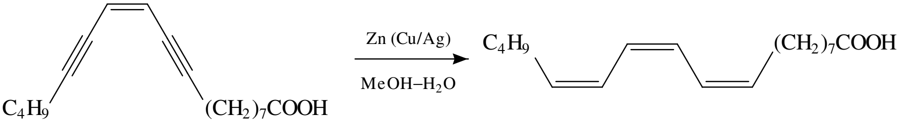
TABLE 29. Dienes through selective hydrogenation of enynes

Eneyne	Diene	Reference
		278a
		278b
		278c

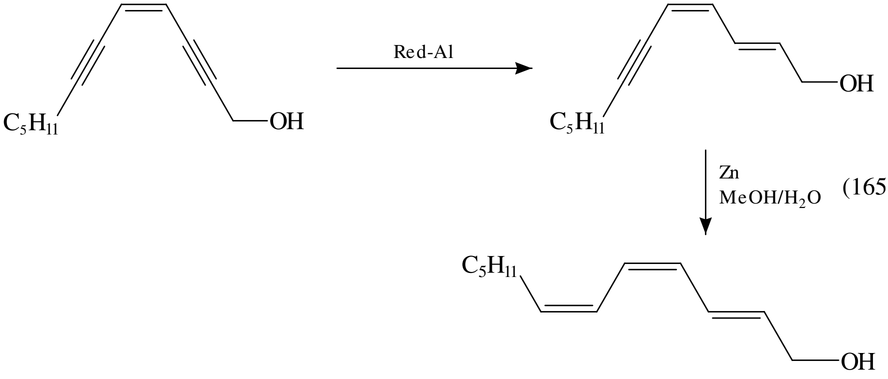


(163)

Carbon–carbon triple bonds in enynes can also be reduced to *E*-double bonds in high isomeric purity with powerful hydride reducing agents such as LAH^{281}, sodium bis-(ethoxymethoxy)aluminium hydride (Red-Al^{R})^{282} and *n*-BuLi, DIBAH^{282}. Linstrumelle and coworkers reported the synthesis of several trienes and polyenes of defined stereochemistry from enynes by transforming a carbon–carbon triple bond to either a *Z*-double bond using Zn/MeOH–H_2O or an *E*-double bond using Red-Al^{R} (equations 164 and 165)^{283}.



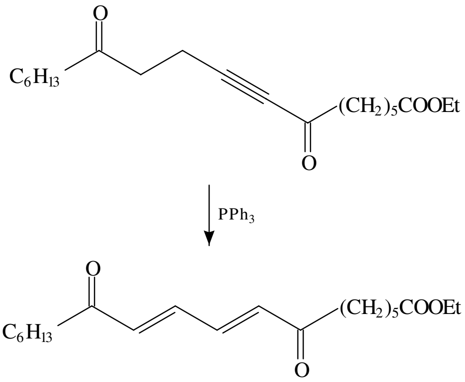
(164)



(165)

B. Isomerization Reactions

Isomerization of alkynes to dienes is a useful synthetic approach since alkyne derivatives are readily available. Even though alkyne migrations along the chain under basic conditions are well known, isomerizations of isolated alkyne to 1,3-diene do not take place easily. For some alkynones, this reaction takes place readily with triphenylphosphine[284]. Utilizing isomerization of a yne-one as a key reaction, Guo and Lu reported a three-step synthesis of an anti-cancer agent ostopanic acid starting from pent-4-ynal (equation 166)[284a,285].

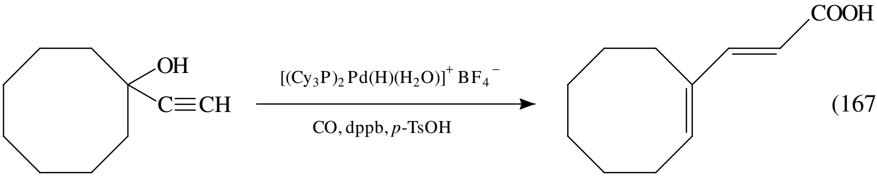


Ostopanic acid

(166)

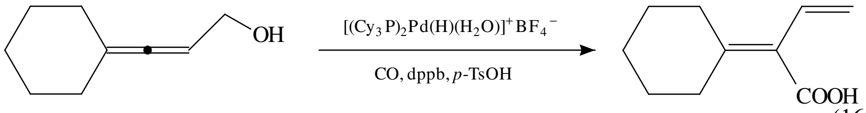
C. Carbonylation and Isomerization via Organometallic Intermediates

Air-stable palladium(0) catalyst, $[(Cy_3P)_2Pd(H)(H_2O)]BF_4$, catalyses carbonylation of propargylic alcohols to generate dienoic acids and esters (equation 167)[286]. Since propargyl alcohols are obtained from carbonyl compounds by acetylide addition reactions, this sequence constitutes a three-carbon homologation. α-Allenic alcohols are converted to α-vinylacrylic acids under similar conditions (equation 168)[287].



(167)

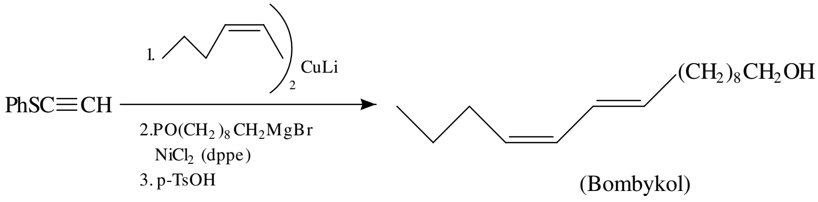
Cy = c-Hex; dppb = 1,4-Bis(diphenylphosphino)butane



(168)

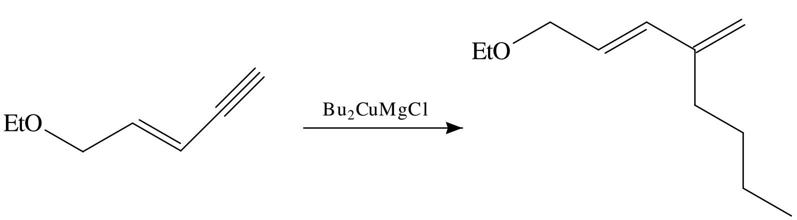
D. Addition of Gilman Reagents

Stereodefined alkenyl cuprates add to alkynes in *syn* fashion to result in 1,3-dienes of predictable stereochemistry[288]. Naso and coworkers used this method for the synthesis of pheromones having *E*,*Z*- and *Z*,*E*-conjugated diene structures[289]. Thus, *Z*-dialkenyl cuprates were added to phenylthioacetylene to yield *E*,*Z*-alkadienyl sulphide intermediate, which undergoes a cross-coupling reaction with Grignard reagents in the presence of a catalytic amount of a Ni(II) complex, leading to the desired dienes (equation 169)[289]. Alkyl cuprates react with vinylacetylene moiety in a regio- and stereoselective manner to result in alkylated 1,3-dienes (equation 170)[290].



P = $CH_3CH_2OCHCH_3$

(169)



(170)

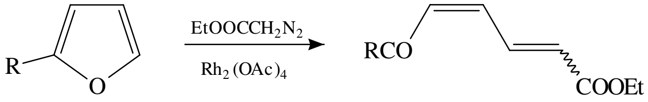
VIII. FROM HETEROCYCLIC COMPOUNDS

A. General Aspects

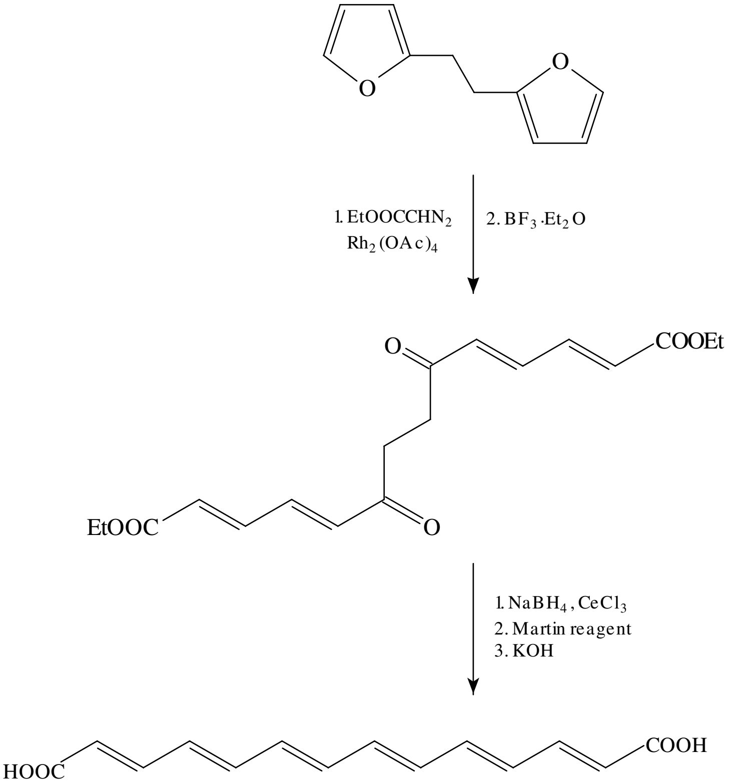
Five- and six-membered oxygen and nitrogen heterocycles, such as furan or pyridine, can be viewed as masked cyclic dienes with predisposed geometry. Appropriate protocols can lead to ring-opening of 5- or 6-membered heterocycles to reveal the diene functionality with well defined stereochemistry. Since substitution reactions can be performed on the heterocycles easily, ring-opening strategy has enormous potential in diene and polyene synthesis[291].

B. From Five-membered Heterocycles

Furan can be viewed as a dienol ether. Wenkert and coworkers found that carbene generated from ethyl diazoacetate using dirhodium tetraacetate add to furan and subsequent *in situ* ring-opening results in 1,4-diacyl-1,3-butadienes (equation 171)[292]. Iodine or BF_3-Et_2O catalysed isomerization of the mixture of diene products results in bifunctional *E*,*E*-dienal ester. Application of this strategy on a bifuran compound resulted in tetraene product which could be elaborated to the hexaene dicarboxylic acid natural product, corticrocin (equation 172)[292]. An intramolecular version of the above strategy was employed for the synthesis of several β-ionone terpenes[293].

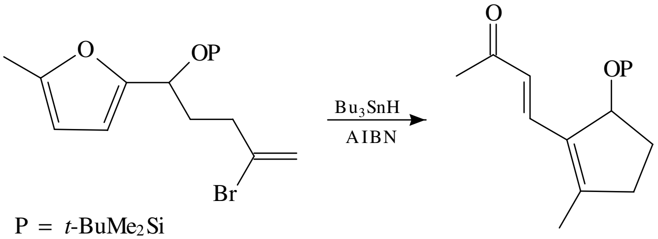


(171)



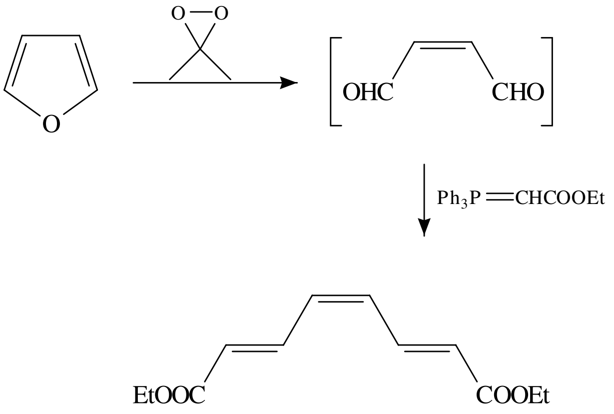
(172)

Parsons and coworkers found that intramolecular addition of vinyl radicals, generated *in situ* from the corresponding vinyl bromide and tri-*n*-butyltin hydride in the presence of azobisisobutyronitrile, to the furan ring results in tandem radical addition–fragmentation sequence leading to the formation of five-membered ring compounds having a dienone moiety (equation 173)[294]. Utilizing this strategy, a short synthesis of a prostaglandin model compound was reported[294].



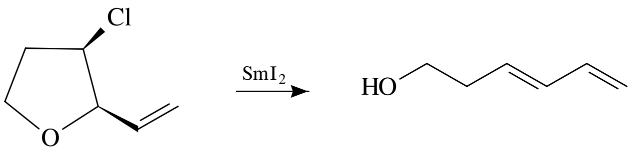
(173)

Furan can be used as a source for malealdehyde. McKervey and coworkers found that oxidation of furan with dimethyldioxirane results in malealdehyde, which can be trapped *in situ* with a variety of Wittig reagents to generate dienes and polyenes (equation 174)[295]. The same sequence with substituted furans gives ketodienealdehydes and ketodieneesters[295].



(174)

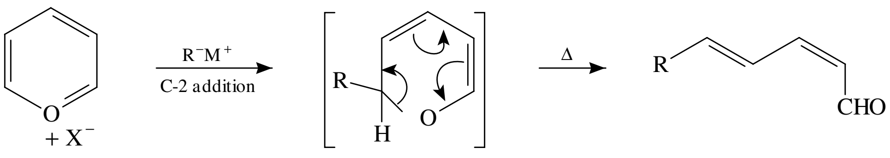
Crombie and Rainbow reported synthesis of terminal dienes of high *E*-selectivity via samarium diiodide mediated scission of 2-vinyl-3-chlorotetrahydrofuran (equation 175) or the corresponding pyran derivatives[296]. Interestingly, both *cis*- and *trans*-2-substituted 3-chlorotetrahydrofurans give the same diene, indicating the involvement of identical intermediates formed by electron transfer from samarium diiodide.



(175)

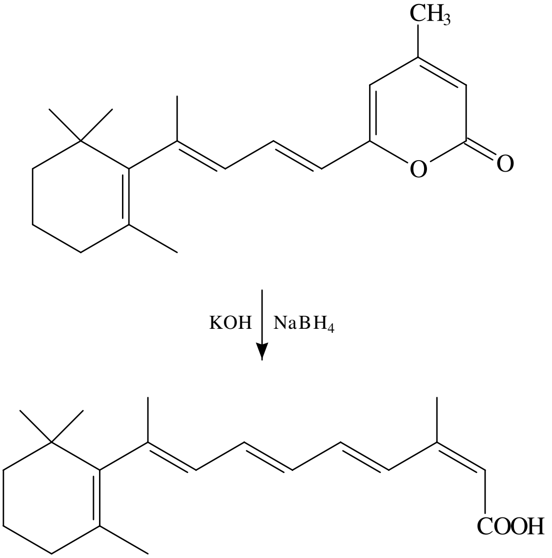
C. From Six-membered Heterocycles

Taylor and coworkers have utilized pyrylium perchlorate[297,298] or pyrylium tetrafluoroborate[299] as a source of five-carbon 2*Z*,4*E*-dienal synthons for diene and polyene synthesis. This method involves C-2 addition of an organometallic reagent to the pyrylium salt followed by electrocyclic ring-opening of the intermediate 2*H*-pyran to give *Z*,*E*-dienal (equation 176) of high stereochemical purity. Taylor applied the above strategy for the synthesis of several diene and triene derivatives which are shown in Table 30[298b,299,300]. Bestmann and coworkers reported an efficient synthesis of 13*Z*-retinoic acid where the 11,13-diene moiety was generated by reductive ring-opening of substituted 2-pyrone (equation 177)[299b,c].



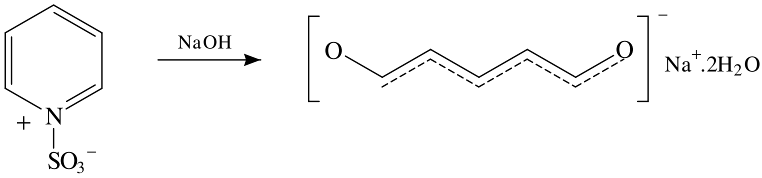
$X = ClO_4, BF_4$

(176)

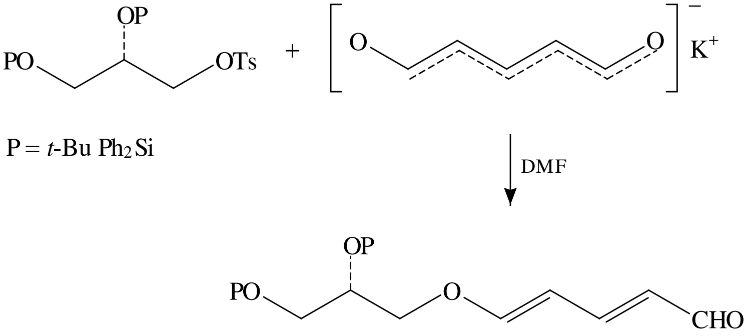


(177)

Treatment of 1-pyridinium sulphonate with sodium or potassium hydroxide generates sodium or potassium salts of 5-hydroxy-2,4-pentadienal (glutaconaldehyde), which are starting materials for a variety of transformations (equation 178)[171b,301]. For example, the reaction of the potassium salt with a carbon electrophile has been used for the preparation of a dienol aldehyde (equation 179)[171b] which was an intermediate in the total synthesis of a mutagen, (S)-3-(dodeca-1,3,5,7,9-pentaenyloxy)propane-1,2-diol.

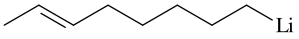
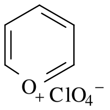
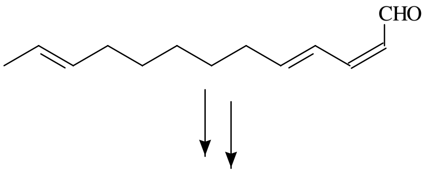
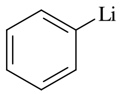
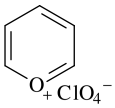
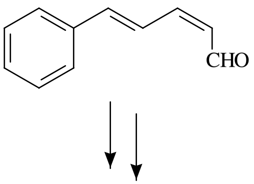
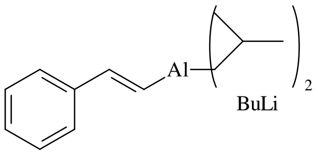
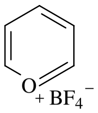
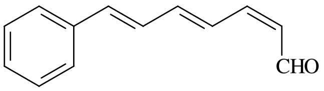


(178)



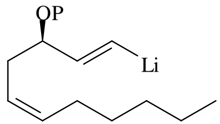
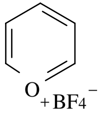
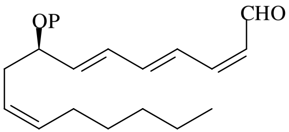
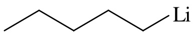
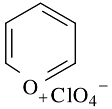
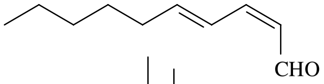
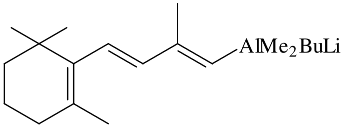
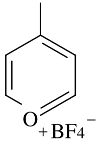
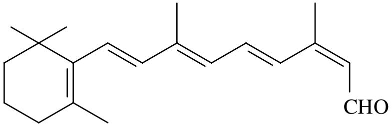
(179)

TABLE 30. Dienes and polyenes from ring-opening of pyrylium salts

Substrate	Reagent	Product	Reference
		 Umbraculumin A	300a
		 Lignarenone A and Lignarenone B	300b
			299a

continued overleaf

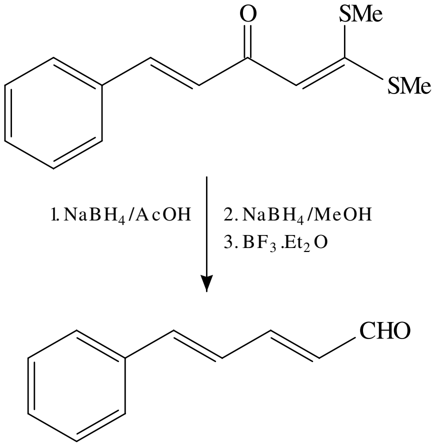
TABLE 30. (*continued*)

Substrate	Reagent	Product	Reference
 P = TBDMS		 $\downarrow\downarrow$ (+)LTB$_4$ methyl ester and (−)(5R)-LTB4 methyl ester	300c
		 $\downarrow\downarrow$ (3Z, 5E)-Undeca-1,3,5-triene	298b
		 (13Z-Retinal)	300d

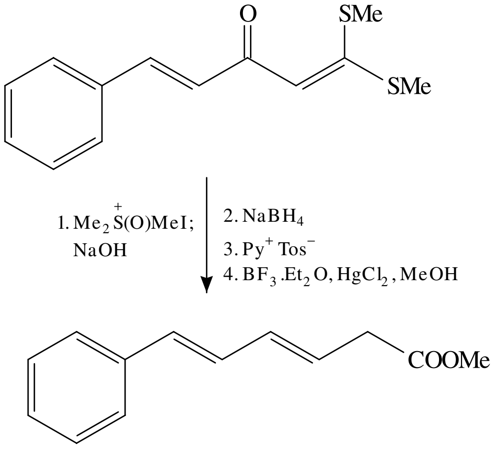
IX. MISCELLANEOUS

A. Oxoketene Dithioacetals

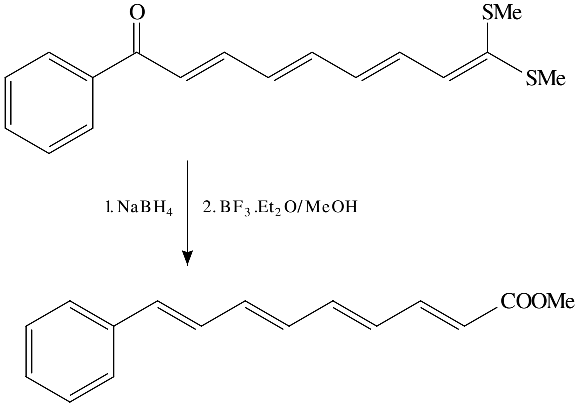
α-Oxoketene dithioacetals are versatile three-carbon synthons in which the carbonyl group can be manipulated either in 1,2-fashion or 1,4-fashion. The ketene dithioacetal portion is a masked ester and the 1,4-reduction product of α-oxoketene dithioacetals, the β-oxodithioacetals, are masked β-ketoaldehydes. Junjappa and Ila have utilized these synthones for the synthesis of diene and polyene aldehydes and esters. For example, sequential 1,4-reduction, 1,2-reduction and hydrolysis of α-oxoketene dithioacetals release the α,β-unsaturated aldehyde. Dienals and polyenals result when this sequence is applied to the substrates having conjugated double bonds (equation 180)[302]. On the other hand, sequential cyclopropanation, 1,2-reduction, dehydration and hydrolysis of the α-oxoketene dithioacetals result in diene esters (equation 181)[303]. Polyene separated oxoketene dithioacetals on 1,2-reduction and hydrolysis yield polyene esters in good yield (equation 182)[304]. This reaction constitutes a method for carbonyl transposition across the polyene chain.



(180)



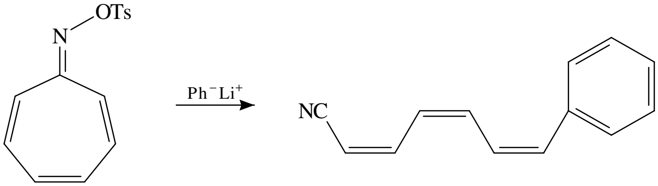
(181)



(182)

B. Trienes from Tropone Oxime Tosylate

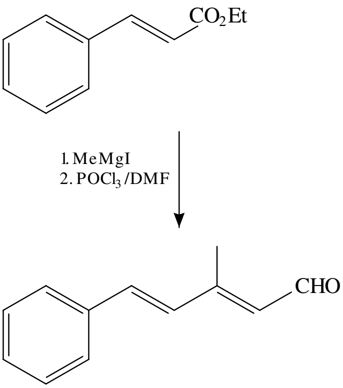
Machiguchi, Nozoe and coworkers have very recently observed that in contrast to chemical reactivity of tropones, the tosylate of tropone oxime undergoes a facile ring-opening to 6-substituted (*Z*,*Z*,*Z*)-1,3,5-hexatriene nitriles on reaction with various nucleophiles[305]. For example, reaction of phenyl lithium results in the corresponding hexatriene carbonitrile (equation 183).



(183)

C. Dienals via Vilsmeier Reaction

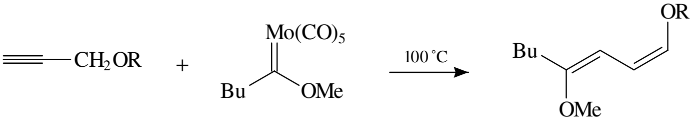
Cinnamic acid esters can be converted to dienals via Grignard addition and Vilsmeier reaction (equation 184)[306].



(184)

D. Carbene Insertion Reactions

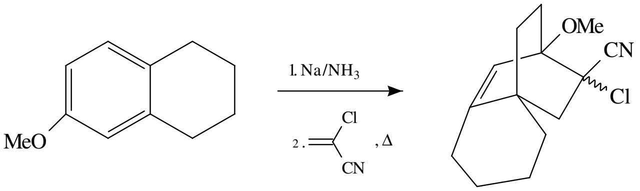
(*Z*,*Z*)-1,4-Dialkoxy-1,3-dienes can be readily prepared from propargyl ethers and molybdenum carbene complexes (equation 185)^{307}. High stereoselectivity in this reaction may be due to the formation of stable vinyl hydride complex with the enol ether.



(185)

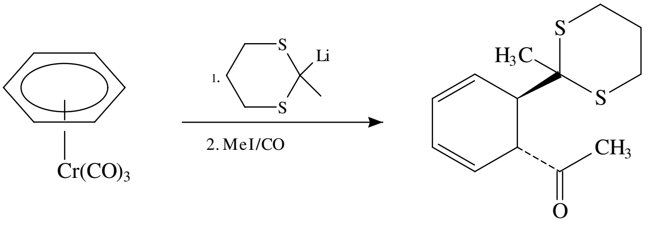
E. From Arenes

Reduction of aromatic compounds to dihydro derivatives by dissolved metals in liquid ammonia (Birch reduction) is one of the fundamental reactions in organic chemistry^{308}. When benzene derivatives are subjected to this reduction, cyclohexa-1,4-dienes are formed. The 1,4-dienes obtained from the reduction isomerize to more useful 1,3-dienes under protic conditions. A number of syntheses of natural products have been devised where the Birch reduction of a benzenoid compound to a cyclohex-1,3-diene and converting this intermediate in Diels−Alder fasion to polycyclic products is involved (equation 186)$^{308f-h}$.



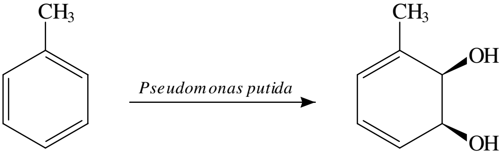
(186)

Arenes can be transformed to *trans*-disubsituted 1,2-dihydroarenes via temporary complexation with the electrophilic $Cr(CO)_3$ group, followed by addition of a nucleophile and an electrophile across the arene double bond (equation 187)^{309}.



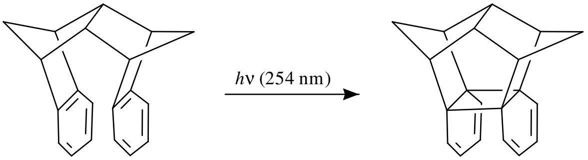
(187)

Benzene and other arenes can be oxidized to *cis*-1,2-cyclohexadienediol enantiospecifically using a mutant of *Pseudomonas putida* through microbial techniques (equation 188)^{310}.



(188)

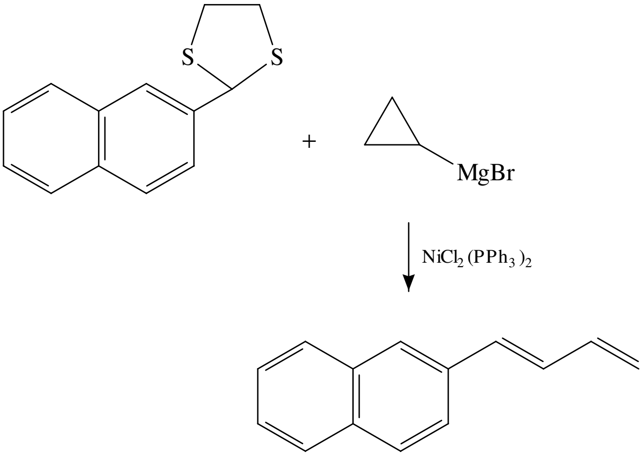
Photochemical 6π-6π cycloaddition of two benzene rings, in principle, produces benzene dimers having two 1,3-dienes units[311]. However, as expected, the dimers are unstable and revert back to benzene rings easily. Prinzbach and coworkers found that two benzene rings, locked in face-to-face relationship, undergo 6π-6π photocycloaddition on irradiation with monochromatic 254-nm light (equation 189)[312]. This reaction was used to generate bisdiene intermediate en route to pagodane.



(189)

F. Cyclopropane Ring-opening

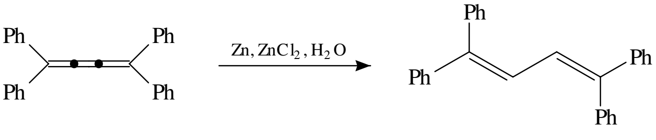
Cyclopropyl organometallic compounds readily undergo ring-opening to give homoallyl organometallic intermediates, which undergo β-elimination to furnish butadienes[313]. Cyclopropylmagnesium bromide reacts with dithioacetals under nickel catalysis to give cyclopropylcarbinyl nickel intermediates, which on ring-opening and spontaneous elimination result in dienes (equation 190)[314].



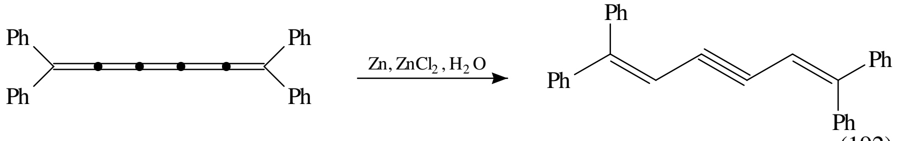
(190)

G. Selective Reduction of Allenes

Aryl group substituted butatrienes and hexapentaenes can be selectively reduced with $Zn{-}ZnCl_2{-}H_2O$ to result in aryl-substituted 1,3-butadienes and hexa-1,5-dien-3-ynes, respectively (equations 191 and 192)[315].



(191)



(192)

X. ACKNOWLEDGEMENTS

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