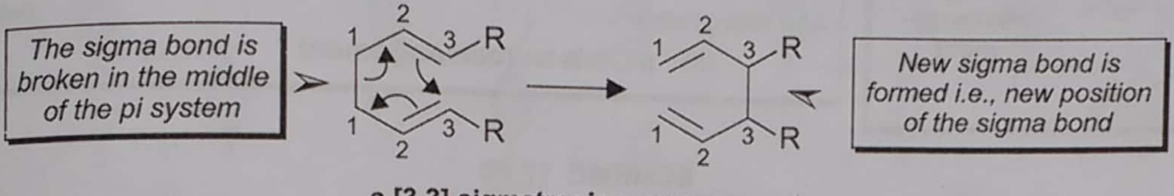
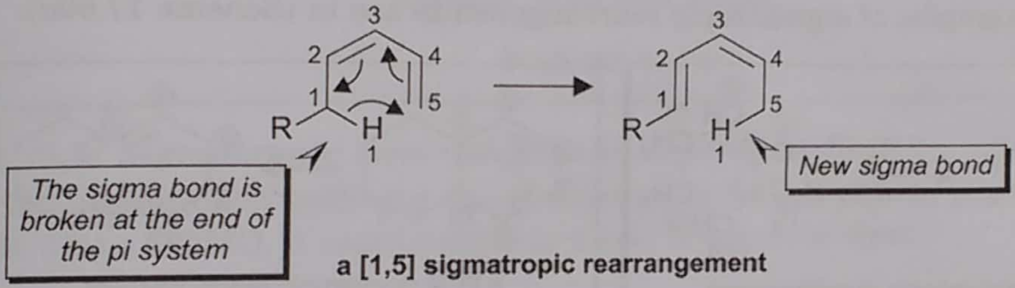
17.7 SIGMATROPIC REARRANGEMENTS

A sigmatropic rearrangement is a concerted intramolecular shift of an atom or a group of atoms. During this arrangement a σ bond is broken in the reactant and a new σ bond is formed in the product and the π bonds rearrange. The following points may be noted:

- The number of π bonds does not change, both the reactant and the product contain the same number of π bonds.
- The σ bond that cleaves can be in the middle of the π system or at end of the π system (Scheme 17.67).



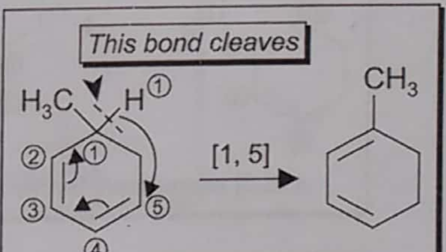
a [3,3] sigmatropic rearrangement



a [1,5] sigmatropic rearrangement

SCHEME 17.67

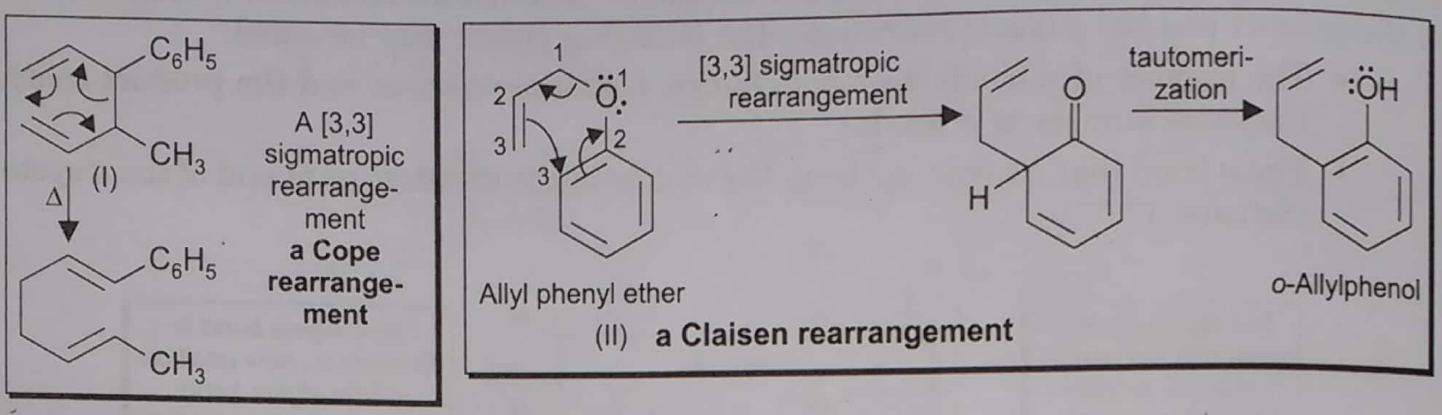
- The σ bond that breaks is bonded to an allylic carbon.
- To identify the order of a sigmatropic shift [*i*, *j*] first identify the σ bond which is broken in the reaction. Then assign number 1 to both the atoms involved in this bond, then the atoms in each direction from the bond being cleaved, upto and including the atoms which form the new σ bond in the product are numbered as atoms 2,3 and so on. The numbers assigned to the atoms that form the new bond, separated by commas are put within the brackets to show the reaction order (Scheme 17.67). Similarly the migration of hydrogen (Scheme 17.68) is another example of [1,5] sigmatropic shift. The order [1,5] is not due to the fact that hydrogen migrates from C1 to C5 but since the hydrogen (one of the two atoms given the number 1) forms part of the new σ bond and had also formed part of the old σ bond. Only all the atoms taking part in the reaction have to be counted. Thus the rearrangement of cyclohexadiene (Scheme 17.68) cannot be labelled as [1,3] shift since the methylene group linking 1 and 5 is not involved in the reaction.



SCHEME 17.68

- Since in these reactions a change in the position of one σ bond takes place, Woodward and Hofmann coined the term "sigmatropic shifts".
- A [3,3] sigmatropic rearrangement of a 1,5-diene (when the six atoms involved are all carbons) is known as the Cope rearrangement (I, Scheme 17.69).

- The oxygen analog of the Cope rearrangement is called the Claisen rearrangement. Often one of the π bonds is part of an aromatic ring (II, Scheme 17.69). Allyl vinyl ethers also undergo Claisen rearrangement.

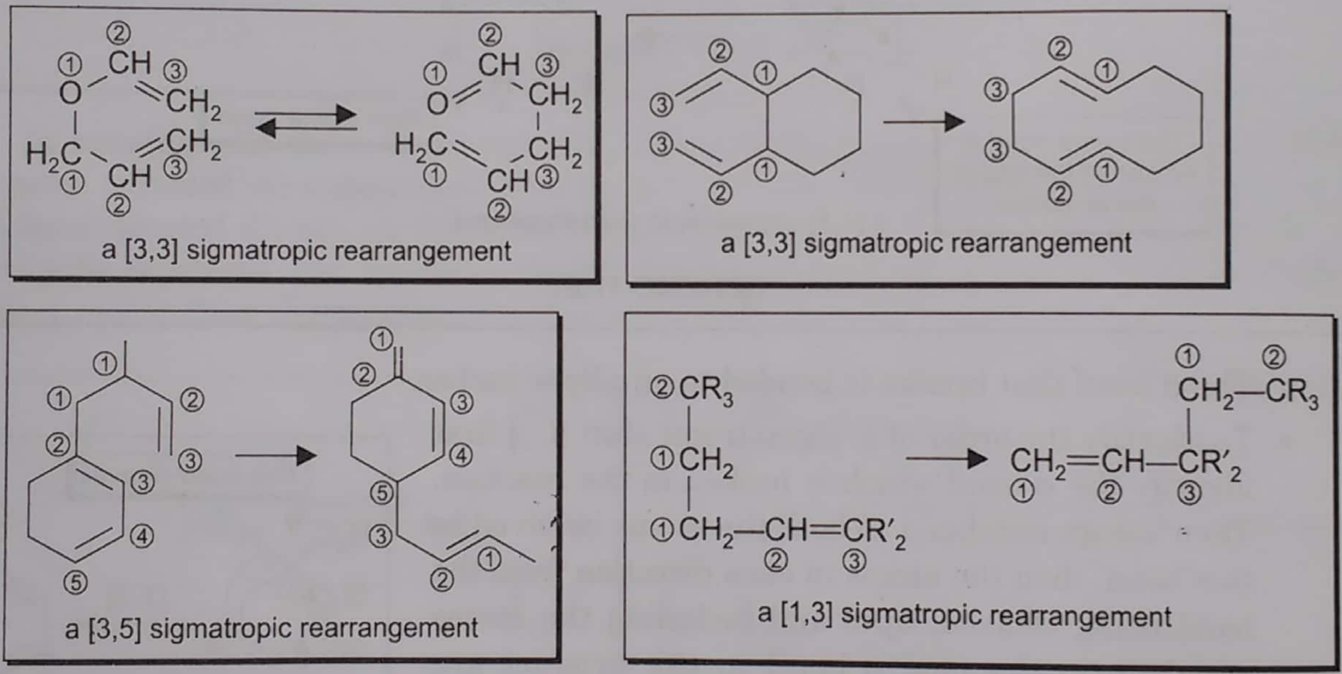


(I) A [3,3] sigmatropic rearrangement **a Cope rearrangement**

(II) **a Claisen rearrangement**

SCHEME 17.69

- More examples of sigmatropic rearrangements are in (Scheme 17.69*a*).



a [3,3] sigmatropic rearrangement

a [3,3] sigmatropic rearrangement

a [3,5] sigmatropic rearrangement

a [1,3] sigmatropic rearrangement

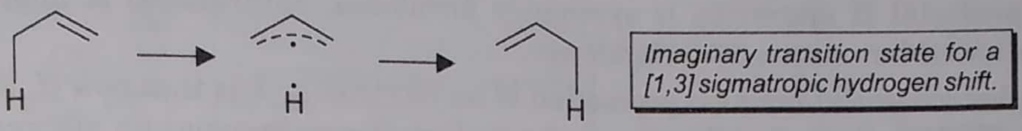
SCHEME 17.69a

A. Sigmatropic Migration of Hydrogen

(i) Introduction.

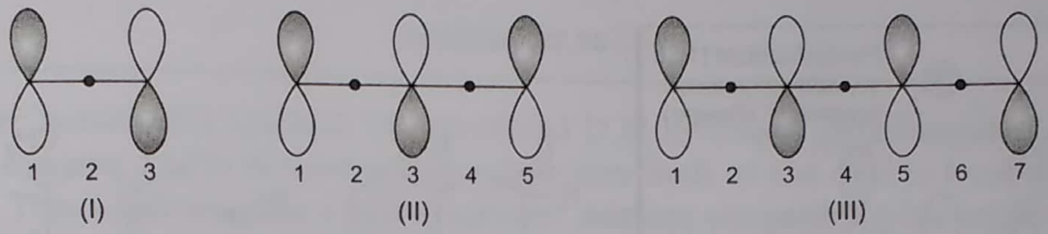
A hydrogen atom is reported to migrate from one end of a system of π bonds to the other, under thermal or photochemical rearrangements. In the transition state the hydrogen must be in contact with both ends of the chain at the same time. There are two distinct processes by which a sigmatropic migration can occur. If the hydrogen moves along the top or bottom face of the π-system *i.e.,* migrating group remains associated with same face of the conjugated system throughout the process, the migration is termed *suprafacial.* When the hydrogen moves across the π system either from top to bottom or vice versa *i.e.,* the migrating group moves to the opposite face of the π-system during the course of migration then it is called *antarafacial.*

In a given sigmatropic rearrangement, the migrating group is bonded to both the migration source and the migration termini in the transition state. It is imagined that the migrating H atom breaks away from the rest of the system which is treated as a free radical. Thus in a simplest case involving a [1,3] shift of hydrogen (Scheme 17.70), the frontier orbital analysis treats this system as a hydrogen atom interacting with an allyl radical. The electron of the hydrogen atom is in a 1*s* orbital which has only one lobe. The HOMO of an allylic free radical depends on the number of carbons in the π-framework (Scheme 17.71).



Imaginary transition state for a [1,3] sigmatropic hydrogen shift.

SCHEME 17.70

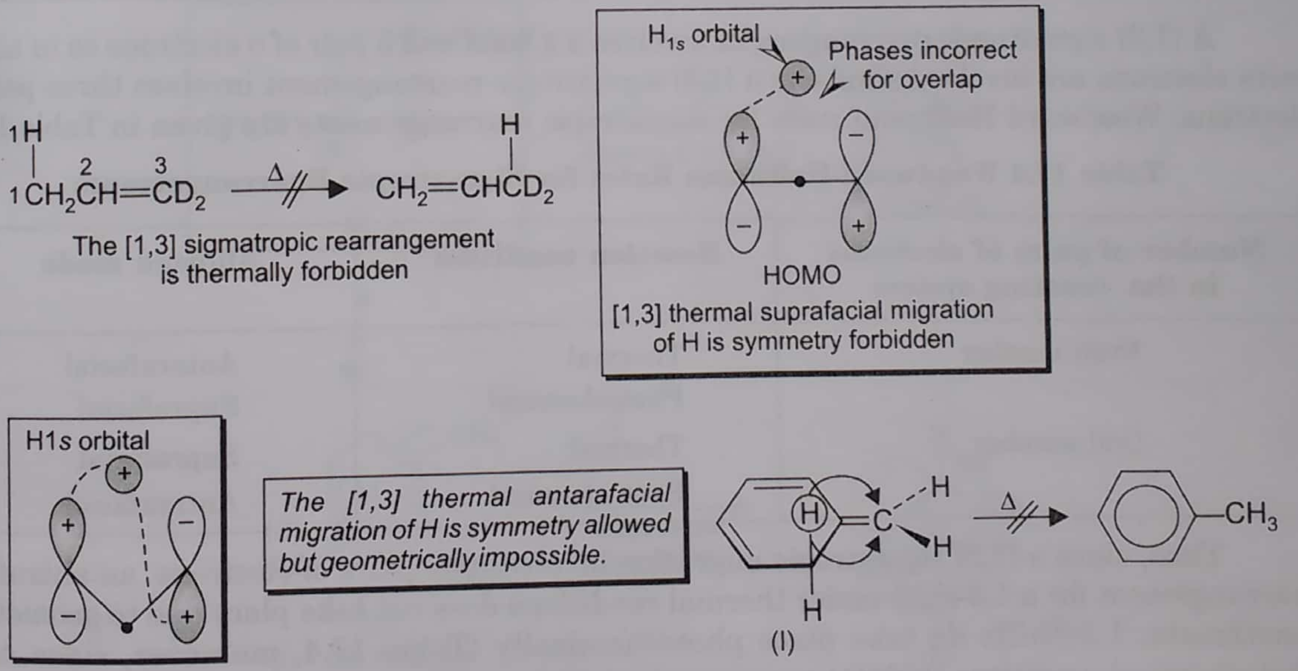


The HOMO of the *allylic* radicals

SCHEME 17.71

(ii) [1,3] Sigmatropic Rearrangement (Hydrogen Shift).

In the migration of hydrogen the H must move from a plus to plus or from minus to a minus lobe of the HOMO, it cannot move to a lobe of opposite sign.



The [1,3] sigmatropic rearrangement is thermally forbidden

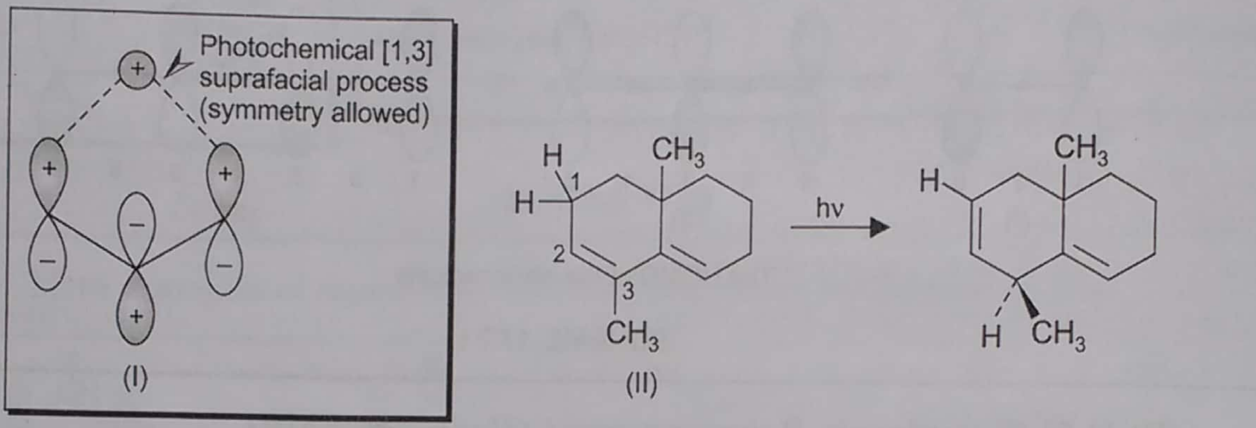
[1,3] thermal suprafacial migration of H is symmetry forbidden

The [1,3] thermal antarafacial migration of H is symmetry allowed but geometrically impossible.

SCHEME 17.72

During a thermal [1,3] sigmatropic migration of a hydrogen, the overlap of the hydrogen 1*s* orbital with the HOMO of the allyl radical (I, Scheme 17.71, asymmetric) is bonding at one end and antibonding at the other end for the suprafacial migration (Scheme 17.72). Thus [1,3] sigmatropic suprafacial migration of hydrogen (under thermal conditions) is symmetry-forbidden (Scheme 17.72). However, in the antarafacial process (Scheme 17.72) the hydrogen atom shall have to cross over the *pi* system to the other face to form a four membered ring transition state, a geometrically very difficult situation. Thus over all thermal [1,3] sigmatropic rearrangements are rare. The stability of the triene (I, Scheme 17.72) which is not thermally isomerized to toluene, which is thermodynamically more stable is due to a symmetry-forbidden process (suprafacial H migration is symmetry forbidden, antarafacial H migration though symmetry allowed but sterically forbidden).

In a photochemical reaction promotion of an electron means that now (I, Scheme 17.73) becomes the HOMO. Suprafacial pathway for [1,3] shift now becomes an allowed process and antarafacial pathway forbidden. Thus, the compound (II, Scheme 17.73) displays a [1,3] hydrogen shift under photochemical conditions.



The [1,3] sigmatropic rearrangement is photochemically allowed

SCHEME 17.73

A [1,3] sigmatropic rearrangement involves a π bond and a pair of σ electrons so in all two pairs electrons are involved similarly a [1,5] sigmatropic rearrangement involves three pairs of electrons. Woodward Hoffmann rules for sigmatropic rearrangements are given in Table 17.4.

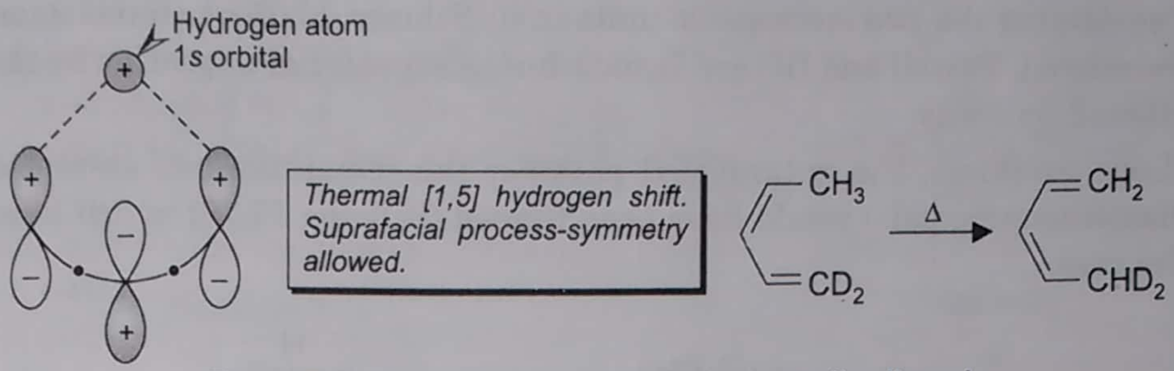
Table 17.4 Woodward-Hoffmann Rules for Sigmatropic Rearrangements

Number of pairs of electrons in the reacting system	**Reaction condition**	**Allowed mode**
Even number	Thermal	Antarafacial
	Photochemical	Suprafacial
Odd number	Thermal	Suprafacial
	Photochemical	Antarafacial

Thus, since a [1,3] sigmatropic migration involves two pairs of electrons, an antrafacial rearrangement for a 1,3-shift under thermal conditions does not take place due to geometrical constraints. 1,3-Shifts do take place photochemically [Table 17.4, moreover, since under photochemical conditions HOMO becomes symmetric (see, Scheme 17.73) hydrogen can migrate by suprafacial pathway].

(iii) [1,5] Sigmatropic Hydrogen Shift.

The [1,5] sigmatropic shift of hydrogen or deuterium atoms is well known. These involve three pairs of electrons, thus these occurs via a suprafacial pathway under thermal conditions (see Table 17.4). These shifts can be analyzed by examining a hydrogen atom and a pentadienyl radical whose HOMO (see III, Scheme 17.71) is bonding at both the migration origin and the migration terminus. Thus the migration maintains orbital symmetry when the migrating group remains on the same side of the conjugated system (suprafacial process, Scheme 17.74).

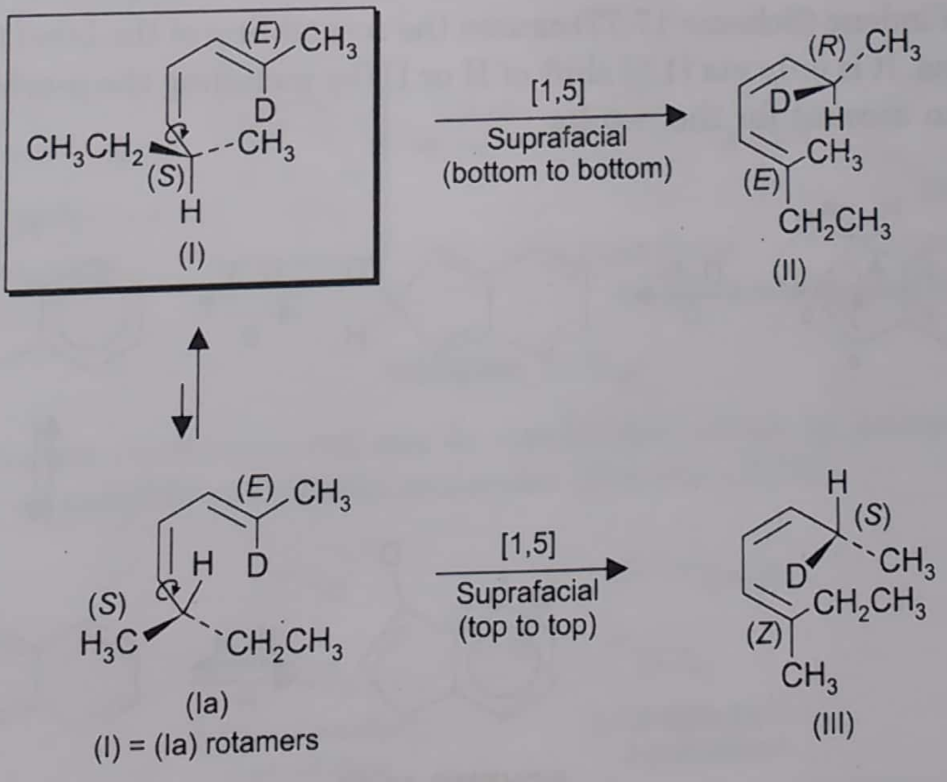


The [1,5] sigmatropic rearrangement is thermally allowed

SCHEME 17.74

Another remarkable example of suprafacial [1,5] hydrogen shift thermally, is in the 1,3-diene (I, Scheme 17.75) of known stereochemistry both at the double bond and at the stereocenter. This 1,3-diene gave a two component mixture compatible with only suprafacial migration. These results are explained as under:

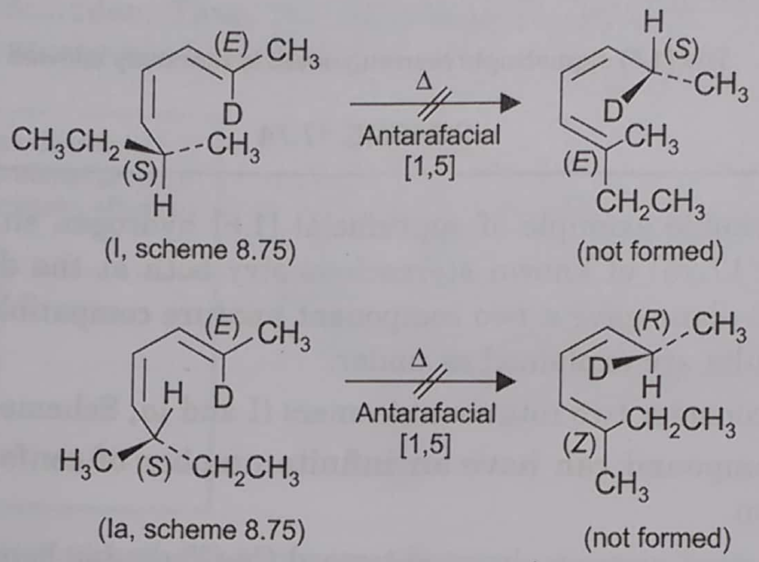
- One has to consider two rotational isomers (I and I*a*, Scheme 17.75) for the reaction.
- Recall, a compound can have an infinite number of conformations but only one configuration.
- In (I) the methyl group is directed toward C4-C5 double bond while in (I*a*) it is now ethyl group that is directed toward C4-C5 bond.



SCHEME 17.75

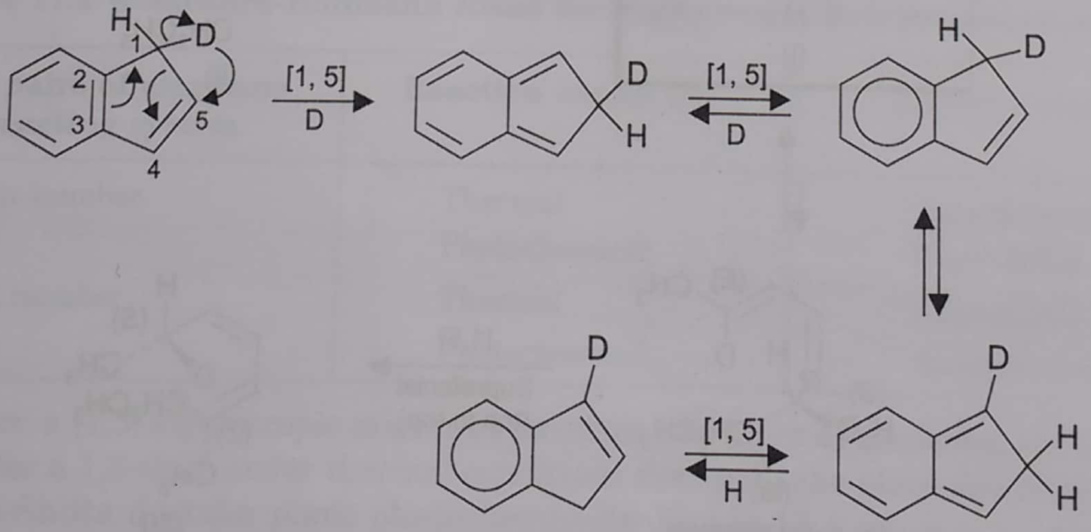
- There are two suprafacial [1,5] pathways for the hydrogen in these two conformations (I and I*a* Scheme 17.75) "top to top" as in (I) or "bottom to bottom" as in (Ia).
- Each of these suprafacial pathways gives a product with specific stereochemistry and both are formed.

- Considering the two stereogenic units in (I, Scheme 17.75) 4 stereoisomers could be considered. Two (II and III) are formed during suprafacial migration by the symmetry allowed pathway.
- If one considers, the antarafacial pathway the remaining two stereoisomers (as a diastereomeric pair) would have been formed (Scheme 17.76) which however, is not the case.



SCHEME 17.76

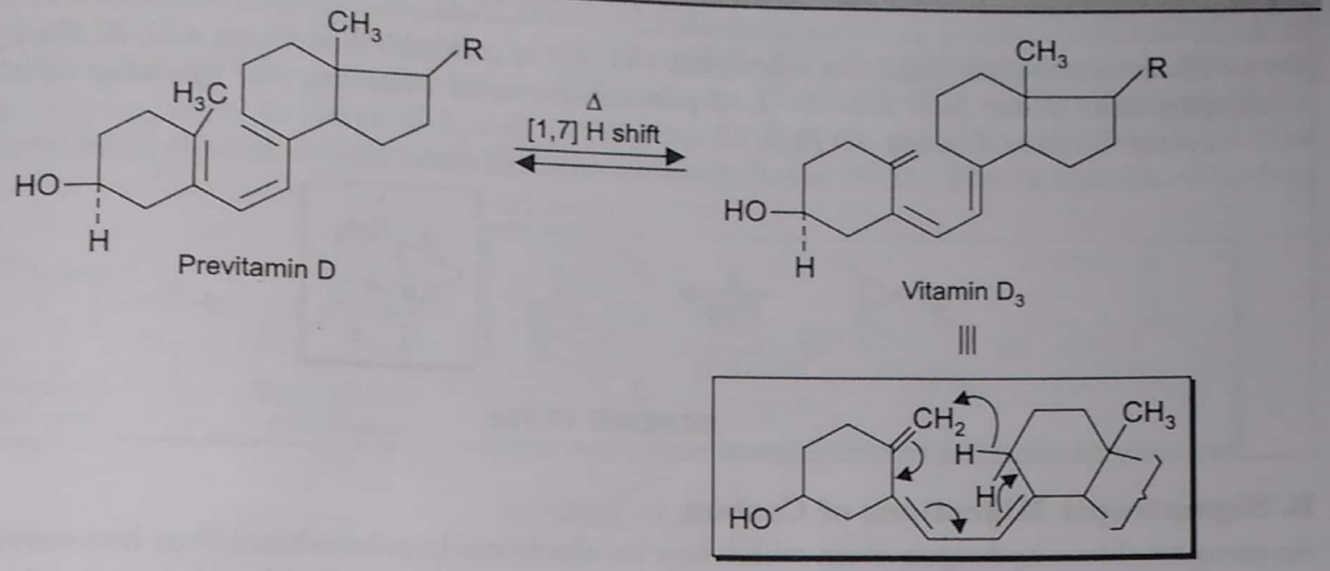
Heating of indene (Scheme 17.77) causes the scrambling of the label to all the three non-aromatic positions. It is only via [1,5] shift of H or D (by including the *p*-orbitals of the benzene ring) that one can account for the results.



SCHEME 17.77

(iv) [1,7] Sigmatropic Hydrogen Shift

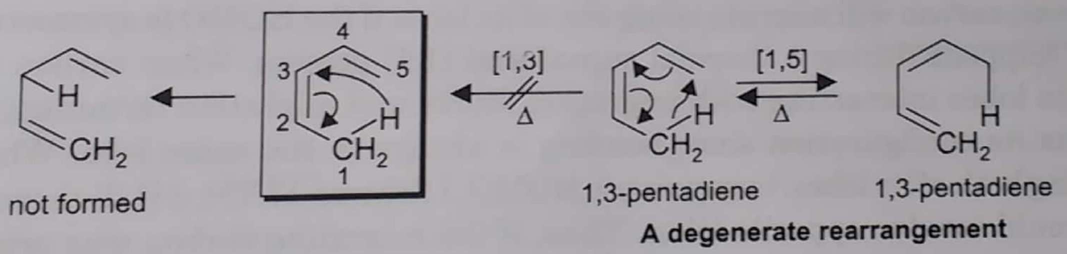
In the case of [1,7] hydrogen shifts, in a triene, the orbital symmetry rules (see III, Scheme 17.71) predict that the transfer of hydrogen must be antarafacial compared to [1,3] shift, the transition state is not much strained and the shift is sterically feasible. This is seen in the thermal interconversion of vitamin D series (Scheme 17.78).



SCHEME 17.78

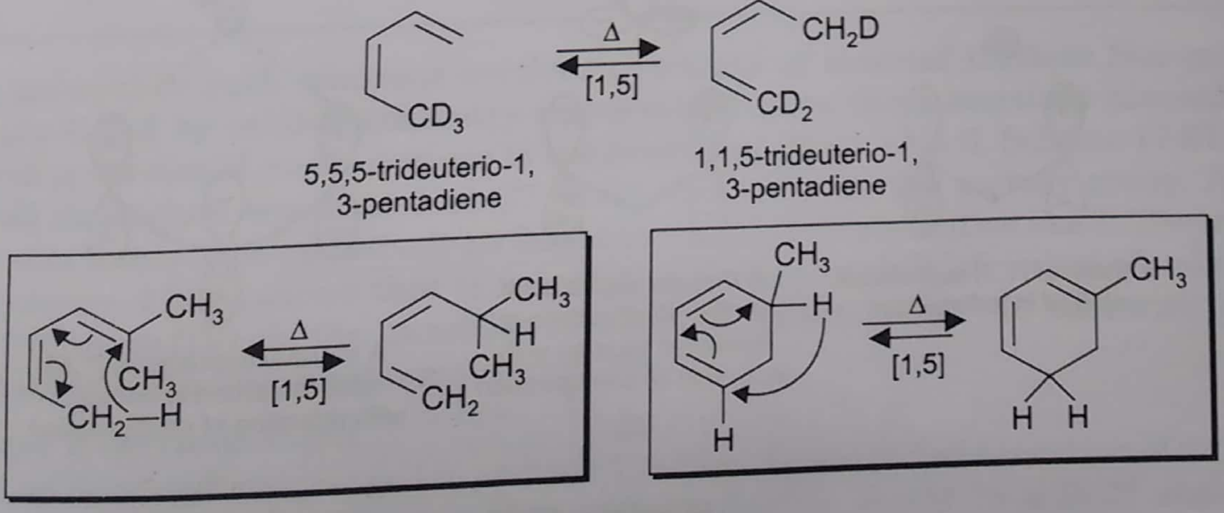
More on sigmatropic rearrangements (Degenerate rearrangements)

1, 3–Pentadiene on heating regenerates itself via a [1, 5] shift of hydrogen, this kind of process in which a reactant rearranges to itself is termed degenerate rearrangement (Scheme 17.78a). Significantly as expected the [1, 3] shift is symmetry forbidden.



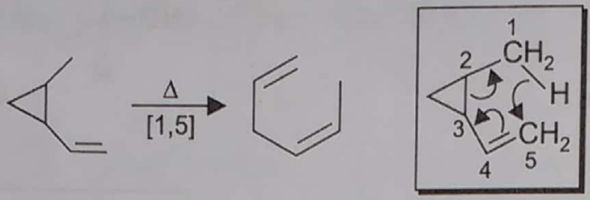
SCHEME 17.78a

The degenerate rearrangement can be established either by isotopically labeled molecules or suitably substituted molecules (Scheme 17.78b).



SCHEME 17.78b

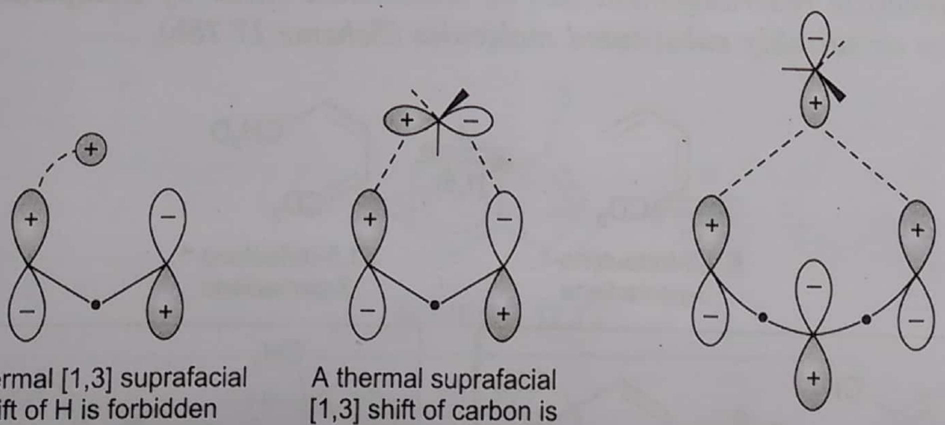
Three membered rings can often play the role of a double bond and a [1, 5] H shift can take place just like in 1, 3-pentadiene and involves the opening of the cyclopropane (Scheme 17.78c).



SCHEME 17.78c

B. Sigmatropic Migrations of Carbon

As compared to a hydrogen atom which has its electrons in a 1*s* orbital that has only one lobe, a carbon free radical (free imaginary transition state) has its odd electron in a *p* orbital which has two lobes of opposite sign. Recall that a [1,3] sigmatropic suprafacial migration of hydrogen (thermally) is symmetry forbidden while an antarafacial reaction though allowed is geometrically improbable (see Schemes 17.72–17.74). Interestingly an additional possibility would exist if an alkyl group (carbon) rather than a hydrogen was potential migrator. A [1,3] shift can now be suprafacial migration (I, Scheme 17.79) if the migrating group does so antarafacially *i.e.,* it would result in inversion of configuration of the migrating group. Thus carbon can simultaneously interact with the migration source and the migration terminus using either one of its lobes or both of its lobes (Scheme 17.79). Considering suprafacial rearrangement, carbon will migrate using one of its lobes if the HOMO is symmetric (II, Scheme 17.79). This happens during a thermal suprafacial [1,5] process. When carbon migrates with only one of its lobes interacting with migration source and migration terminus, the migrating group retains its configuration since bonding is always to the same lobe. When the carbon migrates using both of its lobes. (asymmetric HOMO, I Scheme 17.79), a [1,3] thermal suprafacial migration would involve opposite lobes. Thus, if the migrating carbon was originally bonded *via* its positive lobe, it must now use its negative lobe to form the new C—C bond. The stereochemical outcome of such a process is the inversion of configuration in the migrating group.



A thermal [1,3] suprafacial shift of H is forbidden

A thermal suprafacial [1,3] shift of carbon is however allowed with inversion of configuration

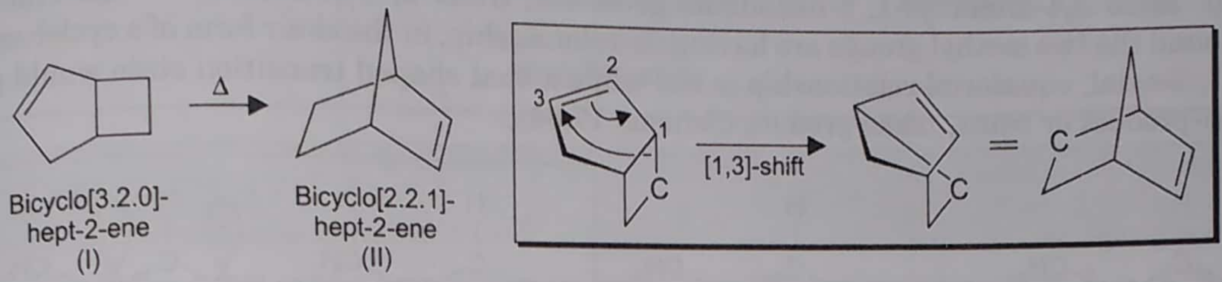
(I)

A thermal suprafacial [1,5] shift of carbon is allowed with retention of configuration

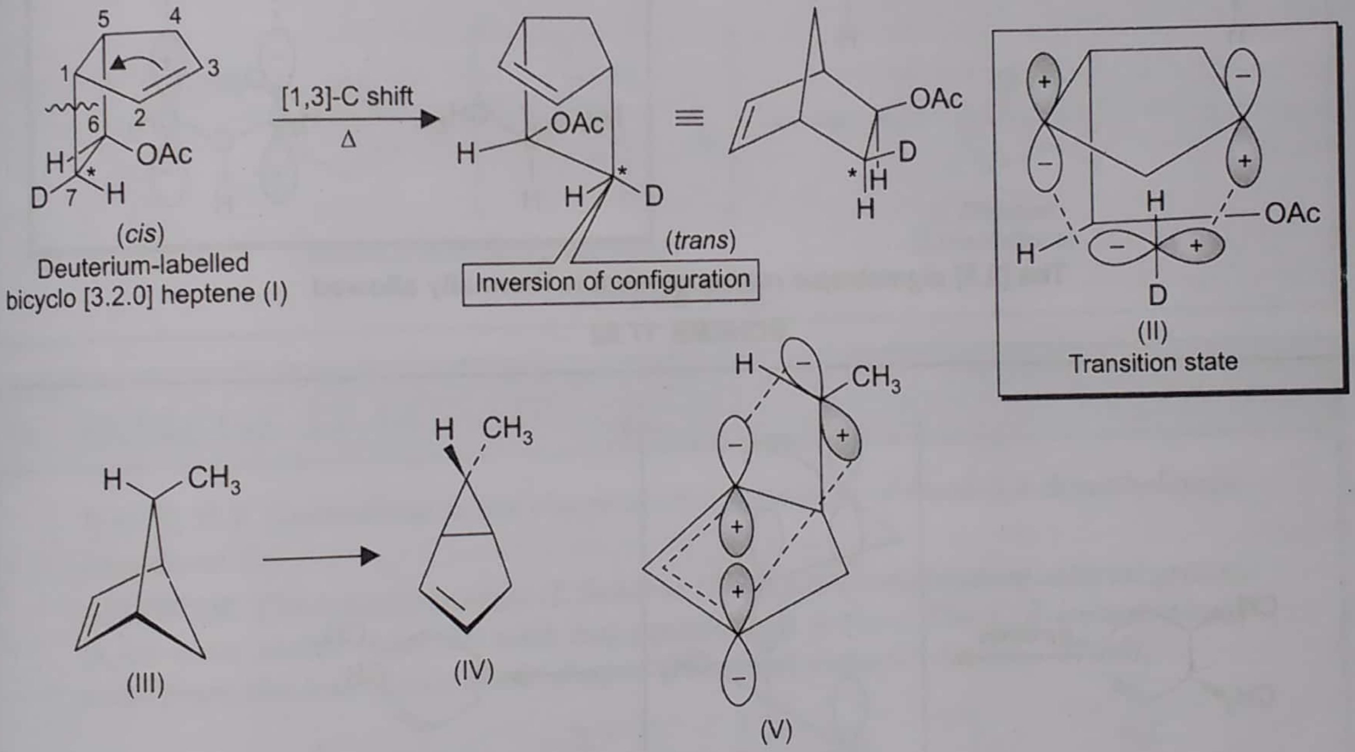
(II)

SCHEME 17.79

In summary, a suprafacial [1,5] thermal rearrangement proceeds with retention of configuration at the migrating carbon, while the related [1,3] suprafacial process proceeds with inversion. In the thermal conversion of (I, Scheme 17.80) to (II) a carbon atom migrates across an allyl system to leave C-1 and ending up at C-3 via a [1,3] shift. The inversion of configuration is observed using suitable substrates (Scheme 17.81). The [1,3] shifts of carbon



SCHEME 17.80

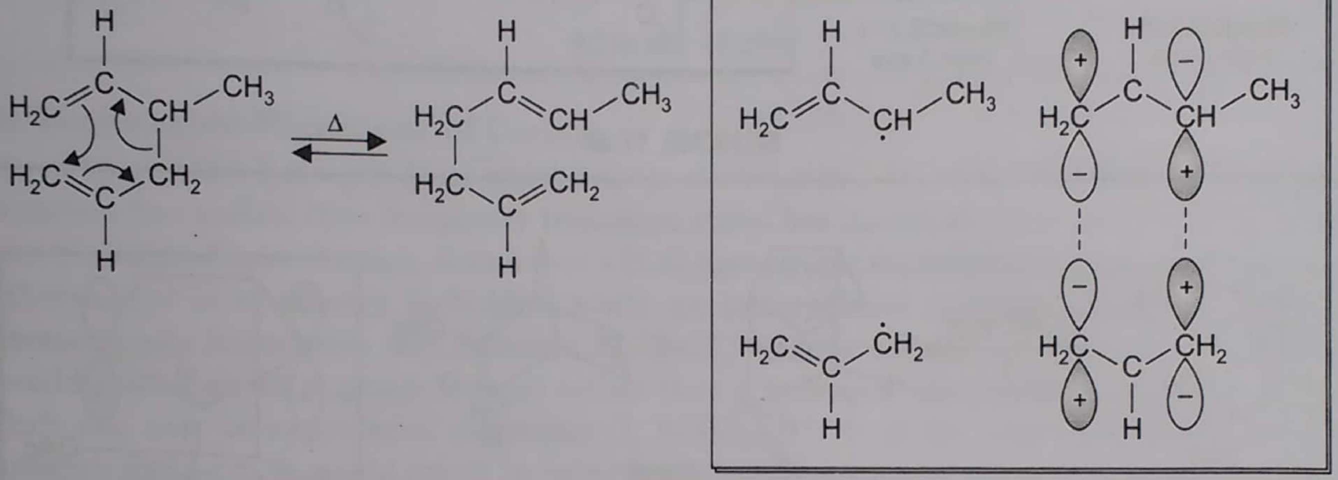


SCHEME 17.81

(*i.e.*, alkyl groups) in such reactions involve expansions of strained three-or four-membered rings. As predicted by orbital symmetry conservation rules these reactions proceed almost entirely with inversion of configurations in the migrating group as in (I, Scheme 17.81). In this case, a label deuterium was placed at C7 which was *trans* to the acetoxy group. After the reaction, it was found to be exclusively *cis* due to inversion of configuration at C7. The transition state (II, Scheme 17.81) shows that it is a [1,3] sigmatropic shift of carbon. Similarly (III, Scheme 17.81) gives (IV) via the transition state (V) by a suprafacial [1,3] shift with inversion at the migrating carbon under thermal conditions.

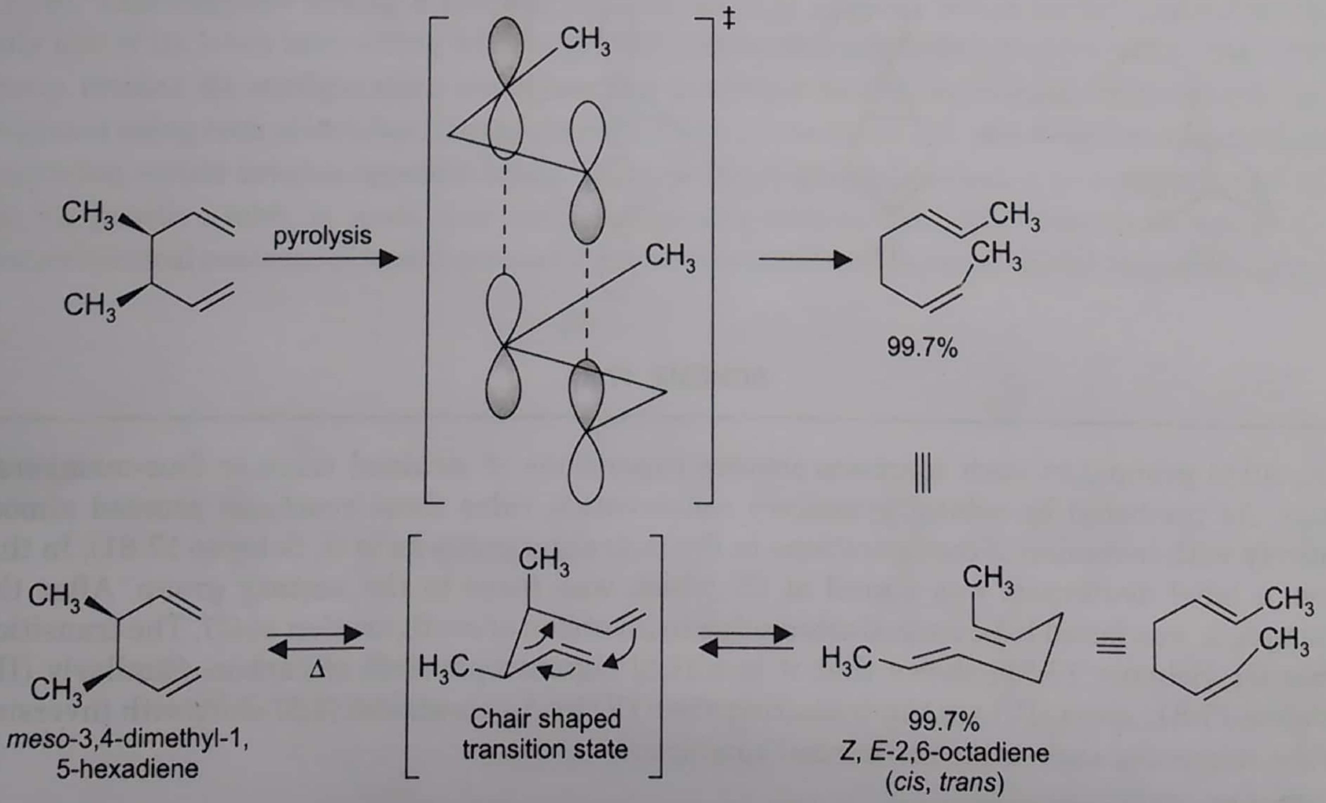
C. The Cope Rearrangement

A 1,5-diene on heating is rearranged to another 1,5-diene by concerted formation of a 1, 6-bond, breaking of the 3,4-bond and migration of both double bonds in a [3,3] sigmatropic rearrangement known as Cope rearrangement (see, Scheme 17.69). The compound rearranges by a [3,3] sigmatropic pathway and is also hypothetically pictured as split into two allyl radicals (Scheme 17.82). Interaction of the HOMO's of these allyl radicals is bonding at both ends, so the reaction is thermally allowed. The stereochemical outcome of this rearrangement is in keeping with their occurrence generally through the chair-shaped transition states (Scheme 17.83). *Meso* 3,4-dimethyl-1, 5-hexadiene gives *cis*, *trans*-2, 6-octadiene (in the starting compound the two methyl groups are having *cis*-relationship, in the chair form of a cyclohexane only 1, 2-axial, equatorial relationship is *cis*) while a boat shaped transition state would give *cis*, *cis*-product or *trans*, trans-product (Scheme 17.84).



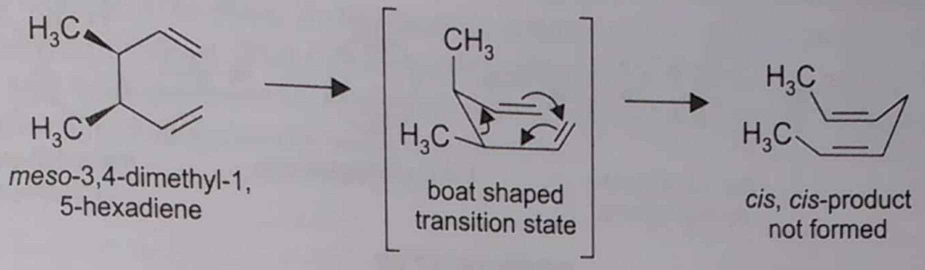
The [3,3] sigmatropic rearrangement is thermally allowed

SCHEME 17.82



Cope rearrangement occurs via a chair shaped transition state

SCHEME 17.83

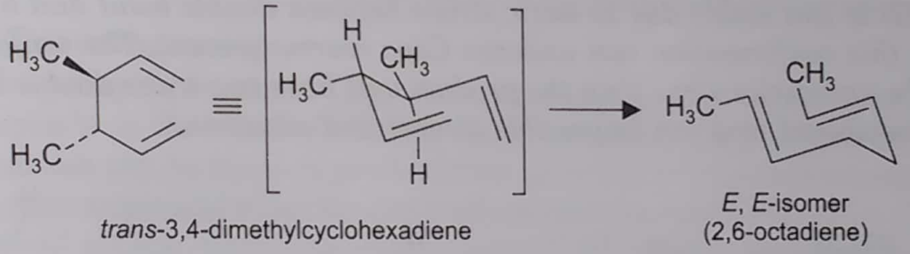


SCHEME 17.84

EXERCISE 17.13

Which diene you expect on pyrolysis of trans-3, 4-dimethylcyclohexadiene ?

ANSWER. *A Cope rearrangement occurs through a chair shaped transition state and the diene expected is E, E isomer of 2, 6-octadiene (Scheme 17.85).*

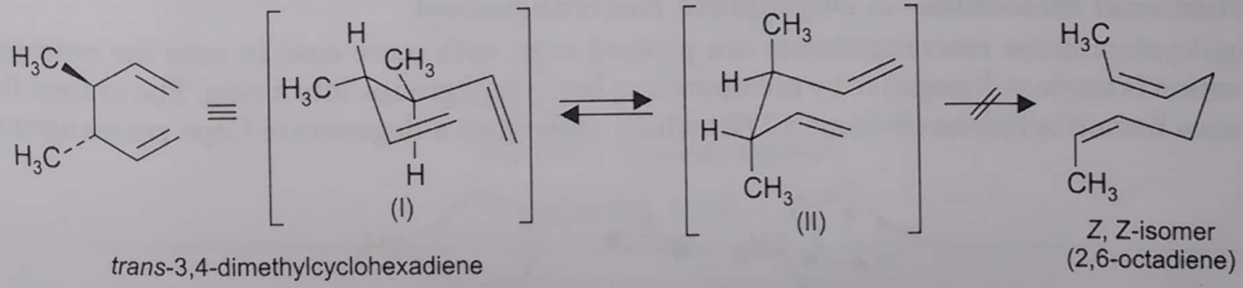


SCHEME 17.85

EXERCISE 17.14

Why Z, Z-2, 6-octadiene is not the product of pyrolysis of trans-3,4-dimethylcyclohexadiene ?

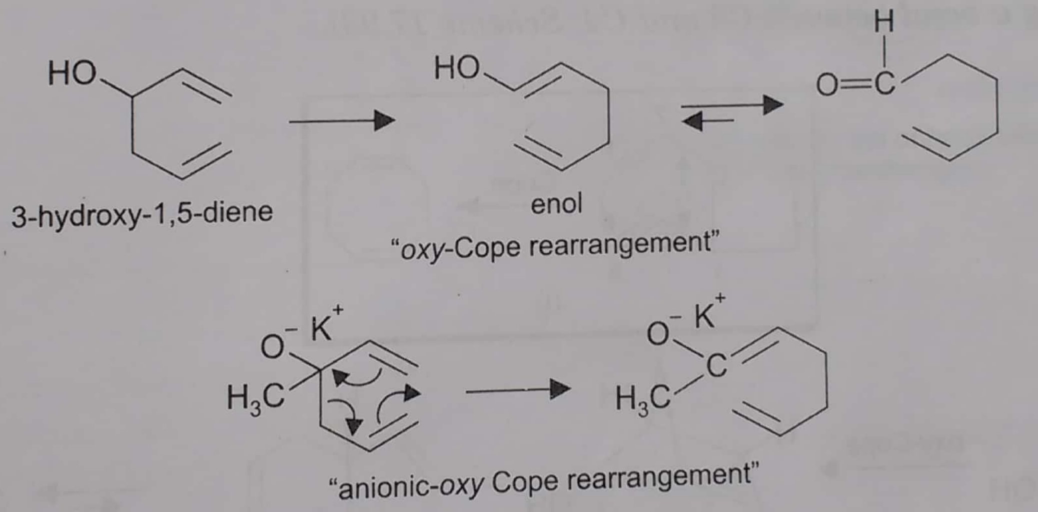
ANSWER. *The transition state (I, Scheme 17.86) with two pseudoequatorial groups is far more stable than (II) with two pseudoaxial groups. The Z, Z-isomer would arise from the less stable chair shaped transition state (II, Scheme 17.86).*



SCHEME 17.86

E. Oxy-Cope Rearrangement

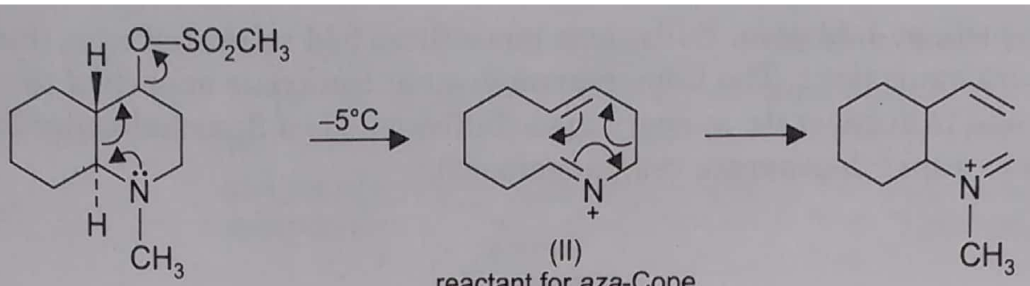
As seen in other pericyclic reactions Cope rearrangement is also reversible and the position of equilibrium depends on the relative stability of the isomers. This problem can be checked and the forward reaction can be made to predominate provided the product reacts further. This is so in oxy-Cope rearrangement when the reactant contains an oxygen group on C3 or C4 position. The alcohol variant of Cope rearrangement (Scheme 17.90) is called the oxy-Cope rearrangement and when the alkoxide derivative is used it is referred to as the "anionic oxy-Cope rearrangement. The rates of sigmatropic rearrangements are enhanced and the temperatures for the reactions are drammatically decreased compared to parent alcohols.



SCHEME 17.90

F. Aza-Cope Rearrangement

It is well known that the presence of oxygen atom adjacent to the π bond accelerates the Cope rearrangement. Similarly a nitrogen usually as an iminium salt fragment in the diene also induces an aza-Cope rearrangement. Thus the reactant (II, Scheme 17.91) derived from (I) underwent a fast aza-Cope rearrangement at low temperature.



(I)

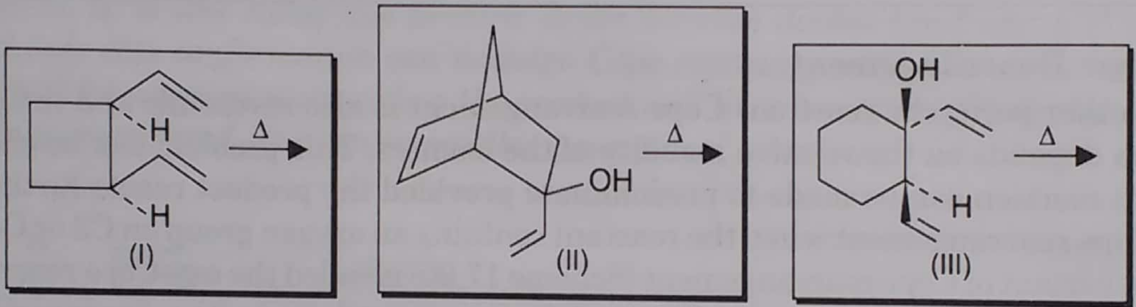
(II)
reactant for *aza*-Cope
rearrangement

***Aza*-Cope rearrangement**

SCHEME 17.91

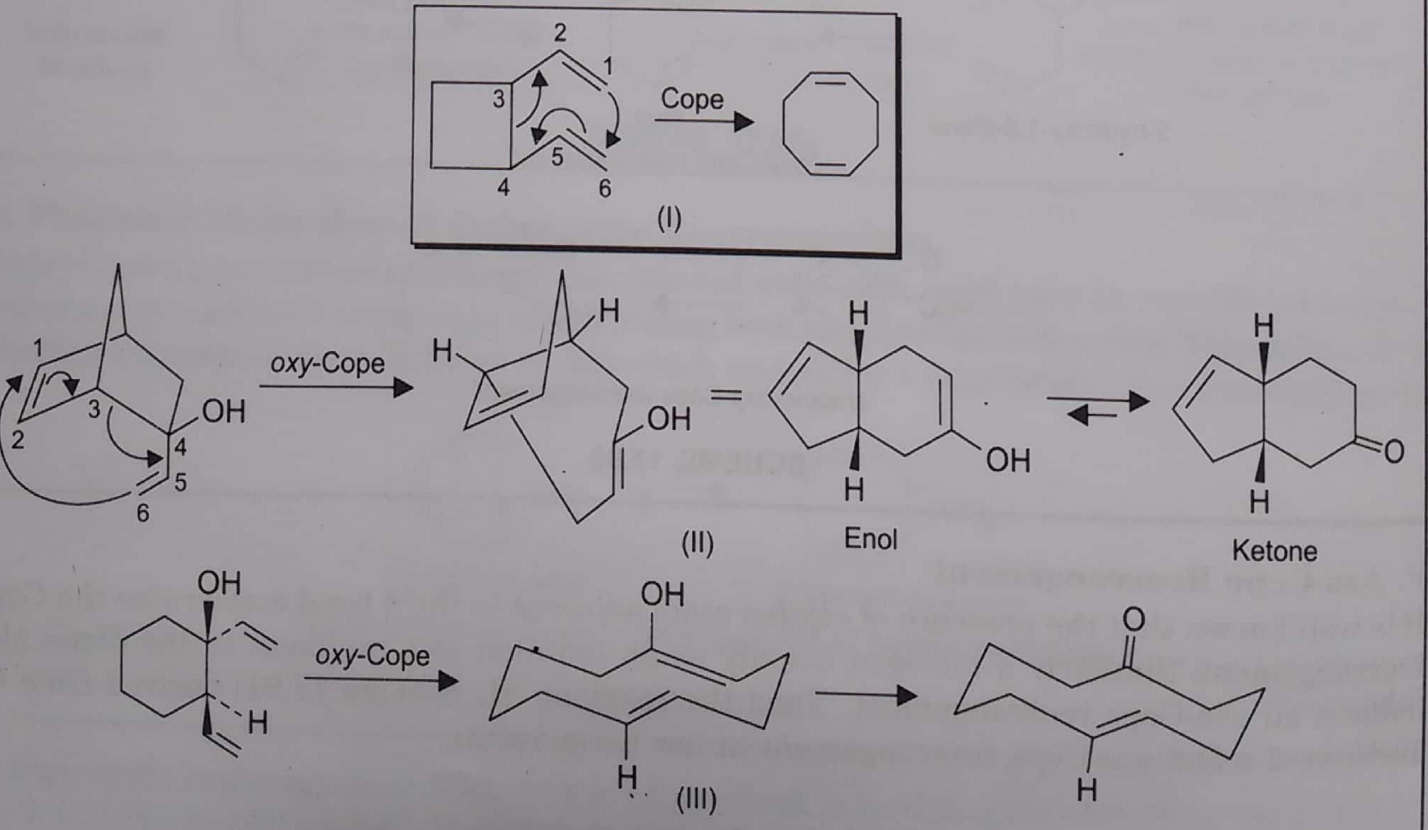
EXERCISE 17.16

Write the structure of products from the reactions (Scheme 17.92).



SCHEME 17.92

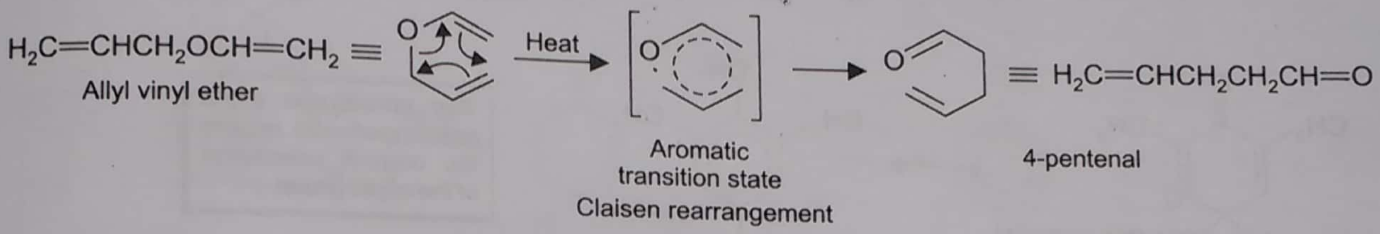
ANSWER. *Always look for the presence of a 1, 5-diene unit which will hint towards a Cope rearrangement (draw the arrow to form a bond between C1 and C6 and breaking a bond between C3 and C4, Scheme 17.93).*



SCHEME 17.93

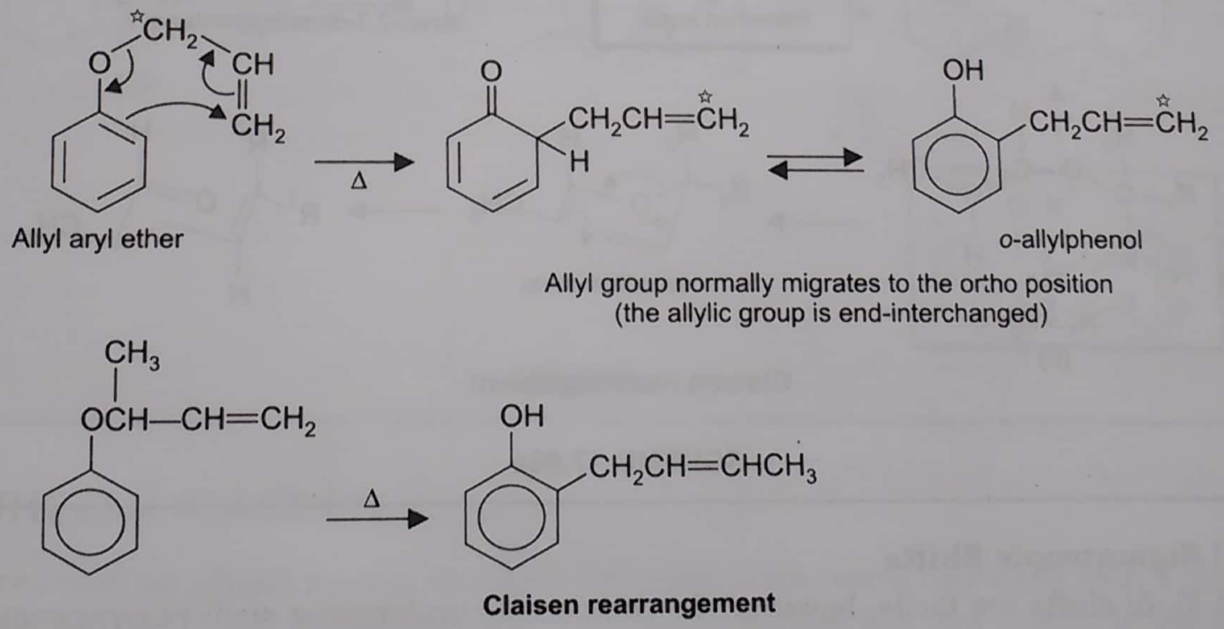
G. The Claisen Rearrangement

Claisen rearrangement also involves a [3,3] sigmatropic pathway like Cope rearrangement, however, in Claisen rearrangement the substrates incorporate one or more heteroatoms in place of carbon in the 1,5-hexadiene system. The simplest example of Claisen rearrangement is the thermal conversion of allyl vinyl ether to 4-pentenal (Scheme 17.94). The transition state involves a cycle of six orbitals and six electrons. With six electrons the transition state has aromatic character. Similarly allyl aryl ethers on heating rearrange to *o*-allyl phenols.



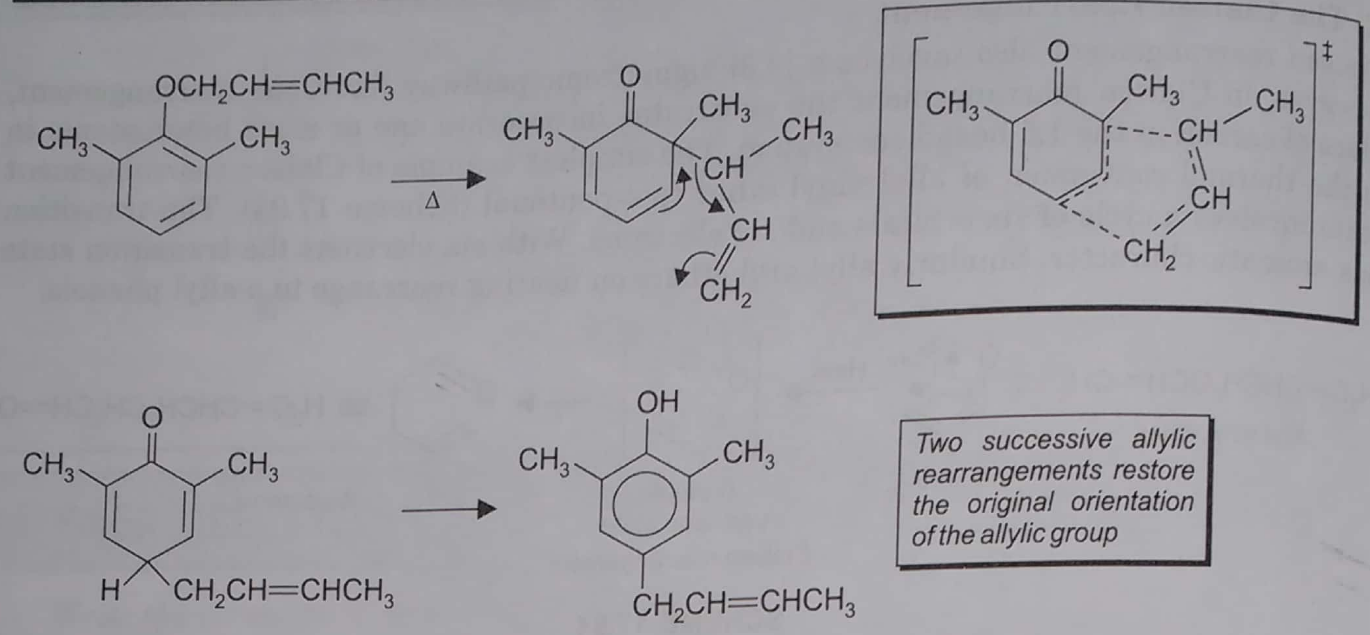
SCHEME 17.94

Studies using migrating groups labelled with ^{14}C or with substituents show that the allylic group is end-interchanged during the *ortho* rearrangement (Scheme 17.95). These and other results which show that the Claisen rearrangement is intramolecular provide strong support for a concerted mechanism. When both *o*-positions are occupied the allyl group migrates to the *p*-position (Scheme 17.96).



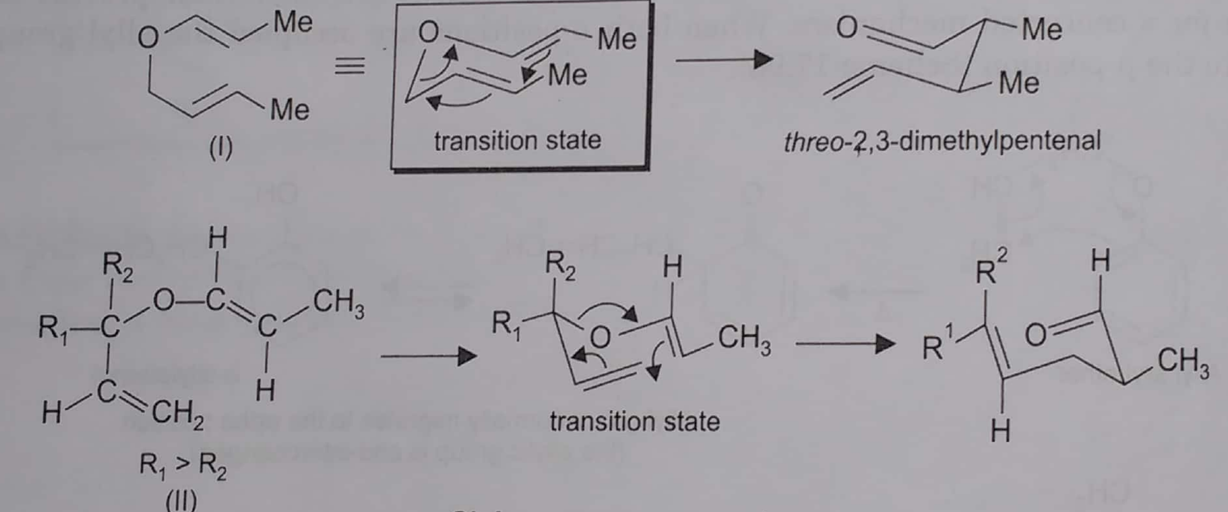
SCHEME 17.95

Like Cope rearrangement reliable stereochemical predictions can be made from a chair-like transition state (Scheme 17.96*a*). In (I) the methyl groups occupy pseudoequatorial positions in the transition state. Similarly in (II) the major product will have *E* configuration of the newly created double bond due to placement of the bulkier substituent in the pseudo equatorial position.



Two successive allylic rearrangements restore the original orientation of the allylic group

SCHEME 17.96



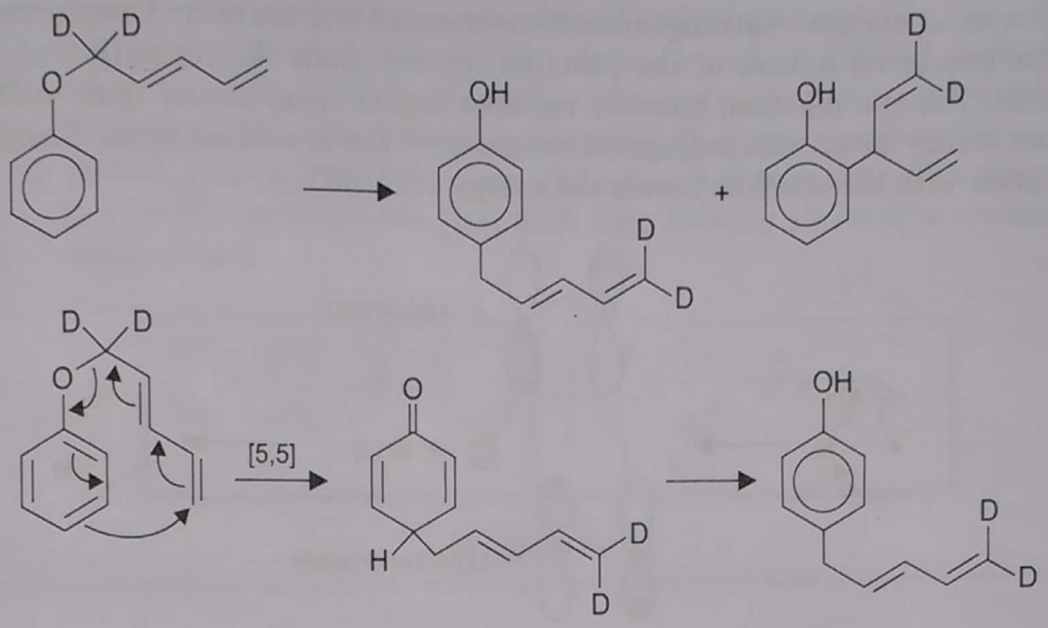
Claisen rearrangement

SCHEME 17.96a

H. [5, 5] Sigmatropic Shifts

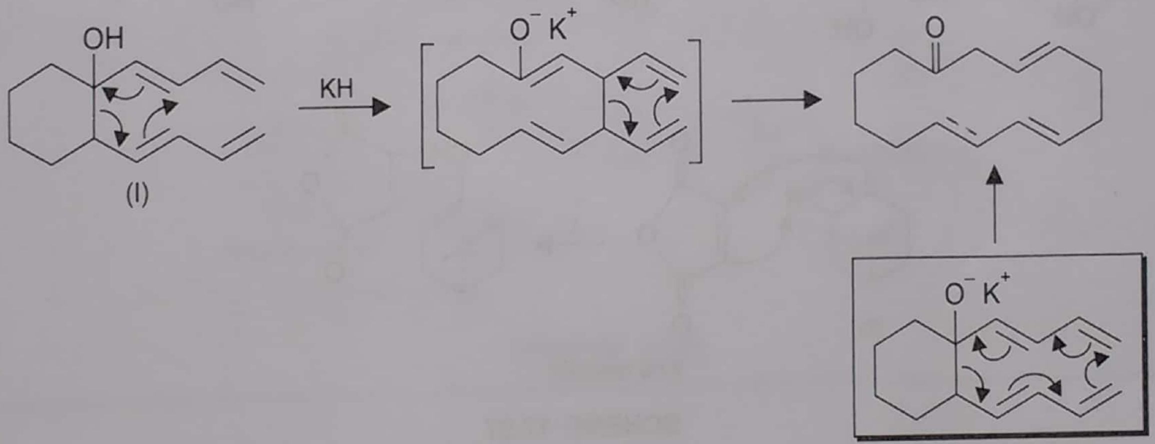
Thermal [5, 5] shifts are facile, however the compounds undergoing such rearrangement are not common. One type of substrates are pentadienyl ethers which give 4-pentadienylphenols as the major products along with minor products arising from *ortho*-Claisen rearrangement (Scheme 17.96*b*). With the help of deuterium labeling it has been shown that major products arise from direct [5, 5] sigmatropic shifts and not by two consecutive [3, 3] shifts.

It is proved that [5, 5] shifts occur very fast in negatively charged compounds. An interesting reaction is oxy-Cope rearrangement of (I, Scheme 17.96*c*) the arrangement does not proceed by a sequence of consecutive [3, 3] shifts, however it is indeed a result of [5, 5] shifts, (Scheme 17.96*c*).



[5,5] Sigmatropic shifts

SCHEME 17.96b



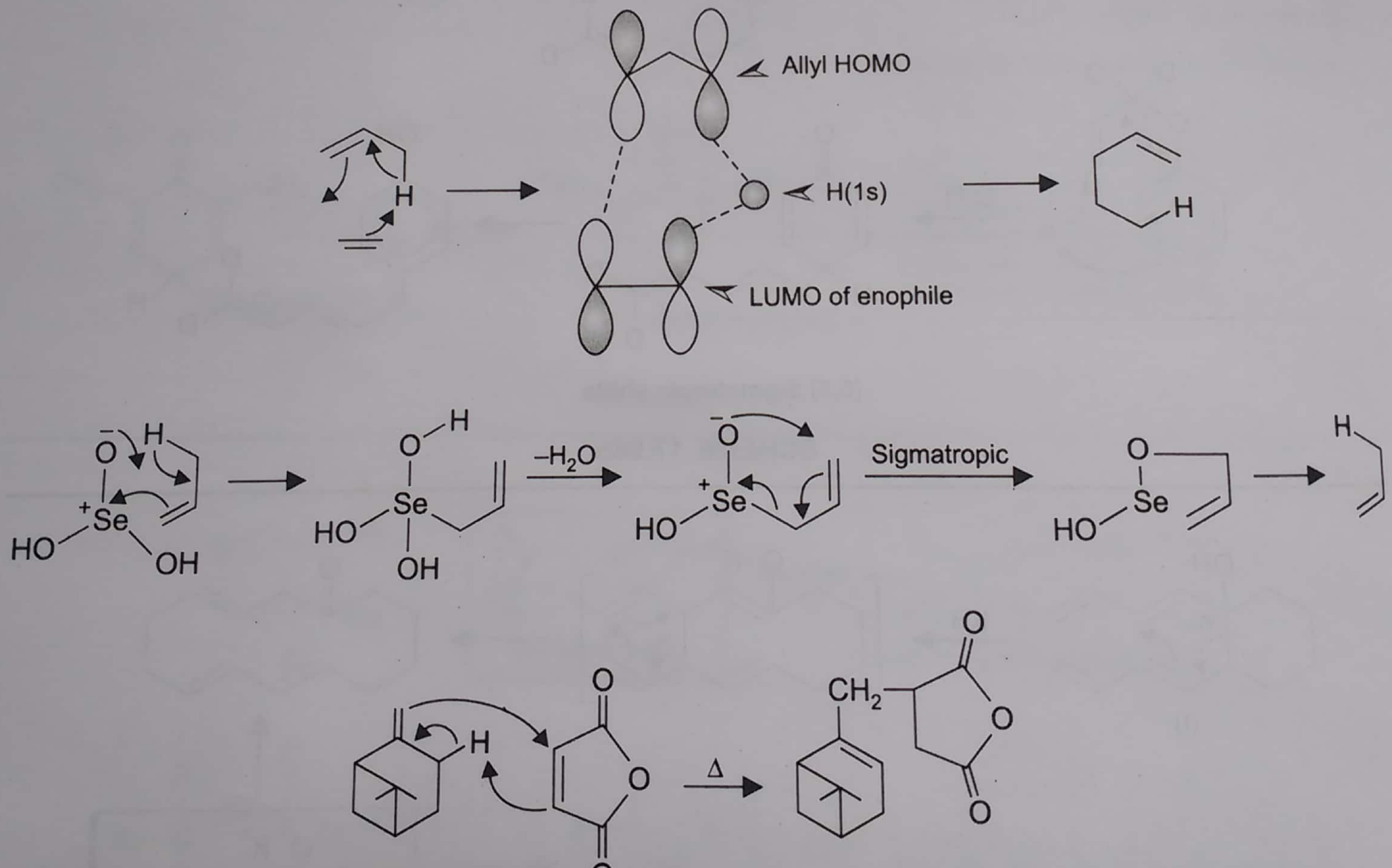
SCHEME 17.96c

17.8 THE ENE REACTION

In this reaction an alkene having an allylic hydrogen atom reacts thermally with a dienophile (C=C, C=O, N=N etc., called enophile) with the formation of a new σ bond to the terminal carbon of the allyl group. This is followed by the 1,5-migration of the allylic hydrogen and subsequent change in the position of allylic double bond. The reaction thus resembles both cycloaddition and a [1,5]-sigmatropic shift of hydrogen.

Mechanistically, the reaction is a concerted process, there being little charge development in the transition state. It shows a primary kinetic isotope effect to show C—H bond breaks in the rate determining step (the reverse process occurs in the pyrolysis of esters). The interaction of a hydrogen atom with the HOMO of the allyl radical and the LUMO of the enophile (Scheme 17.97) is a symmetry allowed process. A good example of ene reaction is found during allylic oxidation of alkenes with selenium dioxide.

The reaction shows a primary kinetic isotope effect of C—H bond breaking in the rate determining step. The ene reaction of β-pinene with maleic anhydride (Scheme 17.97) gives the product without skeletal rearrangement of the strained four membered ring in the β-pinene, to show the concerted nature of the reaction (rather than the formation of a cationic intermediate). The ene reaction, however requires higher temperature than in Diels-Alder reaction, but occurs faster with conjugated enones with Lewis acid catalysts. Coordination of the Lewis acids with the enophile lowers the energy of LUMO.



(I)

Ene reaction

SCHEME 17.97