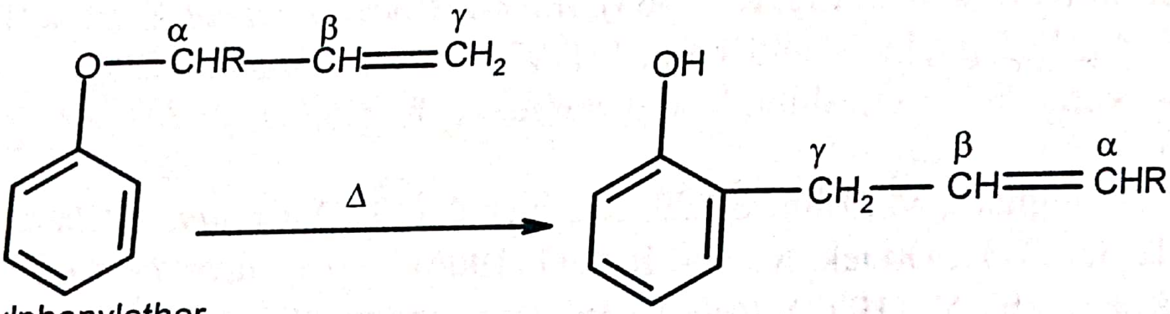
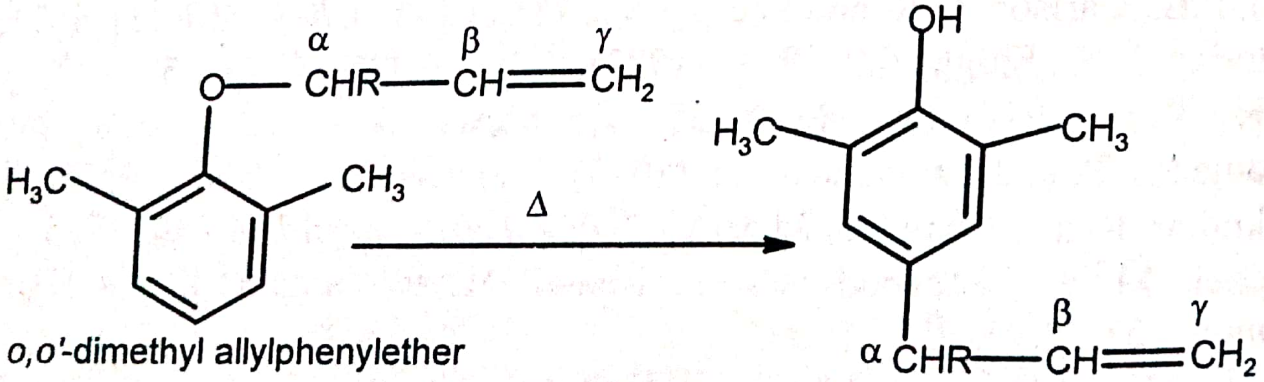
The *Claisen rearrangement*[1] is an example of pericyclic reactions, and belongs to the category of [3,3]-*sigmatropic rearrangements*. The *Claisen rearrangement* involves intramolecular thermal conversion of allyl aryl ethers to allylphenols. The allyl group in the substrate migrates from the ethereal oxygen to the ring carbon *ortho* to it. But when both the *ortho*-positions are blocked, migration occurs at the respective *para*-position.



allylphenylether

o-allylphenol
(*ortho*-migrated product)



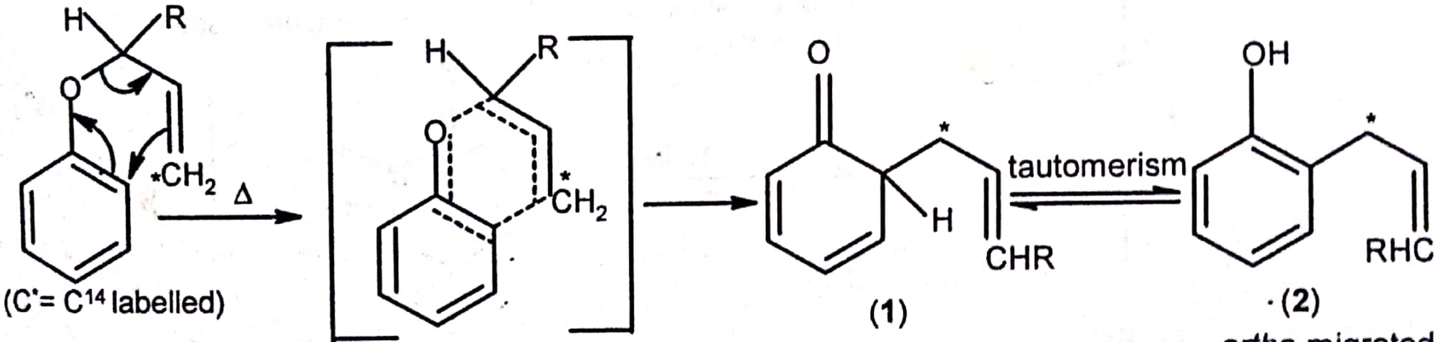
o,o'-dimethyl allylphenylether

o,o'-dimethyl allylphenol
(*para*-migrated product)

During *ortho*-migration the allyl group always undergoes an allylic shift — the carbon atom α to the ethereal oxygen atom in the substrate becomes γ to the ring in the product. However in *para*-migration, the allylic group is found exactly as it was in the starting ether. When the *para-* and both *ortho*-positions are filled, there is no reaction at all — migration to the *meta*-position has not been observed.

Mechanism

The *Claisen rearrangement* follows the first order kinetics. The rearrangement is strictly intramolecular and the mechanism is a concerted pericyclic [3,3]-sigmatropic rearrangement[2]. The reaction proceeds through a cyclic six-membered transition state in which the rupture of the oxygen-allyl bond is *synchronous* with the formation of a carbon–carbon bond at an *ortho*-position. A cyclohexadienone intermediate (**1**) is thus formed, which subsequently undergoes rapid tautomerism to yield the more stable aromatic compound (**2**).



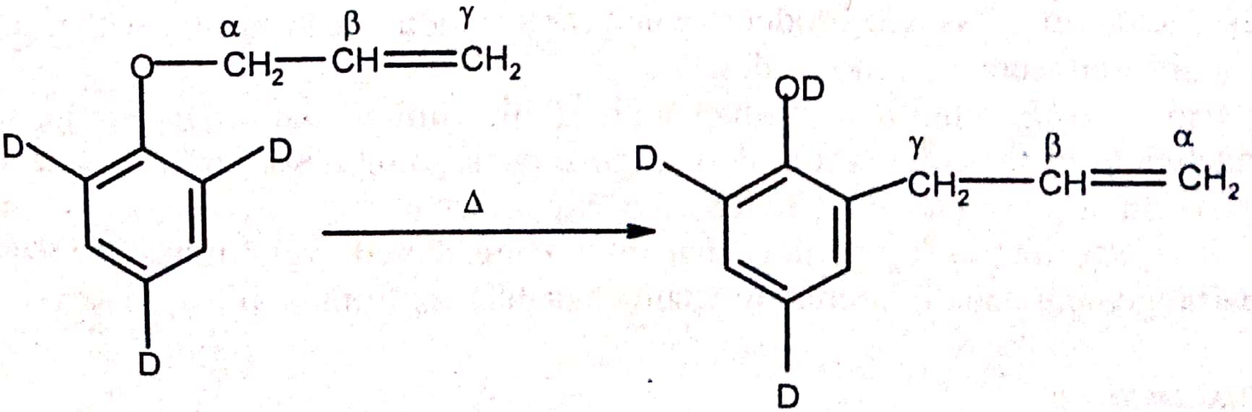
(C*= C14 labelled)

(six-membered cyclic transition state;large negative value for entropy of activation is indicative of more ordered transition state.)

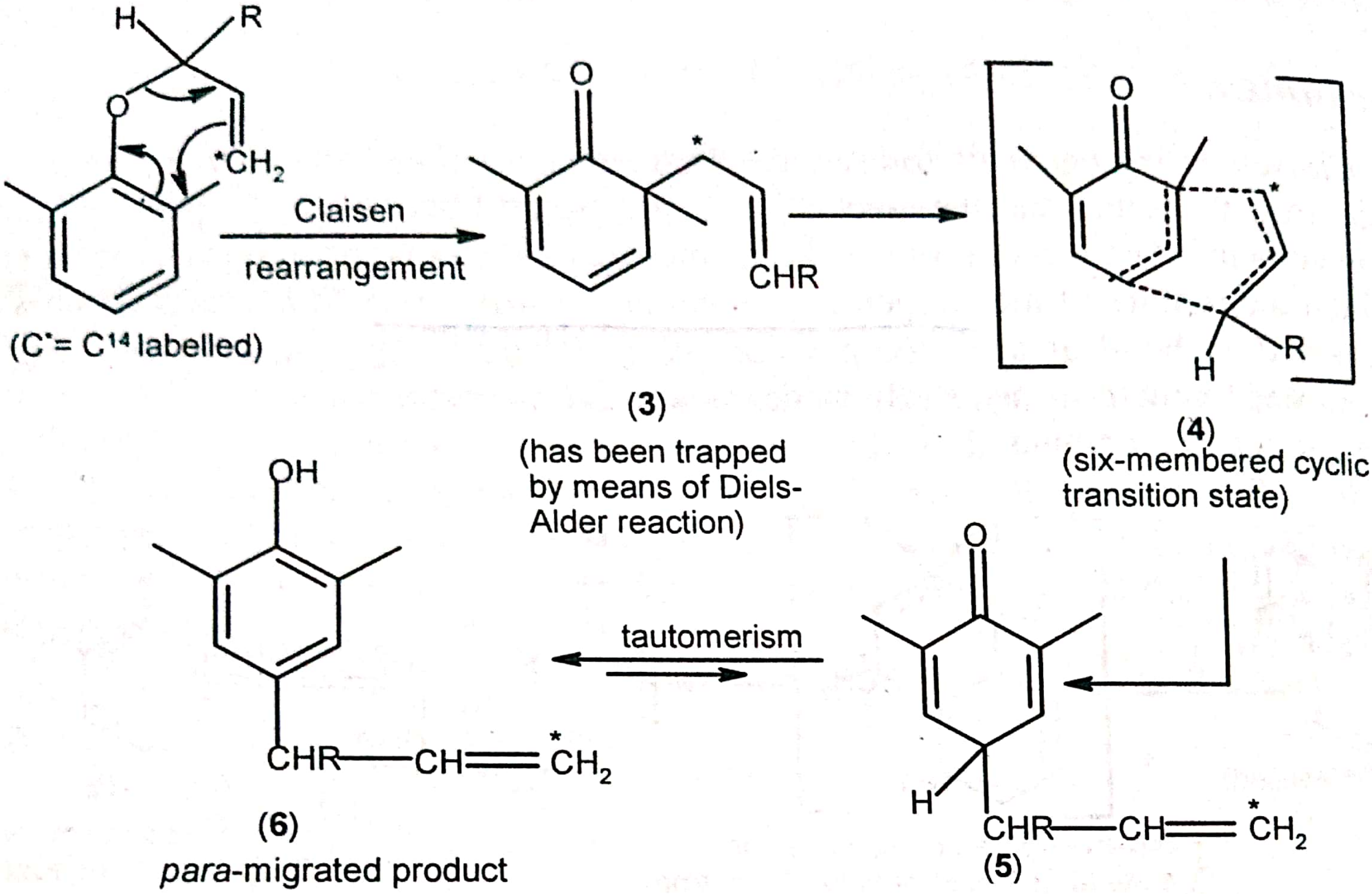
(1)

(2) *ortho*-migrated product

Supportive evidence for the migration of *o*-hydrogen in the dienone (**1**) may be drawn from the experimental work of Kistiakowsk *et al.* (1942).



In case of *para*-migration (occurs when both the *ortho*-positions are blocked) the first step leads to the formation of *ortho*-substituted cyclohexadienone (**3**), but the absence of hydrogen atom at the *ortho*-position prevents aromatization. It undergoes further rearrangement involving migration of the allyl group, again through cyclic six-membered transition state (4) yielding (5) that finally tautomerizes to the *para*-substituted product (6).



The *intramolecular mechanistic approach* is evidenced from the following facts that the reaction —

(i) requires no catalyst,

(ii) is of first order kinetics,

(iii) yields no crossover products when the reaction is carried out with a mixture of two different substrate molecules,

(iv) gives *ortho*-migrated product with allylic shift of the allylic group, while the attachment of the migrated moiety at *para*-position remains the same, due to double inversion, as derived from ^{14}C-labelling experiments.

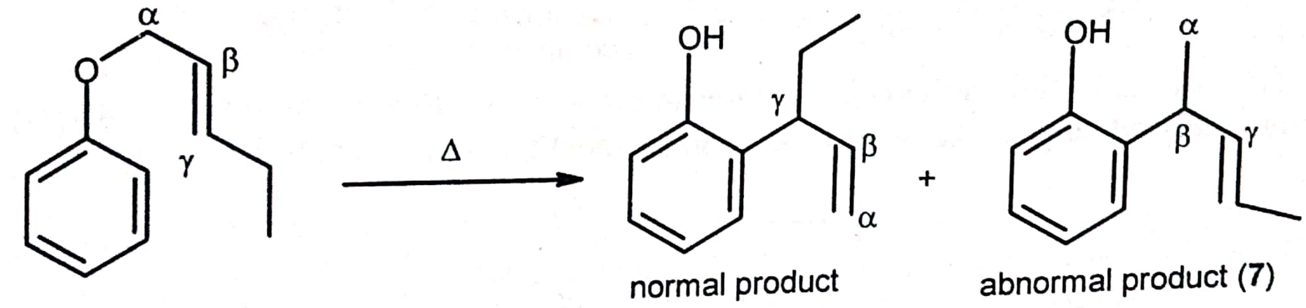
It is also interesting to note that the six-membered cyclic transition state of this rearrangement usually prefers to attain chair-like conformation[3].

Some major points regarding this type of rearrangement are being cited:

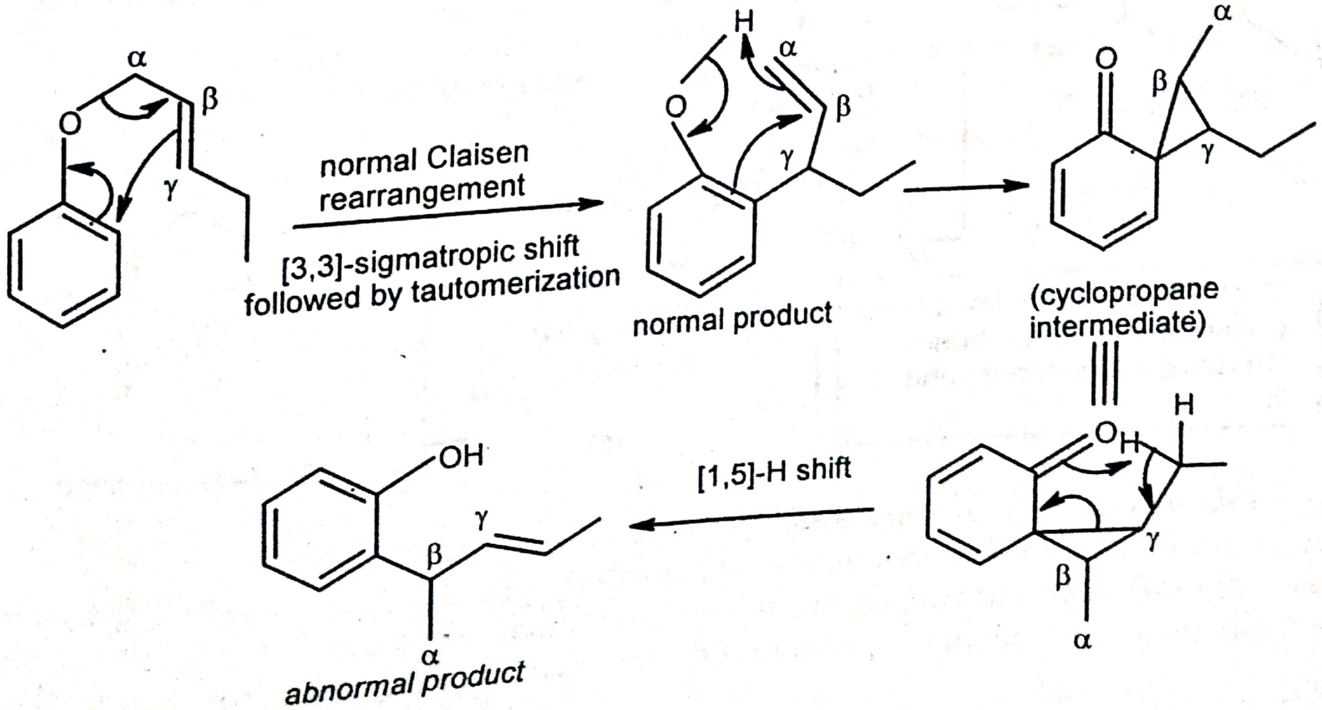
(a) The electronic nature of substituents, if present on the ring, has no so much influence on the rate of the *Claisen rearrangement*. This is because of the fact that the reaction mechanism does not involve ions. Although the effect is small, electronreleasing substituents have been found to enhance the reaction rate, and electron-withdrawing ones to decrease the rate at a minor scale.

However, the reaction rate has been observed to become greatly influenced by solvent effect; trifluoroacetic acid is usually employed as a good solvent for carrying out the reaction at room temperature.

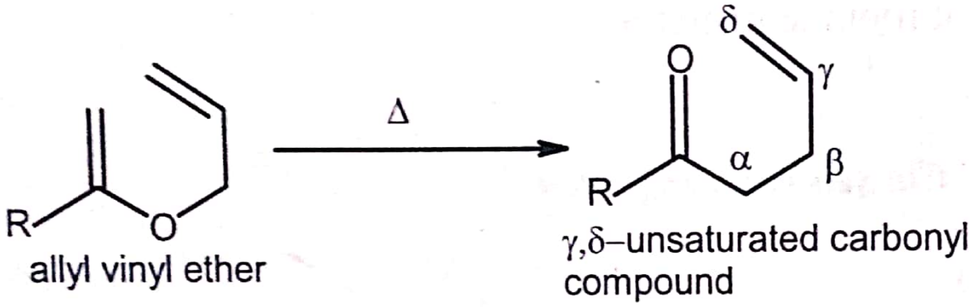
(b) "*Abnormal" Claisen rearrangement*[4]



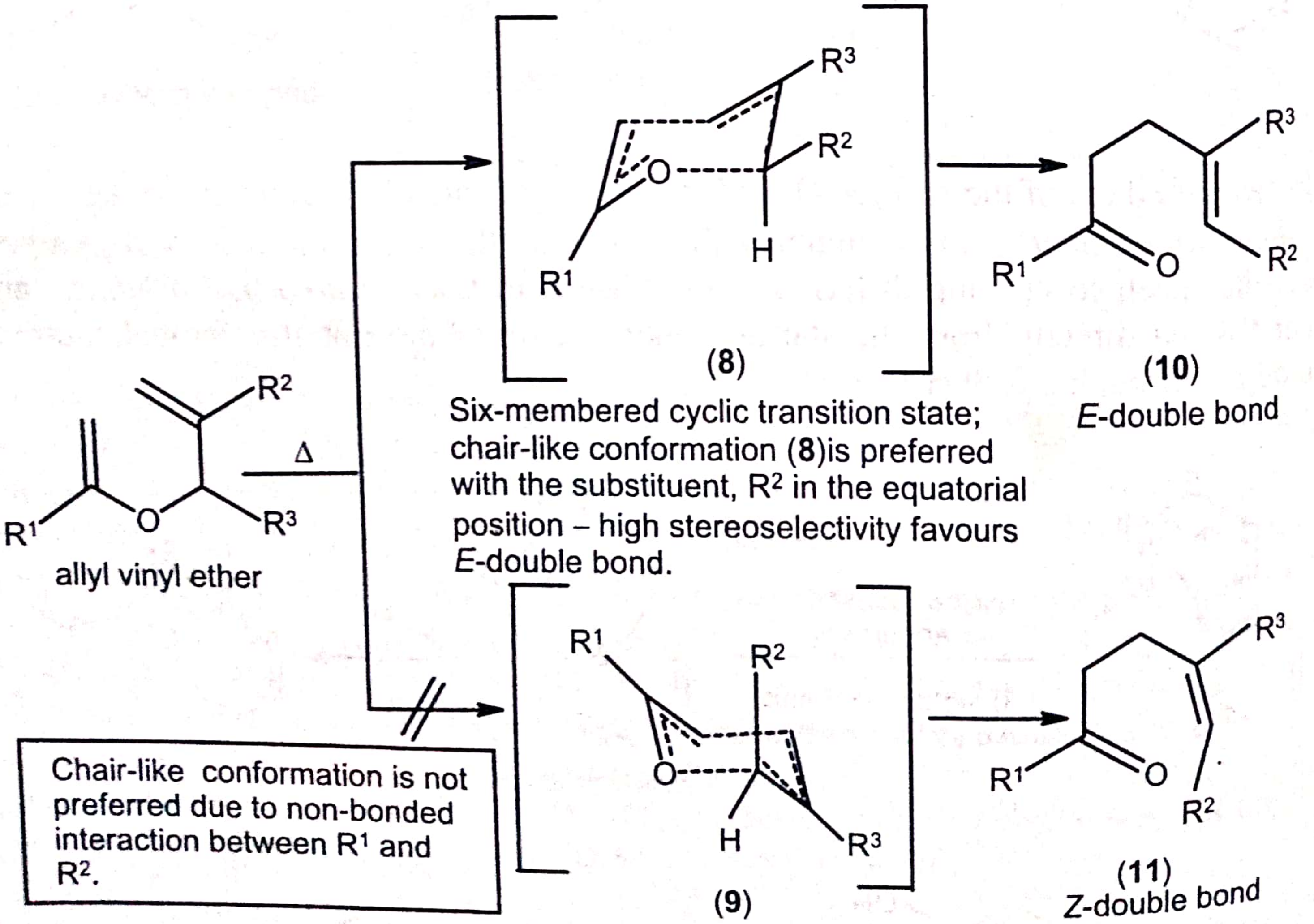
In case of ethers of the type, ArO–C–C=C–R, having an alkyl group at γ-position, an '*abnormal product*' (7) is sometimes obtained —— the β–carbon instead of γ-carbon attaches itself to the ring. It has been established that such '*abnormal products*' are not formed directly from the starting ether, but from the initially formed 'normal product' through a further rearrangement —



c) Allyl vinyl ethers[5] also undergo the *Claisen rearrangement* in similar fashion via concerted step six-membered cyclic transition state. In such cases there is no energetic driving force for tautomerism to restore aromaticity, and thus enone is the end product.



The reaction offers an excellent stereoselective route to γ,δ-unsaturated carbonyl compounds (aldehydes, ketones, esters and amides) from allyl alcohols.



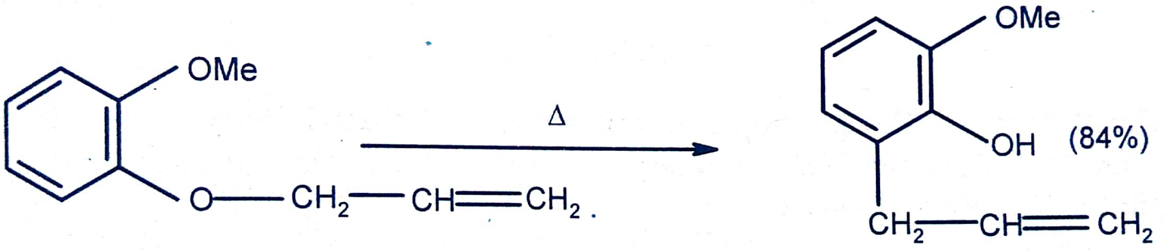
Six-membered cyclic transition state; chair-like conformation (**8**)is preferred with the substituent, R^2 in the equatorial position – high stereoselectivity favours *E*-double bond.

Chair-like conformation is not preferred due to non-bonded interaction between R^1 and R^2.

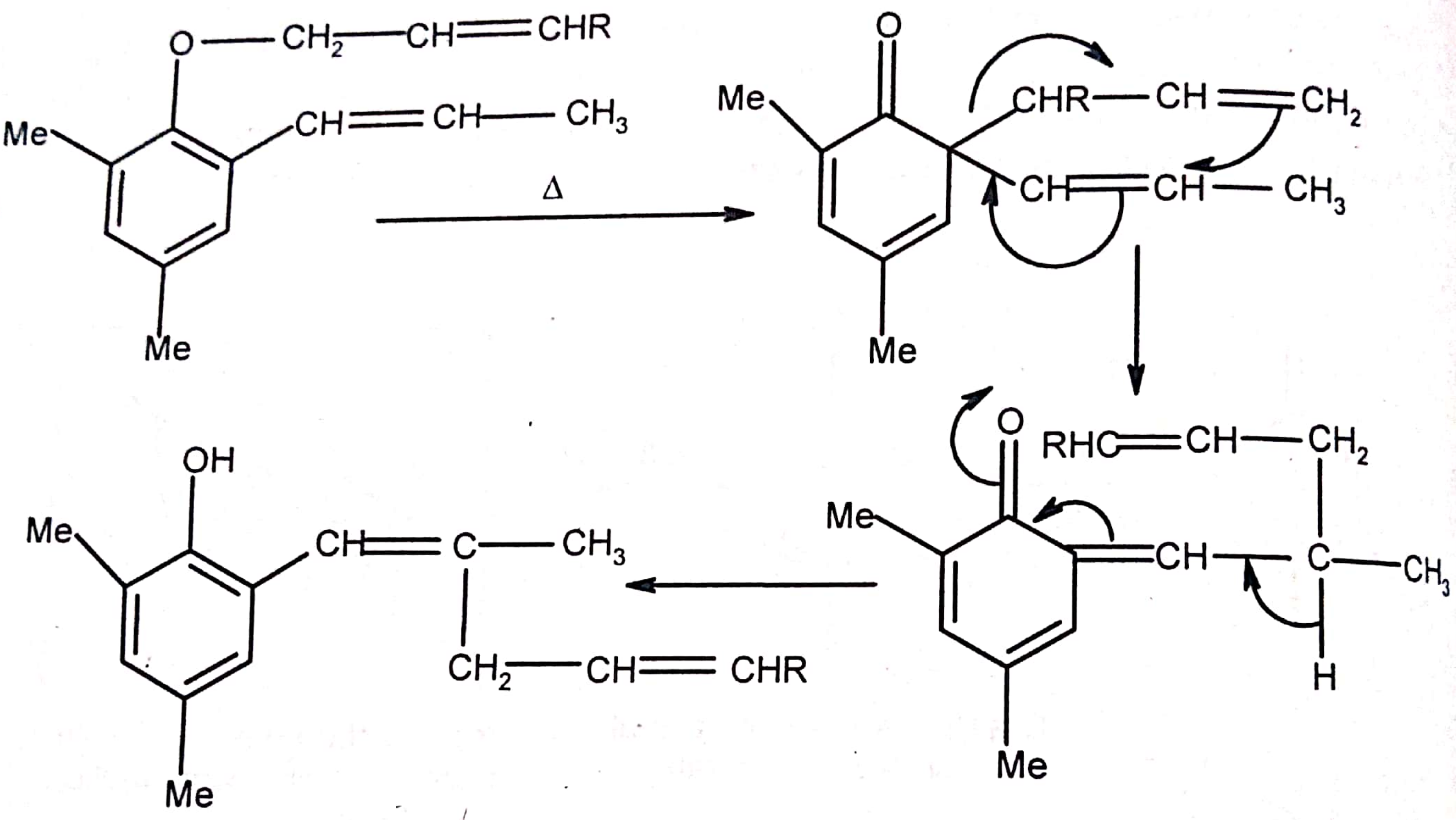
Applications

The classical *Claisen rearrangement* and its extensions are of tremendous utility in organic syntheses. Some are mentioned here:

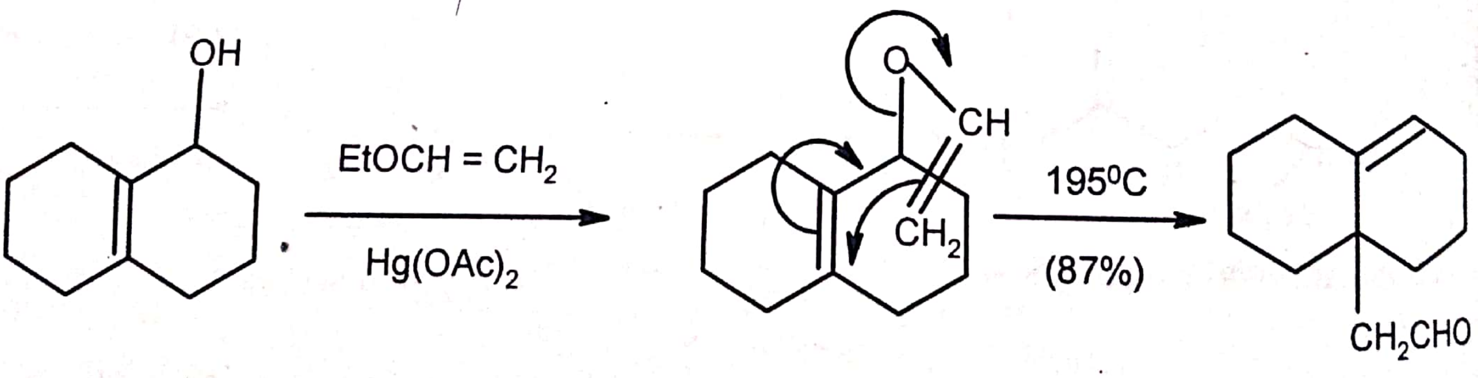
1)

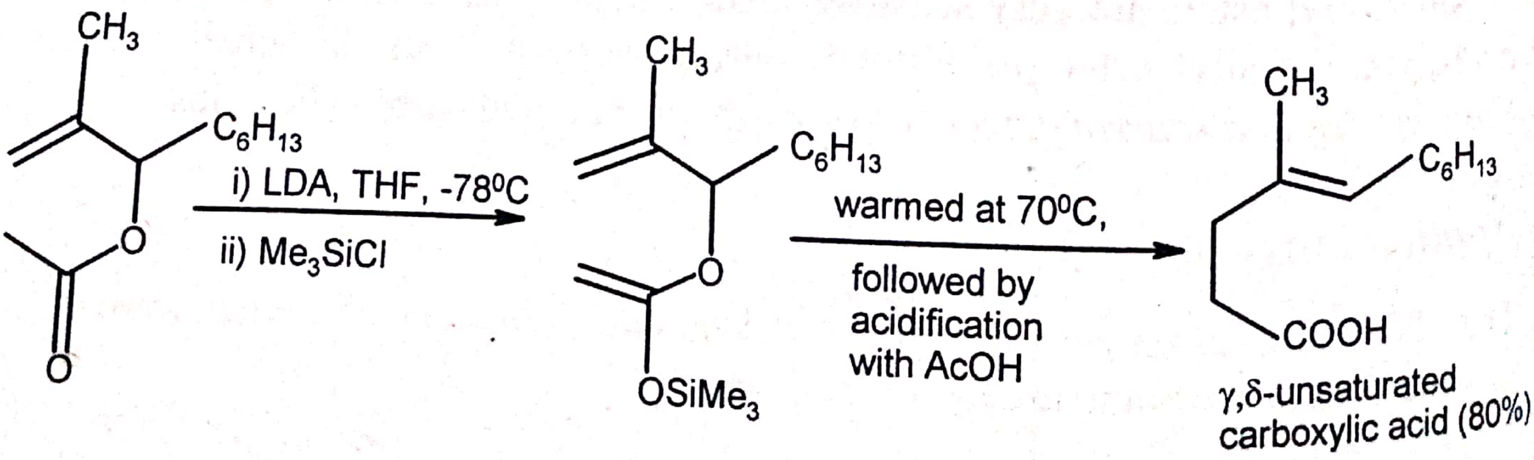


2)


O—CH₂—CH=CHR
Me
CH=CH—CH₃
Me
Δ
O
Me
CHR—CH=CH₂
CH=CH—CH₃
Me
O
RHC=CH—CH₂
Me
=CH—C—CH₃
H
Me
OH
Me
CH=C—CH₃
CH₂—CH=CHR
Me

3)


OH
EtOCH = CH₂
Hg(OAc)₂
O
CH
CH₂
195⁰C
(87%)
CH₂CHO


CH₃
C₆H₁₃
O
O
i) LDA, THF, -78⁰C
ii) Me₃SiCl
CH₃
C₆H₁₃
O
OSiMe₃
warmed at 70⁰C,
followed by
acidification
with AcOH
CH₃
C₆H₁₃
COOH
γ,δ-unsaturated
carboxylic acid (80%)