

**DAMIETTA
UNIVERSITY**

**CHEM-405:
PERICYCLIC REACTIONS**

LECTURE 7

Dr Ali El-Agamey

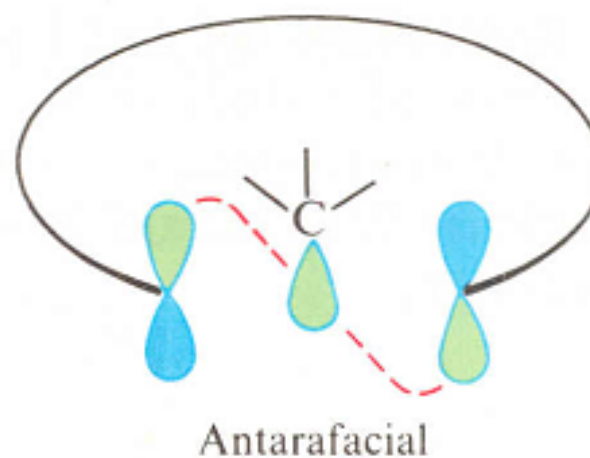
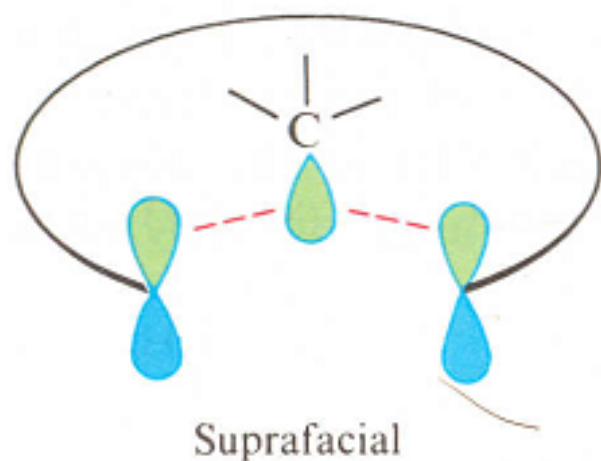
Sigmatropic Rearrangements

Migration of Carbon¹

➤ As compared to a hydrogen atom, which has only **one lobe** (1s orbital), the carbon free radical has **two lobes of opposite phases** (p orbital). Thus carbon can simultaneously interact with the migration source and the migration terminus using either **one of its lobes** or **both of them**.¹

Sigmatropic Rearrangements

Migration of Carbon¹

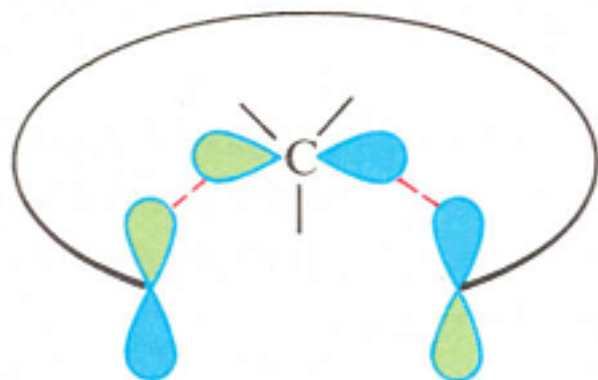


Retention in G

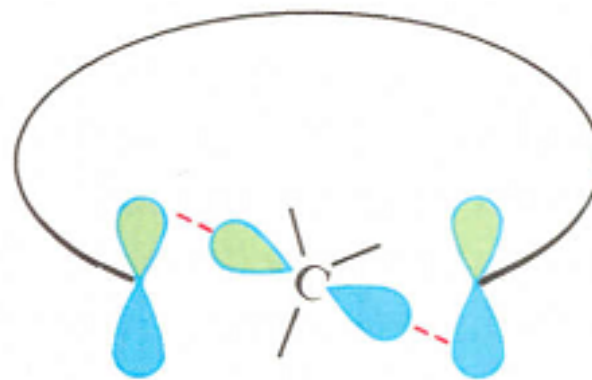
- Bonding through the **same lobe** on carbon means attachment to the same face of the atom, that is to say, *retention of configuration in the migrating group*.¹

Sigmatropic Rearrangements

Migration of Carbon¹



Suprafacial



Antarafacial

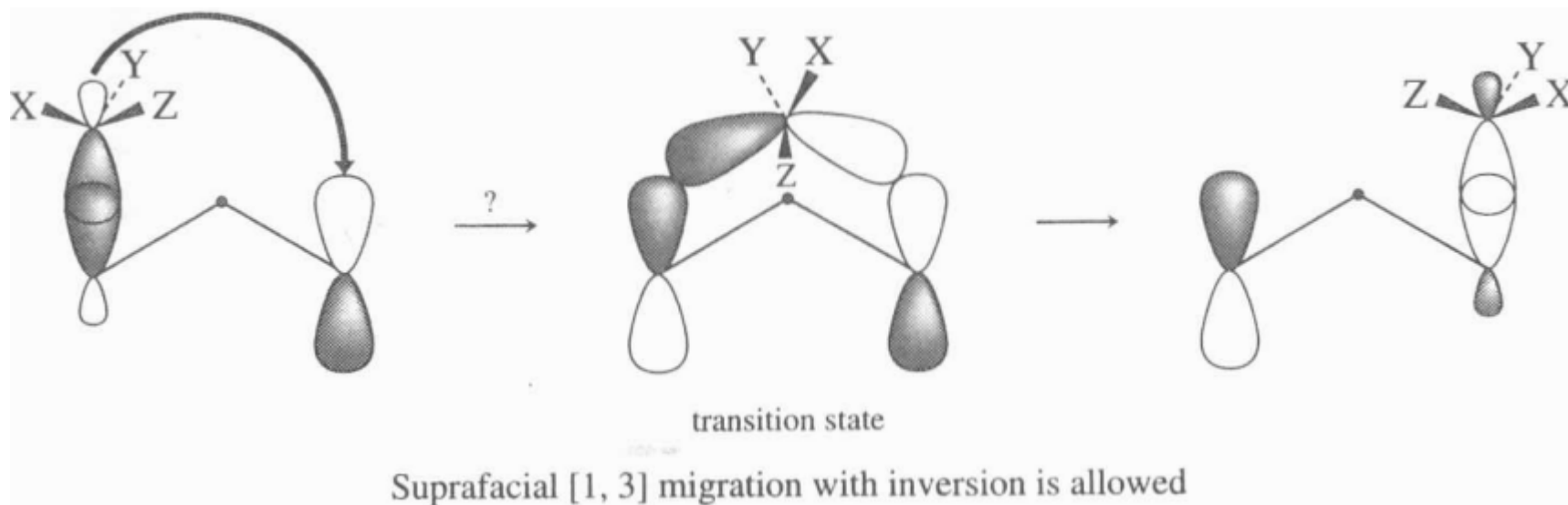
Inversion in G

- Bonding through **different lobes** of a p orbital- these lobes are on opposite faces of carbon- leads to an *inversion of configuration in the migrating group*.¹

Sigmatropic Rearrangements

[1,3] alkyl shift:

Migration of Carbon¹

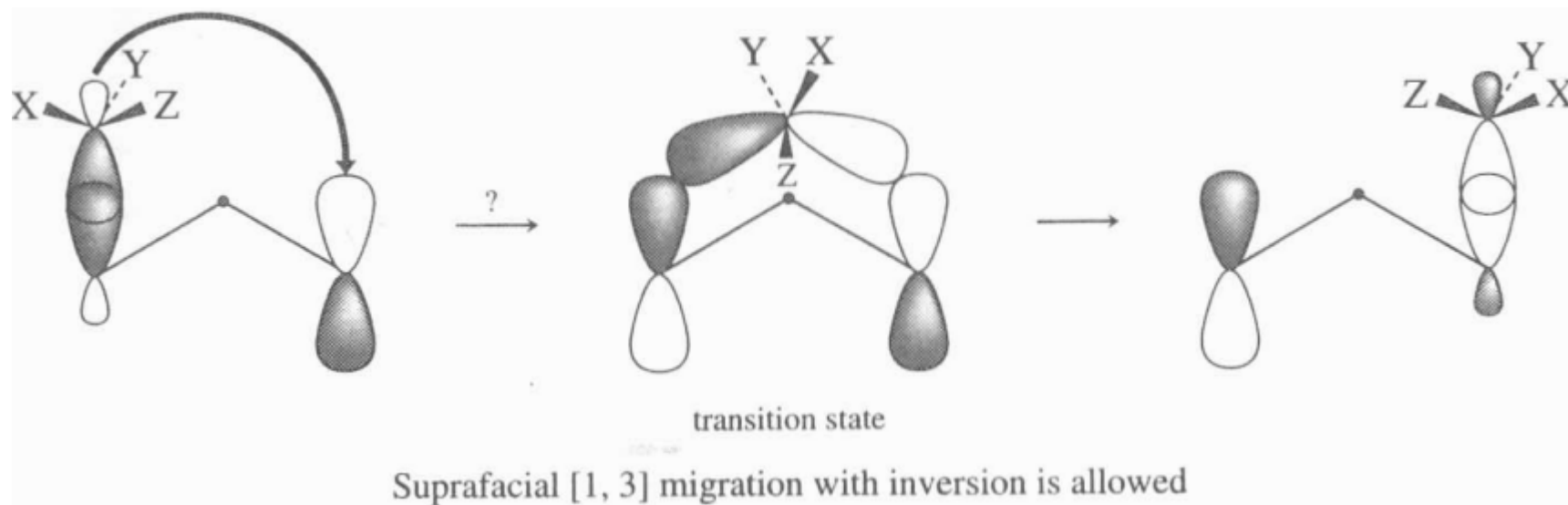


- Suprafacial migration with retention of configuration of the migrating group would again be **forbidden**.
- An antarafacial migration with retention, while **theoretically allowed** would be **very unlikely** to occur.
- A suprafacial migration forming a new bond to the "**back**" lobe of the migrating orbital would also be **theoretically allowed**. This process would result in **inversion** of the configuration of the migrating group.

Sigmatropic Rearrangements

Migration of Carbon¹

[1,3] alkyl shift:



- It would obviously require **grossly distorted bonds in the TS** and would be an **unlikely process**, although perhaps **not quite so unlikely** as a migration to the opposite face of the pi system.¹
- Not surprisingly, there **do not** seem to be any examples of [1,3] alkyl shifts in **open-chain alkenes**. However, [1,3] shifts of alkyl groups can occur if the reactions involve **expansions of strained** three-membered or four-membered rings.¹

Sigmatropic Rearrangements

Migration of Carbon¹

[1,3] alkyl shift \longrightarrow ar or si

[1,5] alkyl shift \longrightarrow ai or sr

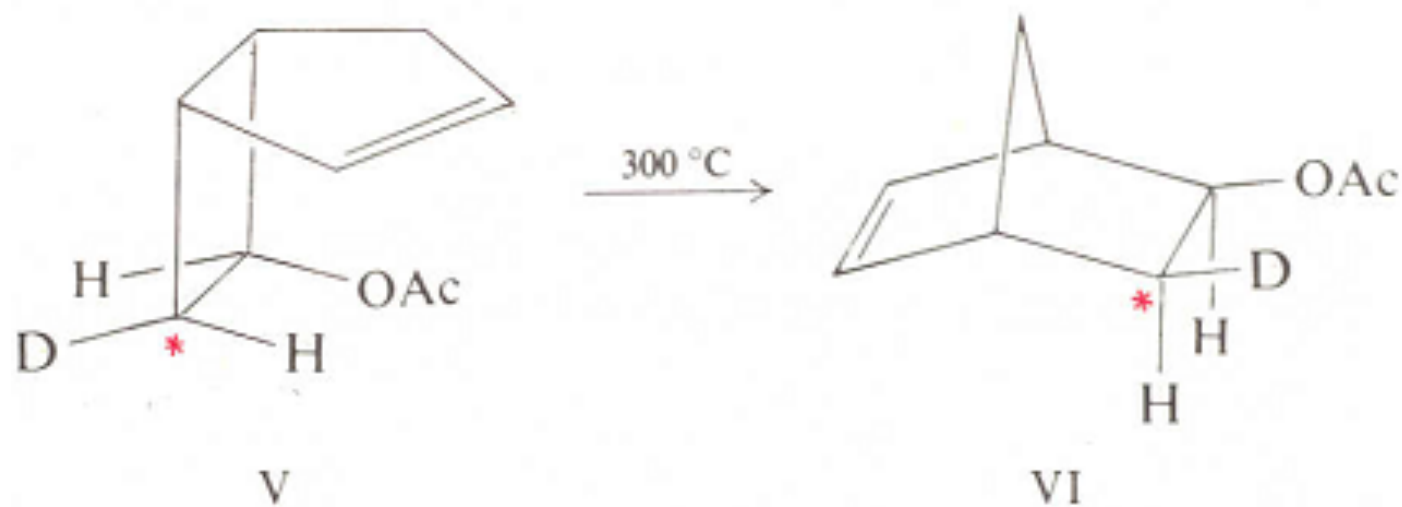
[1,7] alkyl shift \longrightarrow ar or si

Where **s** and **a** refer to suprafacial and antarafacial, and **r** and **i** to retention and inversion of configuration at the migrating center.²

Sigmatropic Rearrangements

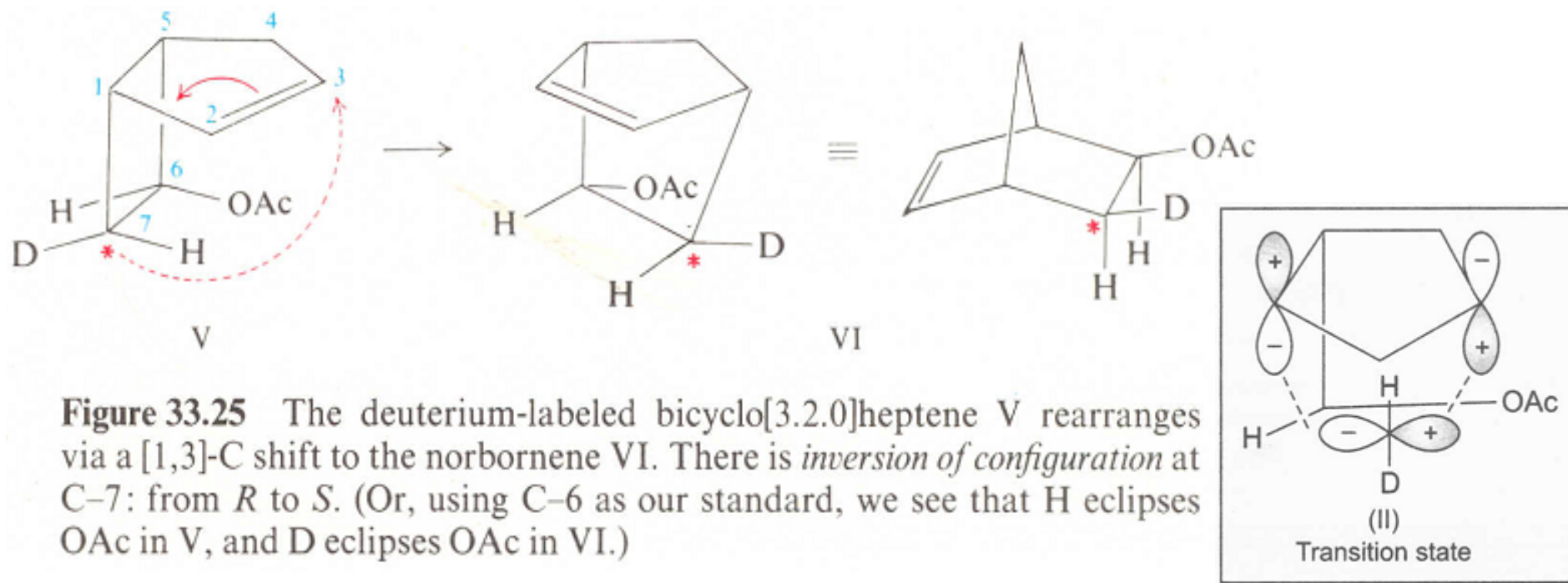
Migration of Carbon¹

These prediction have been confirmed by experiments:



Sigmatropic Rearrangements

Migration of Carbon¹

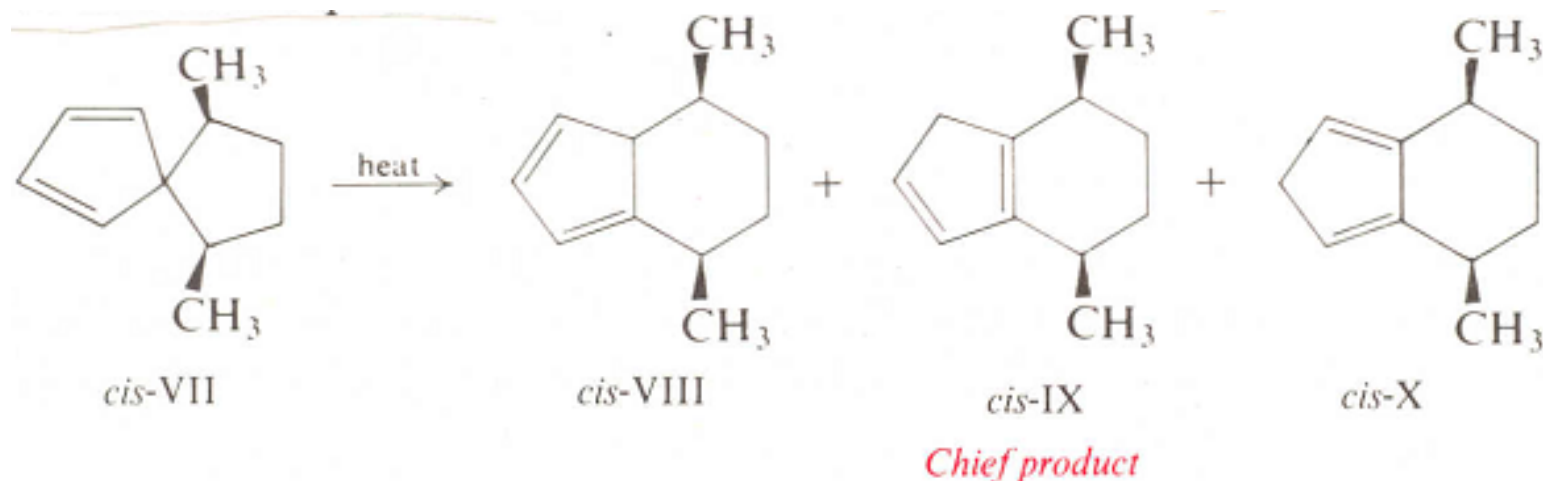


- This reaction proceeds by a [1,3] migration and with *complete inversion of configuration in the migrating group*.¹

Sigmatropic Rearrangements

Migration of Carbon¹

- **Homework:** Write a reasonable mechanism for the following reaction.
Note: the reaction involves 1,5-alkyl and 1,5-H shifts.



- This reaction is completely stereoselective and stereospecific.¹

LEARNING OUTCOMES

LECTURE 8

➤ **(1) The Woodward-Hoffmann rules for [1,n] sigmatropic rearrangements**

-[1,2] cationic shift -[1,2] anionic shift

➤ **(2) Photochemical Sigmatropic Rearrangements**

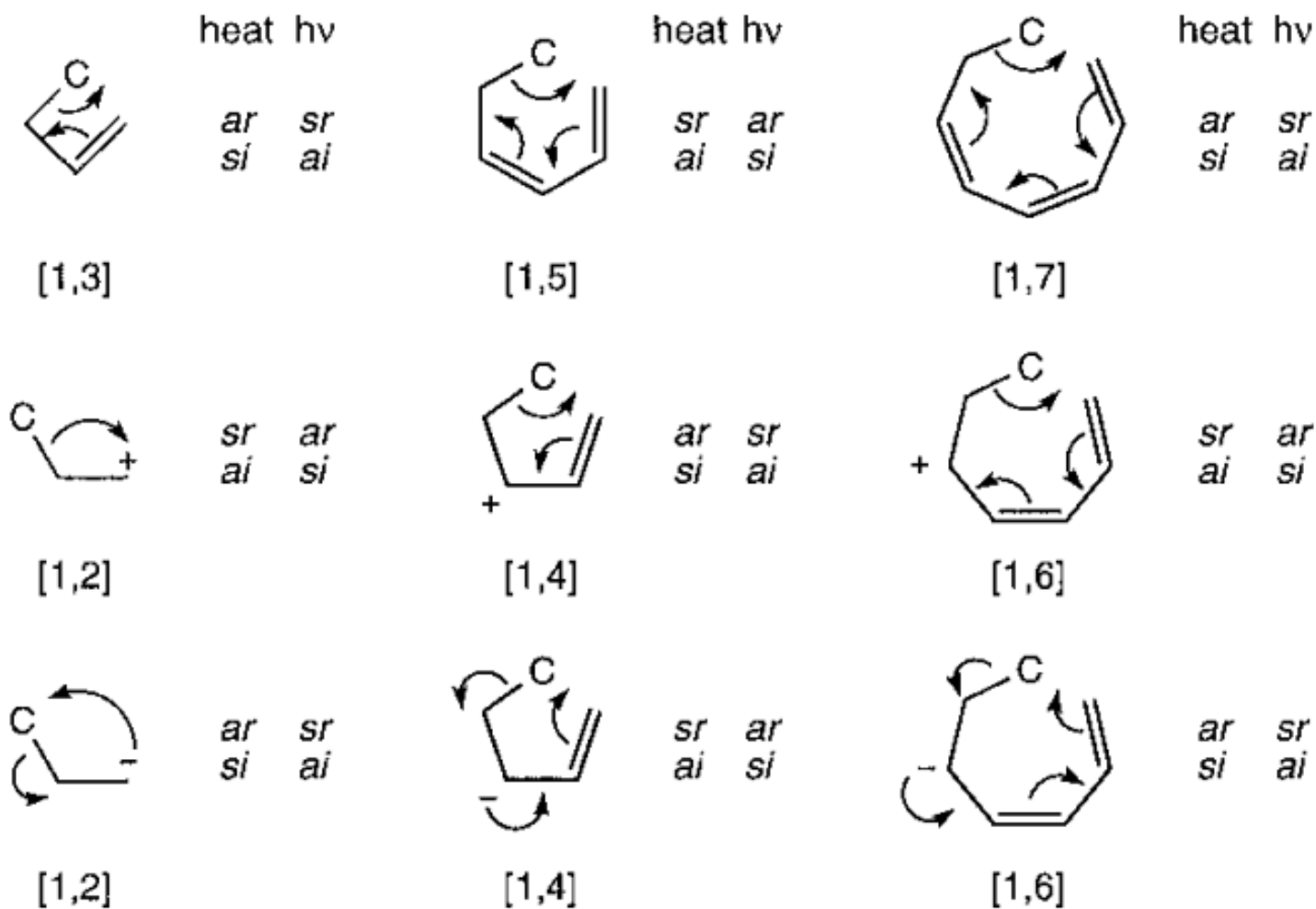
➤ **(3) [m,n] Sigmatropic Rearrangements**

(a) [3,3] sigmatropic rearrangements:

-Cope rearrangement -oxy-Cope rearrangement -anionic oxy-Cope rearrangement -Claisen rearrangement -Ireland-Claisen rearrangement

(b) [5,5] sigmatropic rearrangements

The Woodward-Hoffmann rules for [1,n] sigmatropic rearrangements¹



➤ If the migrating group is **hydrogen**, the pathways involving **inversion** must be **ignored**.

The Woodward-Hoffmann rules for [1,n] sigmatropic rearrangements¹

$(4n + 2)$ electrons \longrightarrow e.g. 2 or 6 or 10 electrons

$(4n)$ electrons \longrightarrow e.g. 4 or 8 or 12 electrons

$(4n + 2)$ electrons



suprafacial shift with retention (or antarafacial shift with inversion but impossible in practice)

The Woodward-Hoffmann rules for [1,n] sigmatropic rearrangements¹

- (4n) electrons are the opposite

(4n) electrons



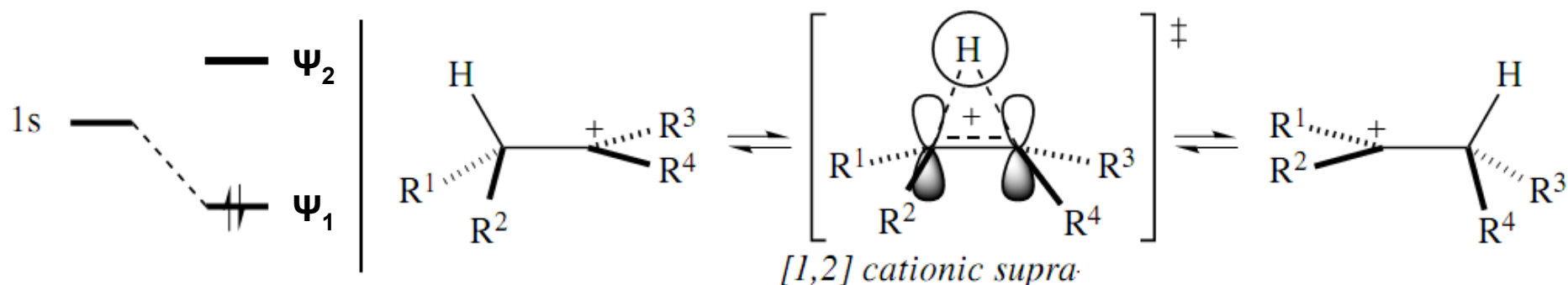
suprafacial shift with inversion (or antarafacial shift with retention)

- Photochemical reactions follow the reverse of the thermal rule.

Sigmatropic Rearrangements¹

[1,2] cationic shift:

- In the cationic [1,2] hydride shift (**two**-electron reaction), there are one-atom component, the H atom, and two-atom component.
- **No matter** how the two electrons are distributed between the two components, *the dominant HOMO–LUMO interaction in the TS is between the 1s orbital of the one-atom component and Ψ_1 of the two-atom component.*

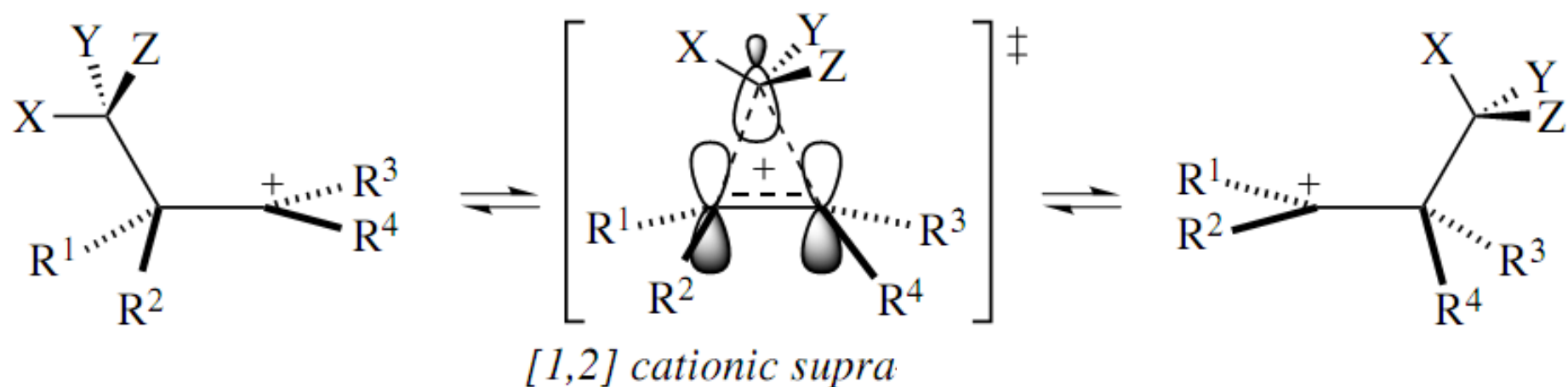


- The H atom is always classified as a suprafacial component, as the 1s orbital is monophasic.

Sigmatropic Rearrangements¹

[1,2] cationic shift:

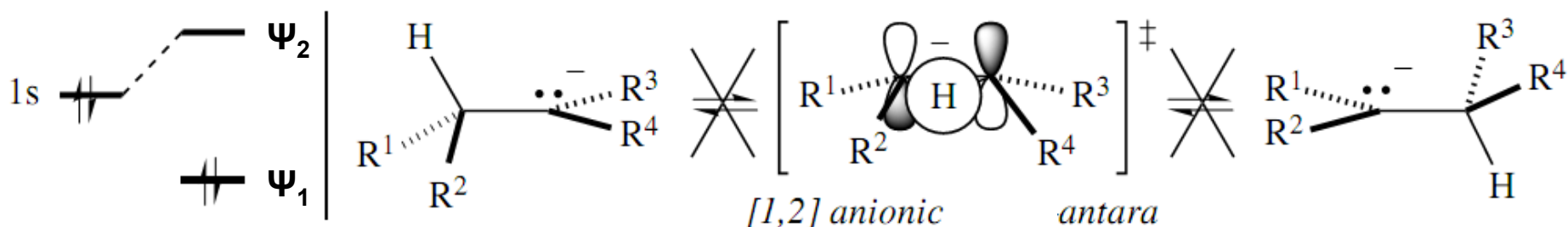
- Likewise, in the cationic **[1,2] alkyl shift**, both components must be **suprafacial**. The migrating group **retains its configuration** because of the requirement for suprafaciality.



Sigmatropic Rearrangements¹

[1,2] anionic shift:

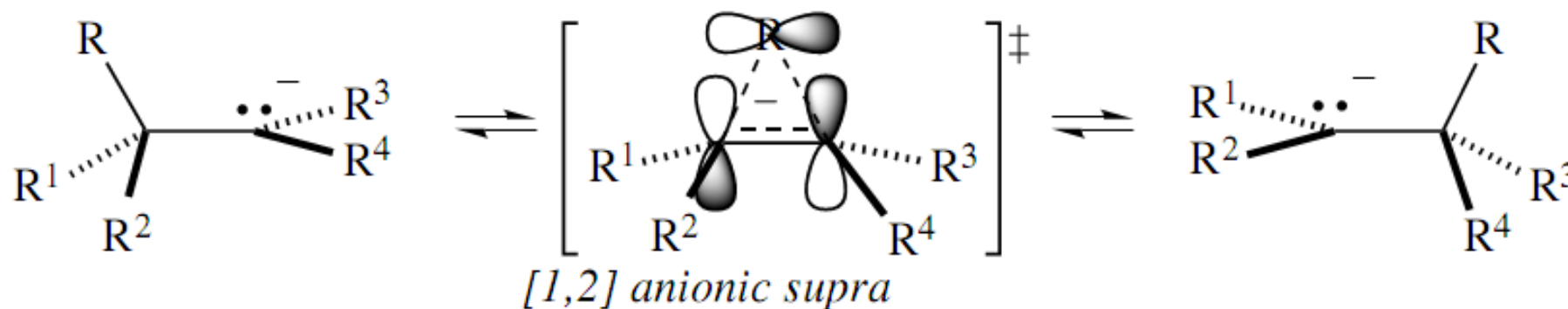
- By contrast, in the [1,2] anionic H shift, the dominant FMO interaction is **between** the **1s** orbital of the one-atom component and Ψ_2 of the two-atom component.
- The H atom must have partial bonds to the top and bottom faces of the two-atom component simultaneously. Because this arrangement is **geometrically impossible**, [1,2] anionic H shifts are **thermally disallowed reactions**.



Sigmatropic Rearrangements¹

[1,2] anionic shift:

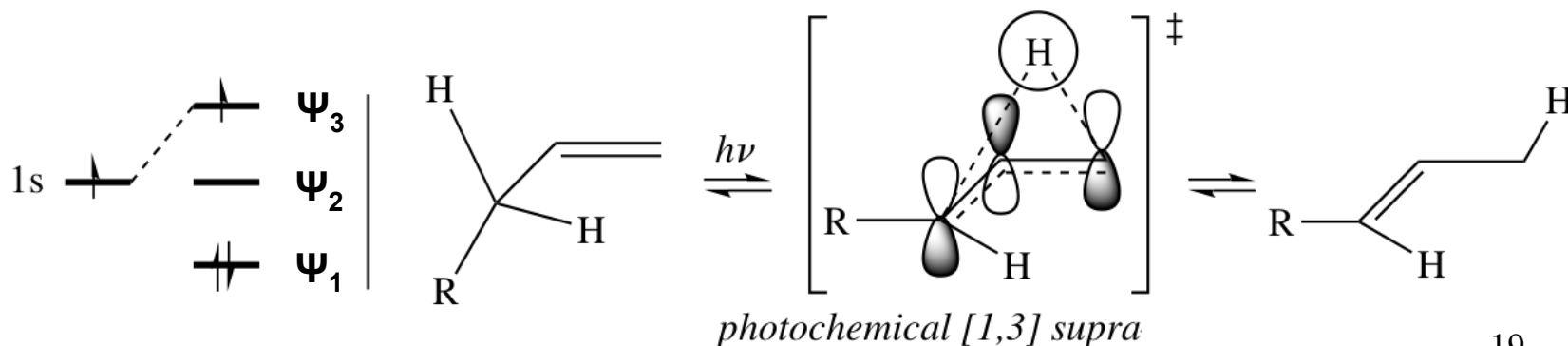
- In the case of the **alkyl shift**, the **configuration is inverted**. In fact, the geometric requirements for anionic [1,2] alkyl shifts are so stringent (**severe, inflexible**) that the reactions are **extremely rare**.



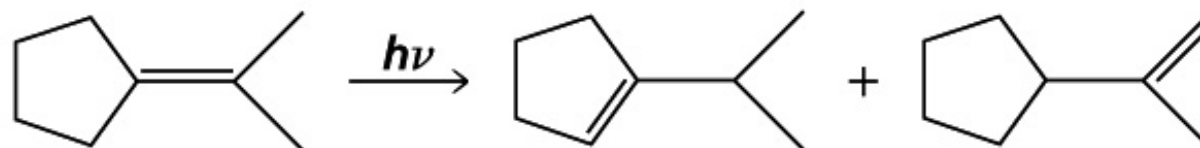
Photochemical Sigmatropic Rearrangements

Migration of Hydrogen

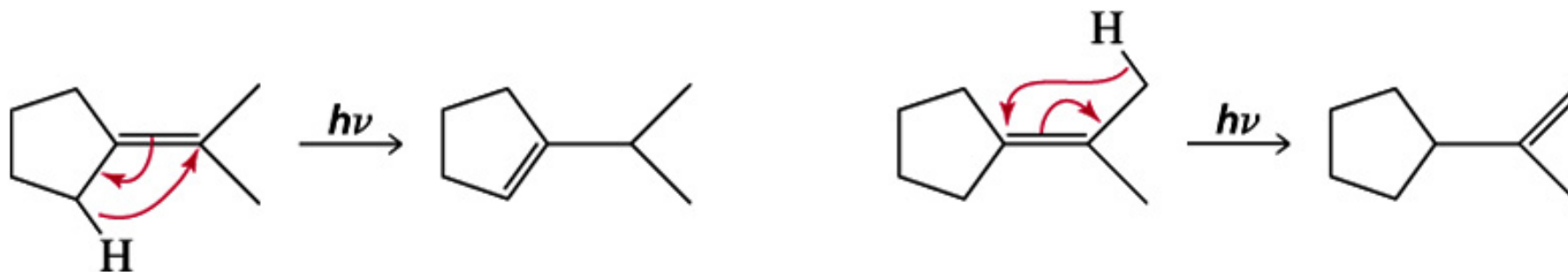
- Photochemical sigmatropic rearrangements are extremely rare.³⁻⁴
- For photochemical rearrangements, predictions are exactly reversed.¹
- In a photochemical [1,3] sigmatropic rearrangement, the stereochemical requirement changes because under these conditions, the HOMO of the three-atom component is Ψ_3 (symmetrical), not Ψ_2 (antisymmetrical).²



1,3-hydrogen shifts

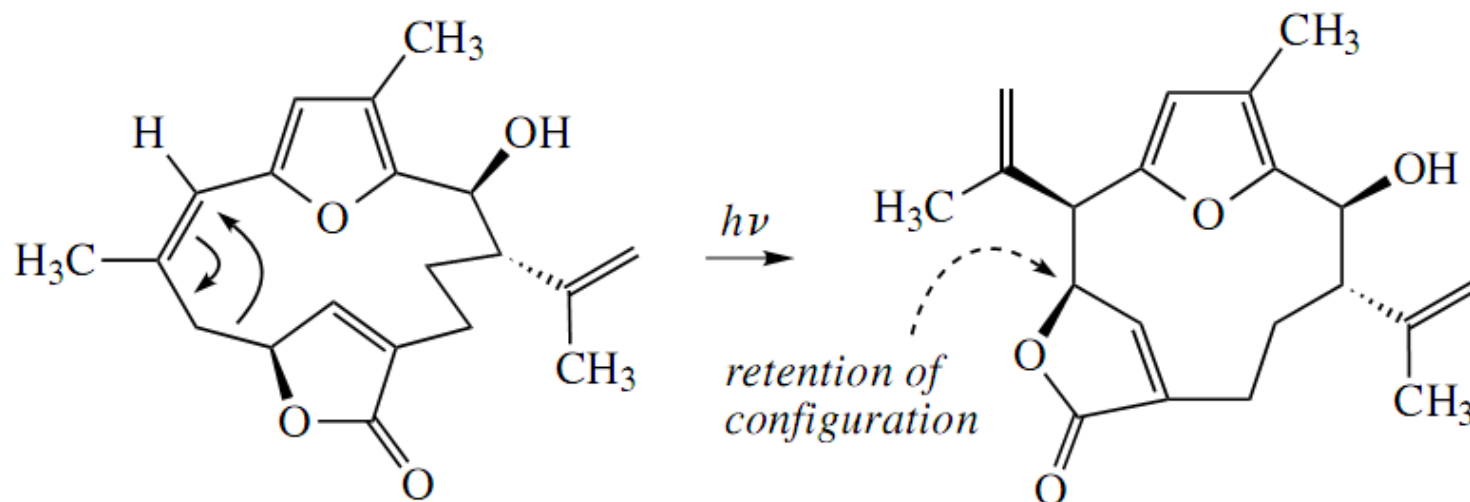


Mechanism???



Photochemical Sigmatropic Rearrangements

Photochemical [1,3] alkyl shift:

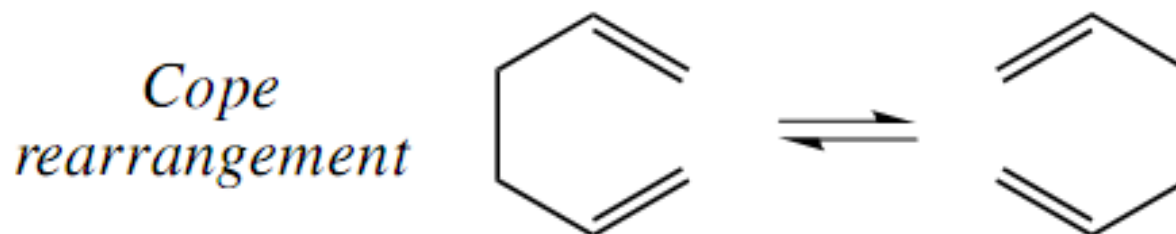


- This photochemical [1,3] sigmatropic rearrangement proceeds suprafacially with respect to both components, resulting in **retention of configuration** about the migrating one-atom component, a stereogenic alkyl group.¹
- The reaction **fails** to proceed at all under thermal conditions.¹

[m,n] Sigmatropic Rearrangements

[3,3] sigmatropic rearrangements:

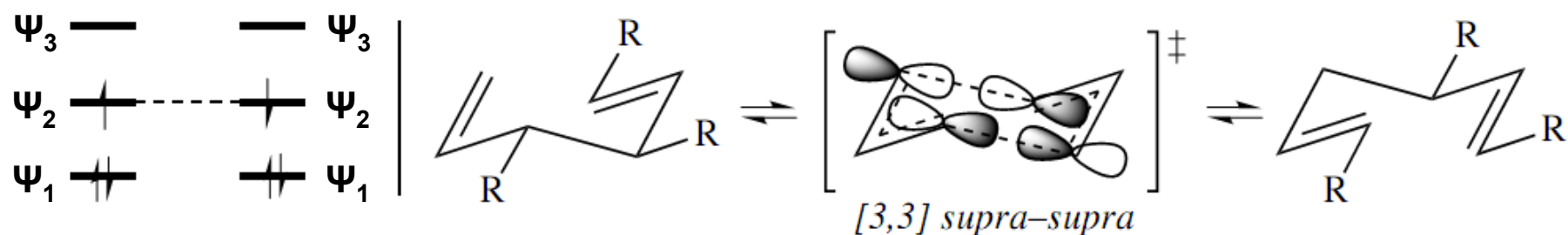
- The [3,3] sigmatropic rearrangements (Cope and Claisen rearrangements) are the most widely used sigmatropic rearrangements and are probably the most widely used pericyclic reactions after the Diels–Alder reaction. In the Cope rearrangement, a **1,5-diene** isomerizes to **another 1,5-diene**.¹
- The **Cope rearrangement** is a [3,3]-sigmatropic rearrangement **with only carbon atoms** in the ring. In its simplest version it is not a reaction at all.²⁻³



[m,n] Sigmatropic Rearrangements

[3,3] sigmatropic rearrangements:

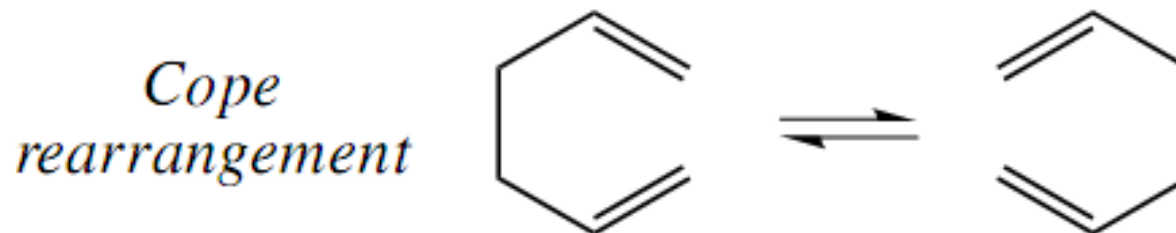
- The [3,3] sigmatropic rearrangement is a **six-electron reaction**. **No matter** how the six electrons are distributed between the two three-atom components, the dominant FMO interaction in the TS is between Ψ_2 of one component and Ψ_2 of the other component. The reaction proceeds suprafacially with respect to both components.¹



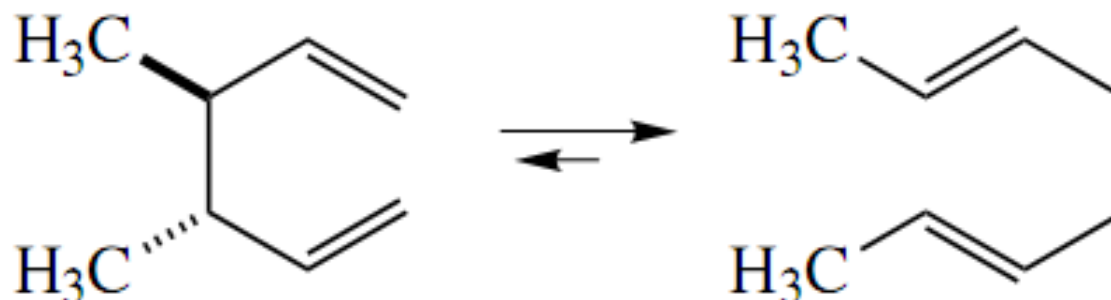
[m,n] Sigmatropic Rearrangements

[3,3] sigmatropic rearrangements:

- The Cope rearrangement of the simplest 1,5-diene, 1,5-hexadiene, is **degenerate**: the starting material is **identical** with the product, and the equilibrium constant for the rearrangement is 1.¹



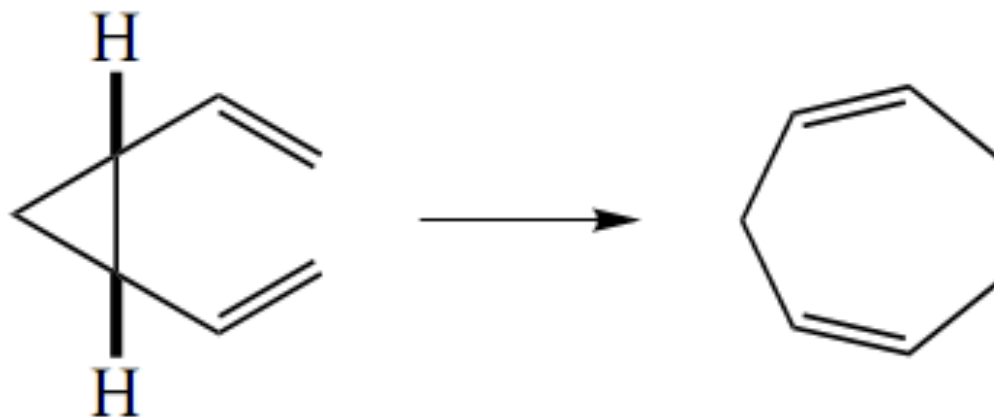
- Substituents may shift the equilibrium to one side or the other. For example, the equilibrium between 3,4-dimethyl-1,5-hexadiene and 2,6-octadiene lies on the side of **the more substituted pi bonds**.¹



[m,n] Sigmatropic Rearrangements

[3,3] sigmatropic rearrangements:

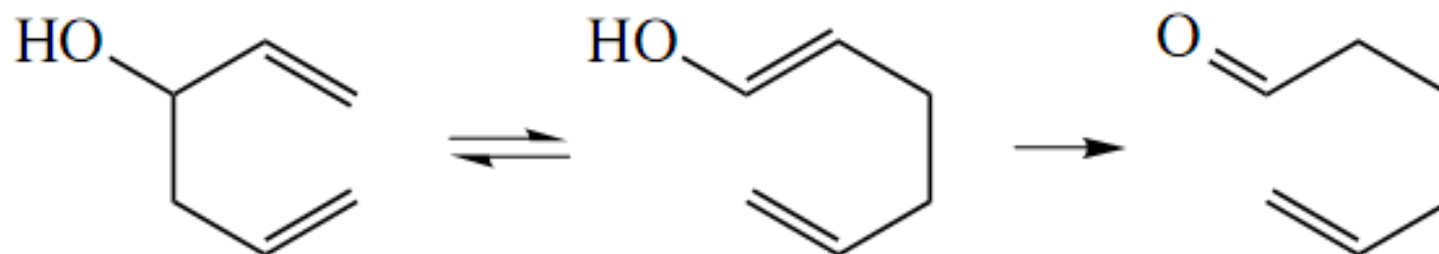
- Cope rearrangement occurs at exceptionally low temperatures when the single bond is part of a small **strained ring** and the **two double bonds are cis** to each other.¹



[m,n] Sigmatropic Rearrangements

[3,3] sigmatropic rearrangements:

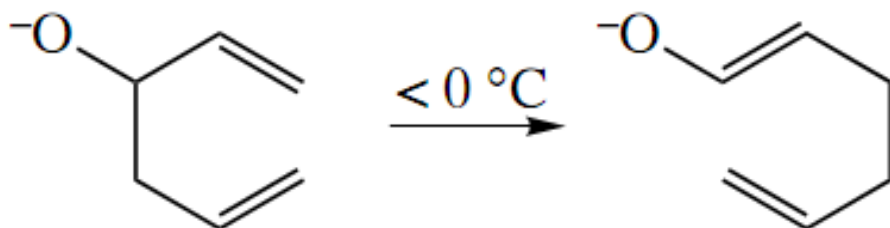
- The **position** of the Cope equilibrium can also be altered **by removing** the product 1,5-diene from the reaction mixture.¹
- In the ***oxy-Cope rearrangement***, a 3-hydroxy-1,5-diene undergoes the Cope rearrangement to give **an enol**, which isomerizes quickly to a δ,ϵ -unsaturated carbonyl compound. The latter compound is a **1,6-diene**, not a 1,5-diene, so it is incapable of undergoing the Cope rearrangement in the retro direction.¹



[m,n] Sigmatropic Rearrangements

[3,3] sigmatropic rearrangements:

- Oxy-Cope rearrangements proceed at especially low temperatures when the alcohol is **deprotonated**. The *anionic oxy-Cope* rearrangement is accelerated compared with the neutral reaction because the negative charge is more delocalized in the TS than in the starting material. **The driving force** for the anionic oxy-Cope rearrangement is no longer removal of the product diene from the equilibrium but simply **delocalization of the negative charge**.¹

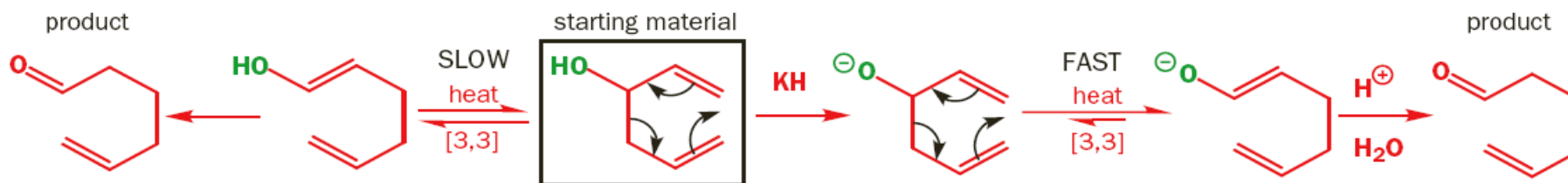


*negative charge more delocalized
in TS and product than in SM*

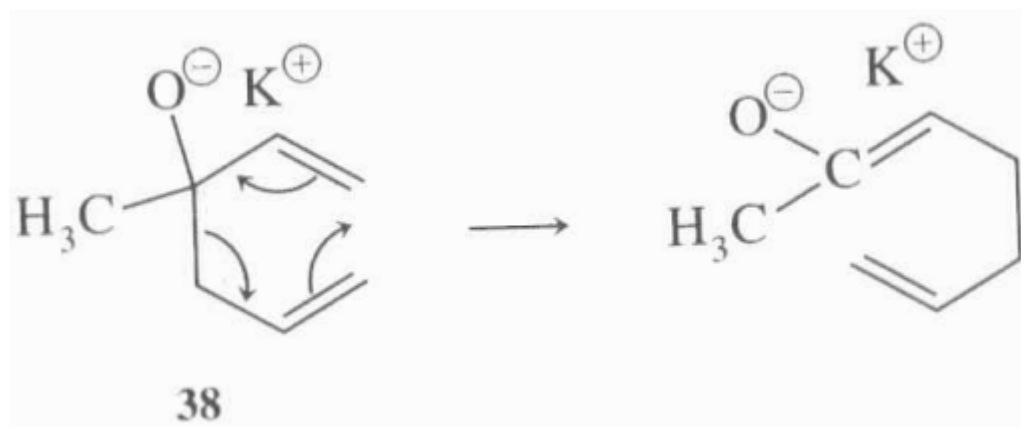
[m,n] Sigmatropic Rearrangements

[3,3] sigmatropic rearrangements:

Base catalysis



➤ That is to say sigmatropic rearrangements **are catalyzed by bases**. For example; the "oxy-Cope rearrangements" of the potassium salts of 3-hydroxy-1,5-hexadienes, such as **38**, have been found to proceed as much as **10¹² times** as rapidly as the rearrangements of the parent alcohols.¹

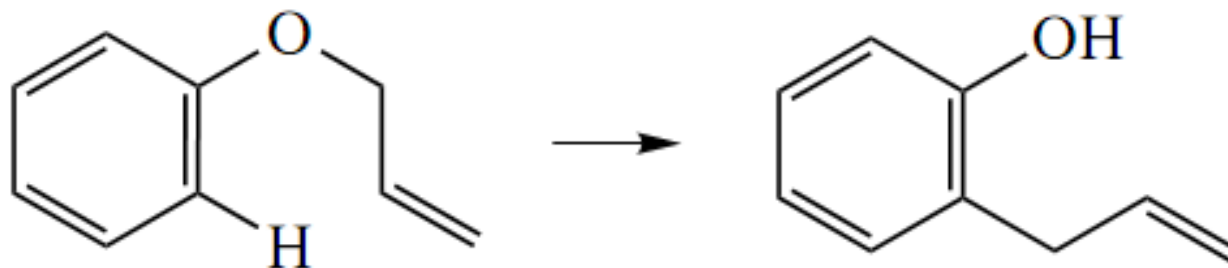
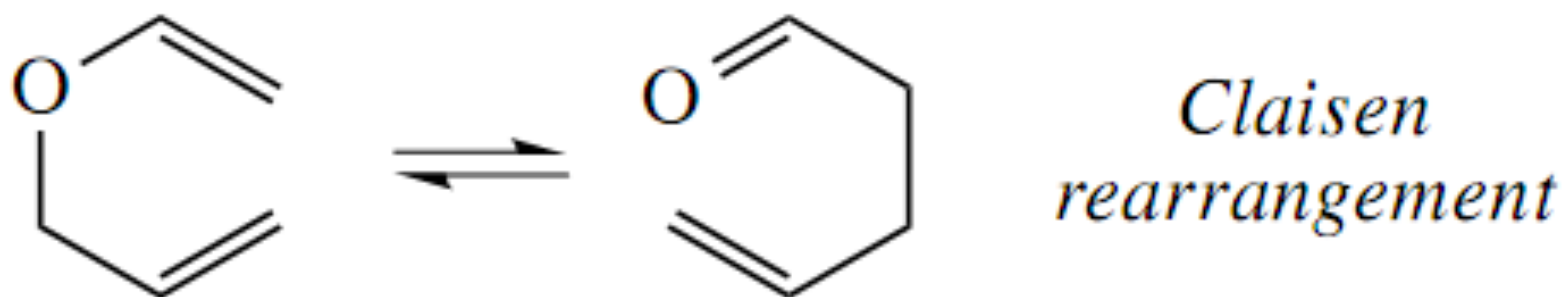


[m,n] Sigmatropic Rearrangements

[3,3] sigmatropic rearrangements:

Claisen rearrangement:

➤ In the Claisen rearrangement, an **allyl vinyl ether** isomerizes to a **γ,δ -unsaturated carbonyl** compound.¹

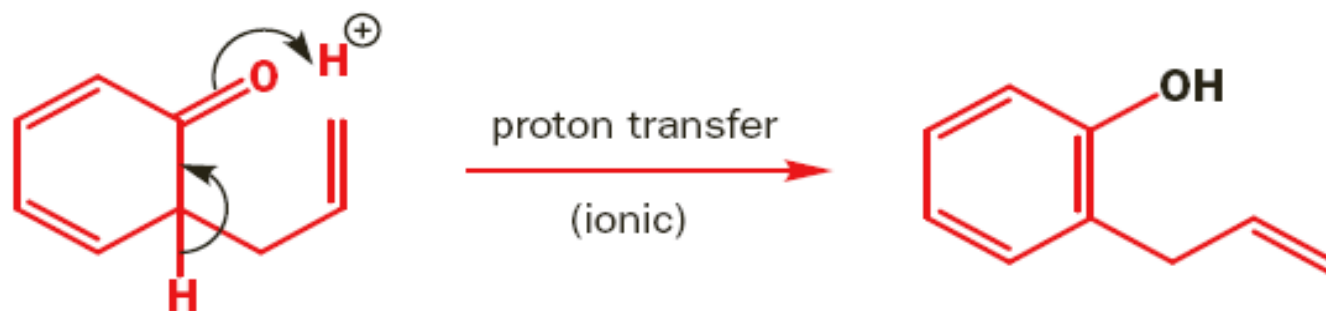
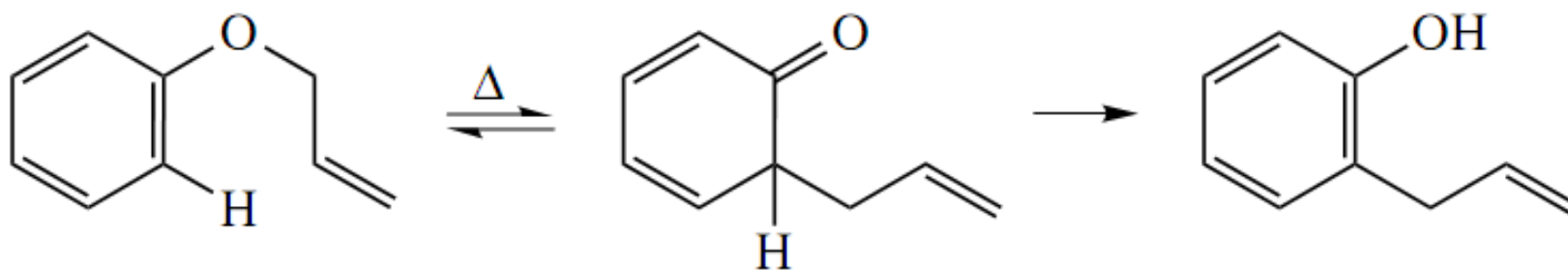


[m,n] Sigmatropic Rearrangements

[3,3] sigmatropic rearrangements:

Claisen rearrangement:

Mechanism

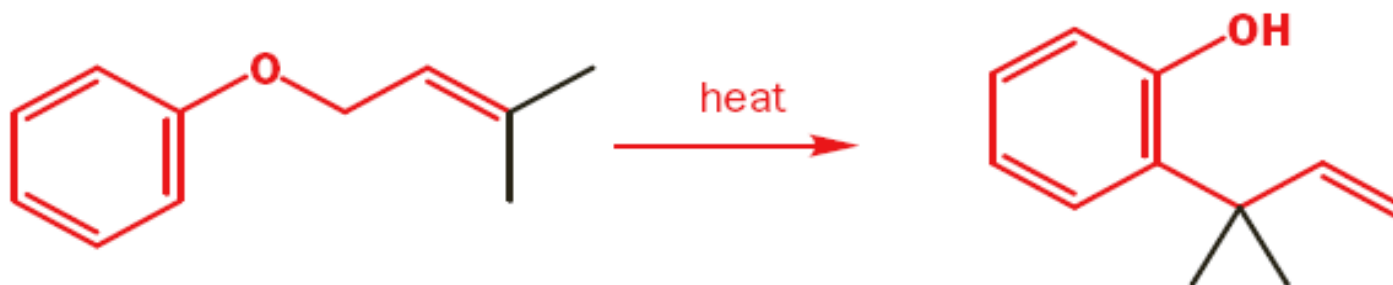


[m,n] Sigmatropic Rearrangements

[3,3] sigmatropic rearrangements:

Claisen rearrangement:

- How do we know that this is the mechanism?¹

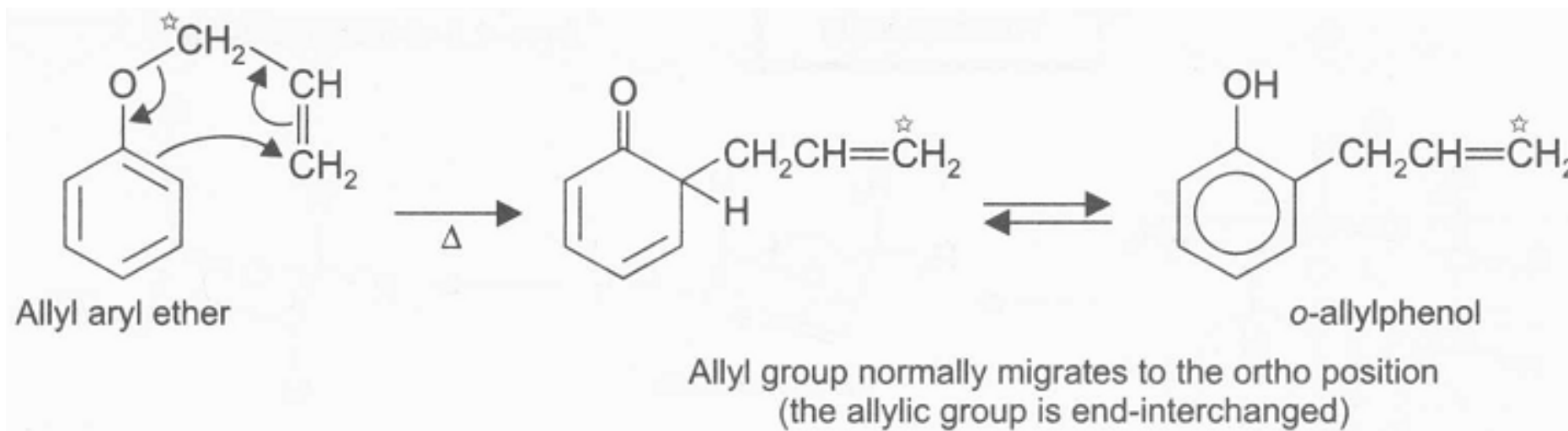


[m,n] Sigmatropic Rearrangements

[3,3] sigmatropic rearrangements:

Claisen rearrangement:

- Studies using migrating groups labelled with ^{14}C .²



SCHEME 17.95

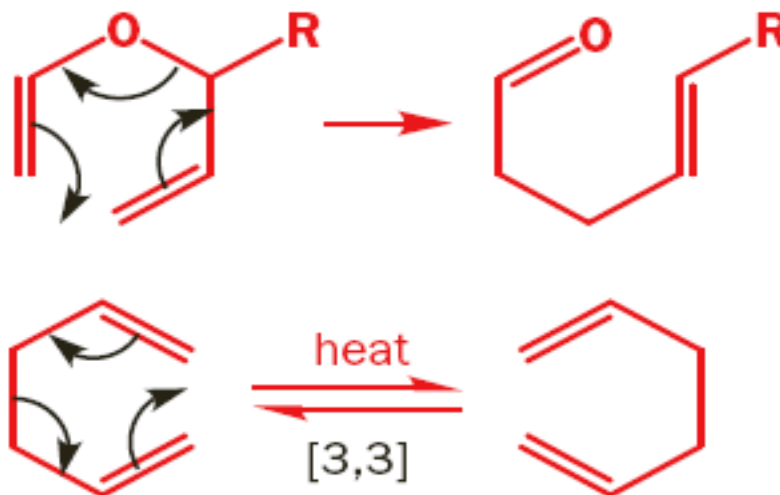
- These results indicate that Claisen rearrangement proceed by a **concerted mechanism**.²

[m,n] Sigmatropic Rearrangements

[3,3] sigmatropic rearrangements:

Claisen rearrangement:

- Which way will they go?
- Orbital symmetry tells us that [3,3]-sigmatropic rearrangements are **allowed** but says nothing about **which way they will go**. They are allowed in either direction. So why does the Claisen rearrangement always go in this direction?¹



[m,n] Sigmatropic Rearrangements

[3,3] sigmatropic rearrangements:

Claisen rearrangement:

➤ The combination of a carbonyl group and a C–C sigma bond made the keto form **more stable** than the enol form with its combination of a C=C pi bond and a C–O sigma bond. The same is true here. It is **the formation of the carbonyl** group that drives the reaction to the right. ¹⁻²

➤ *The key to identifying Cope and Claisen rearrangements is the **1,5-diene** in the starting material or in the product.*

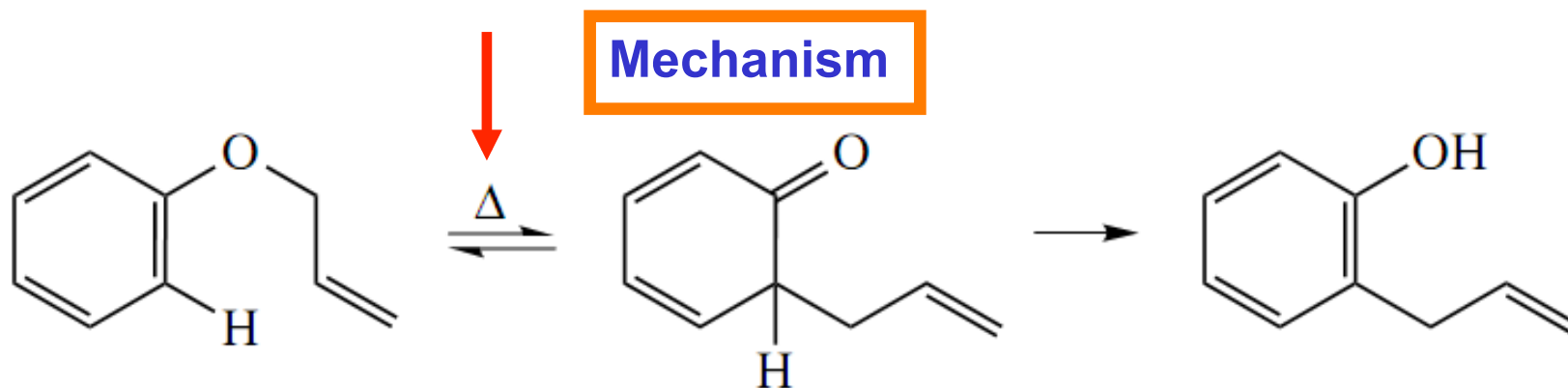
- A γ,δ -**unsaturated carbonyl** compound (a 1,5-heterodiene) can be made by a **Claisen rearrangement**, and

- a δ,ϵ -**unsaturated carbonyl** compound can be made by an **oxy-Cope rearrangement**.²

[m,n] Sigmatropic Rearrangements

[3,3] sigmatropic rearrangements:

Claisen rearrangement:



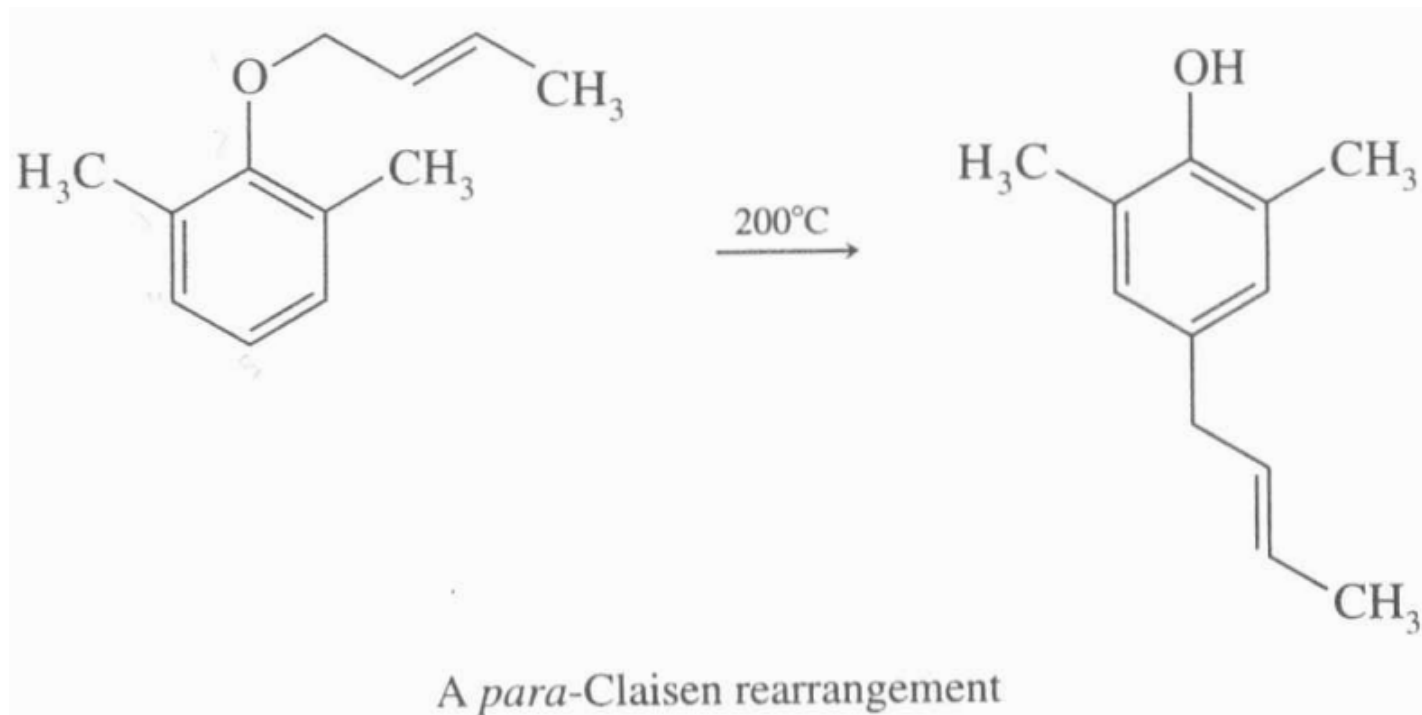
- One might expect that in this particular case, the equilibrium would lie on the side of the **aromatic** compound, not the carbonyl. However, the **carbonyl quickly tautomerizes** (by a nonconcerted mechanism!) to the aromatic 2-allylphenol, which can't undergo the reaction in the **reverse direction**.¹

[m,n] Sigmatropic Rearrangements

[3,3] sigmatropic rearrangements:

Claisen rearrangement:

- When both ortho positions on the aromatic ring are already substituted (and even, to small degree, when one or both are not substituted), the migrating allylic group will shift to the para position, resulting in a **p-substituted phenol**.¹⁻²



[m,n] Sigmatropic Rearrangements

[3,3] sigmatropic rearrangements:

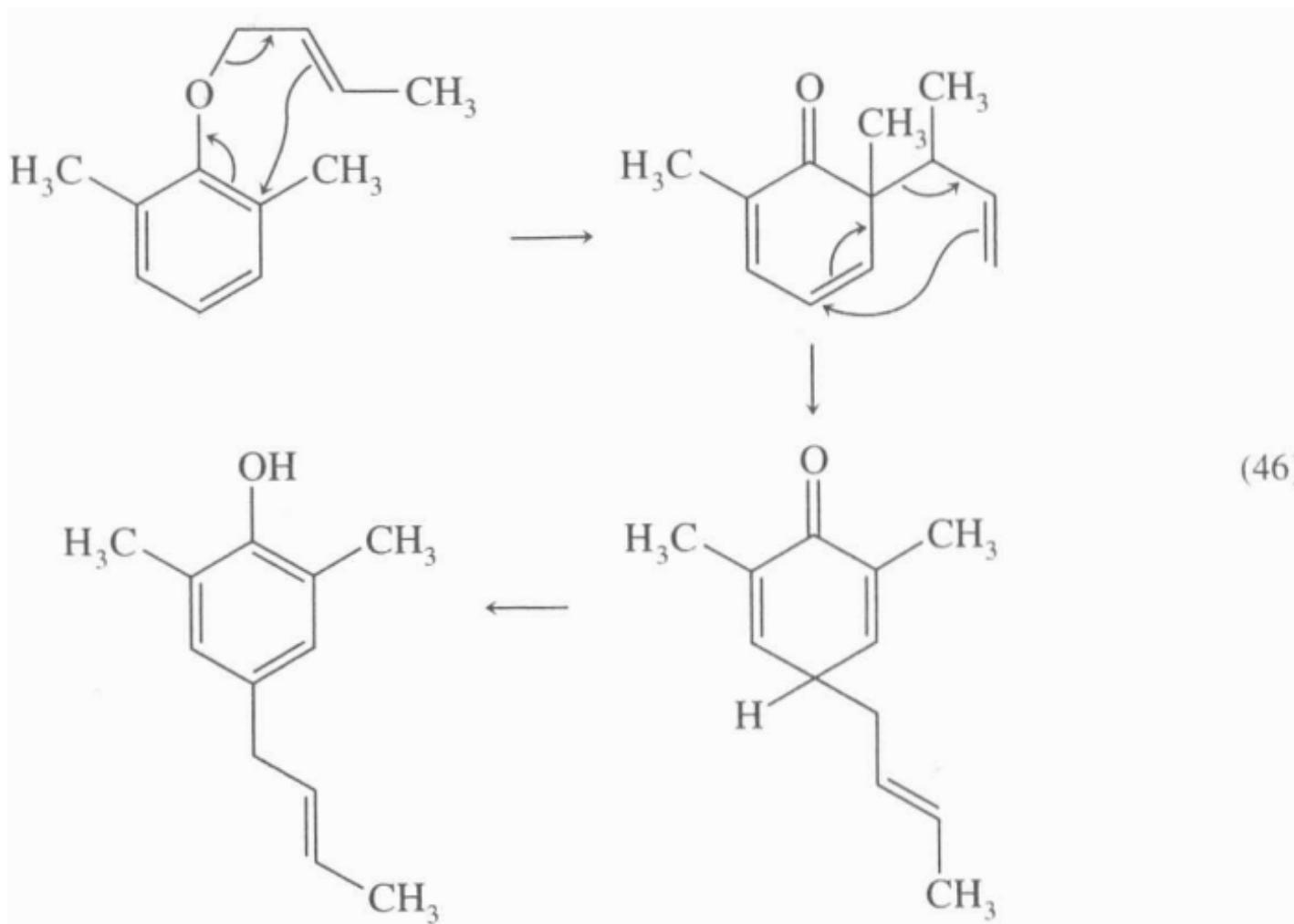
Claisen rearrangement:

- The **direct [1,5] shift mechanism seems unlikely**, in view of the distance between the oxygen atoms and the para positions.¹
- In fact, para-Claisen rearrangements have been demonstrated to proceed by **two successive [3,3] shifts (Eq 46)**. The allylic group first migrates to the ortho position and then undergoes a second [3,3] shift (a Cope migration step) to the para position.¹
- Finally, the **para-cyclohexadienone** formed in the second migration step **tautomerizes** to form a phenol—a process presumably catalyzed by acids or bases.¹
- The rearrangement **is not a direct [3,5] shift**.²
- **Homework:** can you draw the **[3,5] shift product**?

[m,n] Sigmatropic Rearrangements

[3,3] sigmatropic rearrangements:

Claisen rearrangement:

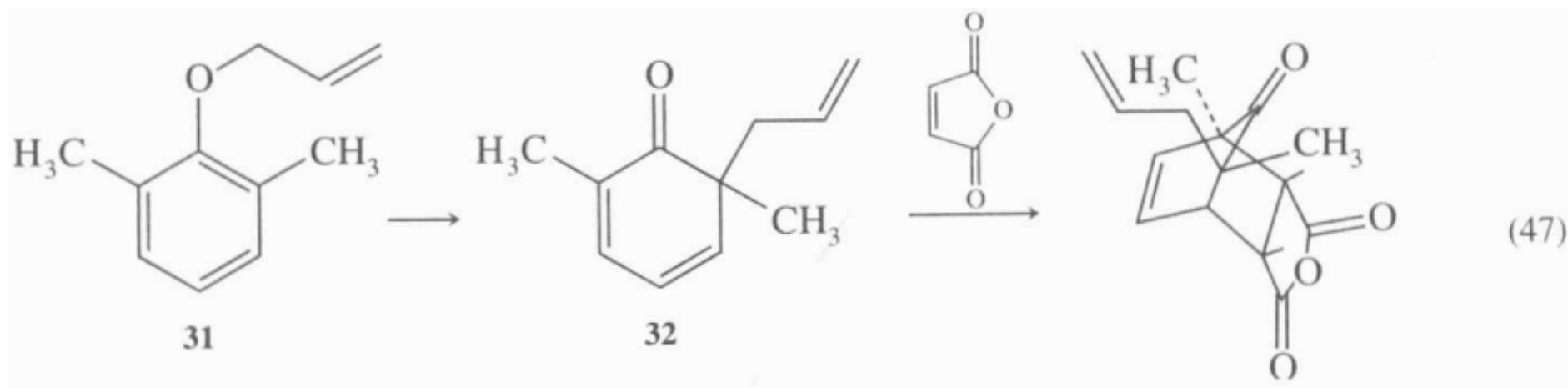


[m,n] Sigmatropic Rearrangements

[3,3] sigmatropic rearrangements:

Claisen rearrangement:

- Several lines of evidence demonstrate that para-Claisen rearrangements proceed via two successive [3,3] shifts rather than a single [1,5] shift:
- (1) The ortho-cyclohexadienone, **32**, formed as the initial intermediate in the rearrangement of ether **31**, **has been trapped** as its Diels-Alder adduct with maleic anhydride.¹

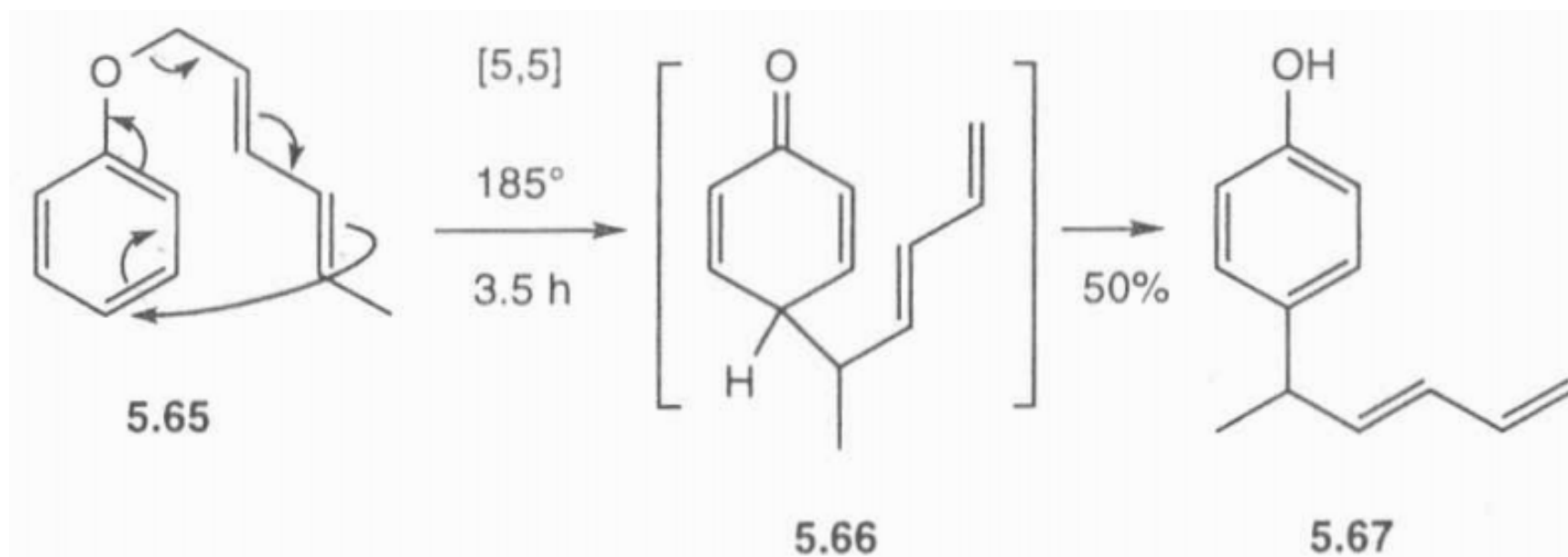


[m,n] Sigmatropic Rearrangements

[5,5] sigmatropic rearrangements:

Claisen rearrangement:

- A longer conjugated system **5.65** allows a more direct delivery to the para position, giving the phenol **5.67** as the major product along with some of the product of a normal Claisen rearrangement.¹

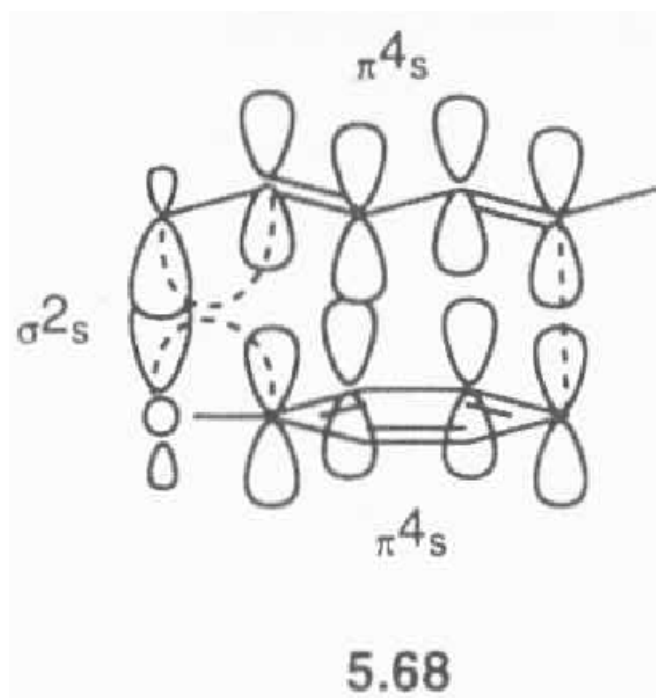


[m,n] Sigmatropic Rearrangements

[5,5] sigmatropic rearrangements:

Claisen rearrangement:

- Similarly, the **terminal methyl** group in **5.65** shows that this is a **[5,5] rearrangement (5.65 to 5.66)** rather than two successive [3,3] rearrangements. The [5,5] rearrangement **is allowed** if it is **all-suprafacial**, a geometry **5.68** that is not difficult to achieve.¹



Questions

- **Homework:** Write the mechanism of the following reaction?

