Rearrangement

Bond re-organization to give a structural isomer of the original compound.

It often involves migration of a group (an atom) from one atom to another within the molecule.

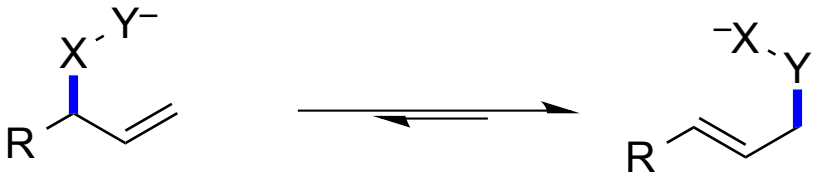
Very often, rearrangment led to a significant structural modification.

Reminder: reaction types we've already learnt: Acid-base; Addition; Substitution; Elimination; Condensation…

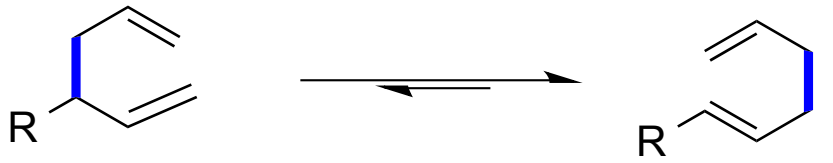
Sigmatropic Rearrangement

Those reactions in which a sigma bond and associated substituent interchanges termini on a conjugated π-system

[1,3]-sigmatropic rearrangement



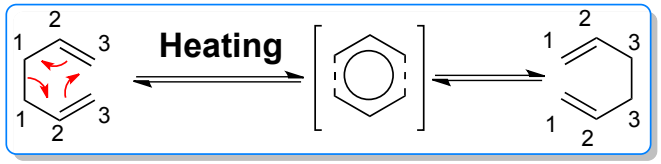
[2,3]-sigmatropic rearrangement



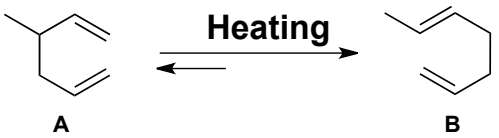
[3,3]-sigmatropic rearrangement

Cope Rearrangement

A thermal isomerization of 1,5-diene to a regioisomeric 1,5-diene. It is a pericyclic reaction with a concerted molecular rearrangement: $4\pi e^-$ + 2σ bonds. Consequently, the transition state has "aromatic character". It belongs to a family of [3,3]-sigmatropic rearrangements



Cope rearrangement is an equilibrium process leading to thermodynamically more stable isomer

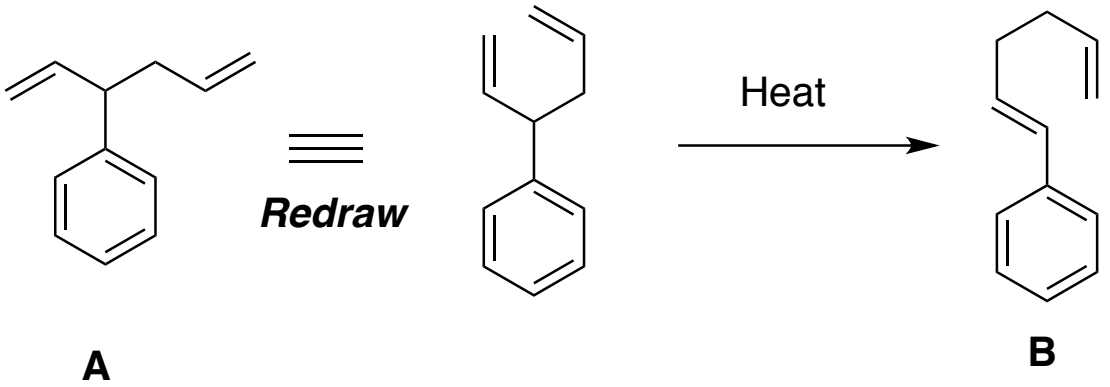


B is the major product, Why?

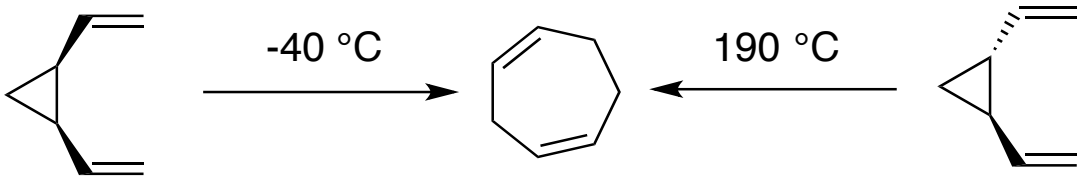
Definition of a pericyclic reactions:
Having a cyclic transition state and proceeding in a concerted manner.

Cope Rearrangement

Key: ***To recognize the 1,5-diene unit***



B is thermodymanically more stable

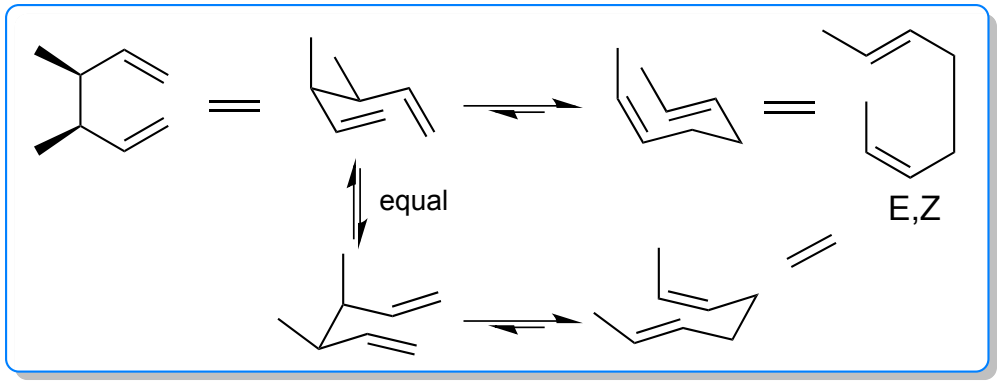


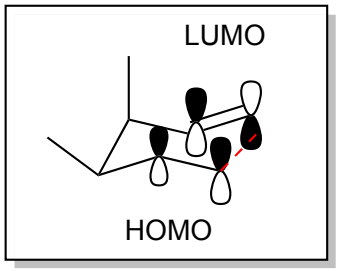
Driving force: Release of ring strain

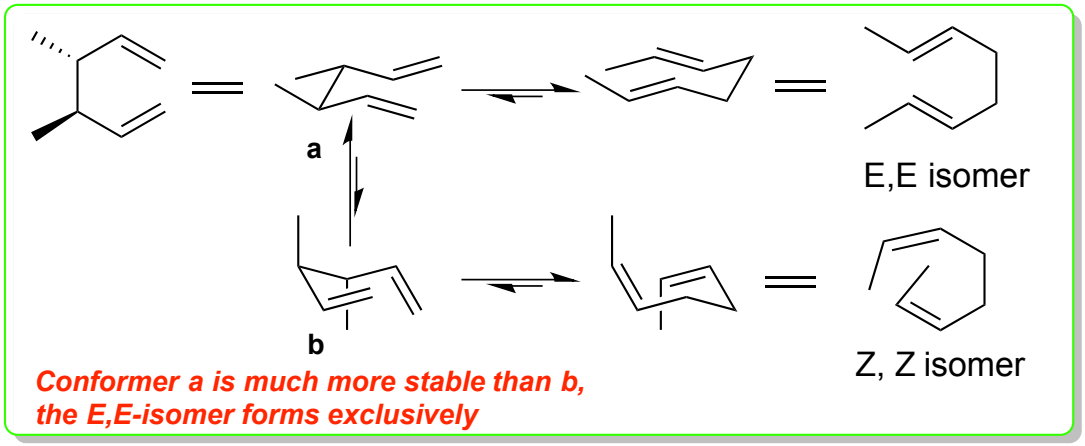
Cyclopropane ring strain: 27 kcal/mol

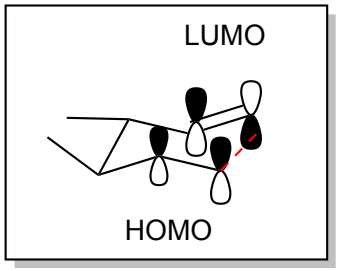
Cope Rearrangement

Key: For linear 1,5-diene, the rearrangement generally went through a chair-like transition state. The TS conformation determines the stereochemistry of the new double bonds



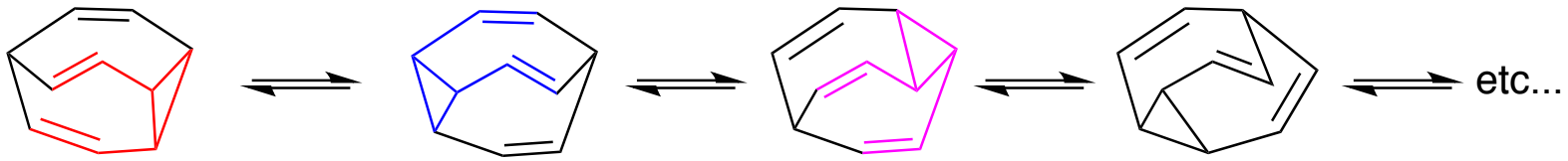






Very similar to Zimmerman-Traxler transition state for the aldol reaction
Avoid 1,3-diaxial interaction in drawing your transition state

Degenerative Cope Rearrangement: Case of Bullevalene



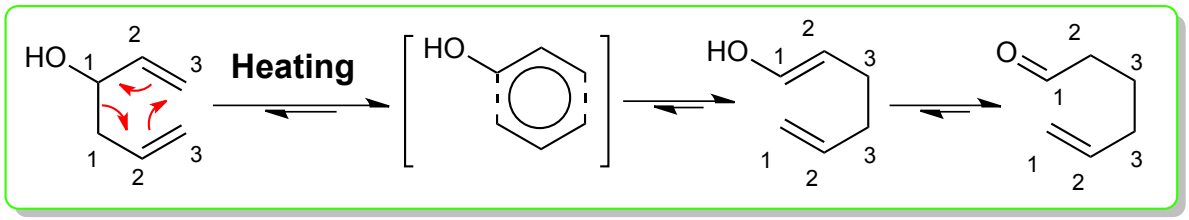
$C_{10}H_{10}$

***Doring's Prediction*:**

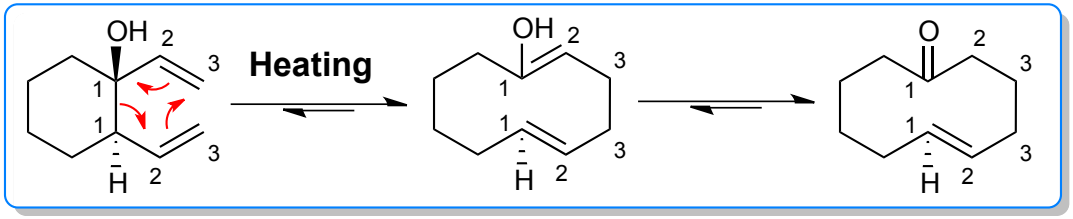
If each of the 10 CH groups of the molecule were individually labeled, there would be 1,209,600 arrangements of the molecule.

Oxy-Cope rearrangement

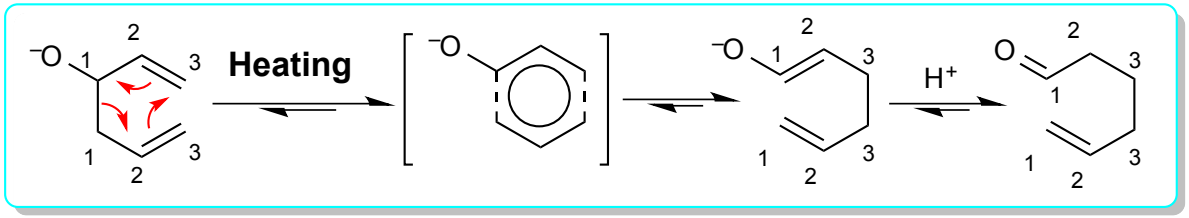
oxy-Cope rearrangement: aldehyde formation is the driving force



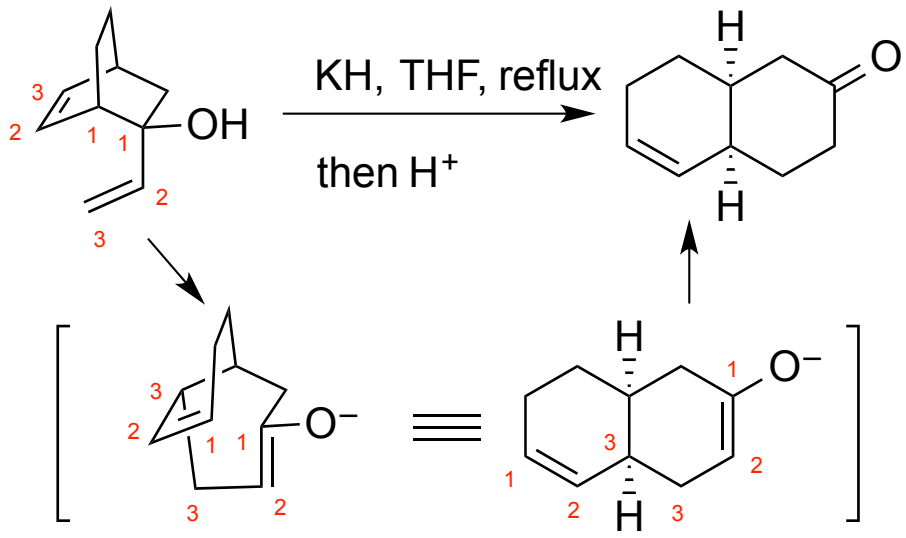
The carbonyl tautomer is more stable, removing the enol from the equilibrium.

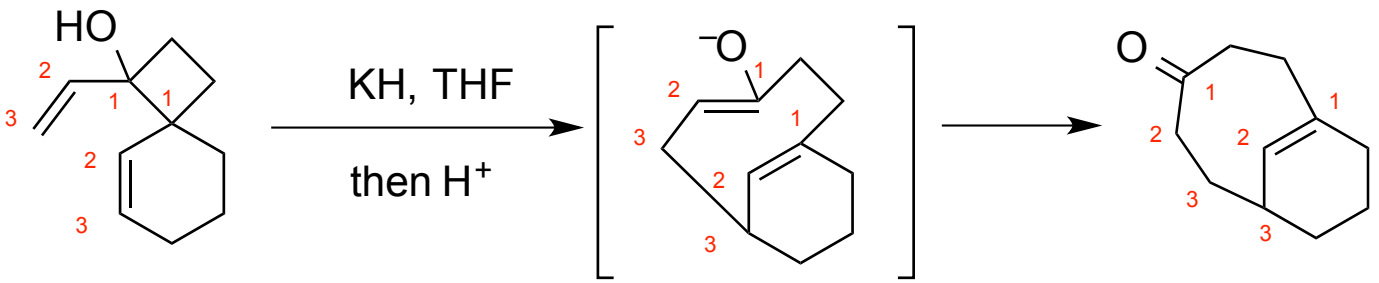


The oxy-Cope rearrangement is significantly accelerated when the hydroxy group is converted to alkoxide. The base-catalyzed reaction is called: **anionic oxy-Cope rearrangement**



Oxy-Cope rearrangement:
Example of complete structural re-organizaiton



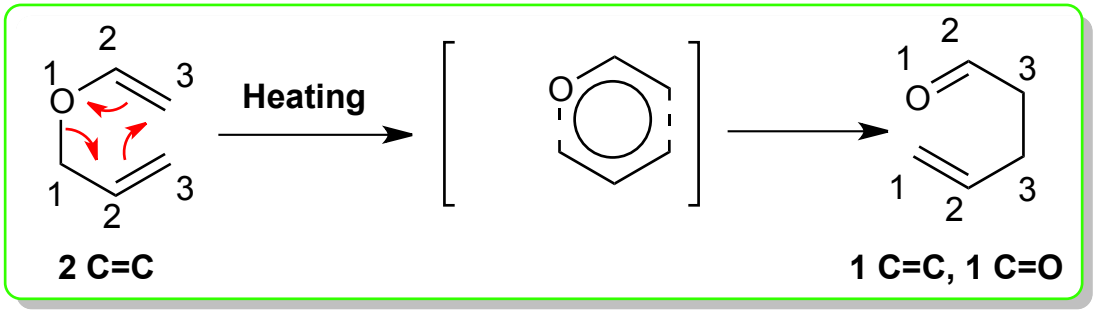


Claisen rearrangement

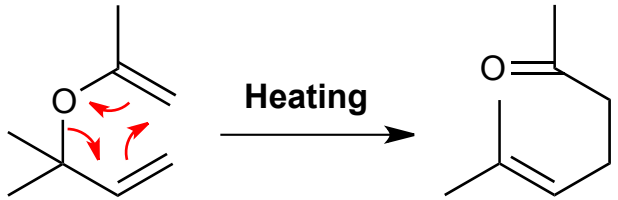
Claisen rearrangement involving a vinyl allyl ether is essentially the same as Cope rearrangement. However, the equilibrium is driven to the product (4-pentenal) which is thermadynamically more stable.

Driving force of the reaction = carbonyl group formation

Comparing the bond dissociation energies: C=C 146 kcal/mol, C=O 172 kcal/mol

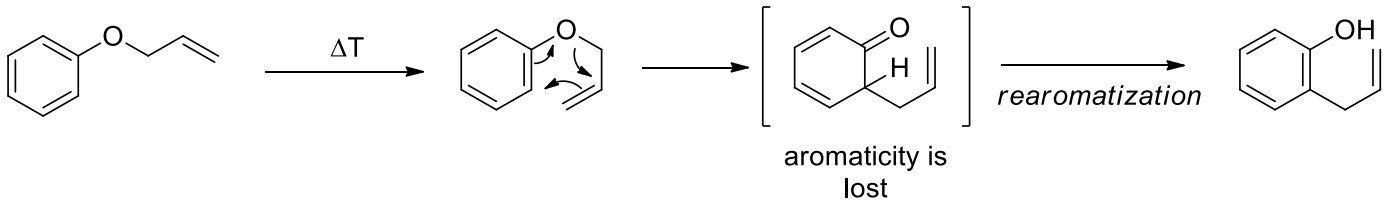


Example:

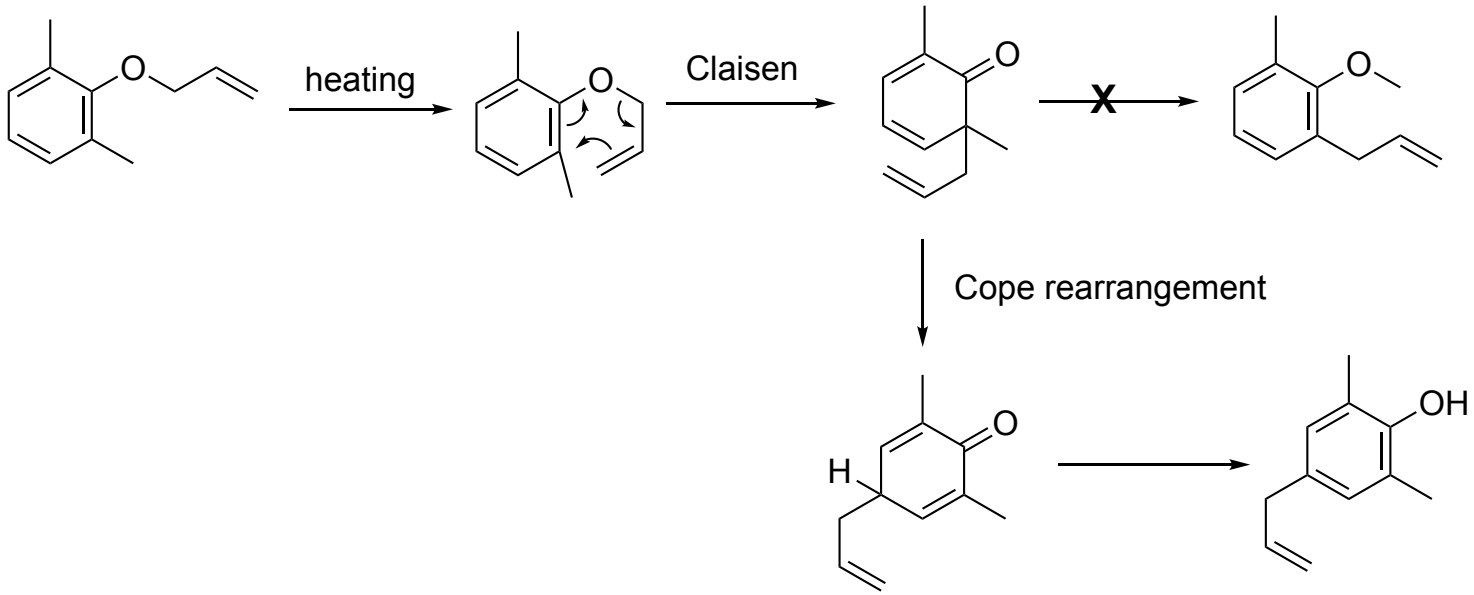


Claisen rearrangement

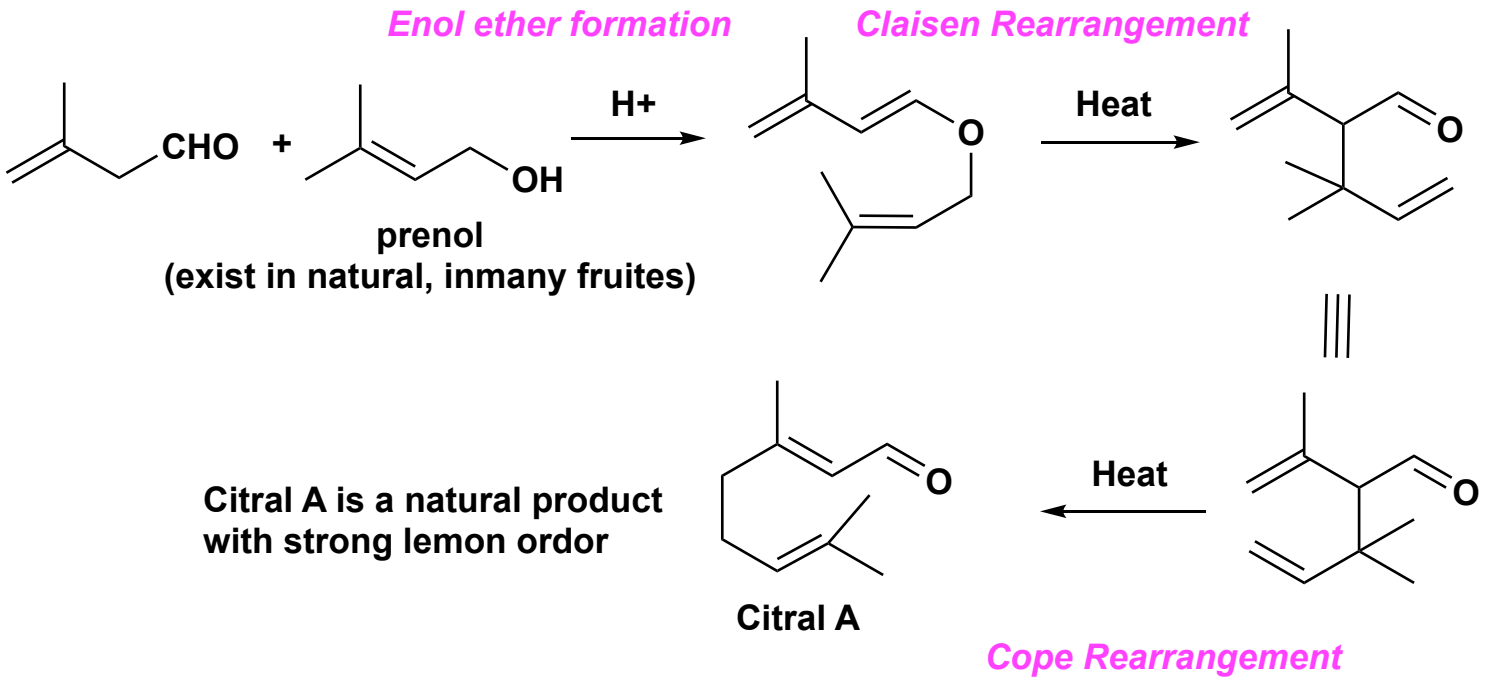
Aromatic Claisen rearrangement:



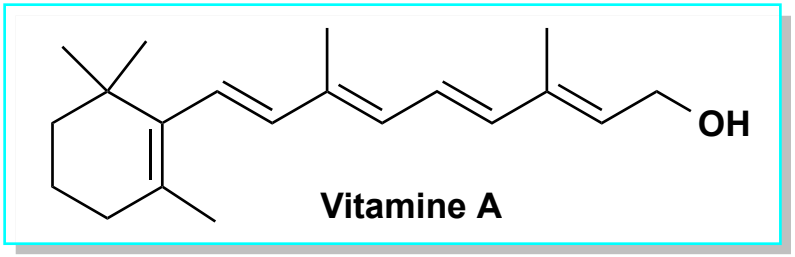
When the *ortho*-positions are occupied:



Industrial Application: Synthesis of Citral

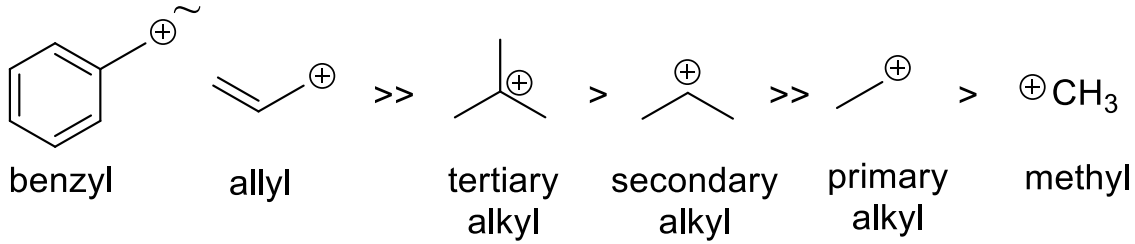


Citral A is a key intermediate in the synthesis of Vitamine A

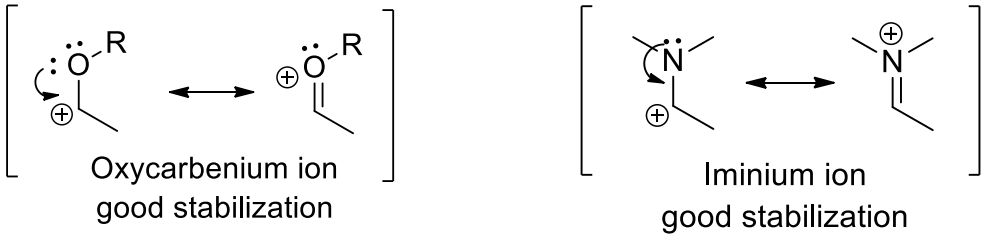


Cationic Rearrangements:

Recapitulation on the stability of carbenium ions:



Even better:

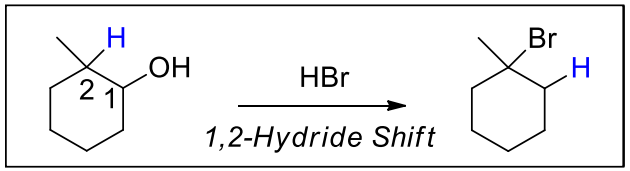


Possible reactions with a cationic intermediate:
Add a nucleophile (S_N1 substitution), Loss a proton (Elimination) and **Rearrangement**

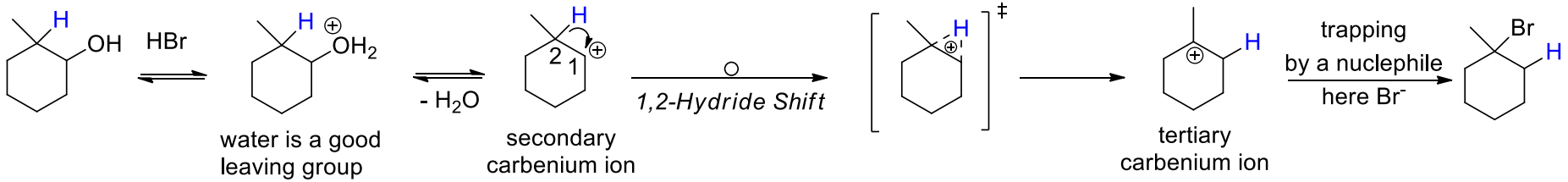
Driving forces and selectivity factors for cationic rearrangements:
*Reaction proceeds to form a better stabilized carbenium ion
*Release of ring strain
*Cleavage/release of small and uncharged molecules, for example: CO or CO_2

Wagner-Meerwein rearrangement: A cationic 1,2-rearrangement involving the migration of an alkyl or a hydride

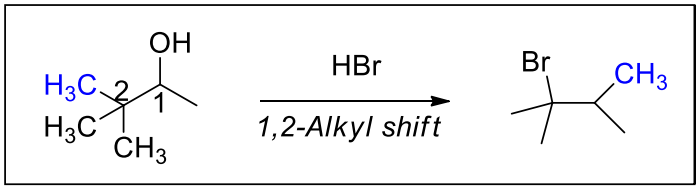
1,2-Hydride Shift (migration of a hydride)



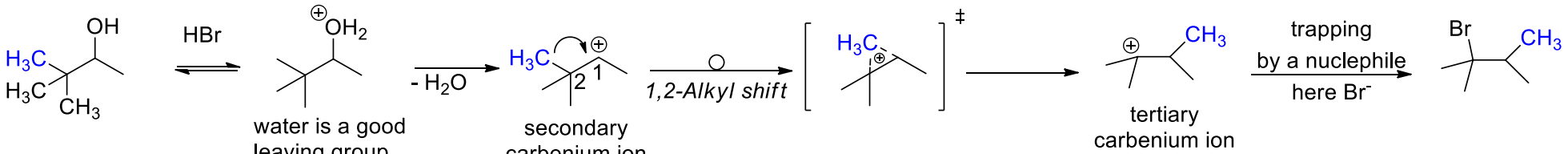
Mechanism:



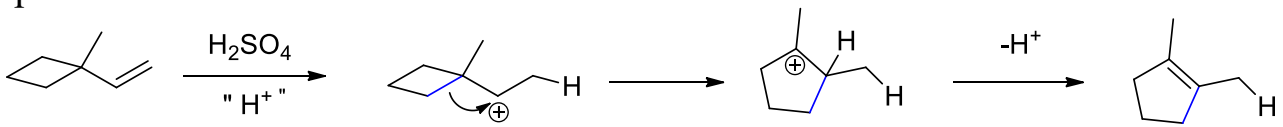
1,2-Alkyl shift (migration of an alkyl group)



Mechanism:



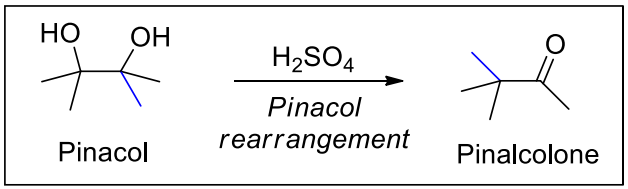
Example:



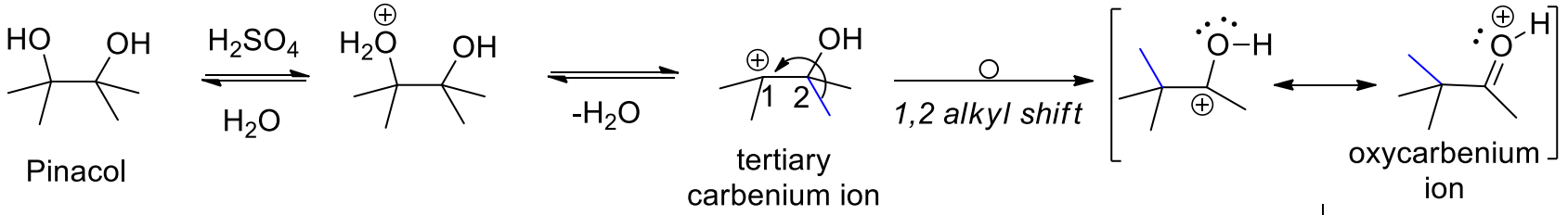
driving force = release of ring strain for the cyclobutane

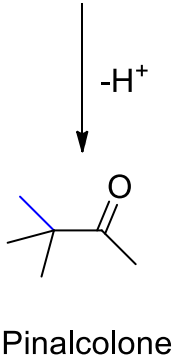
caution: HSO_4^- is not nucleophilic, therefore E1 elimination

Pinacol Rearrangement

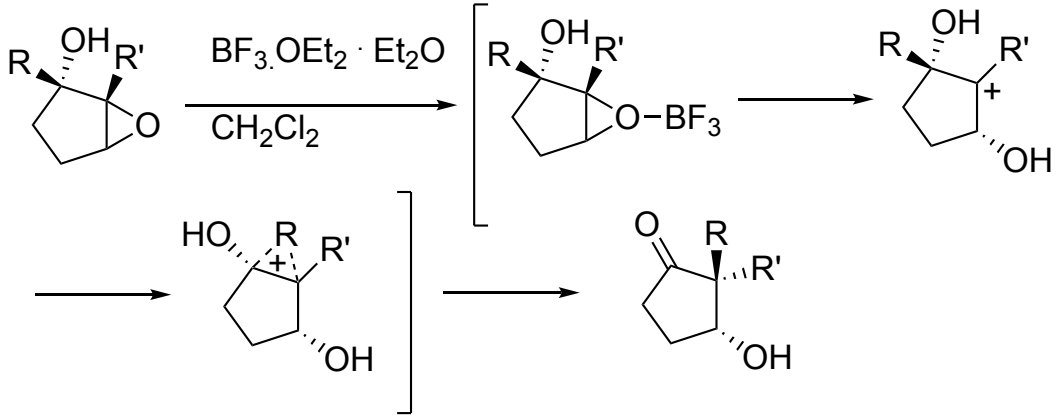


Mechanism:





Semi-pinacol rearrangement



P. J. Walsh, et al. J. *Am. Chem. Soc.* **2003,** *125,* 9544-9545

Pinacol Rearrangement: Examples