Alicyclic Chemistry. Lecture 4

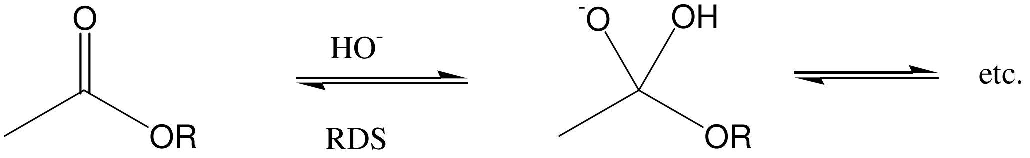
Kinetic Aspects

In general there are two types of phenomenon which affect the relationship between reactivity and conformation. They are Steric Control and Stereoelectronic Control.

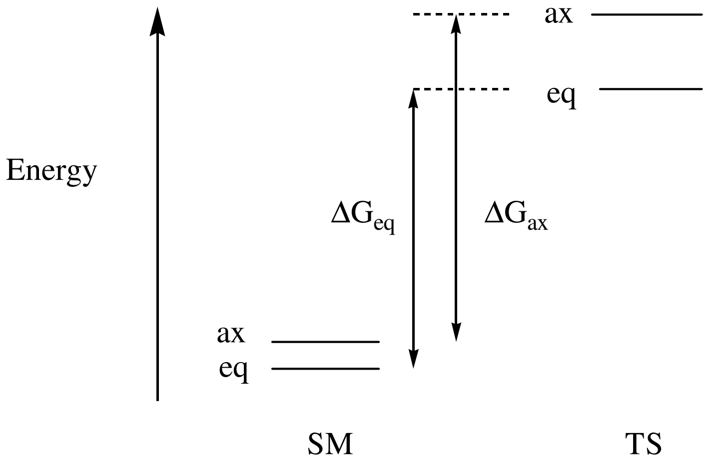
1. Steric Control (1,3-Diaxial Compression)

If we consider the transition state for a reaction involving a substituent in a ring we can conceive of two possibilities in terms of steric compression i.e. that the transition state (TS) is more crowded than the starting material (SM) and that the transition state is less crowded than the starting material.

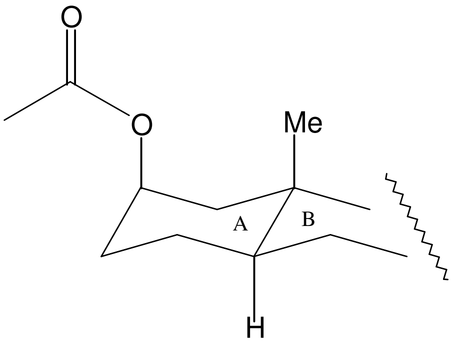
(a) *Base hydrolysis of esters (TS more crowded than SM)*:



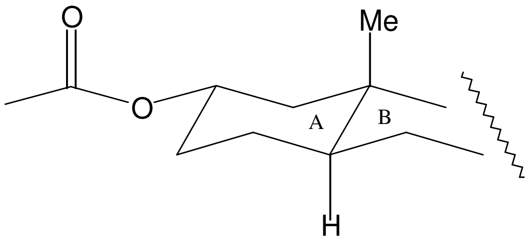
Here the TS resembles the tetrahedral intermediate and hence is bigger than the starting ester group. Thus, if the ester group is axial or equatorial we have in energetic terms the following situation:



Thus, $\Delta G^{\#}_{ax} > \Delta G^{\#}_{eq}$ and therefore $k_{ax} < k_{eq}$ i.e. the rate of hydrolysis of an ester in an axial position will be slower than the rate of hydrolysis of the corresponding equatorial ester, e.g.:

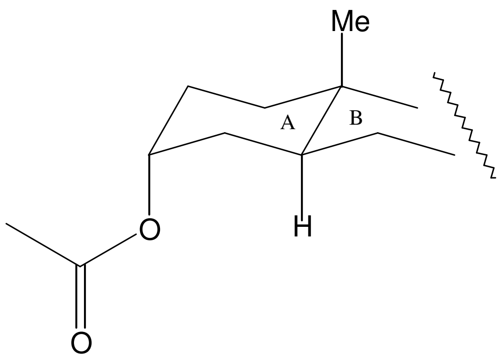


2-β-acetate(ax)

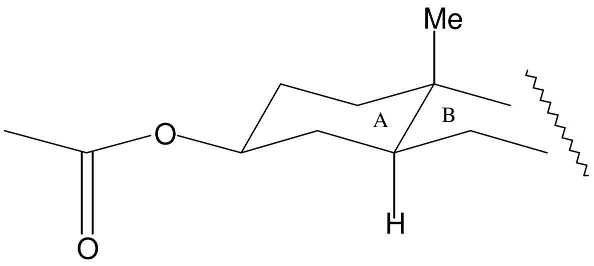


2-α-acetate(eq)

Relative Rate $^{\ominus}$OH / 80^{o}	1	10



3-α-acetate(ax)



3-β-acetate(eq)

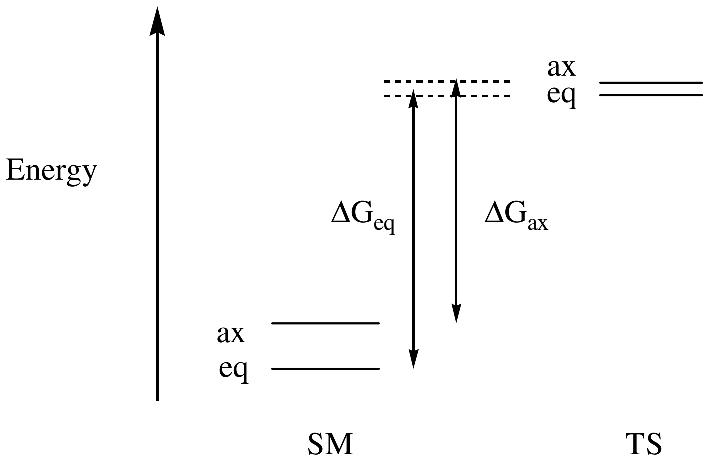
Relative Rate $^{\ominus}$OH / 80^{o}	1	3

Note that the difference between the reactivity of the axial and equatorial compounds is less in the 3-series compared to the 2-series; this is due to the lower 1,3-diaxial compression in the former (OAc vs H instead of OAc vs Me).

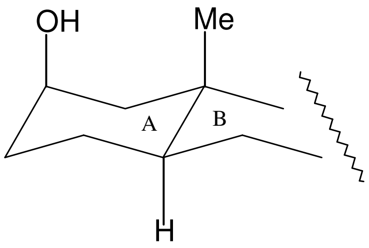
(b) Oxidation of alcohols (TS less crowded than the SM):

$R_2CHOH + CrO_3 \rightarrow R_2CHOCr(O)_2OH \rightarrow R_2C{=}O$

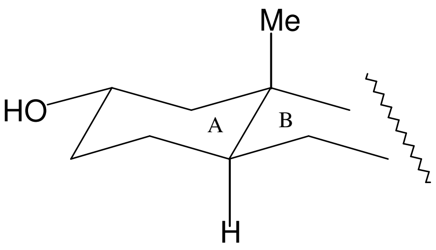
Here it is the second step which is rate limiting and the TS lies between the bulky chromate ester and the much-less hindered carbonyl product i.e the TS is less crowded than the SM. Again, in energy terms we have:



In this case $\Delta G^{\#}_{ax} < \Delta G^{\#}_{eq}$ and thus, $k_{ax} > k_{eq}$ i.e. OH groups in axial positions oxidize faster than those in equatorial positions, e.g.:



2-β-alcohol(ax)



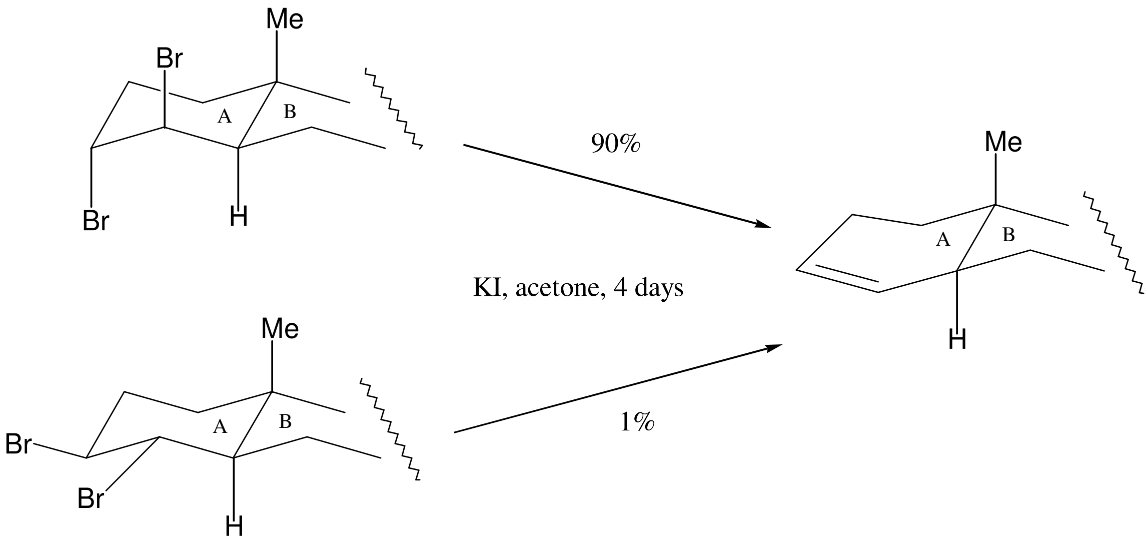
2-α-alcohol(eq)

	2-β-alcohol(ax)	2-α-alcohol(eq)
Relative Rate $^{\ominus}CrO_3$	18	1

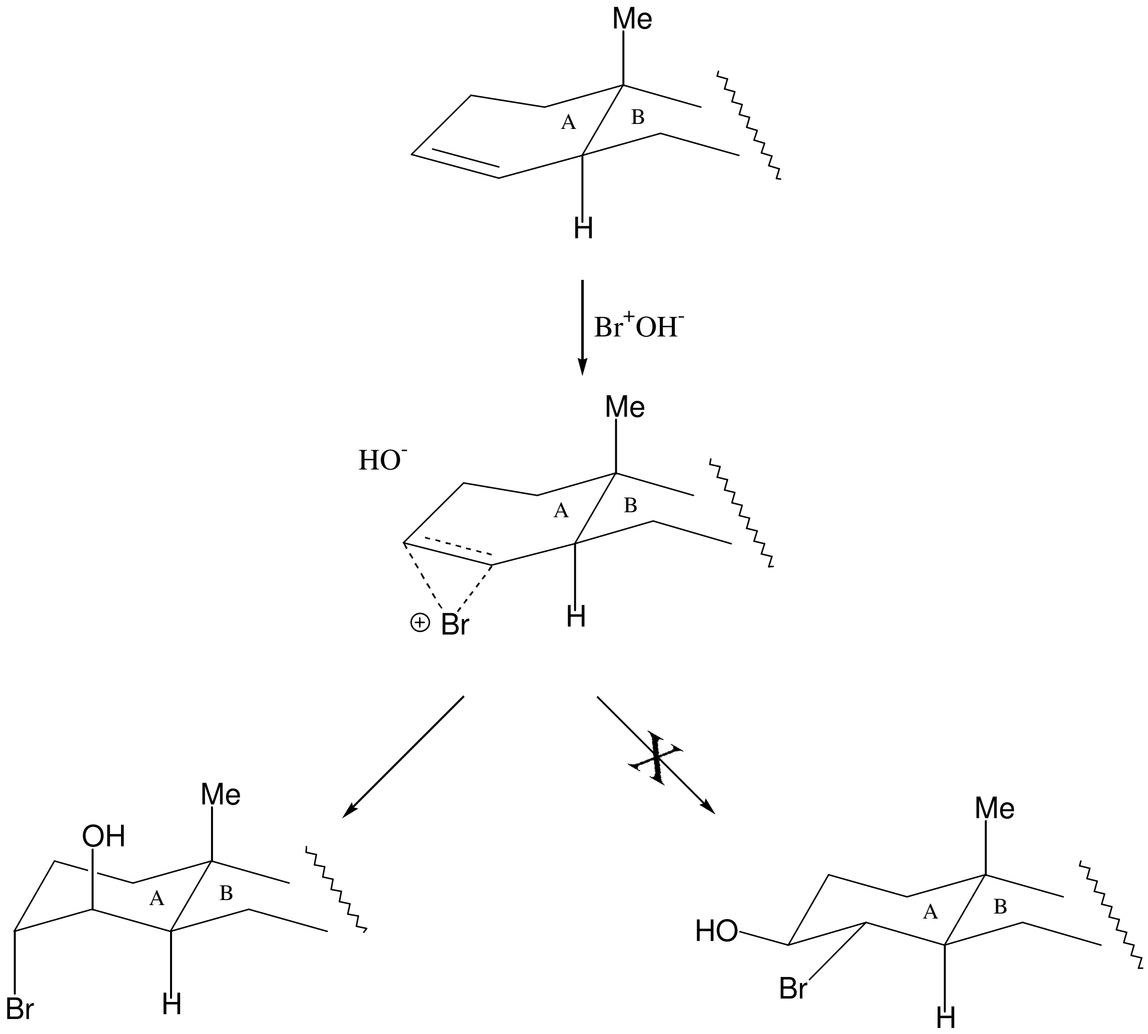
2. Stereoelectronic Control (Anti-periplanar Orbital Overlap)

(a) 1,2-Diaxial Processes: Many reactions require anti-periplanar overlap of orbitals and this is best achieved in cyclohexanes in 1,2-diaxial derivatives. Examples of reactions which illustrate this are:

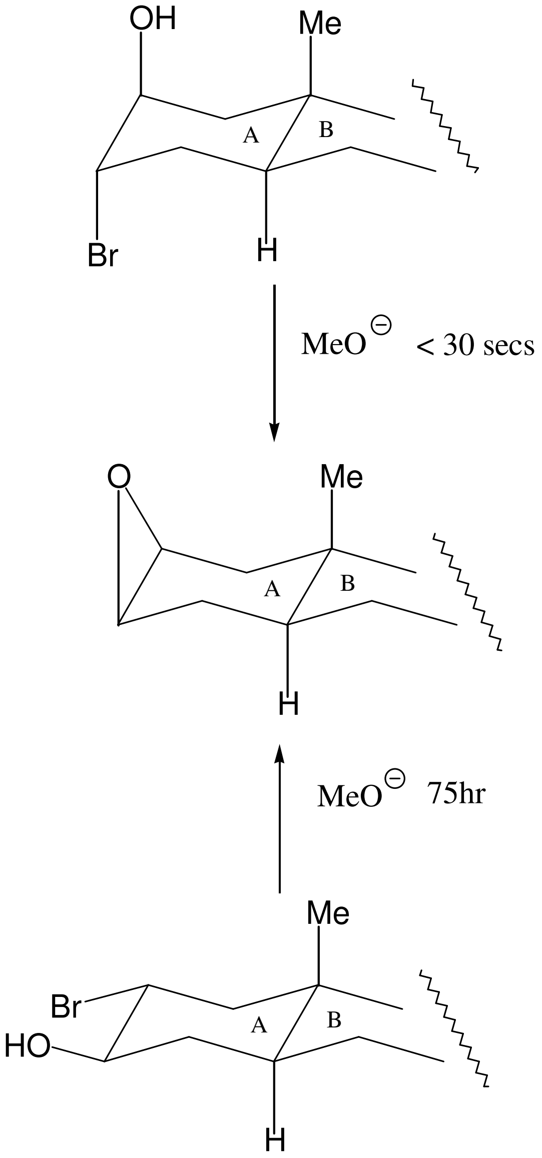
E2-Elimination



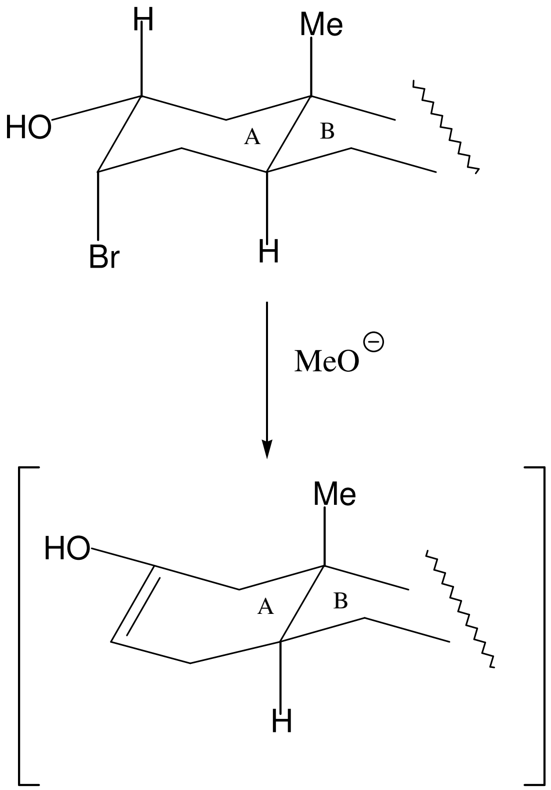
HOBr Addition



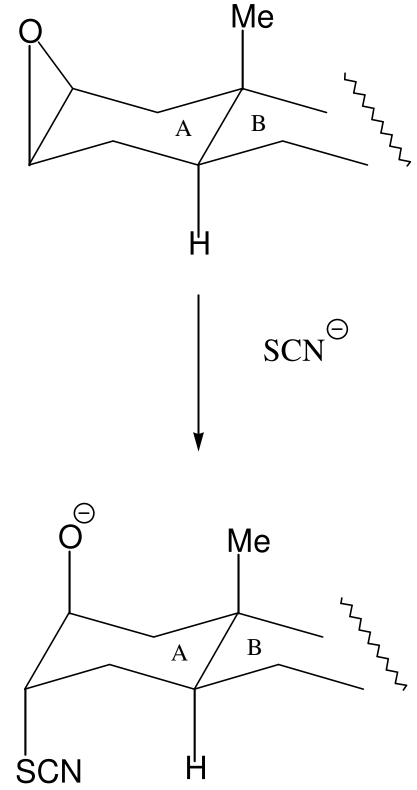
Epoxide Formation



The ability of the neighbouring group to displace a leaving group will depend on whether the orbitals can overlap effectively and the above shows that this can be achieved most readily in a 1,2-diaxial precursor. If we start with the cis-bromoalcohol with an H axial and the Br axial we get elimination to give the enol which rapidly ketonises:

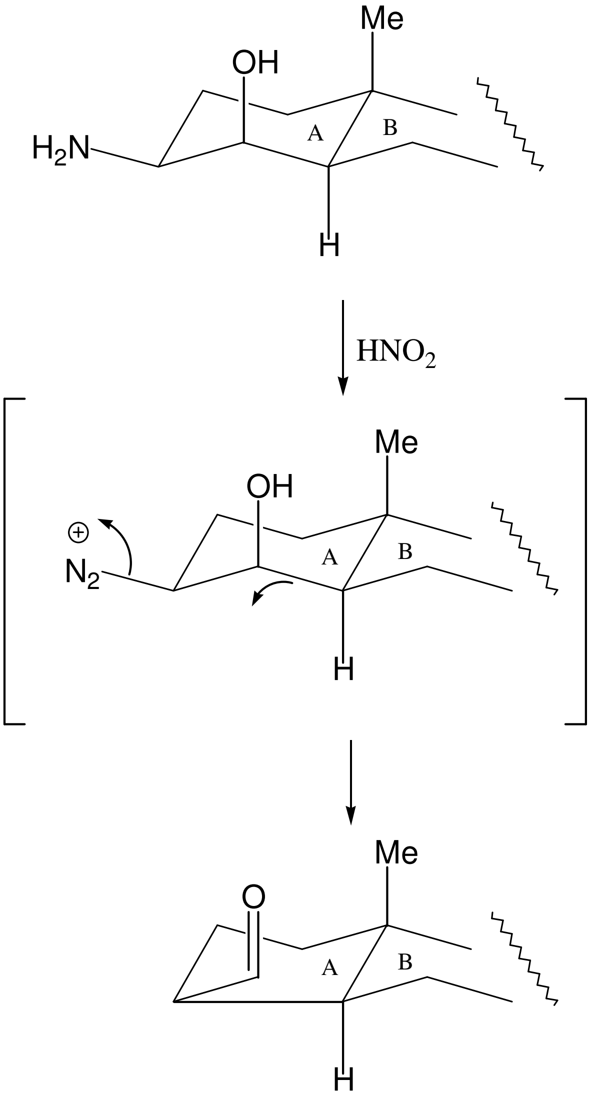


Ring Opening of Epoxides by Nucleophiles



This is really the reverse of the formation of epoxides and therefore attack by nucleophiles should again be axial as above.

(b) Other Anti-Periplanar Processes: Whilst 1,2-diaxial reactions dominate the anti-periplanar processes, we must remember that it is the anti-periplanar nature of these reactions which is the controlling feature and that 1,2-diaxial reactions are only one example of this control. This is clearly indicated in the following example where the substituents are not diaxial but those bonds which are anti-periplanar take over the reaction:



In this case the C4-C5 bond is anti-periplanar to the leaving group and ring A contracts to a five-membered ring.