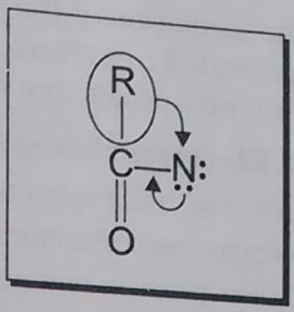
CHAPTER 15

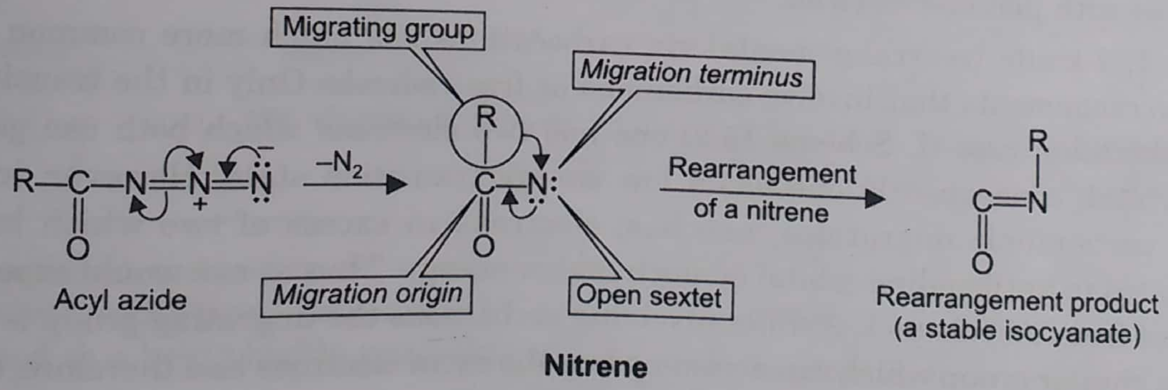
Molecular Rearrangements



When in a reaction on an organic compound, the basic skeleton of the molecule undergoes a change, one then speaks of the occurrence of a molecular rearrangement. The majority of the rearrangements involve a migration from an atom (migration origin) to an adjacent one (migration terminus) and are termed 1, 2 shifts (Scheme 15.1). Most of these rearrangements are intramolecular processes and may occur in:

1. Electron deficient systems

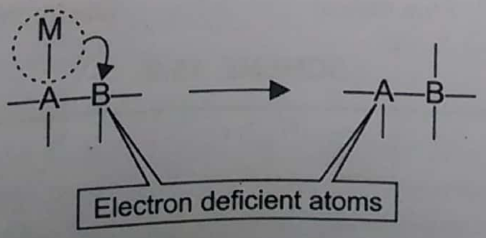
Migrating group moves with its bonding pair of electrons to the migration terminus which is electron deficient with an open sextet. This is seen in the formation of a nitrene (electron deficient nitrogen) during the decomposition of an acyl azide. Once formed the nitrene undergoes a molecular rearrangement (Scheme 15.1). These rearrangements are also called nucleophilic or anionotropic rearrangements.



SCHEME 15.1

The migrating group or atom (M) *e.g.*, M = halogen, RO^-, RS^-, R_2N^-, $(-\overset{|}{\underset{|}{C}}-$ or H)

nigrates from one atom A to an adjacent atom B along with a pair of bonding electrons Scheme 15.1*a*). The essential requirement for the 1, 2-shift involved in this rearrangement is

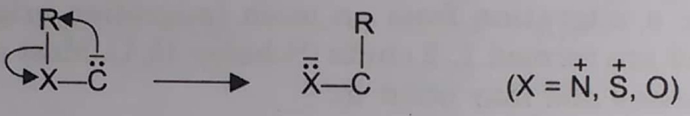


SCHEME 15.1a

the formation of the atom B which has only a sextet of electrons. The electron sextet may be generated in neutral species for examples nitrenes (see, Scheme 15.1) or carbenes and also in cationic species like carbocations, and in electron deficient oxygen and nitrogen.

2. Electron rich systems

In these rearrangements (which are less common), the migration group migrates without its electron pair. An example is prototropic rearrangement where the migrating group is hydrogen. These rearrangements are also termed electrophilic or cationotropic rearrangements. These rearrangements include reactions which are initiated by the formation of an anion (Scheme 15.1*b*) and are usually called anionic rearrangements. Most anionic reactions begin with the removal of a proton by a strong base and these rearrangements may proceed by ionic or free radical pathways.



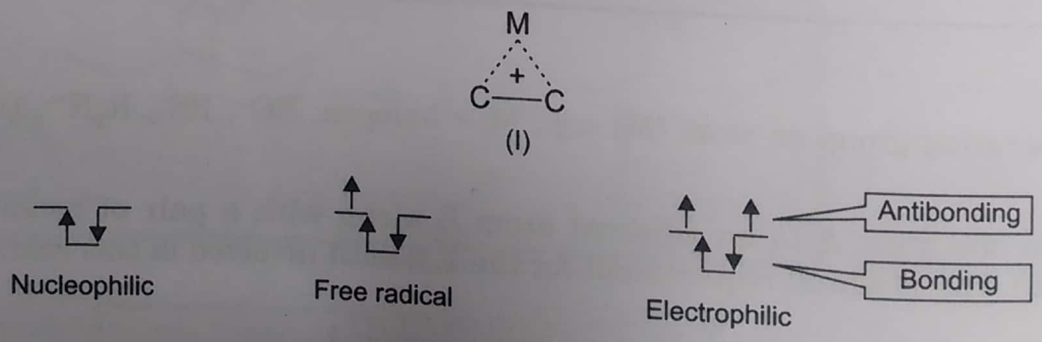
R migrates without its bonding pair

SCHEME 15.1b

3. Free radical rearrangements

The least common of the rearrangements are free radical rearrangements where the migrating group moves with just one electron.

The 1, 2-shifts (rearrangements) via carbocations are much more common than the similar rearrangements that involve carbanions or free radicals. Only in the transition state for the carbocation case (I, Scheme 15.2) one has two electrons which both can go into the bonding orbital, consequently one has a low energy transition state. However, in the free radical or carbanionic migrations, one has, electrons in excess of two which have to be accommodated in antibonding orbital of much higher energy. Thus as one would expect, during 1, 2 shifts of free radicals or 1, 2 shifts involving carbanions the migrating group is generally an aryl or a similar group which can accommodate the extra electrons and therefore, effectively removes these from the three membered transition state.



SCHEME 15.2

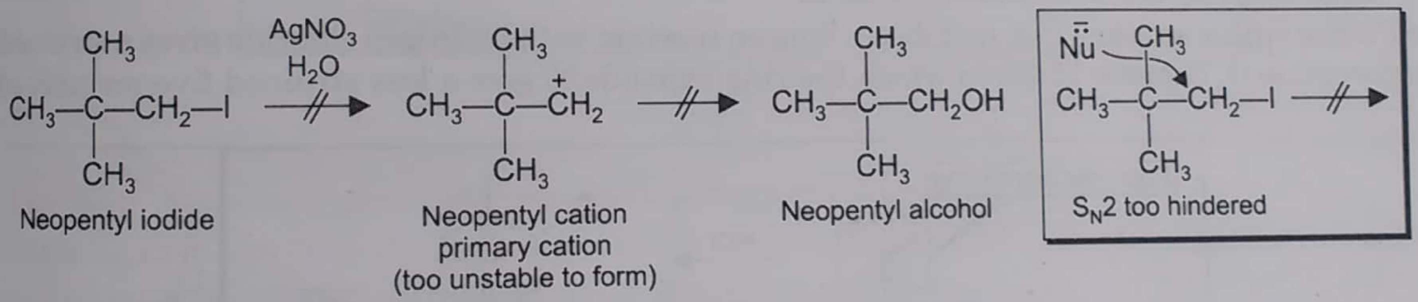
15.1 REARRANGEMENTS TO ELECTRON DEFICIENT CARBON

(A) Wagner-Meerwein Rearrangement (Carbon to carbon migration of R, H and Ar)

1. *A migration of an alkyl group in neopentyl system*

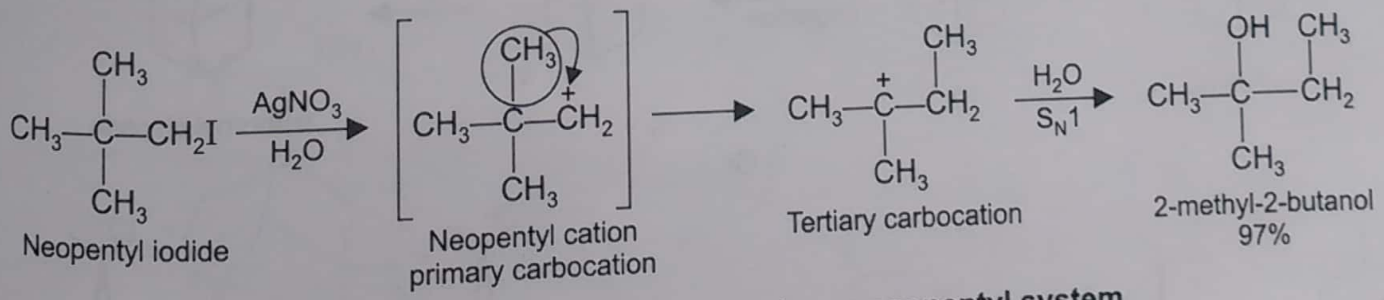
These rearrangements involve the intermediate formation of a carbocation which is an electron deficient open sextet in which a 1, 2 shift (rearrangement) occurs when such a shift leads to the formation of a carbocation of greater stability and this is the driving force of the rearrangement. A further requirement which is often necessary for this rearrangement to occur is the presence of two or more alkyl groups (high degree of substitution) on the migration origin. One of the simplest systems within which carbon (as a methyl group with its bonding pair of electrons) migrates to an electrons deficient carbon atom is the neopentyl system.

Migrations to an electron deficient carbon atom are broadly known as Wagner-Meerwein rearrangements. As an example consider the solvolysis of neopentyl iodide (H_2O, Ag^+). In the absence of Ag^+ ion no reaction is observed at all. Neopentyl iodide cannot display S_N1 reaction since the primary carbocation if formed would be highly unstable and S_N2 reaction is also not observed since the substrate is too hindered. In fact on solvolysis a rearranged alcohol 2-methyl-2-butanol is formed (Scheme 15.3 and 15.3*a*).



SCHEME 15.3

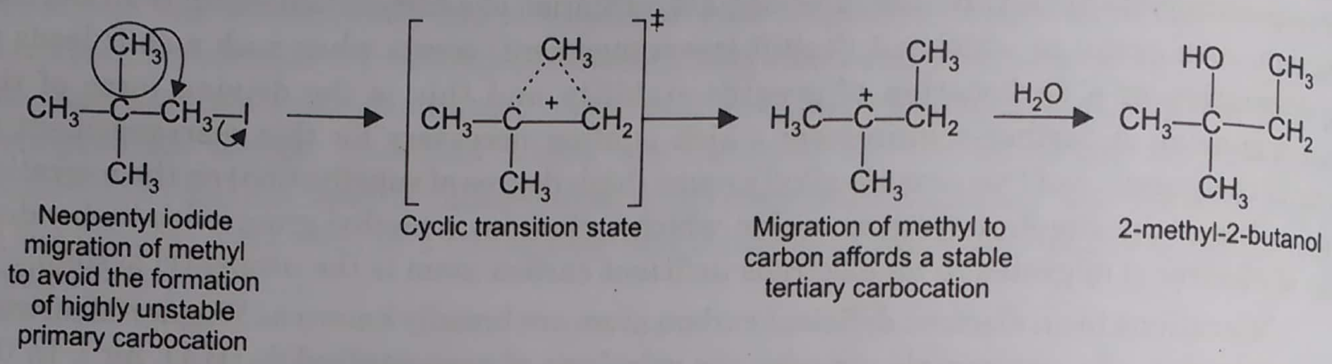
A shorthand method to depict this Wagner-Meerwein rearrangement is in (Scheme 15.3*a*). However, recall from (Scheme 15.3) that the presence of a primary carbocation is highly unsettling and this being highly unstable may not be at all on the reaction pathway.



Wagner-Meerwein rearrangement on a neopentyl system

SCHEME 15.3a

Keeping this in mind a variant of mechanism (Scheme 15.3*b*) is presented to display as if methyl group migrates as iodide departs and by doing so the migrating alkyl group allows the formation of a stable tertiary carbocation. Infact it is suggested that the migration is concerted with the departure of the leaving group. The migrating group infact is never free but keeps on attached with the substrate in some way. It has been demonstrated that if the migrating group is chiral, its configuration is retained in the rearranged product. In summary it is suggested that the migrating group must bridge the migration origin and terminus. Much effort has been spent in determining if such bridged ions are transition states or intermediates and recall this information from chapter 5 on nonclassical carbocations.

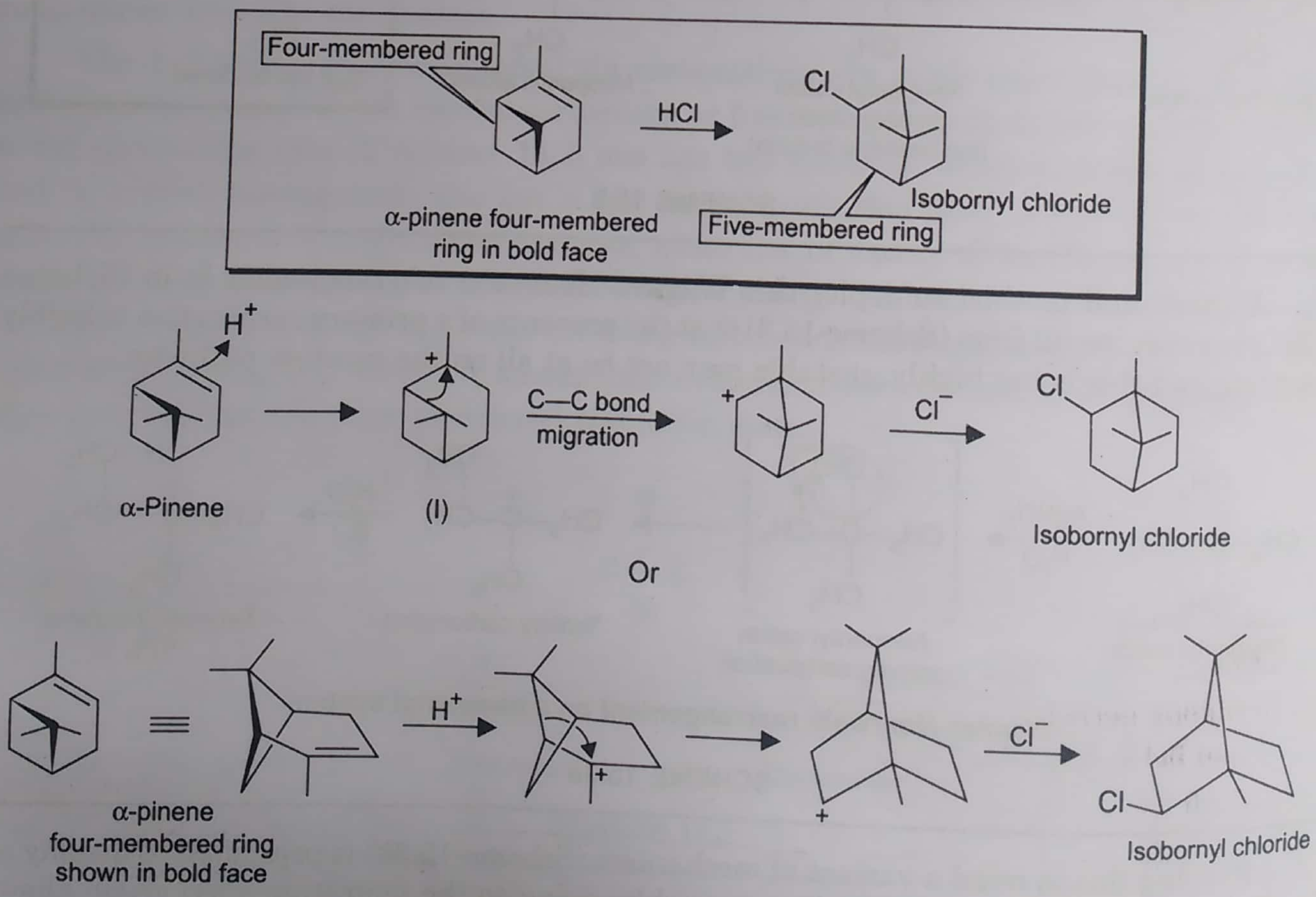


More realistic representation of a 1, 2-shift during Wagner-Meerwein rearrangement

SCHEME 15.3b

2. *Relief of strain via ring expansion provides a driving force for Wagner-Meerwein shift-shift of a carbon-carbon bond*

α-Pinene with a strained four membered ring on reaction with hydrogen chloride gives a strained carbocation (I, Scheme 15.3*c*) in which the ring expands to give a less strained five-membered

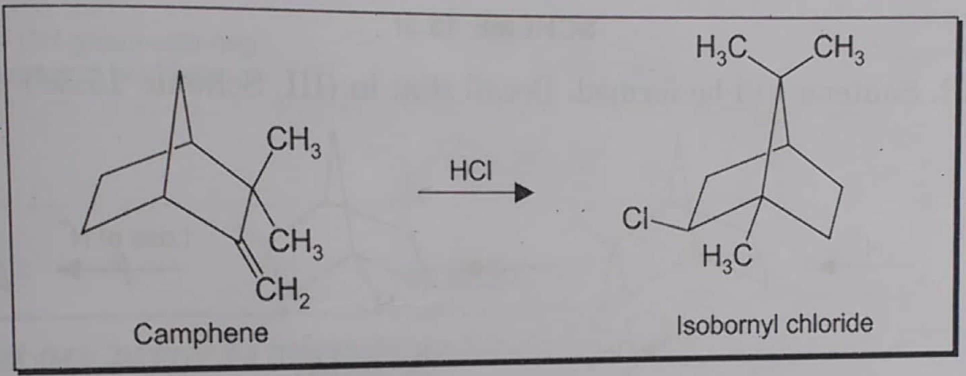


SCHEME 15.3c

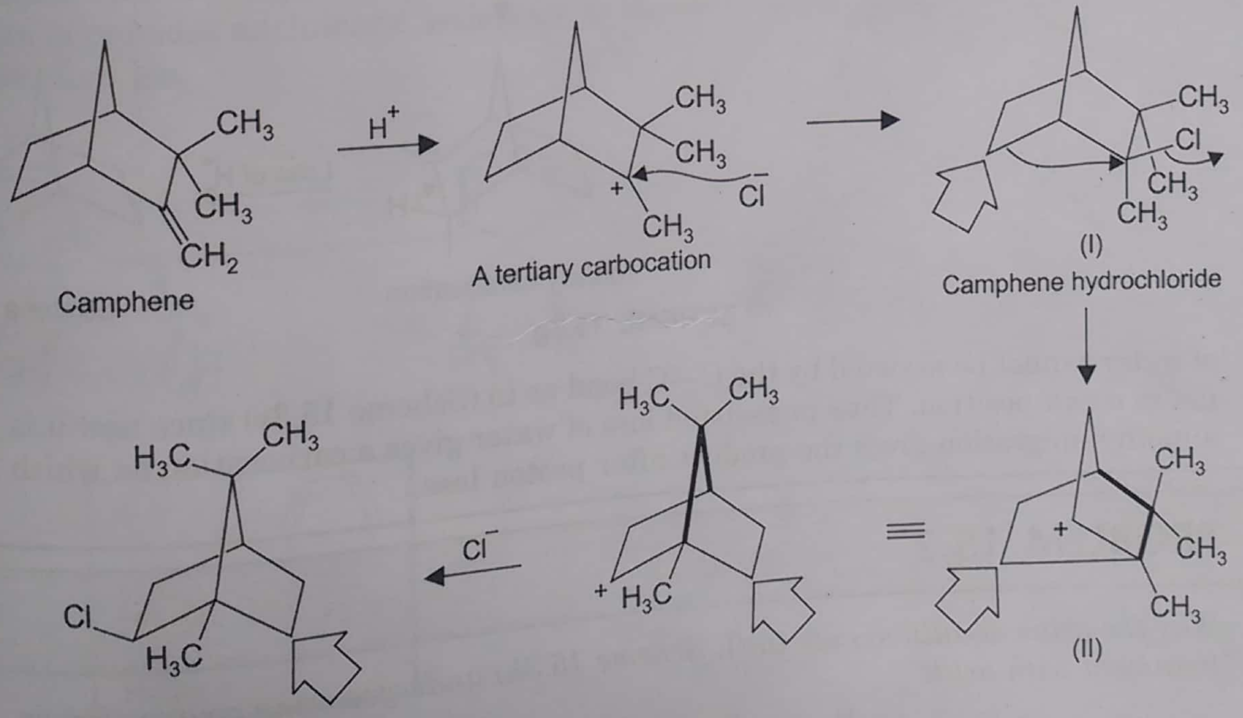
analogue. In this case despite the fact that the rearrangement transforms the initially formed stable tertiary carbocation to a less stable secondary carbocation, relief of ring strain makes the rearrangement favourable.

3. ***The migrating group to be anti-periplanar to the leaving group—a general stereochemical requirement in rearrangements***

Consider the conversion of camphene into isobornyl chloride (Scheme 15.3*d*). Camphene on protonation gives a tertiary carbocation followed by its capture by the chloride ion. The initial product (I, Scheme 15.3*e*) loses chloride assisted by nicely poised C—C bond which acts as a neighbouring group to lend anchimeric assistance via backside attack to give (II) which is then captured by chloride to give isobornyl chloride.



SCHEME 15.3d

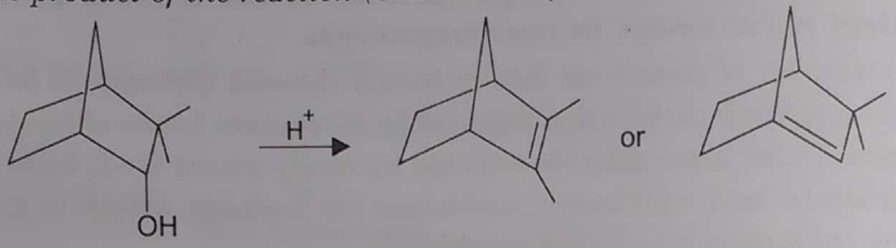


SCHEME 15.3e

This is the case of rearrangement since the participating C—C bond ends up bonded to a different atom.

PROBLEM 15.1

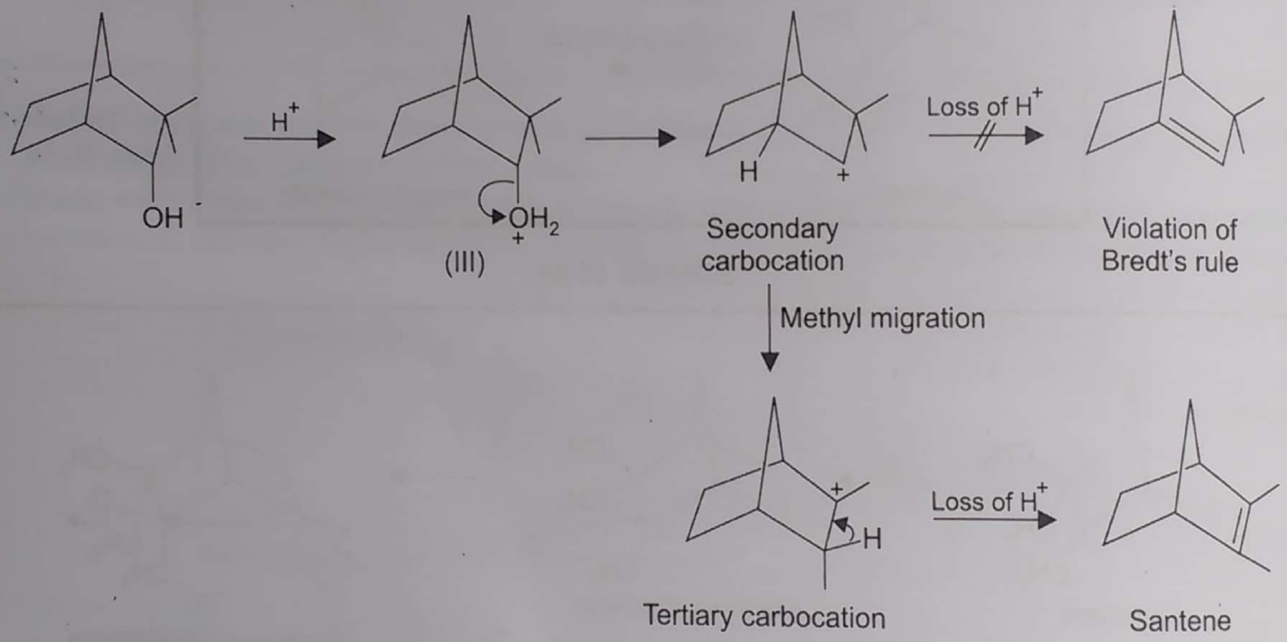
Predict the product of the reaction (Scheme 15.3f) and give the mechanism.



Camphenilol (I) (II)

SCHEME 15.3f

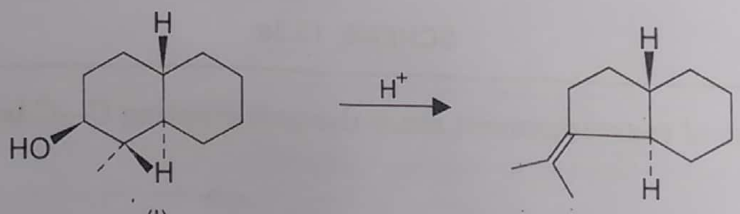
ANSWER. Santene will be formed. Recall that in (III, Scheme 15.3*d*) the loss of water cannot be assisted by the C—C bond as in (Scheme 15.3*e*) since now it is not in a *anti* position. Thus unassisted loss of water gives a carbocation on which a methyl migration gives the product after proton loss.



SCHEME 15.3g

PROBLEM 15.2

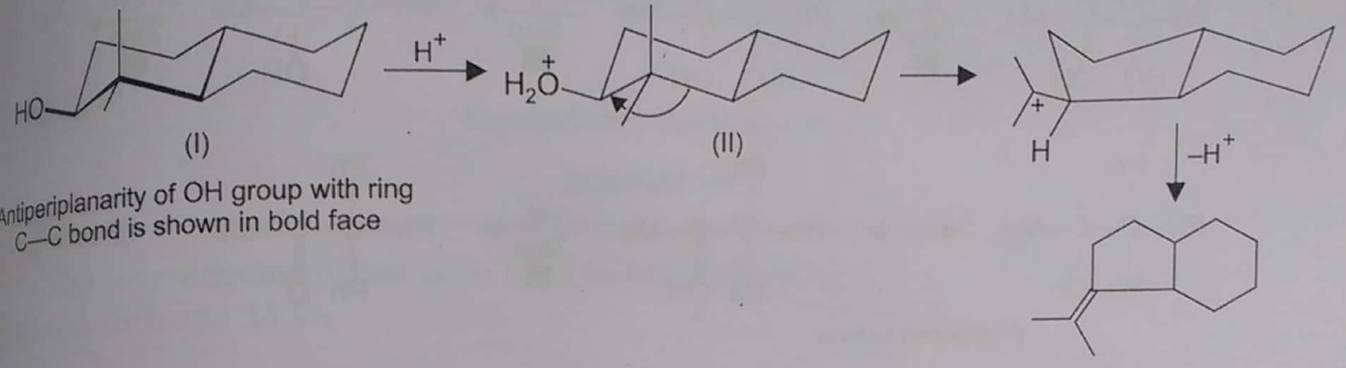
Why the trans decalin system in (I, Scheme 15.3h) undergoes ring contraction on treatment with acid?



(I)

SCHEME 15.3h

ANSWER. *This is a result of Wagner-Meerwein rearrangement. The equatorial OH group is antiperiplanar to a C—C ring residue and the loss of H_2O from (II) is assisted by this C—C bond to give a ring contracted carbocation from which loss of proton gives the product. Recall that this is a molecular rearrangement since the participating C—C bond has ended up bonded to a different carbon atom. In (I, Scheme 15.3i) there is no anti-hydrogen available to the hydroxyl group so as to exclude the possibility of simple dehydration.*

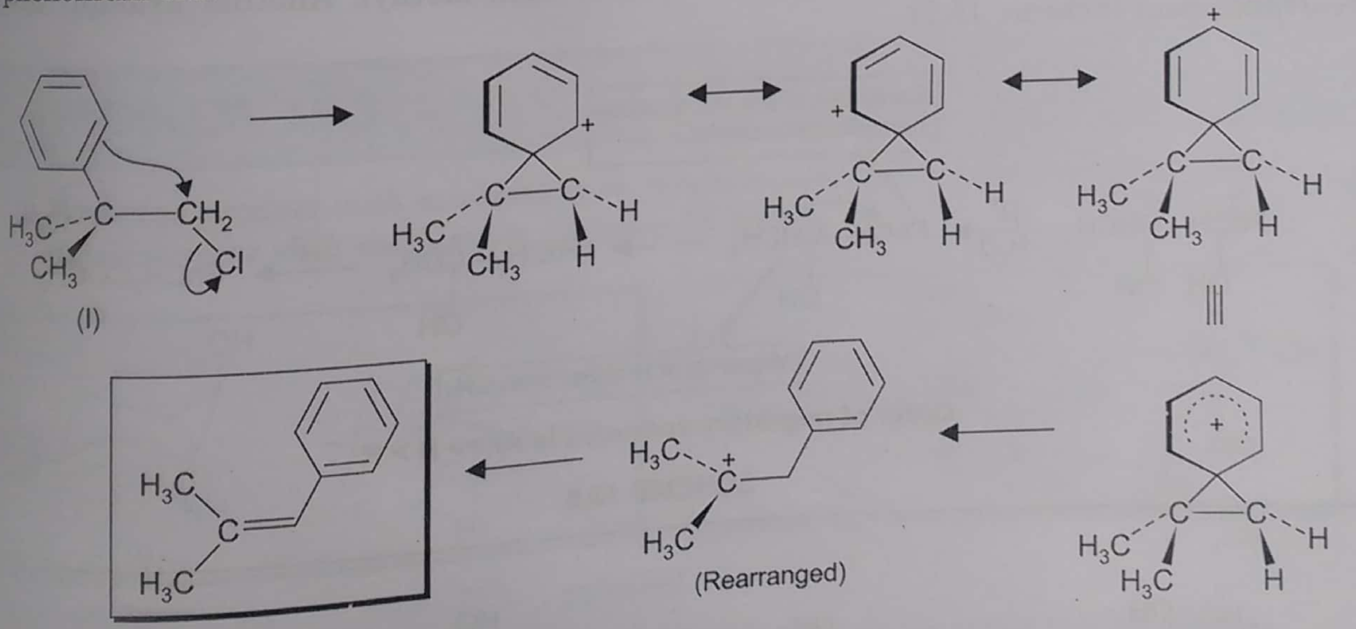


Antiperiplanarity of OH group with ring C—C bond is shown in bold face

SCHEME 15.3i

4. **Aryl groups are prone to migrate and have a far greater migratory aptitude than alkyl groups or hydrogen**

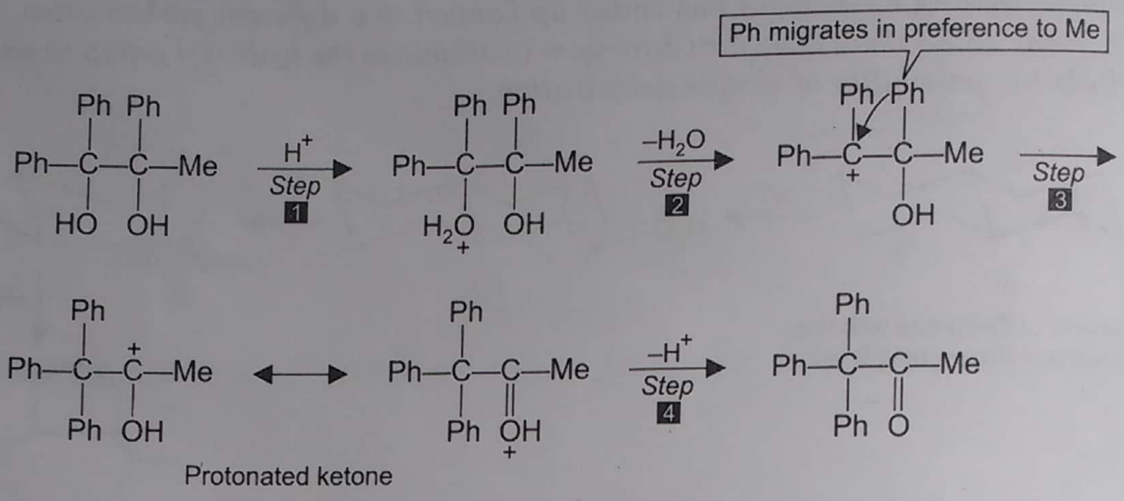
Compared to neopentyl system, in neopentyl iodide (see, Scheme 15.3), the halide (I, Scheme 15.4) undergoes solvolysis with rearrangement several thousand times faster. The aryl group provides anchimeric assistance to the loss of halogen and involves the formation of a phenonium ion.



SCHEME 15.4

(B) Pinacol and Semipinacol Rearrangement

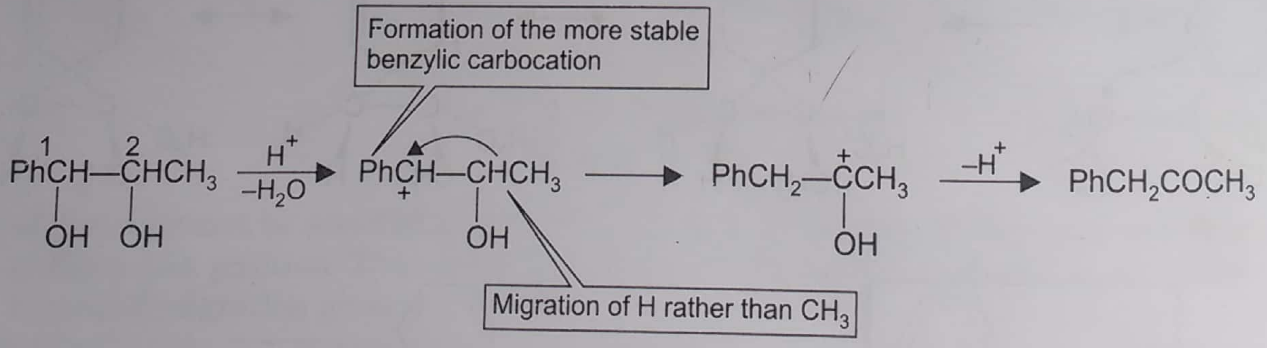
Pinacols (1, 2-diols) on treatment with acids display a rearrangement to ketones (pinacolones). The rearrangement is similar to Wagner-Meerwein shift, but for the fact that here the rearranged intermediate carbocation, the conjugate acid of the ketone is more stabilized than the rearranged carbocation formed in the Wagner-Meerwein shift (Scheme 15.5). Thus in pinacol rearrangement a shift still takes place eventhough the migration terminus may be a tertiary carbocation.



Pinacol rearrangement

SCHEME 15.5

A further observation is that with unsymmetrical glycols the product formation depends mainly by which OH is lost to leave behind the more stable of the two carbocations, and thereafter by which is the better migrating groups (order of migratory aptitude, is Ar > H > R). Thus pinacol (Scheme 15.6) reacts as shown *i.e.*, initial formation of a more stable carbocation (benzylic) and then migration of hydrogen rather than methyl. Another example is the rearrangement (Scheme 15.7).

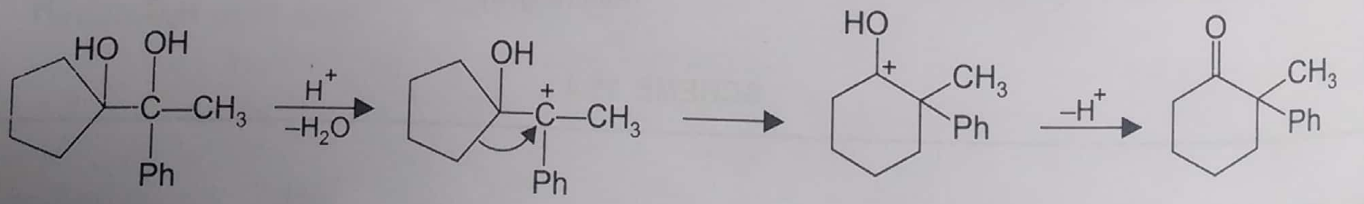


Formation of the more stable benzylic carbocation

Migration of H rather than CH₃

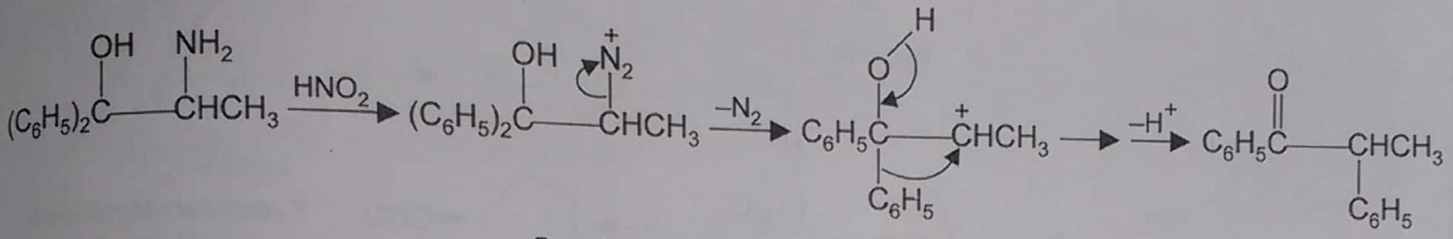
Order of *migratory aptitudes* is Ar >> H > R

SCHEME 15.6



SCHEME 15.7

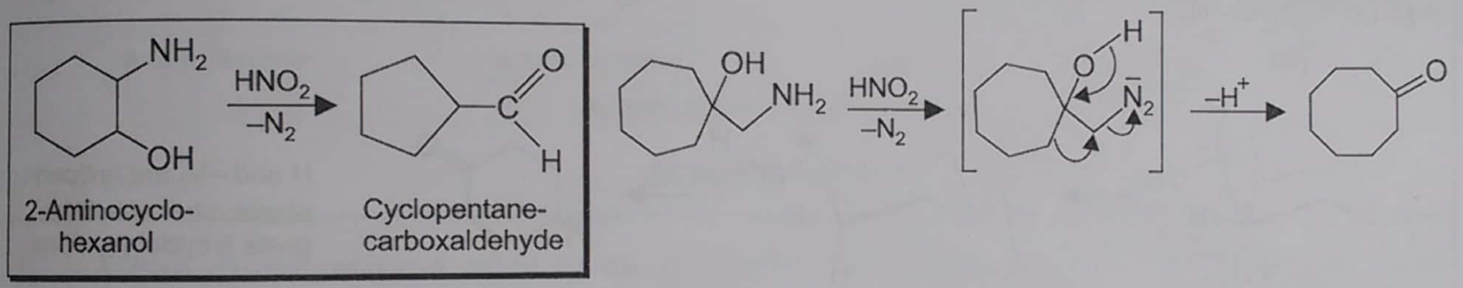
Deamination of α-amino alcohols is closely related with pinacol rearrangement and is called semipinacol rearrangement. These rearrangements are typical where a hydroxyl group provides the electrons to migrate a group and the driving force is provided by the loss of the leaving group other than water (Scheme 15.8).



Semipinacol rearrangement

SCHEME 15.8

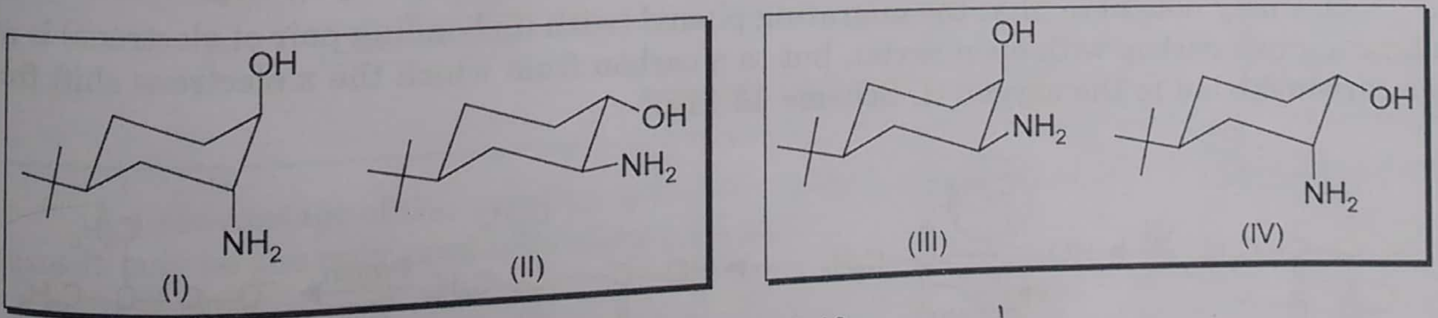
The rearrangement has been used to bring about both ring contraction as well as ring expansion (Scheme 15.9).



SCHEME 15.9

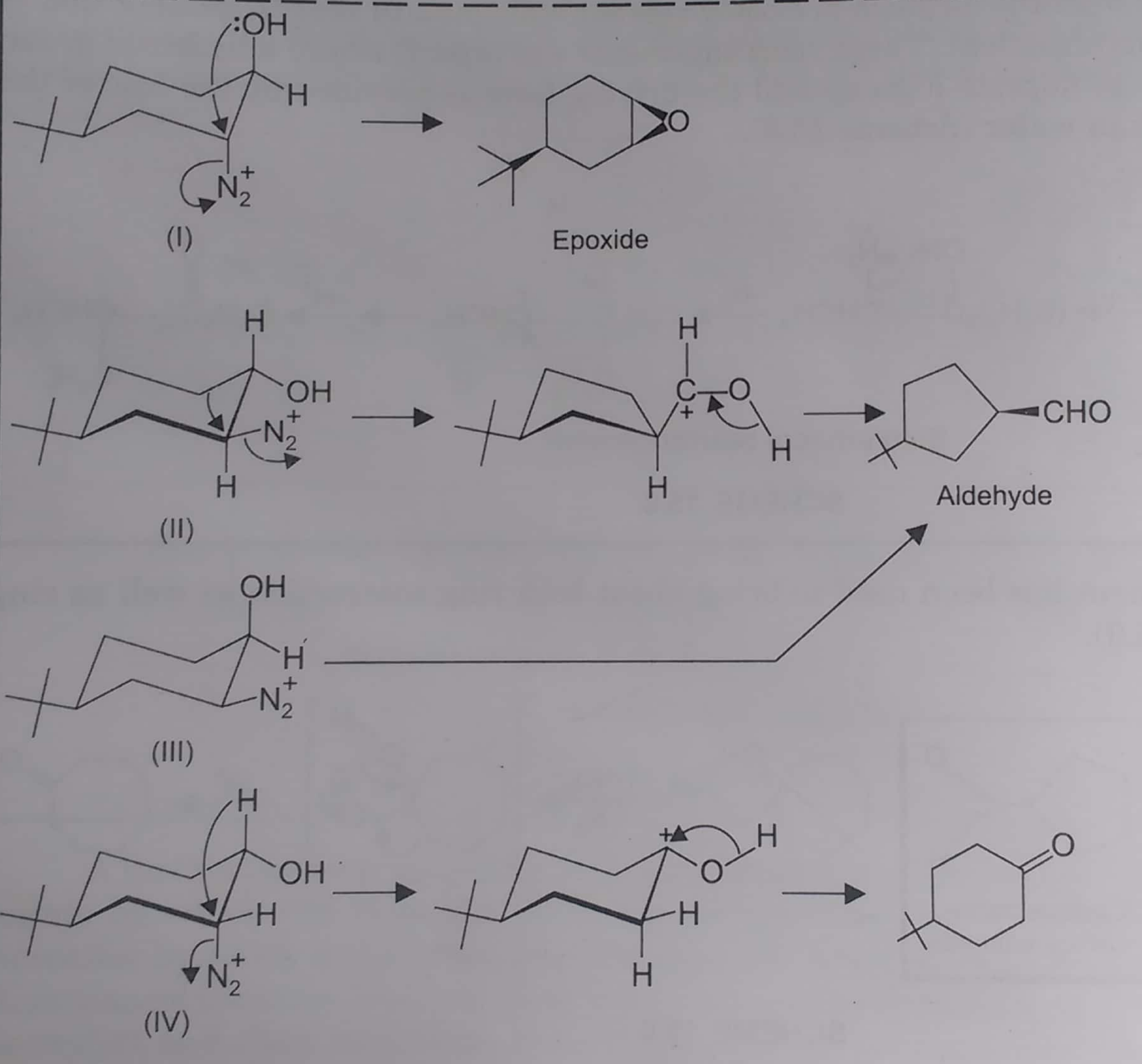
PROBLEM 15.3

Write the product with mechanism on reaction with HNO_2 from each of the four diastereomers with mechanism (Scheme 15.10).



SCHEME 15.10

ANSWER. *In each case t-butyl group locks the ring in the conformation shown. The stereochemical requirement requires an antiperiplanar arrangement between the migrating and leaving group* ($-N_2^+$). *In each of the reactions the OH group provides the electronic push (Scheme 15.11).*



Oxygen of the OH group displaces N_2 to give an epoxide

Equatorial $-N_2^+$ antiperiplanar with C—C bond of the ring

Again equatorial $-N_2^+$ antiperiplanar with the C—C bond of the ring

H and $-N_2^+$ are antiperiplanar, shift of hydride gives a cyclohexanone

SCHEME 15.11