Amrutha. G

1 copy 13 copy Sarika. V

Dr. MOHAMMED MUSTHAFA. TN
MESKC, MKD, Dte Chemistry,
TIRUR. C.K.

CONFORMATIONAL ANALYSIS - I

Unit-3

Conformational Analysis - I

The different spatial arrangement of atoms in a molecule which are readily interconvertible by rotation about single bonds are called conformations. If the energy barrier for conversion of different spatial arrangement is ≥ 100 KJ/mol then it is configurational isomers. If it is less than 40 KJ/mol it is said to be conformational isomers.

→ Conformation of ethane - Jagadamba sing, Gokulachandran

The angle btwn the atoms attached to the front and rear carbon is called the torsional angle (dihedral angle) Staggard conformation has 60° torsional angle., eclipsed conformation has 0° torsional angle. In staggard conformation, the distance btwn H nuclei is 2.55 A°, in eclipsed it is still lesser ie 2.29 A°. The rotational energy barrier is just 12.6 KJ/mol at 298 K. Thus individual conformers cannot be isolated. The rotation about the carbon-carbon single bond in ethane neither completly free nor (2.6 KJ/mol = RT) completly restricted (> 100 KJ/mol)

Torsional strain is the repulsion felt by bonding es of one substituent as they pass the bonding electrons of another substituent.

→ Conformations of butane

Butane has three staggared conformation (one anti and two gache). Anti is the most stable. In gache conformer the largest substituents are adjacent to each other thus have steric hindrance. This steric strain in gache conformer is called gauche interaction. In anti largest substituents are opposite to each other. Butane also have 3 eclipsed conformers (1 fully eclipsed and two eclipsed). All these eclipsed conformers have both torsional and steric

...ative stability ord...

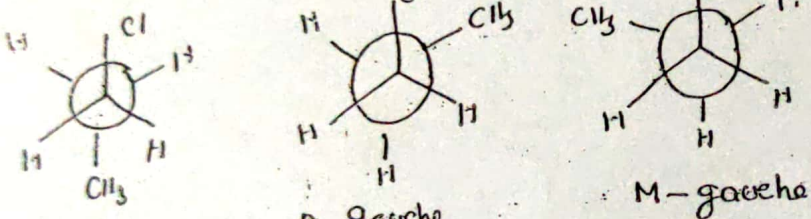
Anti > Gauche > eclipsed > fully eclipse

Two gauche ~~gauche~~ forms of butane are conformational enantiomers while gauche and anti forms are conformational diastereomers

Conformations of halogenoalkanes — Nasipuri

eg: CH_3-CH_2-X X = F, Cl, Br and I

The ~~torsional~~ energy barrier is slightly higher (14-15 kJ/mol) from that of ethane (12.0 kJ/mol) due to increased steric effect of halogen grp than hydrogen. In n-propyl chloride and n-butyl chloride the gauche conformers ~~are~~ (they are enantiomeric) are predominated over anti form due to Vandel-Wals attractive forces (London forces).

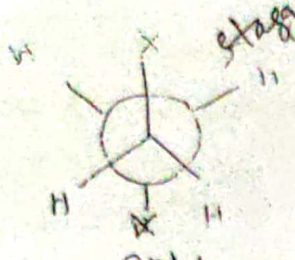


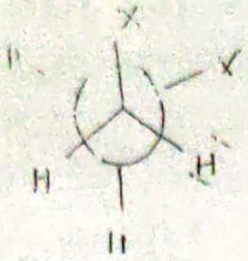
anti P- gauche M-gauche

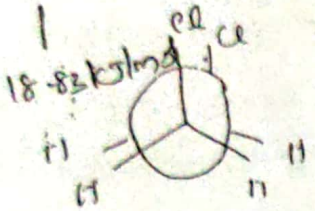
n-propyl chloride | alkane ~~dihalide~~ dihalides

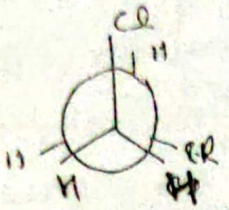
In the gaseous state at 200°C 1,2-dichloro and 1,2-dibromoethanes contain 73 and 85% of the anti conformers (it is 67% only in n-butane). The (higher stability of the anti form in these dihalides in comparison to that in n-butane is due combined effect of steric fact (larger in Br than Cl) and an electronic interaction (dipole-dipole repulsion). In the (liquid state or in the polar solvents, the electrostatic repulsion decreases considerably, due to high dielectric constant of the medium and the ratio of gauche conformers increases than anti forms. The barrier hight in 1,2-dichloro ethane is ≈ 12.8 kJ/mol similar to that in butane due to less H/Cl steric effect.

4.6 > transoid.







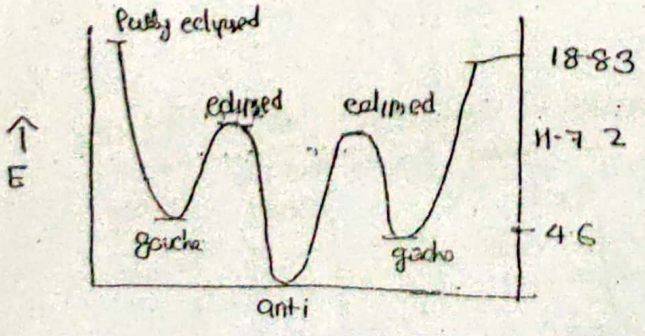


(cisoid)

$CH_2=CH_2$
Cl Cl

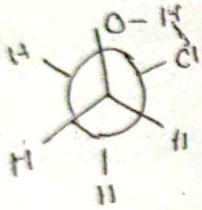
The potential energy of ethylene dichloride undergoes changes on like n-butane only. when one CH_2Cl group is rotated about the C–C bond with other CH_2Cl at rest; there are two positions of minimum energy. One corresponds to the staggard (transoid or anti) form and other to the gauche (skew) form. The gauche conformer has ~ 4.6 KJ/mol more energy than anti form. The fully eclipsed (cisoid) Forms possess about 18.83 KJ/mol more energy than anti form. The ratio of the two forms varies with temp, only the staggard form is present at low temperature.

The stability is affected by dipole-dipole interaction and steric repulsion (H=0 in staggard form and maximum in eclipsed form)

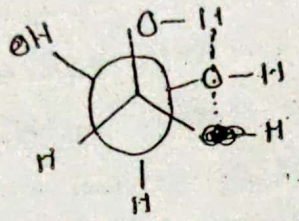


Conformation and intramolecular hydrogen bonding

In 2-substituted ethanols of the type $X-CH_2-CH_2-OH$ where $X = OH, NH_2, F, Cl, Br, OCH_3, NHCH_3, N(CH_3)_2$ the preferred conformations is gauche than anti and eclipsed due to intramolecular H-bonding. Eg: In case of ethylene glycol and ethylene chlorohydrin intramolecular H bonding is possible in gauche form and not in the anti form. This would stabilise the molecule by about 20-29 KJ/mol and this is great enough to make gauche form more stable than anti form.



Ethylene chlorohydrin



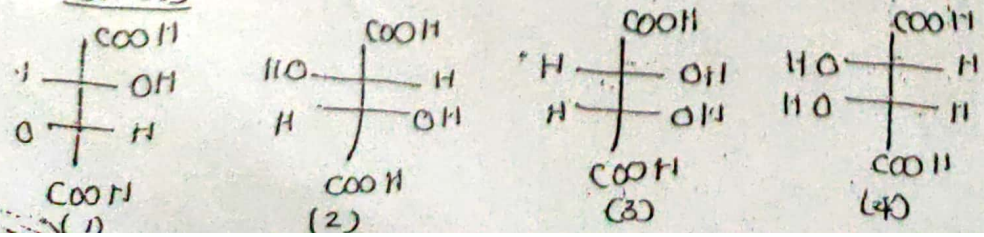
Ethylene glycol

In eclipsed conformer the two group (donor and acceptor) are very close to each other, so vandercual repulsive force come in to play and make the conformation unstable. The anti conformer with the two groups oppositely placed does not permit the formation of intramolecular H bond. The gauche conformation with torsion angle of 60-70° btwn the interacting groups are ideally suitable for intramolecular H bonding.

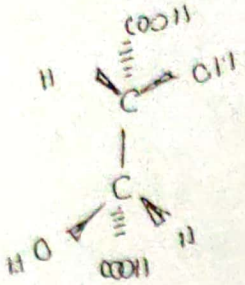
Problems - 1.30 - 1.32

Conformation of tartaric acid - Erythro and threo - Notes from Sapna

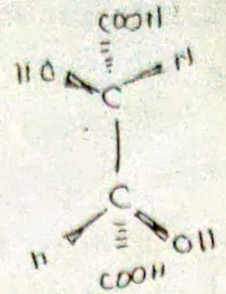
Isomers



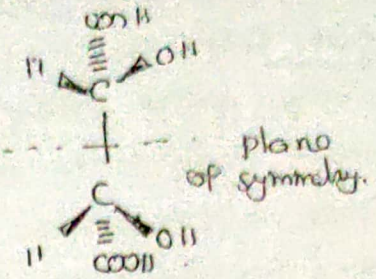
when formula (4) when rotated through 180° (in the plane of the paper) becomes identical with formula (3). Here tartaric acid has three diff isomers (1), (2) and (3).



d-tartaric acid

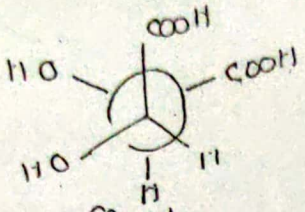


l-tartaric acid

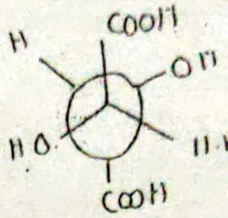


Meso-tartaric acid

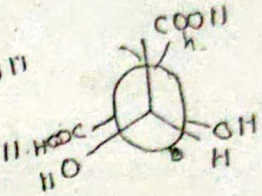
Fully eclipsed



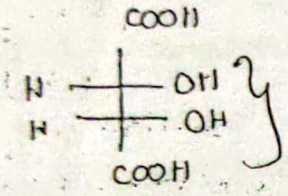
Gauche.



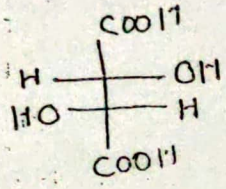
Anti



Eclipsed.



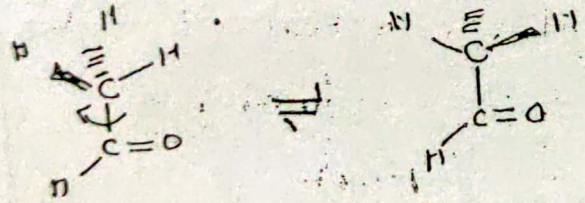
Erythro form

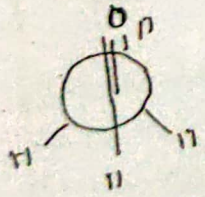


opposite

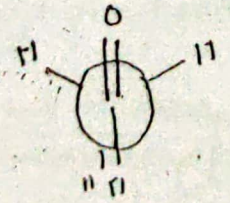
Threo form.

Conformation of Acetaldehyde



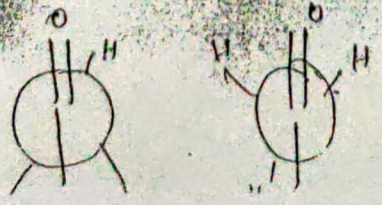


eclipsed



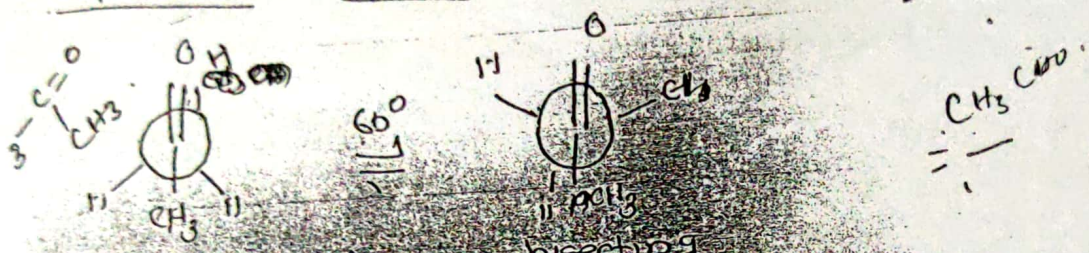
staggard (Bisecting)

more stable



a (-) single bond is connected to a double bond, the double bond at one end of the single bond eclipses a hydrogen at the other end. Acebaldehyde is more stable in the eclipsed conformation (actually the stable conformation has the methyl group rotated about 90 away from perfect eclipsing) than in the staggered one by 1.17 kcal/mol (4.9 kJ/mol) eclipsed conformation has low energy. thus is stable. whereas staggered has high E, least stable

Conformation of acetone



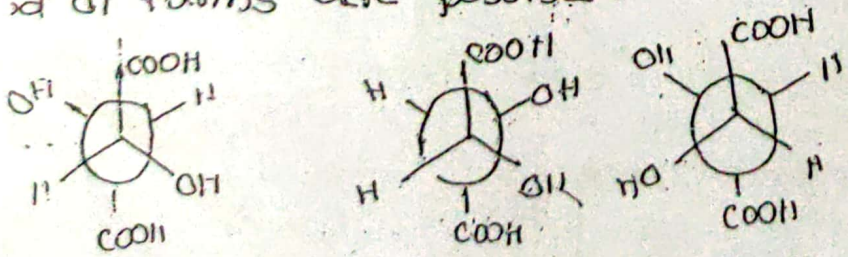
Eclipsed

The preferred conformation of acetone corresponds to that of acetaldehyde in that one hydrogen in each methyl group is eclipsed with the carbonyl oxygen. Similarly dimethyl ketone having conformation the one with both terminal methyl groups similarly eclipsed

Acetone is more stable in eclipsed conformation than in the staggered conformation

Conformation of tartaric acid — Kasim Bros note

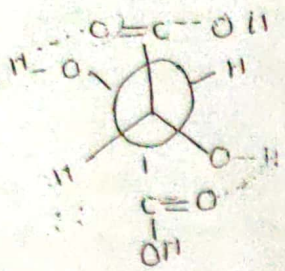
In the case of tartaric acid meso and dl forms are possible.



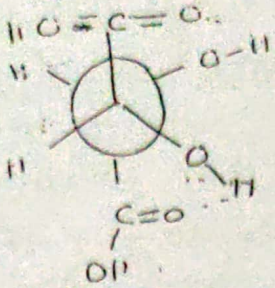
(meso form) (d form) (l-form)

Intermolecular hydrogen bonding is possible btwn >C=O grp of one

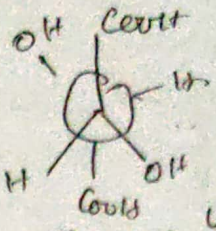
and OH group in the anti and gauche conformation. Thus the meso and dl forms are stable and exist.



meso form



(dl-form)



Meso tartaric acid has a plane of symetry in eclipsed conformation and have centre of symmetry in staggard conformation.

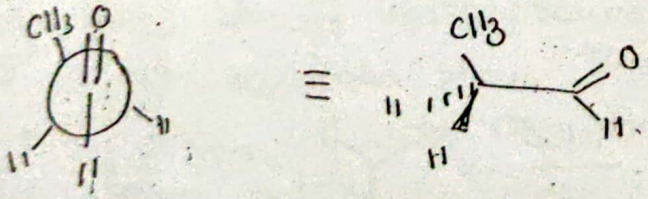
Conformation of aldehydes and ketones - Carey and Sundberg

Rotation around an sp^3-sp^2 bond in acetaldehyde, acetone propionaldehyde etc leads infinit conformations in which eclipsed conformations are preferred over bisected conformation.

Acetaldehyde

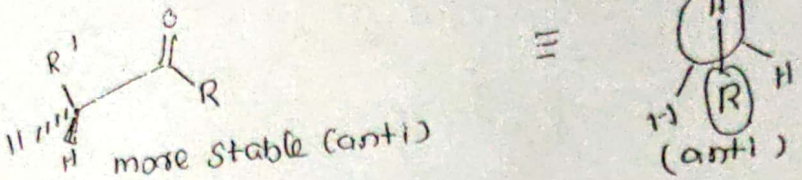
$CH_3-C(=O)-H$; $CH_3-C(=O)-CH_3$

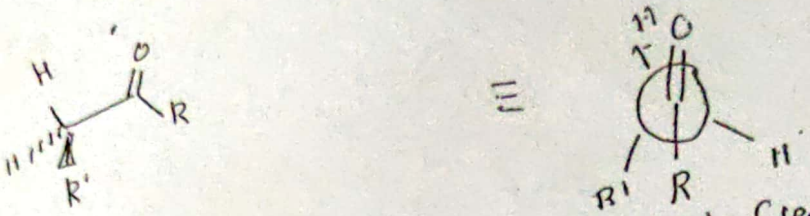
In propionaldehyde the methyl group rather than hydrogen that is eclipsed with the carbonyl group is the most stable conformation.



CH_3-CH_2-CHO

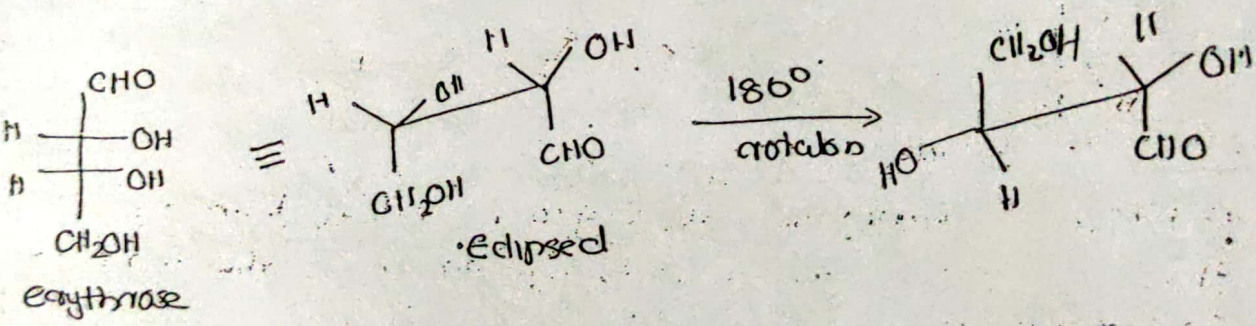
ketones (acetone) also favor eclipsed conformation. The preference is for the conformer in which alkyl group rather than hydrogen is eclipsed with the carbonyl group bec² this conformations allows the two alkyl groups to be anti rather than gauche with respect to other carbonyl substituents

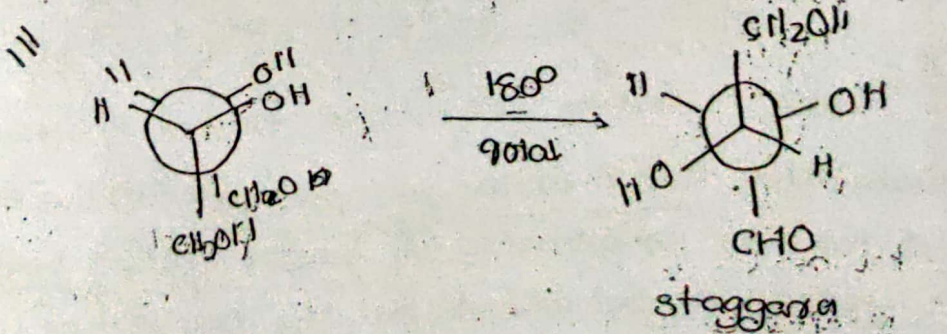




Inversion of Fischer projection in to Sawhorse and Newman formula - and vice versa — Jagadamba singh

Fischer projection represents eclipsed conformation of the molecule, so it can be directly converted in to eclipsed sawhorse or Newman formula. The rotation of front carbon of Sawhorse or Newman by 180° anti gives more stable staggered Sawhorse and newman formula. The reverse process can also be done.





Conformations of cycloalkanes - Jagadamba Singh, Chokkalingam Kalsi

Compds with three and four membered are not as stable as compds with five and 6 membered

rings. According Baeyer strain theory the instability of these small ring compds is due to angle strain (strain induced in a molecule when the bond angles are forced to deviate from the desired tetrahedral bond angle of 109.5°) According to this theory when open chain organic compd having the normal bond angles is converted in to cyclic compd, there is deviation from the normal tetrahedral angle leading to the development of a strain in the molecule. Baeyer assumed the rings are planar. The angles of deviation for different rings are given below.

	Angle strain
cyclopropane	$\frac{1}{2}(109.5-60)^\circ = 24.75^\circ$
cyclobutane	$\frac{1}{2}(109.5-90)^\circ = 9.75^\circ$
cyclopentane	$\frac{1}{2}(109.5-108)^\circ = 0.75$
cyclohexane	$\frac{1}{2}(109.5-120.5)^\circ = -5.25^\circ$
cycloheptane	$\frac{1}{2}(109.5-128.58)^\circ = -9.54$
cyclooctane	$\frac{1}{2}(109.5-135)^\circ = -18.75^\circ$

+ve value = bond angles are compressed
-ve value = bond angles are expanded.

According to Baeyer strain theory cyclopentane is more stable than cyclohexane, but in practice it is not so. The mistake that Baeyer made was to assume that all cyclic compounds are planar. In real sense only cyclopropane is planar and the other cycloalkanes are not.

According to theory of strainless ring cyclic compounds twist and bend in order to achieve a final structure, which minimises the following three kinds strain that can destabilise a cyclic compd.

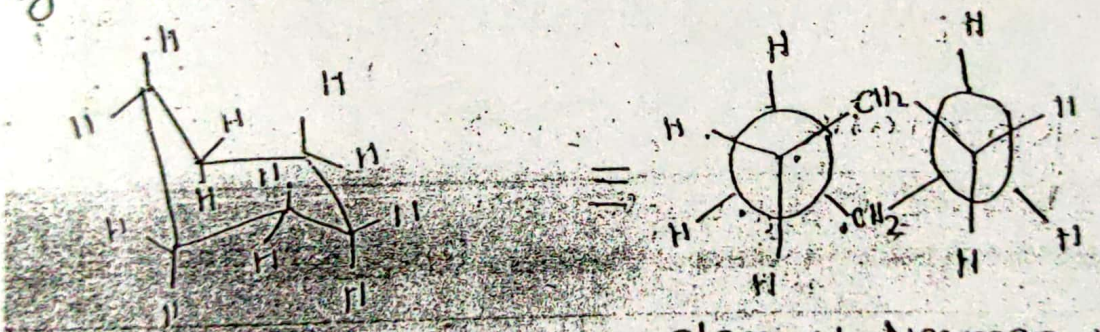
Angle strain (Baeyer strain) – this results when the bond angle is different from the desired tetrahedral bond angle of 109.5°.

Torsional strain (Pitzer strain) – this is caused by repulsion of the bonding $\bar{e}$ (σ-electron) of one substituent with bonding $\bar{e}$s of another substituent on the adjacent atom

Steric strain (Vander Waals strain) – caused by the steric crowding of atoms or groups which approach each other too closely in the structure.

Conformation of cyclohexane

Mohr (1890) proposed that cyclohexane and larger rings are not planar, but they are puckered in which all the angles are tetrahedral and thus the rings are strainless. Cyclohexane exist in two forms which readily undergo interconversion by rotation about single bonds. (boat and chair forms)



Chair conformation.

Staggard Newman projection of the chair conformation

Chair Form

free from angle strain, torsional and steric strain

All C–H bonds are staggard thus torsional strain minimized.

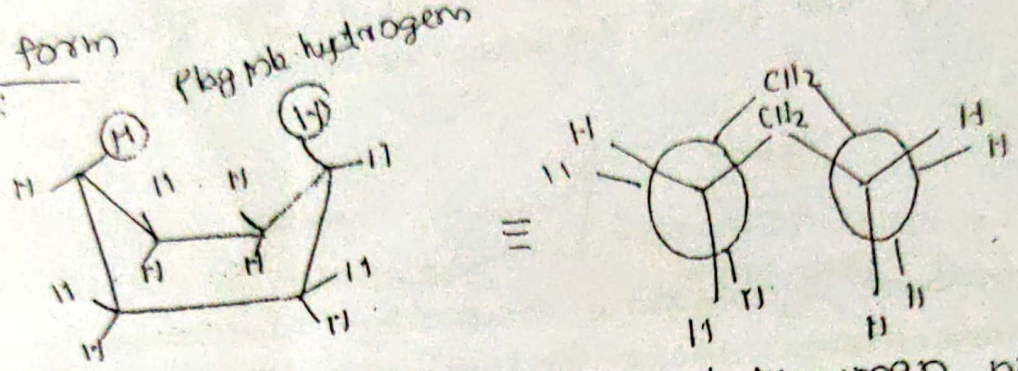
Gauche butane like interaction btwn neighboring methylene groups lead to steric strain

Bond angles are not exactly 109° 30' but 111°, value close to that in acyclic alkanes.

→ The dihedral angles are not exactly 60° but 56° causes slight flattening of the ring

→ The structure has C_3, S_6 axis and centre of symmetry.

Boat form



Eclipsed Newman projection of the boat conformation.

→ has two C_2 axis and 2 σ planes.

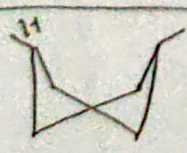
→ There is complete eclipsing of the hydrogen attached to the carbon atom and thus have two eclipsed butane type units. This results torsional strain

→ There is steric repulsion blwn the two hydrogens (flagpole hydrogen) pointing towards each other at C_1 and C_4 and lying only 1.83 Å apart. This causes the steric strain.

→ free from angle strain

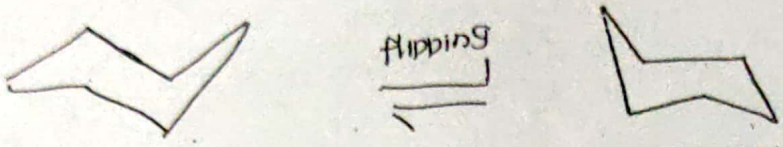
Thus the chair conformation (rigid) is more stable than boat conformation. The energy barrier for the interconversion is 10.8 kcal/m (42 kJ/mol). Thus conformers cannot be separated, however at room temperature most of the cyclohexane molecule (99.9%) exist in the most stable chair conformation.

Twist boat conformation

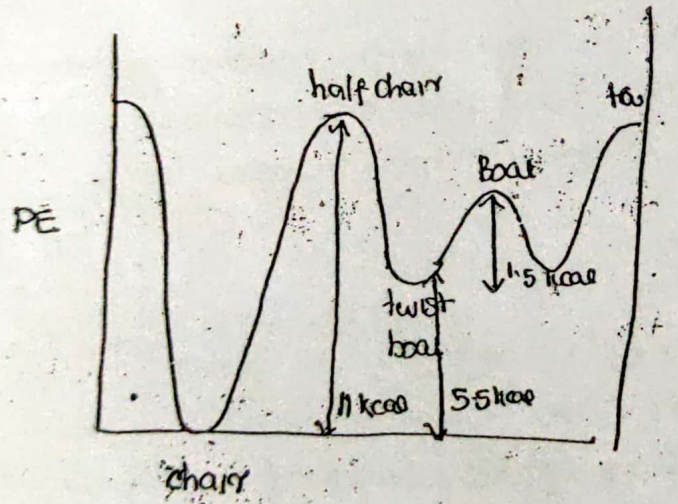


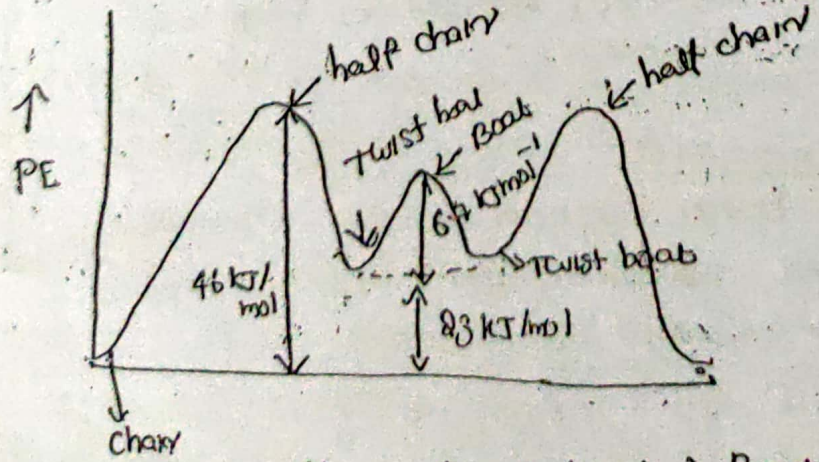
In twist boat conformations flagpole hydrogen are moved apart. Here torsional and steric strains are minimized

In eyet chair conformation of cyclohexane 6 hydrogen are held by bonds which are perpendicular to the average plane of the ring - these are axial bonds The other six bonds holding hydrogens in the average plane of the ring are called equatorial bond



At room temperature, cyclohexane rapidly interconverts (flips) to mirror image chair conformation (then all axial bonds become equatorial and all equatorial becomes axial). At room temperature all hydrogen are equivalent because of rapid flipping. The axial and equatorial hydrogens can be differentiated as two set of proton at $-80^{\circ}C$ due to slow ring flip.





Chair > twist boat > Boat > half chair

Heat chair has highest energy, it is associated with apparent torsional, steric (as well angle strain (angle strain is absent in others)

Conformation of methylcyclohexane - Kalsi

Axial conformer
less stable by 1.8 kcal/mol

Equatorial conformer
more stable

In methyl cyclohexane, the methyl group occupies either equatorial or an axial position

→ In axial conformer, the ~~axial carbon~~ methyl substituent is close to other two axial hydrogens on the same side of the molecule. Thus in axial conformer 1,3-diaxial interaction due to steric repulsion btwn methyl group and axial hydrogen to be. result the conformer less stable.

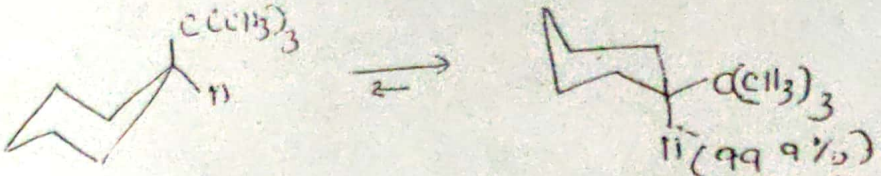
→ Two gauche butane interaction btwn the axial methyl group and the two ring C-C bonds destabilize the axial conformer, while no such interaction exist when the methyl gap is equatorial.

→ at room temp 95% of methyl cyclohexane exist as equatorial and 5% as axial.

→ axial and equatorial conformers ~~are non-superimposable mirror images thus~~ are conformational diastereomers.

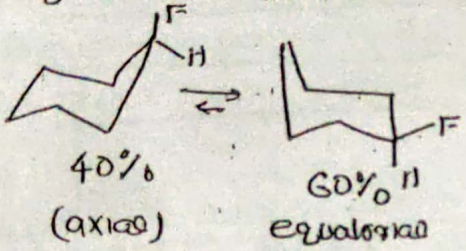
Conformation of tert-Butylcyclohexane

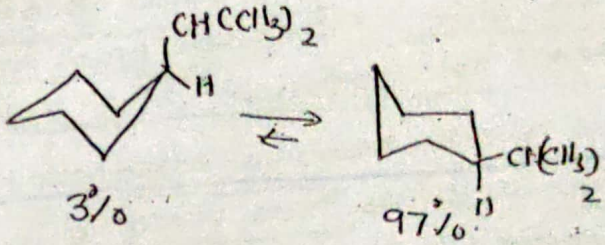
Tert-butyl group is still larger group than methyl group thus the 1,3-diaxial interaction responsible for the destabilising gauche interaction will be further magnified. 99.9% of tert-butyl cyclohexane is maintained in the equatorial form thus the tert-butyl group is used to lock the conformation. the tert-butyl group is referred as 'anchoring group', and the resulting conform are said conformationally biased. (biased)

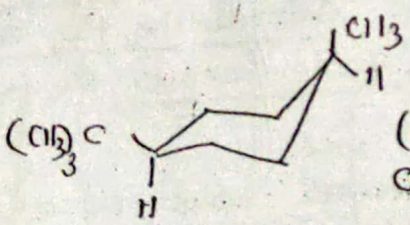


→ ethyle and methyle propyle groups can be rotated, so that a hydrogen is pointed back over the ring to interact with the axial hydrogens, thus their effective steric bulk is not much different from that of a methyle group but t-butyle group causes severe 1,3-diaxial interaction

→ The halogen F, Cl, Br, and I do not differ much in their preferences for the equatorial position, bec a halogen does not require much space (F and It are nearly similar size), C—X bond distance also rises with size of halogen (F<Cl<Br<I). thus we can account following observation.







(tert bulye occupies equatorial So CH_3 bulge be axial in cis-1,4-)

cis-1-tert bulye 4-methye cyclohexane

nformation of disubstituted cyclohexanes

In general disubstituted cyclohexanes the conformation containing both the substituents in equatorial ions will be the preferred conformation, or when this is possible the conformation with bulkier substituent in equatorial position will be the preferred conformation

Disubstituted cyclohexanes – Nasipuri

Disubstituted cyclohexanes do not exhibit any geometrical isomerism but exist in two interconvertible mers by a rapid ring inversion energy barrier

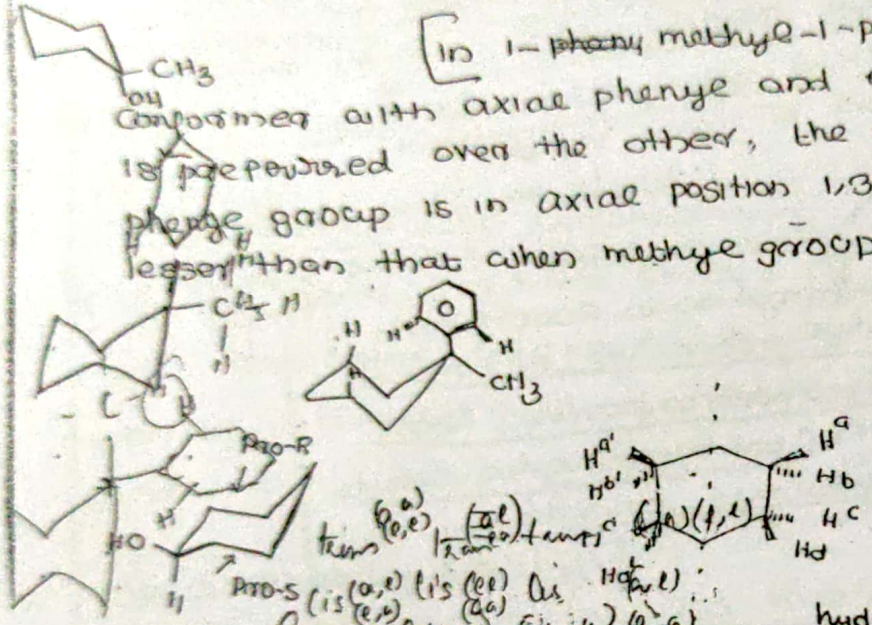
X = x = topomers

X ≠ y = diastereomers

when X = Y as in 1,1-dimethyl cyclohexane, the two conformers are identical (topomers) whe X ≠ Y as in 1-methyl cyclohexanol, the two conformers are diastereomers and present in unequal amounts the conformer with the bulkier substituent in the equatorial position often predominates eg 1-methyl cyclohexanol exist as 70:30 (70% equatorial methyl, 30% axial methyl).

[In 1-phenyl methyl-1-phenyl cyclohexane, the conformer with axial phenyl and equatorial methyl is preferred over the other, the reason is that when phenyl group is in axial position 1,3-diaxial interactions is lesser than that when methyl group

1-phen → more
1-meth → less

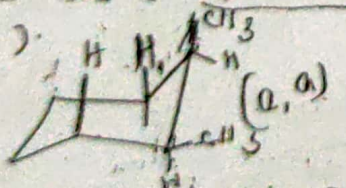


H^a, $H^{a'}$, H^b, $H^{b'}$
H^c, $H^{c'}$, H^d, $H^{d'}$ are enantiotopic, The other CH_2 group exhibit non-equivalent geminal hydrogen which are diastereo topic.

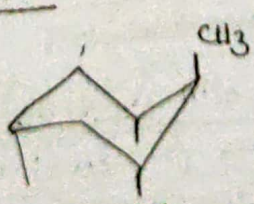
1,2-Disubstituted cyclohexanes

-Jagadamba sing, kalsi

For 1,2-dimethyl cyclohexane, two forms are possible cis (1a, 2e or 1e, 2a) and trans (1a, 2a, or 1e, 2e).



cis-1,2-dimethyl cyclohexane



aa (less stable)

ee (more stable)

in cis-1,2-dimethylcyclohexane, there is one axial methyl group which causes two 1,3-diaxial methyl-hyd

dimethy
(1,1) - X Config → Conformat
(1,1) - CH2 = 2a
Conf
1,1 - axial

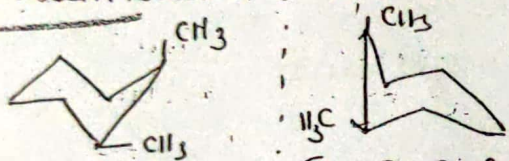
interactions causing strain in trans ee 1,2 dimethyl cyclohexane is more stable than ae (cis) then the stability order.

ee (trans) no 1,3-diaxial interaction > ae (cis) 2 Me/H interaction > aa (trans) 4 Me/H interactions

one Me/H interaction

Enantiomerism :-

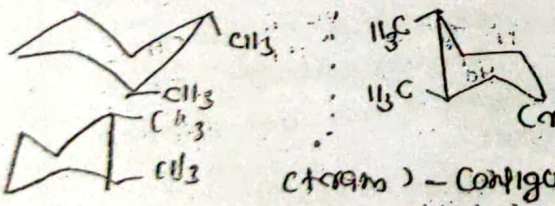
It has two chiral centres hence will have 4 stereoisomers but actually only has three. cis 1,2-dimethyl cyclohexane molecule is not superimposable on its mirror image but the molecule and mirror image are readily interconvertible hence is difficult to measure optical activity (non resolvable racemic modification). It is not a meso compd



(cis)-conformational enantiomers (non resolvable)

(Simple in planner structure it shows a meso compd

The trans 1,2-dimethyl cyclohexane (ee) molecule and its mirror image are not superimposable, hence constitute an enantiomeric pair. (Not interconverted easily ee to aa). They are configurational enantiomers



(trans)-Configurational enantiomers (resolvable)

cis and trans are pair of configurational diastereomers isomers exist as conformational enantiomer whereas are as configurational enantiomers.

case the two substituents in a 1,2-disubstituted are different cyclohexane, then both cis as well as trans isomers are resolvable. The bulkier groups predominantly occupies equatorial position

1-isopropyl-2-methylcyclohexanes

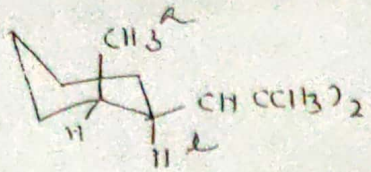
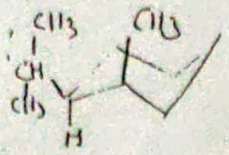
(1,2) different groups cis - trans resolvable

The re
diaste

1,3-D
cis i
trans
two 1,3

(1,2) same groups cis
cis - non resolvable
trans - resolvable
= 4 st
1,3-dim
is achi
hexane
a pair

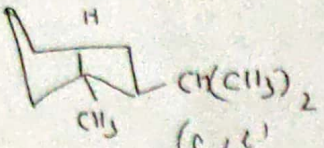
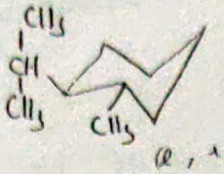
Scanned with CamScanner

(resolvable)

cis -1-isopropyl-2-methyl cyclohexane

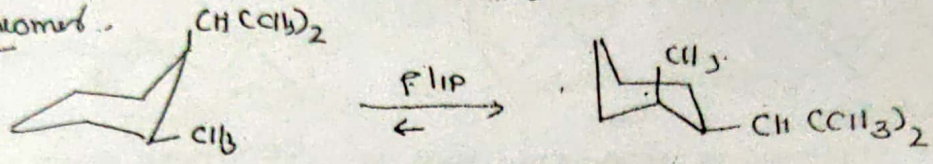
mirror image

Configurational enantiomers

trans isomer

The isomers which results by ring flip is conformational diastereomer.



1,3- Disubstituted cyclohexanes

cis isomer (aa, -less stable) or ee (more stable)

trans isomer (ae or ea)

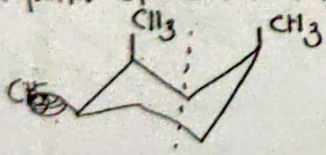
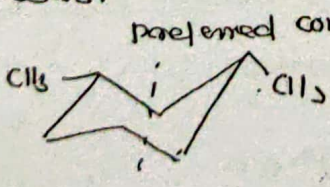
For 1,3-dimethyl cyclohexane, the order of stability

ee > ae > aa

cis trans cis

(more stable)

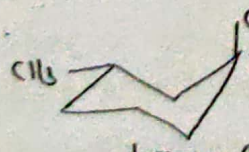
1,3-dimethyl cyclohexane has two chiral centres hence 2^2 = 4 stereoisomers are possible but only 3, bec² cis-1,3-dimethyl cyclohexane has a plane of symmetry and is achiral (meso compd). The trans 1,3-dimethyl cyclohexane does not have plane of symmetry and exist as a pair of enantiomers.

cis (achiral)

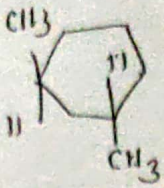
trans

cis (achiral) → meso compd



trans (chiral) - exist as pair of enantiomers (or)

trans (1R, 3R)



trans (1S, 3S)

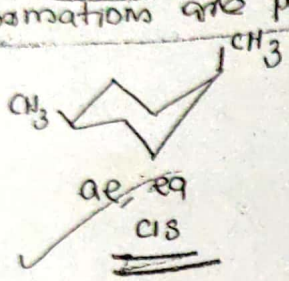
trans (1,2) (1,4)

Cis (1,2) (1,4)

1,4 same as (1,2)

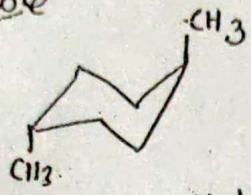
1,4- Disubstituted cyclohexanes

In the case of 1,4-disubstituted cyclohexanes (with identical substituents) one cis and two trans conformations are possible



ae, ea

cis



aa (less stable)

ee (more stable)

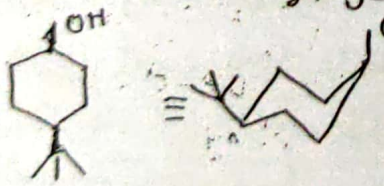
ee > ae > aa

Both cis and trans form have a plane of symmetry hence optically inactive. Thus 1,4 Dimethyl cyclohexane does not have any chiral centre. (exist as cis-trans diastereomers)

t-Butyl groups - locking group - Clayden, Greeves

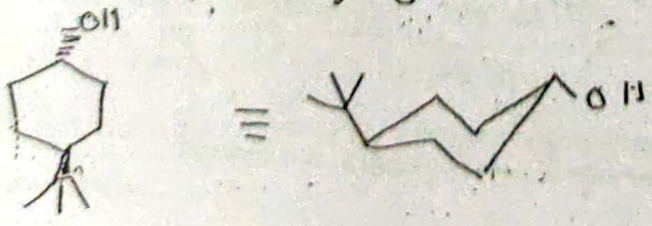
t-butyl group always prefer an equatorial position in a ring (not axial)

eg: cis 4-t-butylcyclohexanol (1,4-isomer)



In the cis diastereomer, the hydroxyl group is forced in to an axial position because of bulky t-butyl group

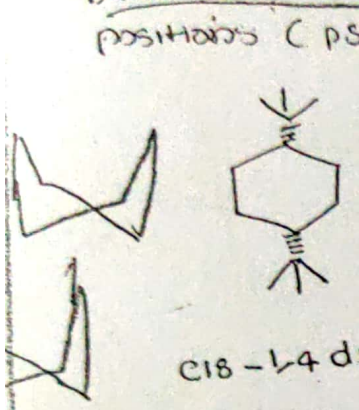
trans- 4- t-butylcyclohexanol



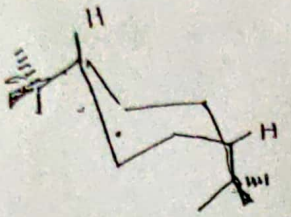
In the trans diastereomer, the hydroxyl group is forced in to an equatorial position (means it will not come in axial position). So it will have only ee conformer not aa one

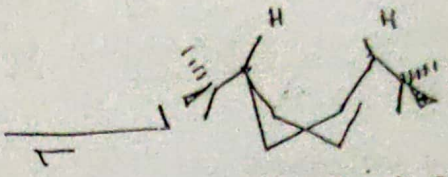
cis -1,4 di-t-butylcyclohexane

→ an axial t-butyl group is really very unfavourable. In cis -1,4- di-t-butylcyclohexane, one t-butyl group would be forced axial if the compd existed in a chair conformation. To avoid this the compound prefers to pucker into a twist boat so that the two large groups can both be in equatorial positions (pseudo equatorial)



cis -1,4 di-t-butylcyclohexane



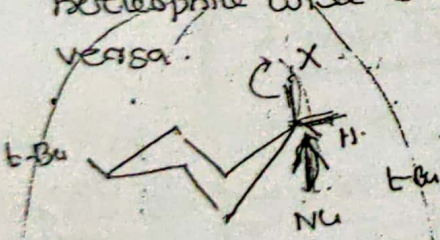


twist boat conformer is lower in G than the chair conformer

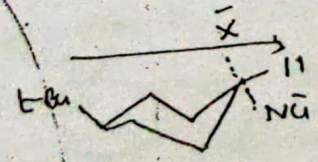
So here t-butyl group locks the conformation. ✓

Reactivity difference when t-butyl group is present

We know SN2 reaction is involved an inversion of config at the carbon centre. If the conformation of the molecule is fixed by a locking group like t-butyl group in SN2 rexn, if the leaving group is axial incoming nucleophile will end up in equatorial position and vice-versa.



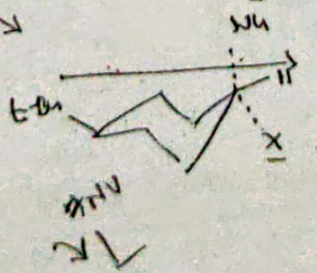
leaving group is axial position (cis)



TS

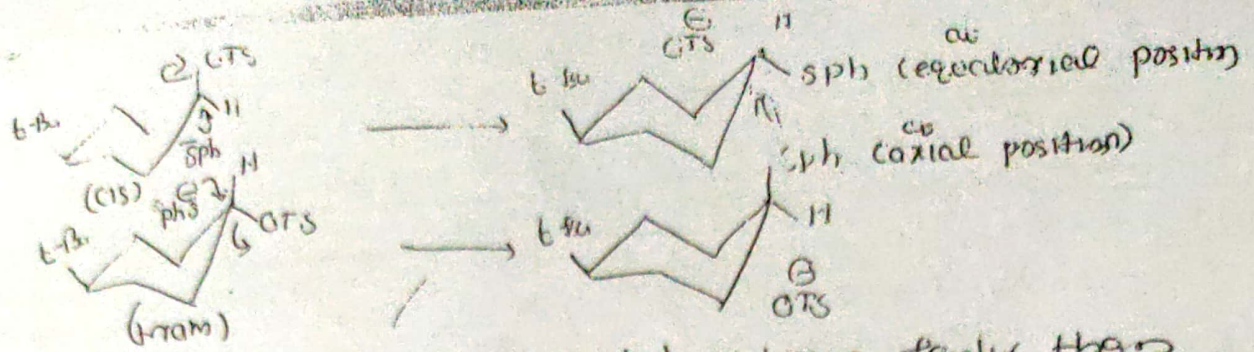
Nucleophile is at equatorial position

leaving group is equatorial

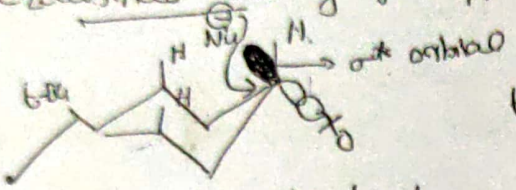


Nucleophile will be at axial position

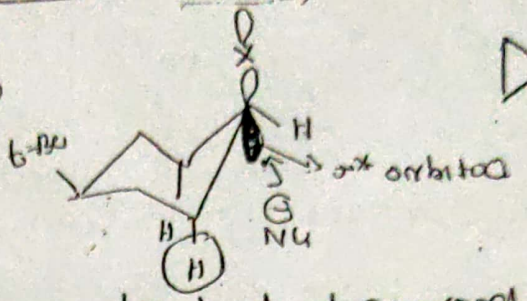
As the t-Bu group locks the conformation in to equatorial position the pdct formed depends on the position of leav in SN2 rexn



→ axial leaving group is substituted 31 times faster than equatorial leaving group.

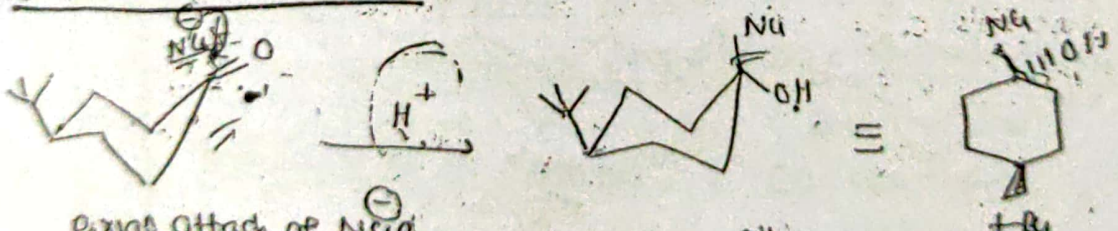


approach is hindered by axial Hs (1,3)

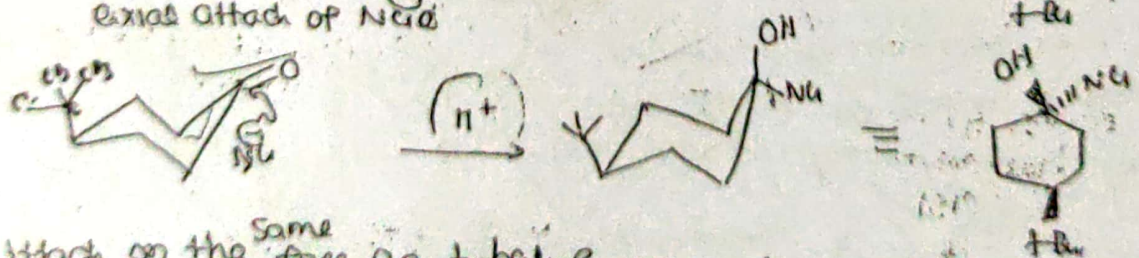


less hindered approach

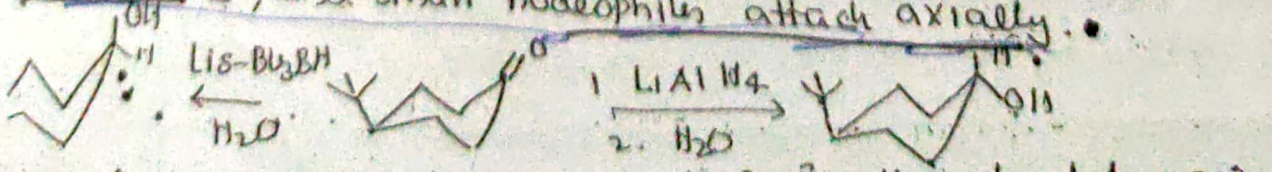
Faster axial substn is mainly due to direction of approach of the nucleophile. The nucleophile must attack the σ^* orbital of leaving group, that is directly behind C–X bond. In the case of equatorial attack, this line of attack is hindered by the axial hydrogen. For an axial leaving group the direction of attack is parallel with the ~~axial~~ axial hydrogens; anti periplanar to the leaving group and approach is much less hindered.



Axial attack of Nu⊖



Attack on the same face as t-butyl group leaves the nucleophile axial and attack on opposite face leaves the nucleophile equatorial. [In general large nucleophile attach equatorially, and small nucleophiles attach axially.

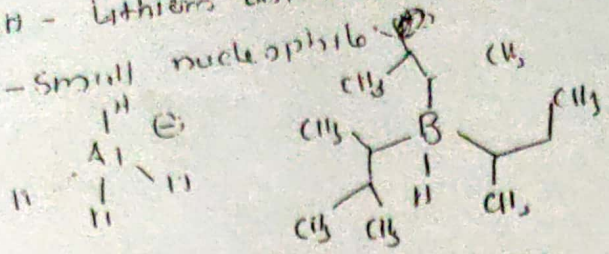


• Large nucleophile : 96% equatorial attach.

• Small nucleophile : 90% axial attach

Lis-BU_3BH - Lithium tri-sec-butyl borohydride

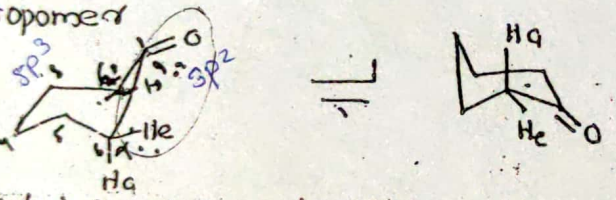
AlH_4^- - Small nucleophile



$LiAlH_4$ $\quad$ Li S-BU_3 BH

Conformation of cyclohexanone - Alkyl ketone effect - Kalsi

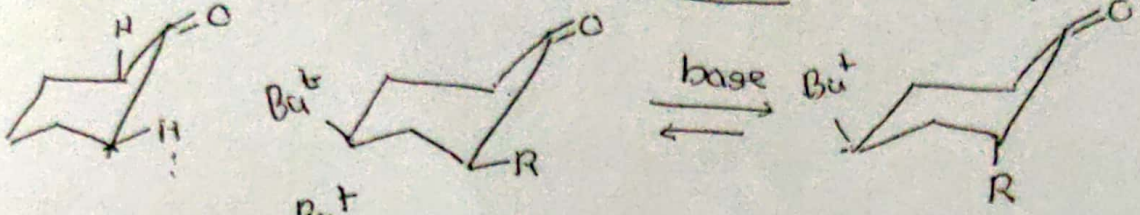
Unlike cyclohexane, the ring in cyclohexanone is buckled slightly from the chair structure in order to accommodate the trigonal carbon (c-c-c bond angle = 120°). thus the equatorial hydrogens on the α-carbon (CC_2) are almost eclipsed with the carbonyl oxygen. An thus an equatorial substituent + destabilized due to steric repulsion. (when C-2 or C-6 H is replaced by alkyl group, this repulsion operate well) In the absence of any complicating factor, cyclohexanone exist almost 99% in the chair form. which on inversion gives a topomer

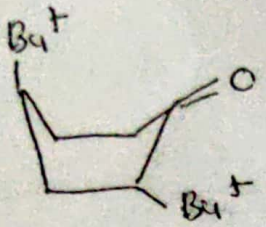


This destabilization decreases the energy difference btwn the axial and equatorial conformers when compared to those in cyclohexane. This decrease is termed as 2-alkylketone effect. which is measured by the difference in $-A G^{\circ} R$ in cyclohexane and $-A G^{\circ} R$ in cyclohexanone. we can consider the 2α effect in 2-alkyl-4-t-butylcyclohexanones. when $R=CH_3$, the difference is negligible, bec² CH_3 group in equatorial position will not experience any appreciable steric repulsion with the >C=O group. Also eclipsing CH_3 with >C=O is electronically favourable like the case of propanal. with increase in size $R=C_2H_5$ a value around 8KJ/mol is obtained for

TTO

the alkylketone effect. When R = i-Pr value = 7 kJ/mol when R = t-butyl the molecule adopts largely boat conformation to avoid t-butyl / C=O eclipsing.

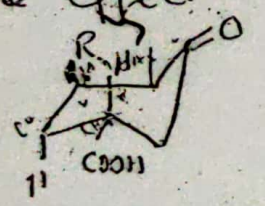




cis-2,4-di-t-butylcyclohexanone

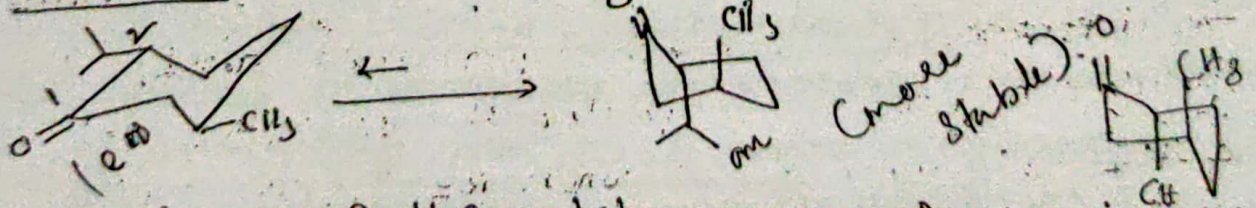
Boat conformation

In the case of a 3-alkylcyclohexanone one 1,3-interaction btwn axial R group and axial H is missing. This is equivalent to one butane-gauche interaction (3.75 kJ/mol) when R = CH_3. This decrease $-\Delta G^\circ$ value of R is termed as 3-alkylketone effect.



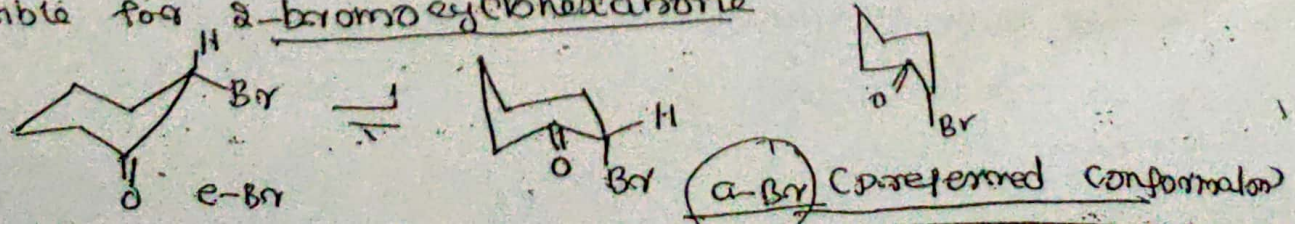
Opposite in axial & equatorial position

In the of menthone the 3-isopropylketone effect and the 3-methylketone effect are cooperating and consequently, the diaxial conformer is much more stabilized than the diequatorial conformer.



Conformation of 2-Halocyclohexanone — Nasipuri

The following two chair forms are possible for 2-bromocyclohexanone



The C-Br and C=O both strongly polar. thus
The C-Br and C=O bonds are both strongly polar. Thus

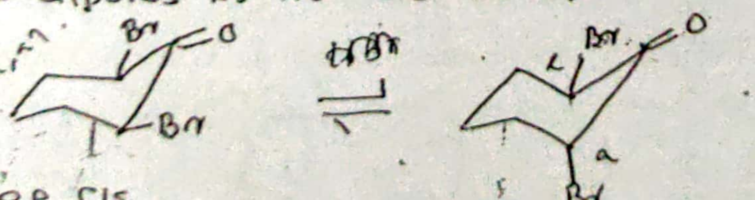
In addition to the steric interaction in the equatorial conformer due to partial eclipsing there also exist a dipole-dipole interaction b/w the two almost parallel dipole C-X and C=O. When the bromine is axial these dipolar interaction is minimum. Thus a-Br is preferred conformation. When however other substituents are present, the 1,3-diaxial interaction may become so large, that it outweigh the dipolar effect and the bromine would now be equatorial. For example in the case of 2-bromo-4,4-dimethyl cyclohexanone, the e-Br conformation is preferred one.

Since the dipole-dipole interaction is solvent dependent, the population of the conformers is affected by the solvent polarity. eg: 2-bromo-4-t-butyl cyclohexanone 78% A

in CCl_4 (solvent of low polarity) = 78% axial isomer

in dioxane (solvent of high polarity) = 63% axial isomer

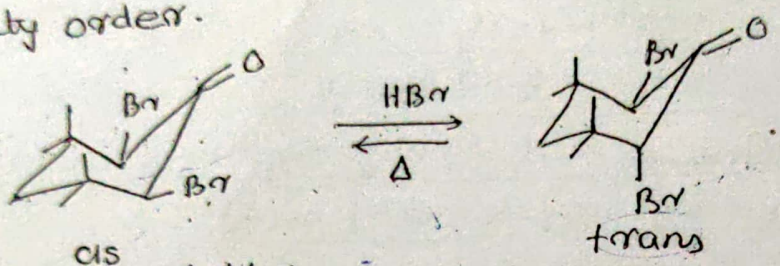
→ In the case of cis and trans isomers of 2,6-dibromo cyclohexanone heating with HBr giving predominantly the trans isomer (more stable), bec² in trans isomer the repulsion of C-Br and C=O dipoles prefer an orthogonal arrangement, rather than all parallel arrangement of the three dipoles in the cis isomer.



ee, cis   e,a trans (more stable)

In 3,3,5,5 tetramethyl-2,6-dibromo cyclohexanone on similar equilibration with HBr give mainly H

cis isomer. This can be explained by relex effect according to which the presence bulky axial group on one side of the ring causes some deformation by opening of the axial bonds. This in turn causes a pinching of the axial groups on H's on the other side of the ring. As a result axial bromine in trans isomer will have more severe gyroaxial interaction with axial hydrogen at 4th position, which reverses the stability order.

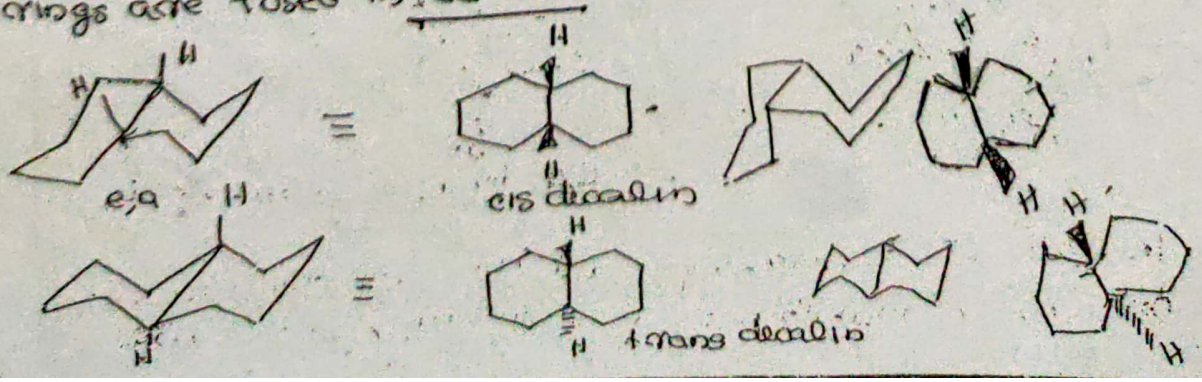


cis (more stable)

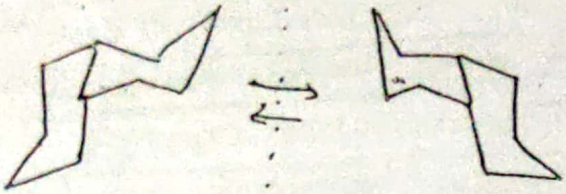
trans

Conformation of fused rings – Decalins

Decalin (bicyclo [4,4,0] decane) exist in two diastereoisomeric forms cis and trans decalins, depending on the way in which the two cyclohexane rings are fused together. In both the diastereoisomers of decalin, the two cyclohexane rings are joined together in the chair conformation. Since the decalin is analogous to a 1,2-disubstituted cyclohexane, in the cis isomer the two cyclohexane rings are fused together in ea form (equatorial bond of one ring is fused with the axial bond of the other), while in the trans isomer, the two rings are fused in ee form



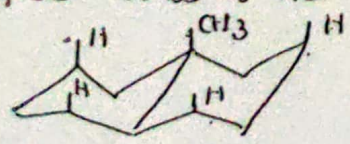
In cis decalin the ring fusion involves ae bonds, hence is flexible and exist in two forms which are inter convertible as a result of conformational flipping. cis decalin is disymmetric in both conformation which are non superimposable mirror images of each other. Because of rapid ring flipping b/wn these forms the compound is a non-resolvable dl pair.



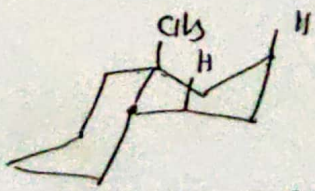
two enantiomeric conformations

Since trans decalin involves two equatorial bonds for the ring fusion, it is a rigid molecule and cannot undergo conformational flipping. ie it cannot be converted into aa conformation, which also does not exist in decalin type of fused ring compounds. Trans decalin has a centre of symmetry and therefore, optically inactive.

cis-decalin has three more gauche butane like interaction than trans decalin. hence trans decalin is more stable than the cis by 2.7 kcal/mole. [In the case of substituted decalins, substituents located at the fusion points of the two rings (angular positions) are axial with respect to one ring, while equatorial with respect to other in cis-decalins. On the other hand in the case of trans decalins, the angular substituents are axial with respect to both the rings.



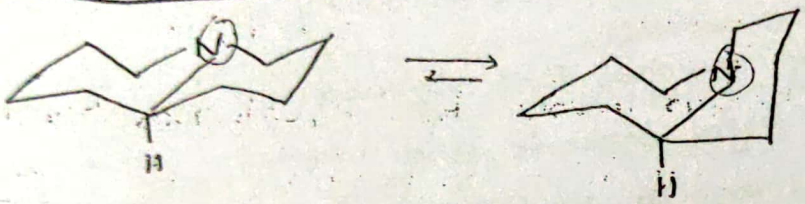
there are 4 sets of 1,3-diaxial interactions involving the bulky methy group and axial hydrogens



Only two sets of 1,3-diaxial interaction with the methyl group.

- When angular methyl group is introduced, the cis form becomes slightly more stable than trans form, bec2 in trans form more 1,3-diaxial interactions are there

- Rotation about C–C bond cannot bring about interconversion of cis and trans decalins. The barrier to interconversion of cis and trans decalin can be decreased by heteroatom subst in some cases eg: in azadecalin. The rapid interconversion of the cis and trans forms in aza decalin is bec2 of easy inversion of config at nitrogen; Thus when nitrogen occupies at bridge head position cis and trans forms cannot be isolated



Anuradha. G