1. Discuss the the relative conformation analysis of 1,2-dimethylcyclohexane.

If we consider cis isomer of 1,2-dimethylcyclohexane, the e,a and a,e both conformer is optically active ads no element of symmetry present. In both conformer three extra gauche butane interaction present and hence both conformer is equally populated. But on flipping it gives the mirror image conformer and hence they are enantimers of each other. So due to internal compensation net optical rotation is zero and they are called invertomer. Theoritically enantiomers should be separable at very low temperature but in practice there are no such reports.

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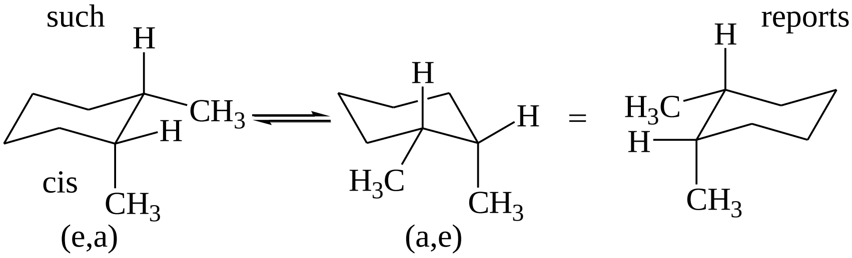
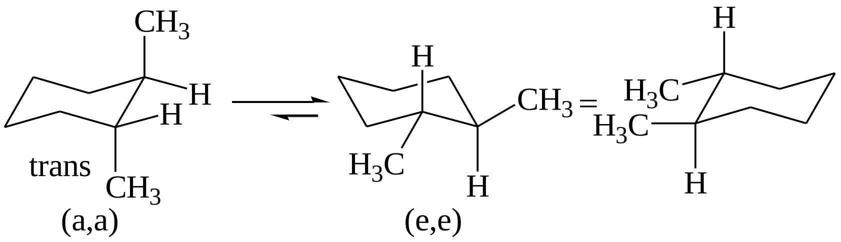
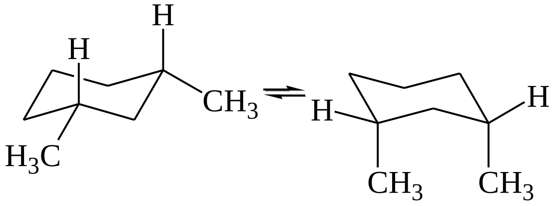


Whereas both the a,a and e,e conformation of trans 1,2-dimethylcyclohexane is optically active , can exists in enantiomers and they are resolvable . Both the a,a and e,e conformer contain a C2 axis passing through C1-C2 and C4-C5 bond. It is obvious that in a,a conformer there is four gauche butane interaction whereas in e,e conformer there is only two gauche butane interaction and hence the e,e conformer is more stable and maximum populated.

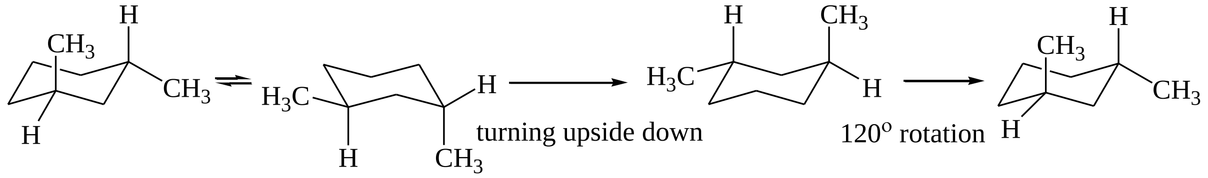


2. Discuss the relative conformation analysis of 1,3-dimethylcyclohexane.

If we look the conformation analysis of cis 1,3-dimethyl cyclohexane, both the e,e and a,a conformer posses a sigma(σ)plane and hence it is optically inactive; no question of resolution arises. In a,a conformer there is two extra gauche butane interaction and hence the e, e conformer is more populated.

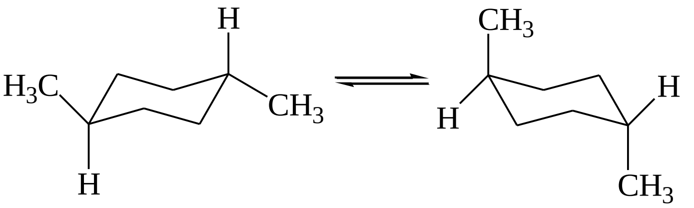


In case of trans isomer, both the e,a and a,e conformer contains one extra gauche butane interaction and hence both conformer is equally populated. But ring invertion itself produces an equivalent conformer and hence it is an example of topomerisation. The planner structure contains a C2 axis and hence it is dissymmetric but puckered structure contain no element of symmetry and hence it is asymmetric molecule.

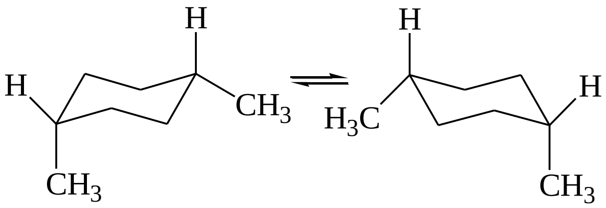


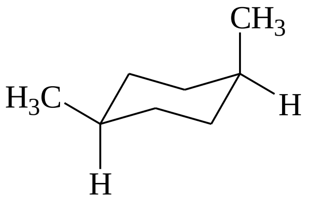
3. Discuss the relative conformation analysis of 1,4-dimethylcyclohexane.

Let us look at the trans isomer of 1,4-dimethylcyclohexane; both the planner structure and puckered structure contain plane of ymmetry and hence molecule is optically inactive and hence no question of resolution. The e,e conformer is more stable and highly populated compared to the a,a confer as the later contain four more gauche butane interaction.



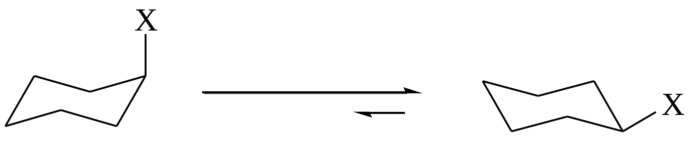
The cis isomer of 1,4-dimethylcyclohexane also contain a sigma plane passing vertically through C1 and C4 and hence compound is optically inactive; no question of resolution. Both the e,a and a,e conformers are equally populated and they are equivalent on ring invertion.





4.Discuss the relative stabilities of monosubstituted cyclohexane.

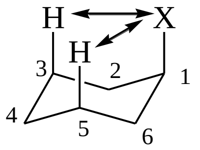
In case of monosubstituted cyclohexane, two different chair conformer exists-with axial substituents called axial conformer and with equatorial substituents called equatorial conformer. Both conformers are in rapid equilibrium by means of inversion but they will not have same energy. In almost all cases, the conformer with axial substituents has higher energy compared to the equatorial conformer and hence the population percentage of axial conformer is far less than the equatorial conformer.



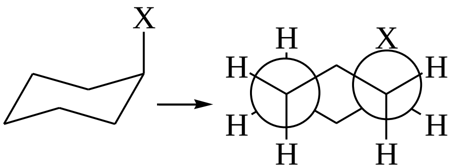
high energy conformation
axial substituent:
axial conformer

low energy conformation
equatorial substituent:
equatorial conformer

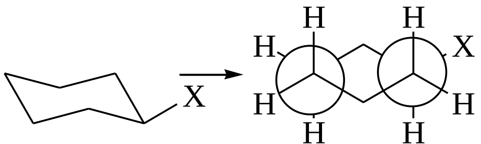
For X= -CH3, the axial conformer is 7.3 KJ/mol higher energy than the equatorial conformer. At 25°C temperature, axial equatorial ratio is 20:1. This higher energy of axial conformer arises from the 1,3- diaxial interaction between the axial substituents (-X) and the axial hydrogens of C3 and C5.



1,3-diaxial interaction

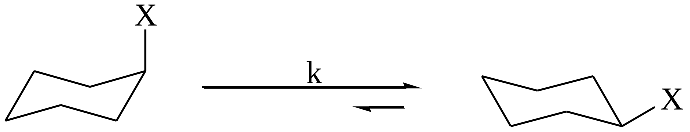


axial conformer



equatorial conformer

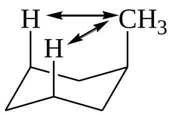
As the size of X increases, the 1,3-diaxial interaction increases and hence the energy of the axial conformer increases or the percentage population of axial conformer decreases.

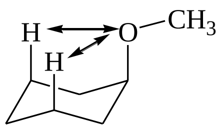


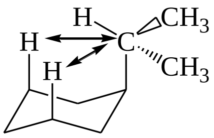
The table below summarises how the equilibrium constant for axial to equatorial ring inversion depends on different substituent. From the table it is clear that as the size of the substituents increases, the equilibrium is shifting towards the equatorial conformer. Although methoxy group is larger compared to methyl or ethyl group, still the equilibrium constant for methoxy substituent is subastantially less than methyl or ethyl substituted cycloheaxane. This is due o the fact that the 1,3 diaxial interaction is effective between the axial hydrogen and the first atom of the axial substituted group. In case of methoxy substituent, although the total size of methoxy is larger than methyl, but the 1,3-diaxial interaction happens between the axial hydrogen and the comparatively smaller oxygen atom of methoxy group and hence the interaction is less active.

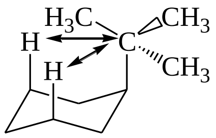
Substituents (-X)	Equilibrium constant (k)	KJ/mol (axial-Equatorial)	% of equatorial conformer
-H	1	0	50
$-CH_3$	19	7.3	95

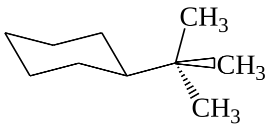
-Et	20	7.5	95
-^{i}Pr	42	9.3	98
-^{t}Bu	>3000	>20	>99.9
-OMe	2.7	2.5	73
-Ph	110	11.7	99











Unusual high equilibrium constant for tertiary butyl group compared to isopropyl group can be explained in terms of relative possibility of interaction. In case of isopropyl group due to free C-C bond rotation, at least once the hydrogen interacts with other two diaxial hydrogen but in case of tertiary butyl group every time the two diaxial hydrogen will meet methyl group and hence the equilibrium will almost shifted towards the inverted ring where the substituent will be at equatorial position.

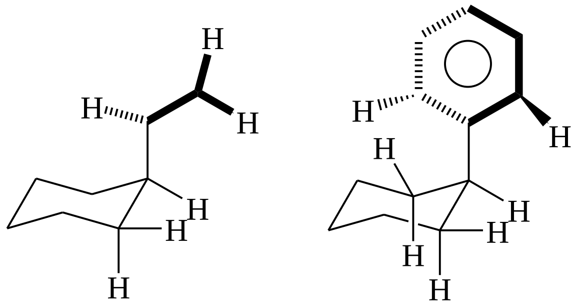
Conformational free energy for linear substituents and halogen substituents

Substituents (-X)	Kcal/mol (axial-Equatorial)
-CN	0.20
-CΞCH	0.41
-NC	0.20
-N=C=O	0.44
-N=N=N	0.45
-F	0.25
-Cl	0.53
-Br	0.48
-I	0.51

The conformational free energy for chlorine, bromine and iodine is almost same although the size of halogen increases is due to the fact that due to enhancement of size, the bond length also increases and hence the 1,3-dipolar interaction decress.

Conformational free energy for plannar group substituents

Substituents (-X)	Kcal/mol (axial-Equatorial)
$-CHO$	0.56
$-COCH_3$	1.02
$-COOCH_3$	1.20
$-COCl$	1.30
$-CH=CH_2$	1.68
$-CH_3$	1.73
-Ph	2.80
$-OH$	0.60
$-OCH_3$	0.63
$-O-CMe_3$	0.73
-O-Ph	0.65
$-O-CO-CH_3$	0.68



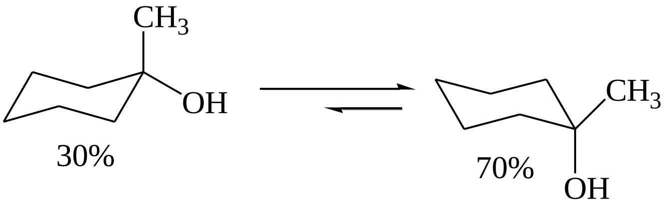
Conformational free energy for substituents in different solvent

Substituents (-X)	Kcal/mol (axial-Equatorial)
-OH (Benzene)	0.60
-OH (Isopropanol)	0.95
$-NH_2$ (Benzene)	1.23
$-NH_2$ (Water)	1.70

In a polar solvent, the effective size of the polar substituent increases due to proper salvation and hence the axial conformer became more unstable compared to the equatorial conformer.

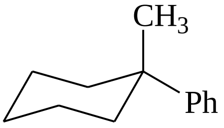
What will be preferred conformation of 1-methyl cyclohexanol ?

The conformational free energy of –OH group (0.60 Kcal/mol) is less than –CH_3 (1.73 Kcal/mole); hence –CH_3 group at equatorial position will be preferred over equatorial –OH group.

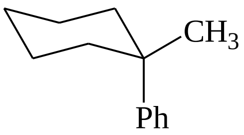


What will be the preferred conformation of 1-methyl-1-phenyl cyclohexane?

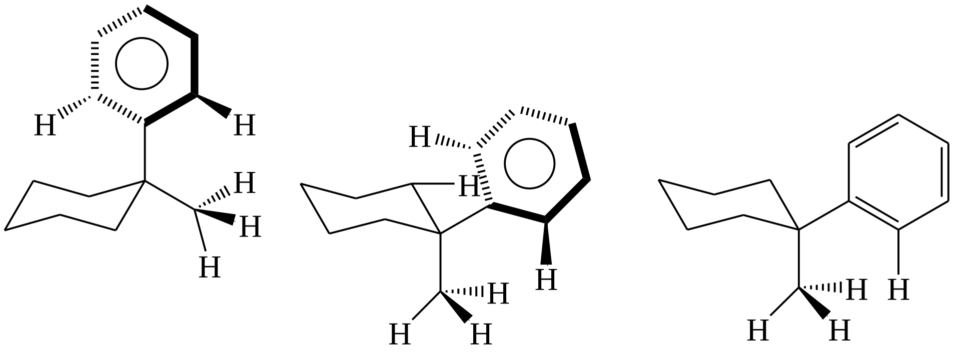
The conformational free energy of –Ph substituent is 2.87 Kcal/mol and 1.73 Kcal/mol for methyl substituents. So, equatorial phenyl conformer will be preferred by 1.14 Kcal/mol however equatorial methyl conformer will be preferred by 0.32 Kcal/mol.



equatorial phenyl

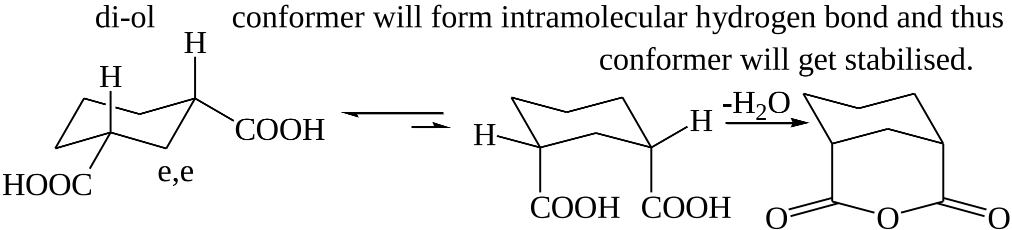


equatorial methyl



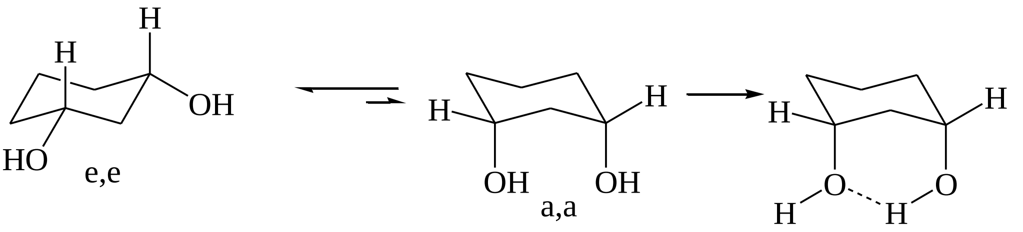
What will be the preferred conformation of cis- cyclohexane-1,3 dicarboxylic acid and cis-cyclohexane-1,3 diol ?

Apparently it seems that both the compound will be more stable in e,e conformer where they will experience minimum 1,3 diaxial interaction. But both the compound will choose a,a conformer. In case of di-carboxylic acid, the a,a conformer will form stable lactone and the a,a di-ol conformer will form intramolecular hydrogen bond and thus both the a,a conformer will get stabilised.



cis- cyclohexane-1,3 dicarboxylic acid

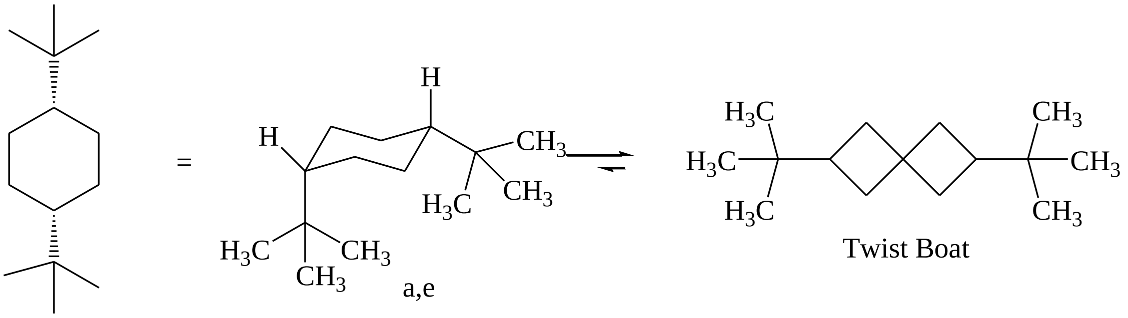
lactone



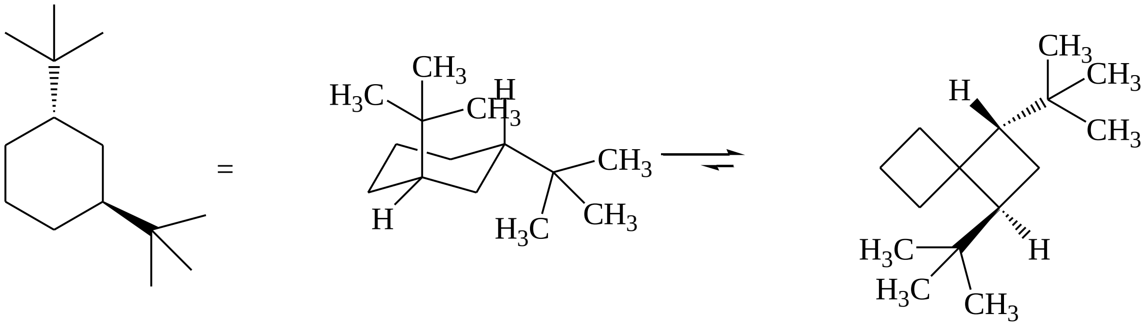
cis- cyclohexane-1,3 diol

intramolecular H-bond

What will be the preferred conformation of cis- 1,4-di-tertiarybutyl cyclohexane and trans-1,3- di-tertiarybutyl cyclohexane ?



cis- 1,4-di-tertiarybutyl cyclohexane

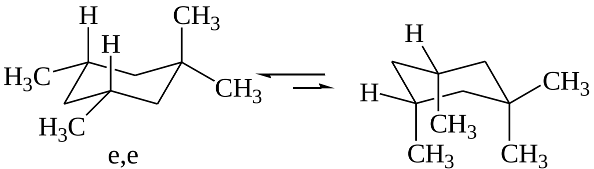


trans- 1,3-di-tertiarybutyl cyclohexane

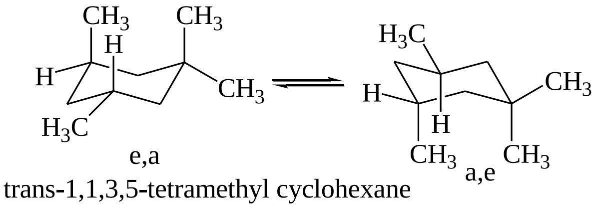
Twist Boat

Both the compound choose a twist boat conformation as in any case in regular cyclohexane conformation any one bulky tertiarybutyl group will face severe 1,3-dipolar interaction.

What will be the preferred conformation of cis-1,1,3,5-tetramethyl cyclohexane and trans-1,1,3,5-tetramethyl cyclohexane ?



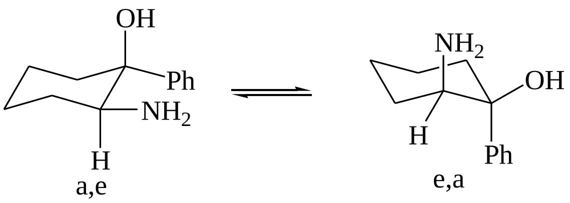
cis-1,1,3,5-tetramethyl cyclohexane



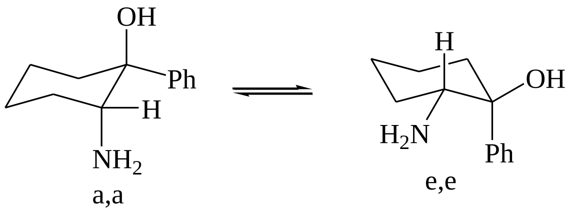
trans-1,1,3,5-tetramethyl cyclohexane

The cis isomer is stable in di-equatorial form as in di-axial conformer it will face severe 1,3-diaxial interaction. The trans isomer will be equally populated in both a,e and e,a conformer as either conformer will face 1,3-diaxial interaction with one axial methyl group.

Draw the preferred conformation of 1-phenyl-2-aminocyclohexanol.

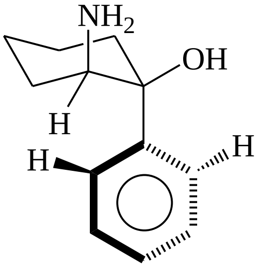


cis-1-phenyl-2-aminocyclohexanol

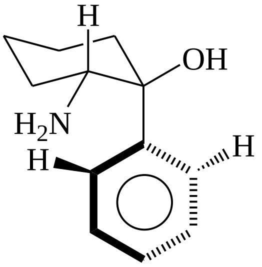


trans-1-phenyl-2-aminocyclohexanol

In case of cis isomer, both the a,e and e,a conformer can make intramolecular hydrogen bond between amine and hydroxyl group. In a,e conformation the equatorial phenyl group at any orientation will experience interation the neighbouring groups. In case of e,a conformer the axial phenyl group will rotate itself perpendicularly so that the ortho hydrogen will face equatorial hydrogens of the ring. As in either conformation amine or hydroxyl group will be at axial position, hence the e,a conformer (axial phenyl) is more stable.



Stable conformer (cis isomer)



Unstable conformer (trans isomer)

In trans isomer, the e,e conformer will orient itself in such a way that the phenyl group will be perpendicular with the ring and hence the ortho hydrogen of phenyl ring will interact with equatorial hydrogen and a amine group. In case of a,a conformer, the equatorial phenyl group will orient itself in such a way that the interaction will be minimum. So, in trans isomer the a,a isomer is most stable conformer.