

Organic Chemistry I

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CYCLOHEXANE: A STRAIN-FREE CYCLOALKANE

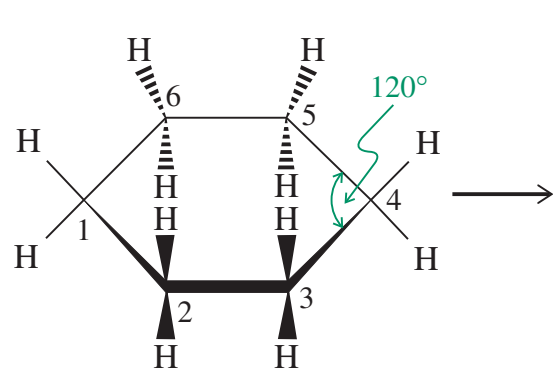
The chair conformation of cyclohexane is strain free

A hypothetical planar cyclohexane would suffer from 12 H–H eclipsing interactions and sixfold bond-angle strain (a regular hexagon requires 120° bond angles). One conformation of cyclohexane, obtained by moving carbons 1 and 4 out of planarity in opposite directions, is in fact strain free. This structure is called the **chair conformation** of cyclohexane (because it resembles a chair), in which eclipsing is completely absent, and the bond angles are very nearly tetrahedral.

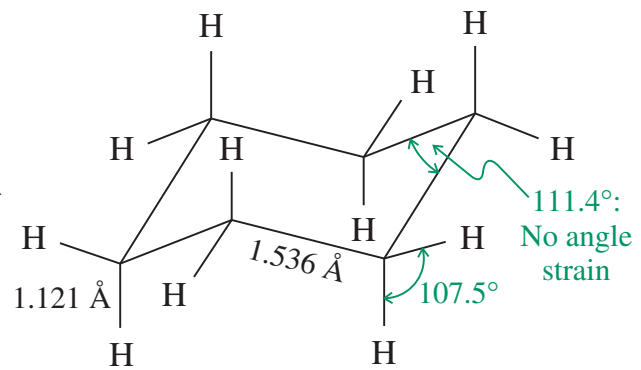
The calculated $\Delta H^\circ_{\text{comb}}$ of cyclohexane ($-944.4 \text{ kcal mol}^{-1}$) based on a strain-free $(\text{CH}_2)_6$ model is very close to the experimentally determined value ($-944.5 \text{ kcal mol}^{-1}$). Indeed, the C–C bond strength, $\Delta H^\circ = 88 \text{ kcal mol}^{-1}$ (368 kJ mol^{-1}), is normal.

The molecular model of cyclohexane enables to recognize the conformational stability of the molecule. If we view it along (any) one C–C bond, we can see the staggered arrangement of all substituent groups along it.

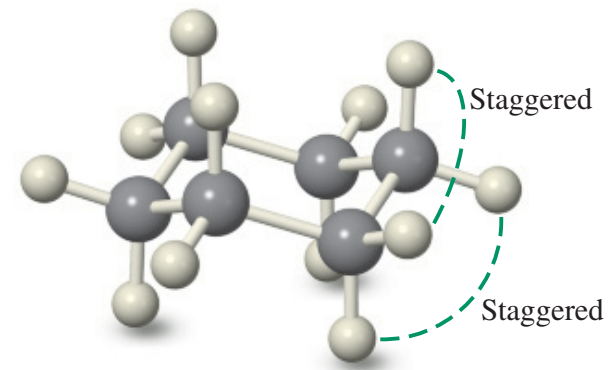
Because of its lack of strain, cyclohexane is as inert as a straight-chain alkane.



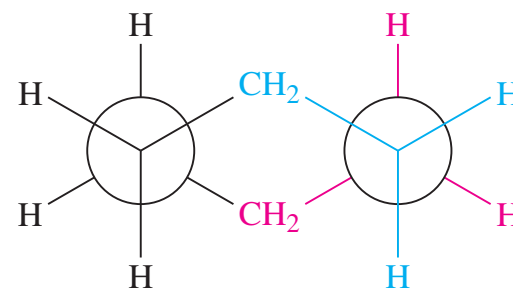
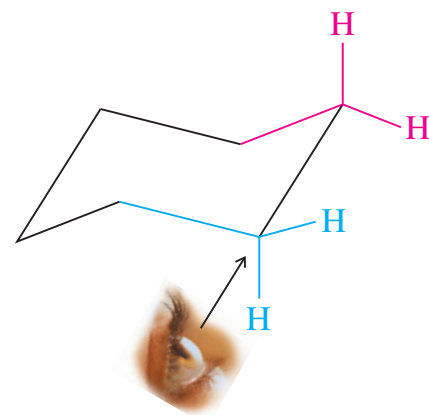
A
Planar cyclohexane
 (120° bond angles;
 12 eclipsing hydrogens)



B
Chair cyclohexane
 (Nearly tetrahedral bond angles;
 no eclipsing hydrogens)



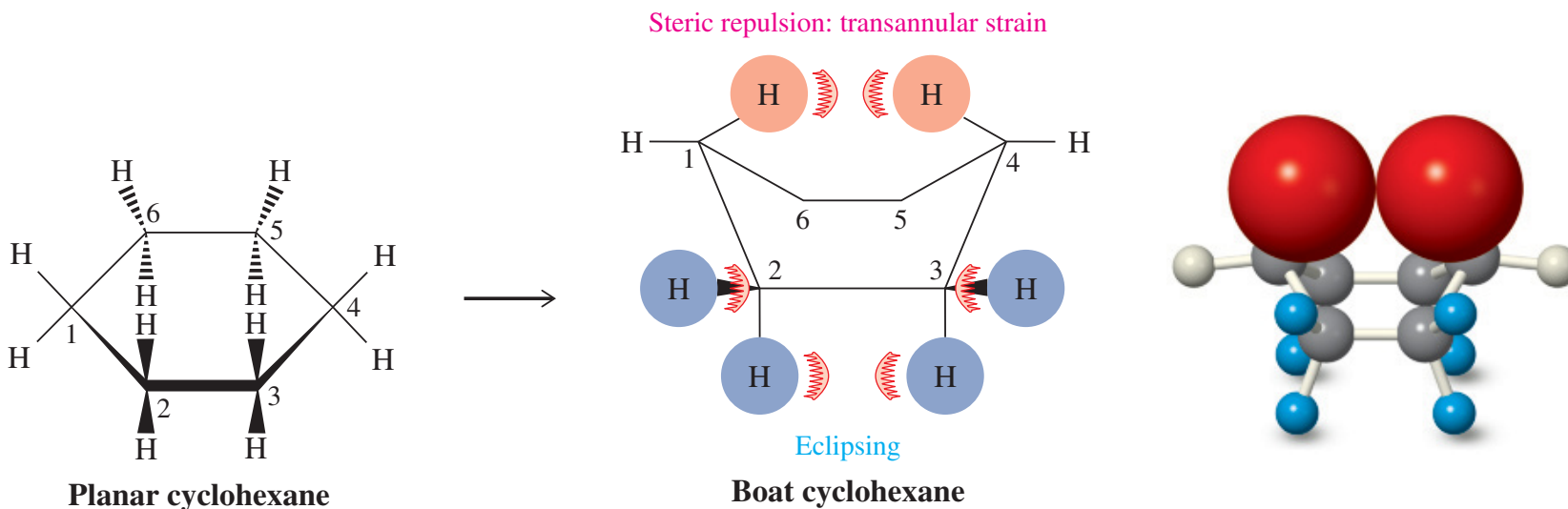
C



Cyclohexane also has several less stable conformations

Cyclohexane also adopts other, less stable conformations. In **boat form**, carbons 1 and 4 are out of the plane in the *same* direction. The boat is less stable than the chair form by 6.9 kcal mol⁻¹. **Reason:** (a) eclipsing of eight hydrogen atoms at the base of the boat, (b) steric hindrance due to the close proximity of the two inside hydrogens in the boat framework.

The distance between these two hydrogens is only 1.83 Å, small enough to create an energy of repulsion of about 3 kcal mol⁻¹ (13 kJ mol⁻¹). This effect is an example of **transannular strain**, that is, strain resulting from steric crowding of two groups across a ring (*trans*, Latin, across; *anulus*, Latin, ring).



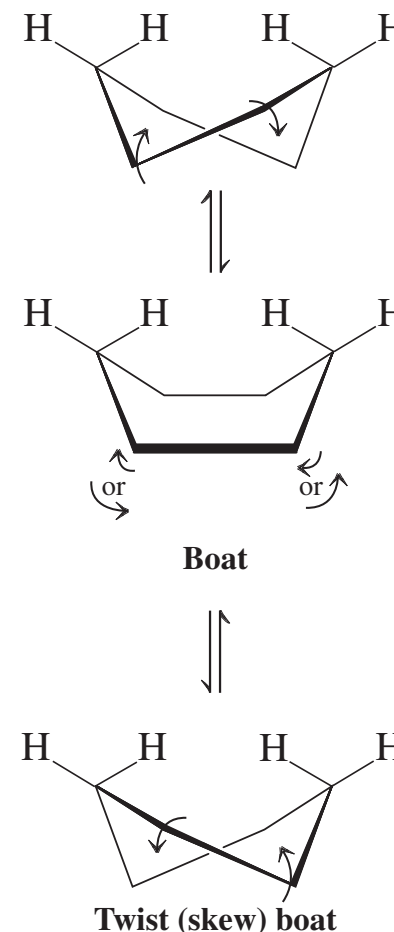
Boat cyclohexane is fairly flexible.

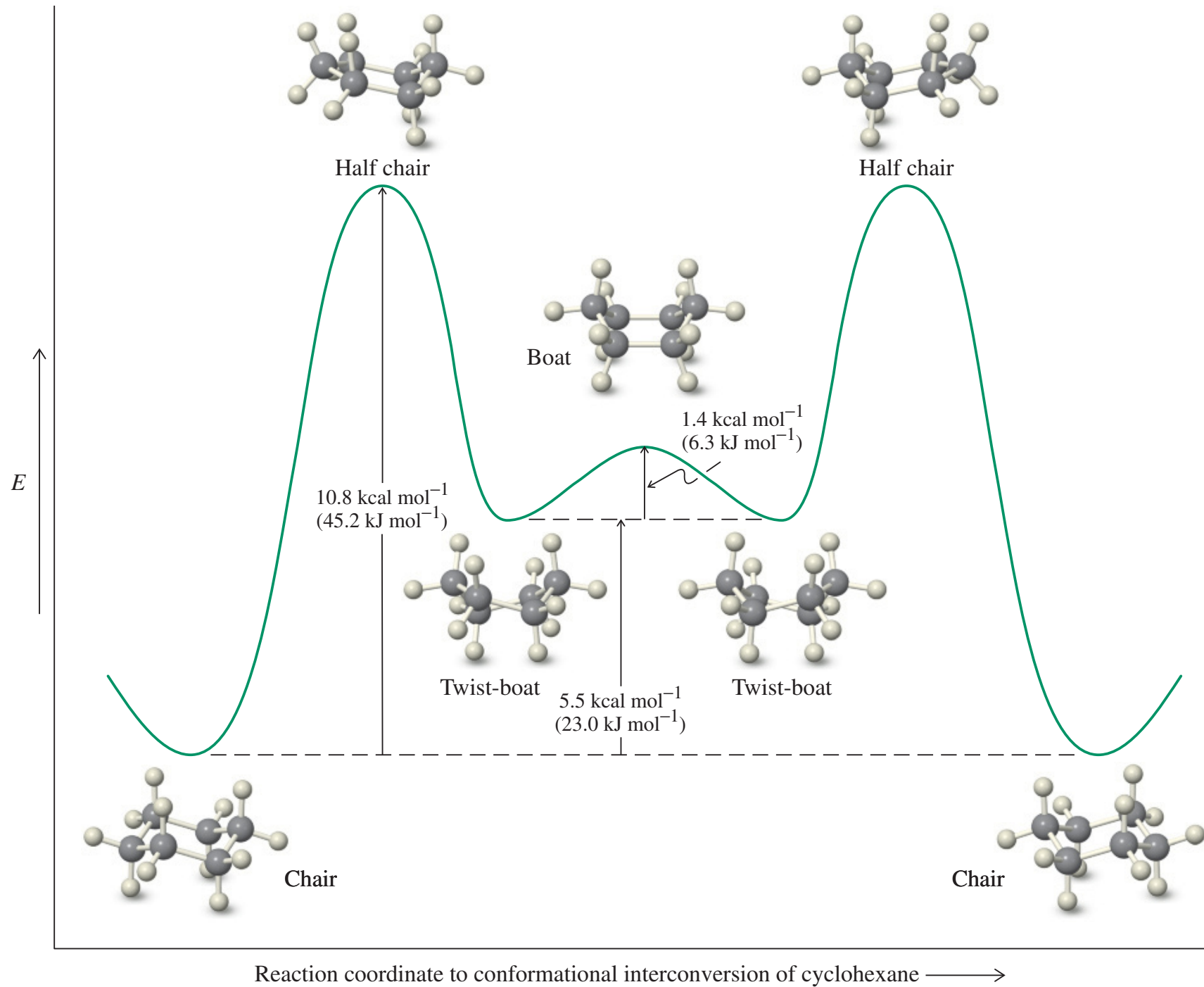
If one of the C–C bonds is twisted relative to another, this form can be somewhat stabilized by partial removal of the transannular interaction (**twist-boat** or **skew-boat** conformation). The stabilization relative to the boat form amounts to about $1.4 \text{ kcal mol}^{-1}$.

Two twist-boat forms are possible. They interconvert rapidly, with the boat conformer acting as a *transition state*.

Thus, the boat cyclohexane is not a normally isolable species, the twist-boat form is present in very small amounts, and the chair form is the major conformer.

The activation barrier separating the most stable chair from the boat forms is $10.8 \text{ kcal mol}^{-1}$.

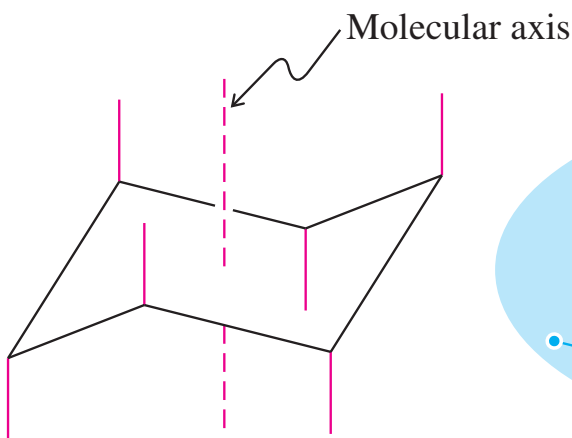




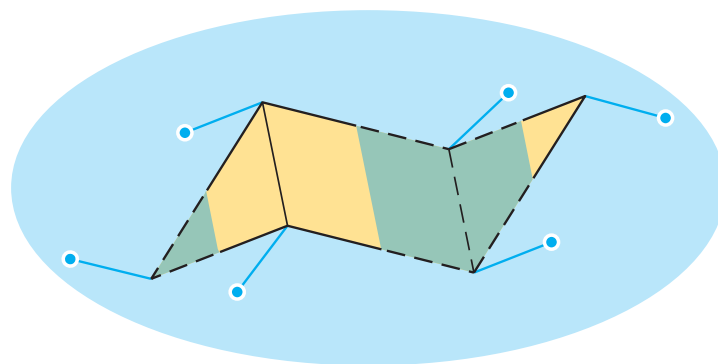
Cyclohexane has axial and equatorial hydrogen atoms

The chair-conformation model of cyclohexane reveals that the molecule has two types of hydrogens.

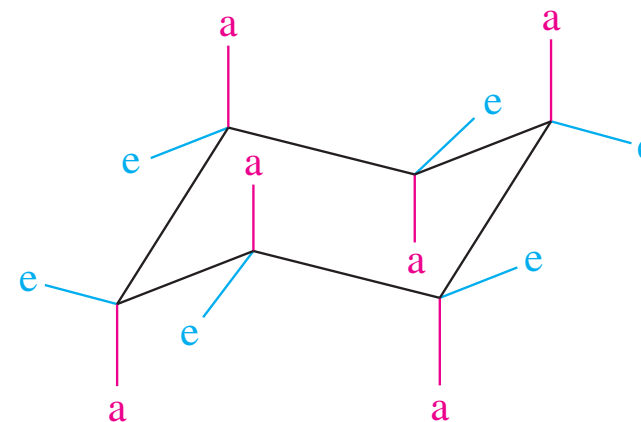
Six carbon–hydrogen bonds are nearly parallel to the principal molecular axis and hence are referred to as **axial**; the other six are nearly perpendicular to the axis and close to the equatorial plane and are therefore called **equatorial**.*



Axial
positions



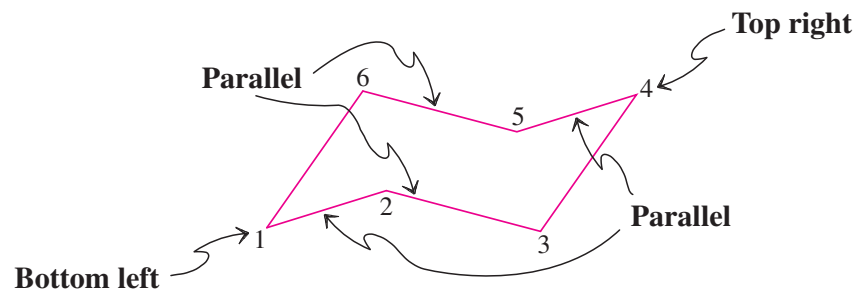
Equatorial
positions



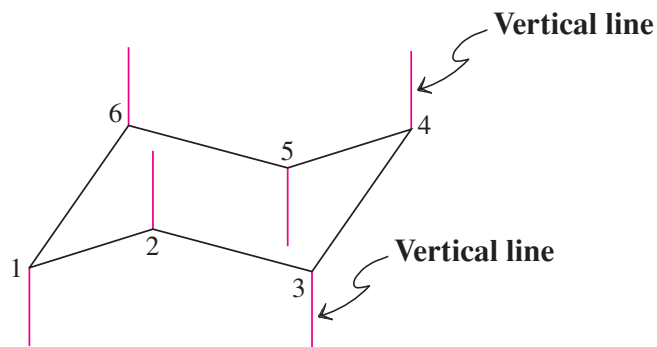
Axial (a) and equatorial (e)
positions

How to Draw Chair Cyclohexanes

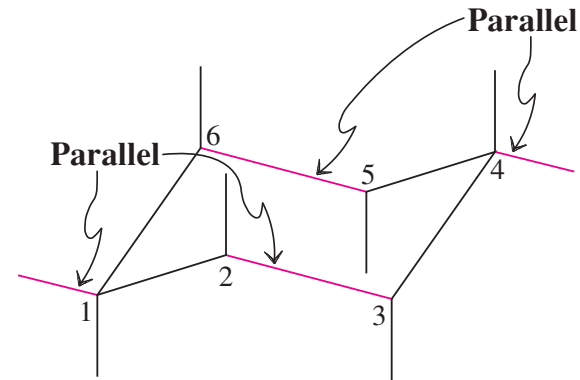
1. Draw the chair so as to place the C2 and C3 atoms below and slightly to the right of C5 and C6, with apex 1 pointing downward on the left and apex 4 pointing upward on the right. Ideally, bonds straight across the ring (namely, bonds 1–6 and 3–4; 2–3 and 5–6; 1–2 and 4–5) should appear parallel to one another.



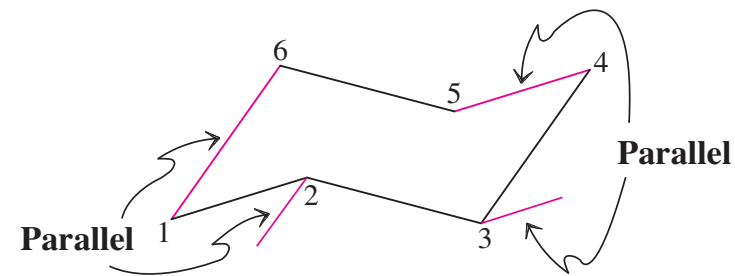
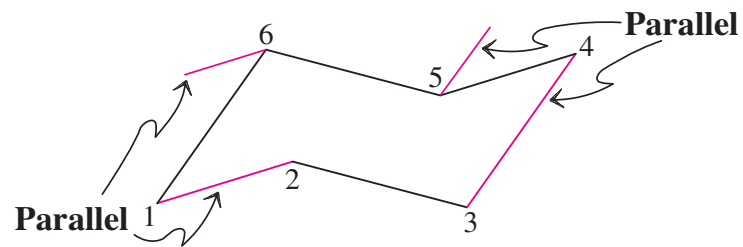
2. Add all the axial bonds as vertical lines, pointing downward at C1, C3, and C5 and upward at C2, C4, and C6. In other words, the axial bonds alternate up-down around the ring.



3. Draw the two equatorial bonds at C1 and C4 at a slight angle from horizontal, pointing upward at C1 and downward at C4, parallel to the bond between C2 and C3 (or between C5 and C6).



4. This rule is the most difficult to follow: Add the remaining equatorial bonds at C2, C3, C5, and C6 by aligning them *parallel* to the C–C bond “once removed,” as shown below.

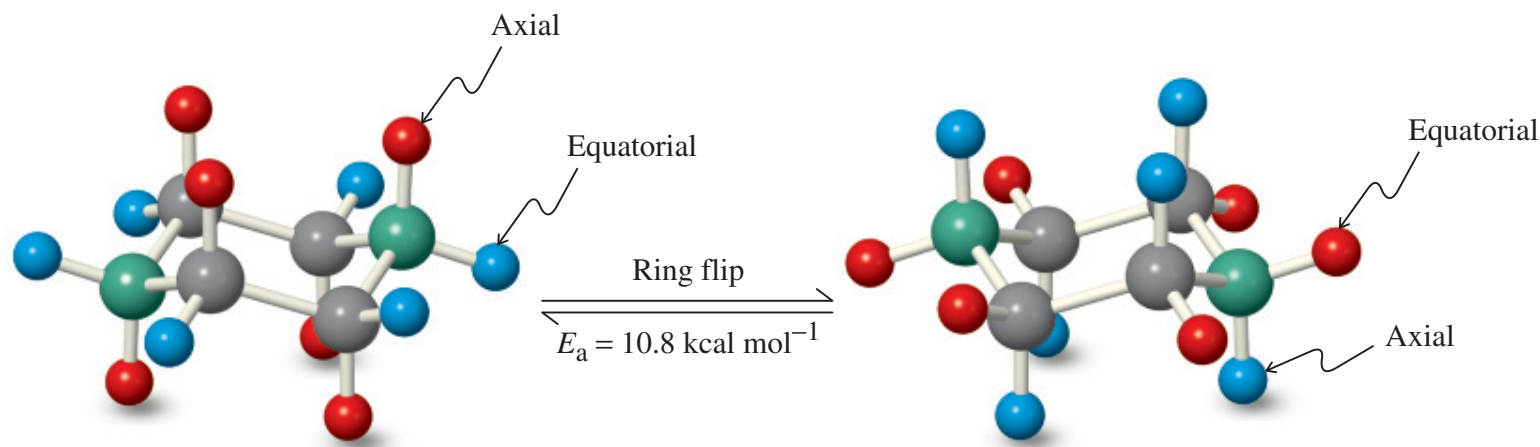


Conformational flipping interconverts axial and equatorial hydrogens

What happens to the identity of the equatorial and axial hydrogens when chair cyclohexane equilibrates with its boat forms?

Cyclohexane undergoes chair–chair interconversions (“flipping”) in which all axial hydrogens in one chair become equatorial in the other and vice versa. The activation energy for this process is $10.8 \text{ kcal mol}^{-1}$. This value is so low at room temperature, the two chair forms interconvert rapidly (approximately 200,000 times per second).

The two chair forms are identical.



SUBSTITUTED CYCLOHEXANES

Axial and equatorial substituents are not equivalent in energy

The chair with a substituent in the equatorial position is different from its conformer, in which the substituent is axial. The preference for one orientation over the other strongly affects the stereochemistry and reactivity of cyclohexanes.

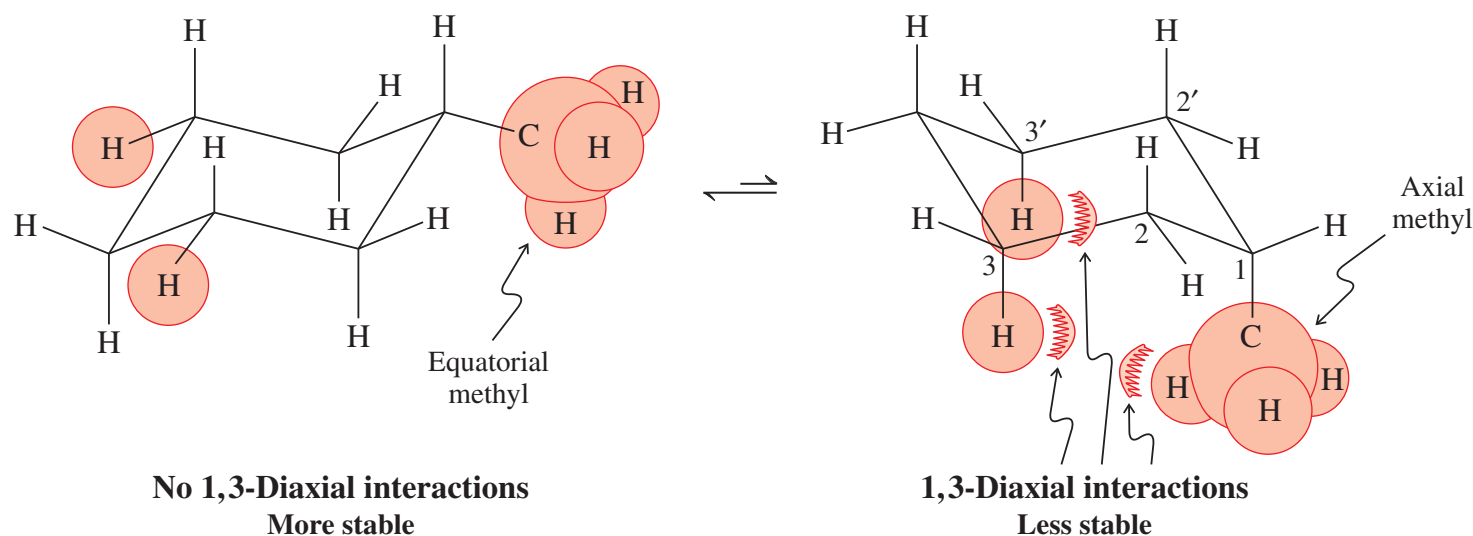
In methylcyclohexane, the methyl group occupies either an equatorial or an axial position. In the equatorial conformer, the methyl group extends into space away from the remainder of the molecule. In contrast, in the axial conformer, the methyl substituent is close to the other two axial hydrogens on the same side of the molecule.

The distance to these hydrogens is small enough (about 2.7 Å) to result in steric repulsion, another example of transannular strain.

Because this effect is due to axial substituents on carbon atoms that have a 1,3-relation (1,3 and 1,3'), it is called a **1,3-diaxial interaction**.

This interaction is the same as that resulting in the *gauche* conformation of butane. Thus, the axial methyl group is *gauche* to two of the ring carbons (C3 and C3'); when it is in the equatorial position, it is **anti** to the same nuclei.

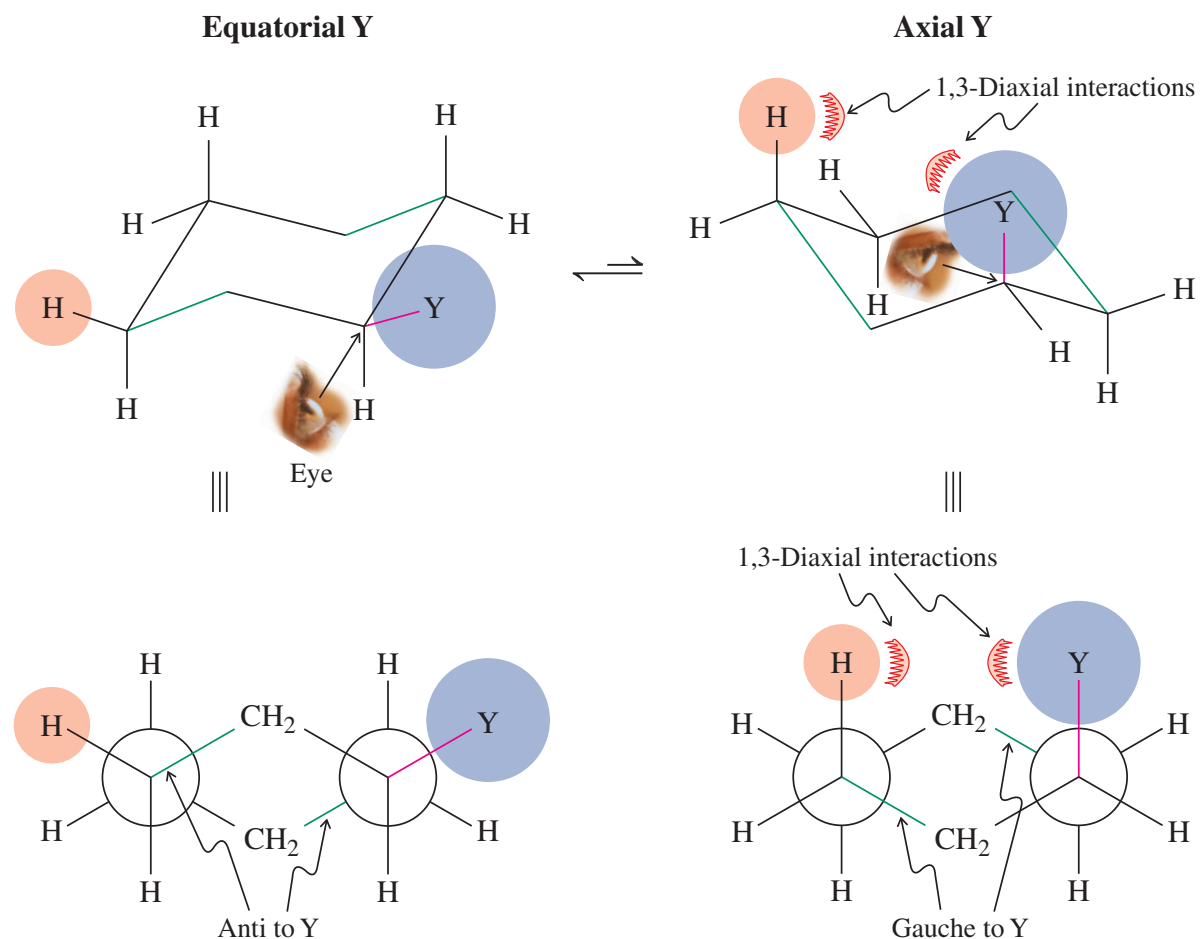
The two forms of chair are in equilibrium. *The equatorial conformer is more stable* by 1.7 kcal mol⁻¹ (7.1 kJ mol⁻¹) and with a ratio of 95:5 at 25 °C. The activation energy for chair–chair interconversion is similar to that in cyclohexane itself [about 11 kcal mol⁻¹ (46 kJ mol⁻¹)], and equilibrium between the two conformers is rapid at room temperature.



Ratio = 95:5

The unfavorable 1,3-diaxial interactions to which an axial substituent is exposed are readily seen in Newman projections of the ring C–C bond bearing that substituent.

In contrast with that in the axial form (*gauche* to two ring bonds), the substituent in the equatorial conformer (*anti* to the two ring bonds) is away from the axial hydrogens.



The energy differences between the axial and the equatorial forms of many monosubstituted cyclohexanes have been measured.

In many cases (but not all), particularly for alkyl substituents, the energy difference between the two forms increases with the size of the substituent, a direct consequence of increasing unfavorable 1,3-diaxial interactions.

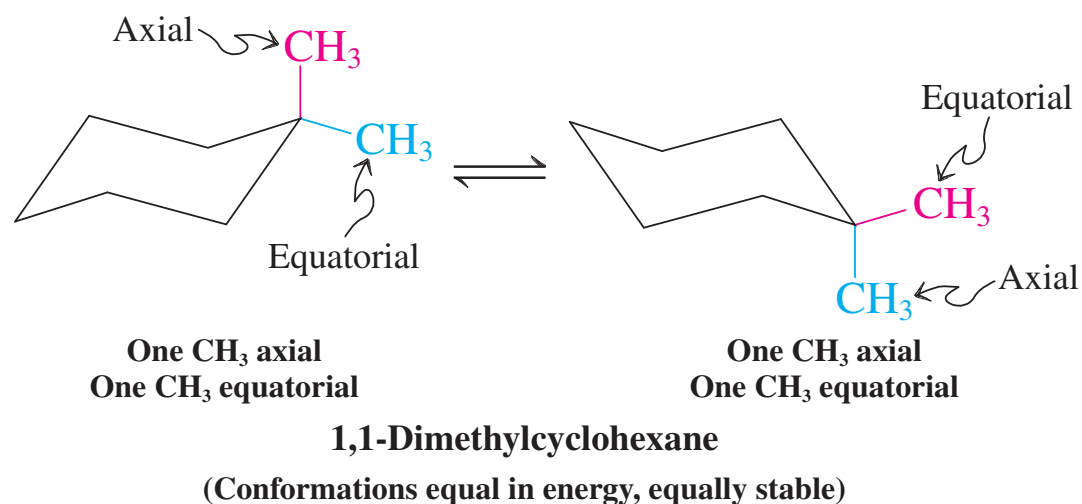
Table 4-3 Change in Free Energy on Flipping from the Cyclohexane Conformer with the Indicated Substituent Equatorial to the Conformer with the Substituent Axial							
Substituent		ΔG° [kcal mol ⁻¹ (kJ mol ⁻¹)]		Substituent		ΔG° [kcal mol ⁻¹ (kJ mol ⁻¹)]	
H	<div>Increasing size</div>	0	(0)	F		0.25	(1.05)
CH ₃		1.70	(7.11)	Cl		0.52	(2.18)
CH ₃ CH ₂		1.75	(7.32)	Br		0.55	(2.30)
(CH ₃) ₂ CH		2.20	(9.20)	I		0.46	(1.92)
(CH ₃) ₃ C		≈ 5	(21)				
<div><div>O</div><div> </div><div>HO-C</div></div>			1.41	(5.90)	HO		0.94
<div><div>O</div><div> </div><div>CH₃-O-C</div></div>		1.29	(5.40)	CH ₃ O		0.75	(3.14)
				H ₂ N		1.4	(5.9)

Note: In all examples, the more stable conformer is the one in which the substituent is equatorial.

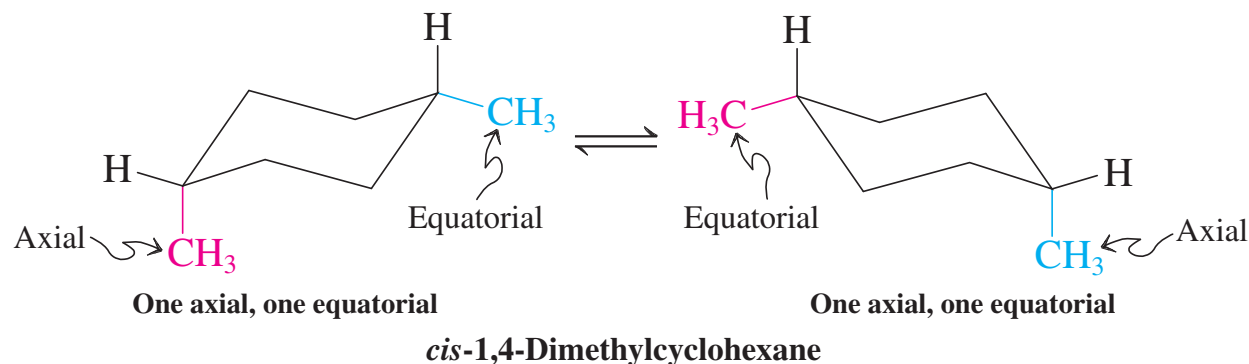
Substituents compete for equatorial positions

To predict the more stable conformer of a more highly substituted cyclohexane, the cumulative effect of placing substituents either axially or equatorially must be considered, in addition to their potential mutual 1,3-diaxial or 1,2-*gauche* interactions.

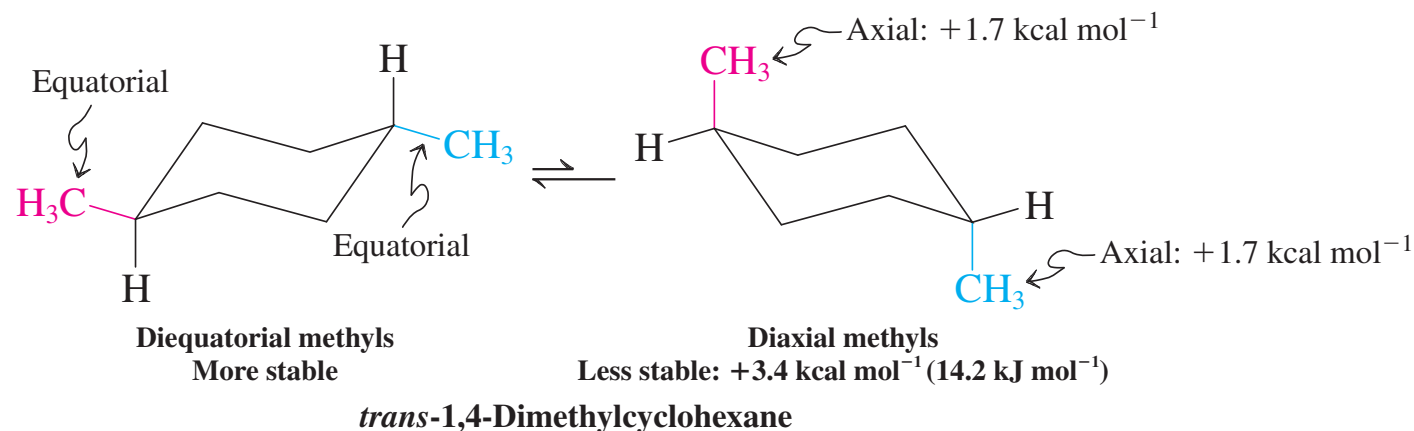
In 1,1-dimethylcyclohexane, one methyl group is always equatorial and the other axial. The two chair forms are identical, and hence their energies are equal.



Similarly, in *cis*-1,4-dimethylcyclohexane, both chairs have one axial and one equatorial substituent and are of equal energy.



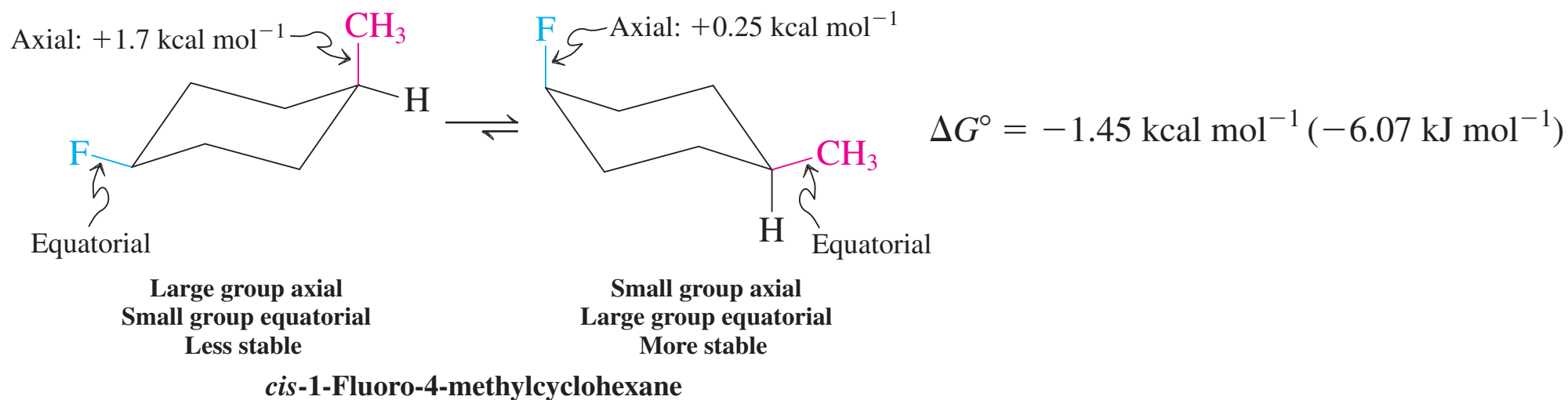
On the other hand, the *trans* isomer can exist in two different chair conformations: one having two axial methyl groups (diaxial) and the other having two equatorial groups (diequatorial).



Experimentally, the diequatorial form is preferred over the diaxial form by 3.4 kcal mol⁻¹, exactly twice the ΔG° value for monomethylcyclohexane.

The ΔG° (diaxial \rightleftharpoons diequatorial) for *trans*-1-fluoro-4-methylcyclohexane is -1.95 kcal mol⁻¹ [- (1.70 kcal mol⁻¹ for CH₃ plus 0.25 kcal mol⁻¹ for F)].

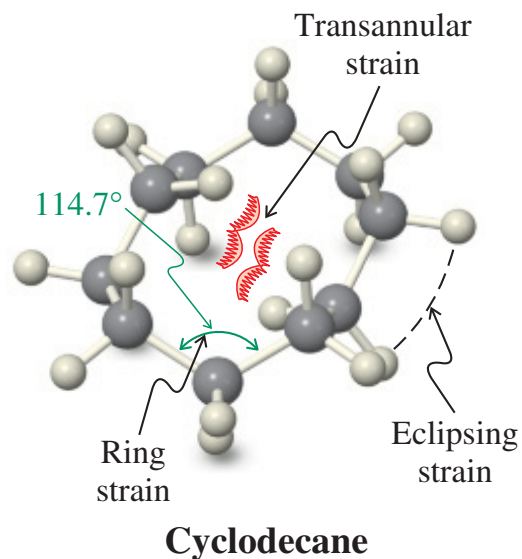
Conversely, in *cis*-1-fluoro-4-methylcyclohexane, the two groups compete for the equatorial positions and the corresponding $\Delta G^\circ = -1.45$ kcal mol⁻¹ [-(1.70 kcal mol⁻¹ minus 0.25 kcal mol⁻¹)], with the larger methyl winning out over the smaller fluorine.



LARGER CYCLOALKANES

It is not possible for medium-sized rings to relieve all of these strain-producing interactions (bond-angle distortion, partial eclipsing of hydrogens, and transannular steric repulsions) in a single conformation.

Essentially strain-free conformations are attainable only for large-sized cycloalkanes, such as cyclotetradecane. In such rings, the carbon chain adopts a structure very similar to that of the straight-chain alkanes, having staggered hydrogens and an all-*anti* configuration.



POLYCYCLIC ALKANES

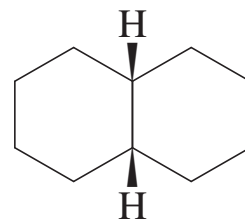
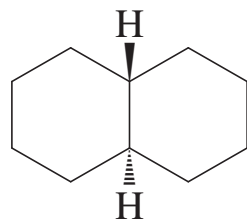
In more complex structures—the bi-, tri-, tetra-, and higher polycyclic hydrocarbons—two or more rings share carbon atoms. Many of these compounds exist in nature with various alkyl or functional groups attached.

Polycyclic alkanes may contain fused or bridged rings

In decalin, two cyclohexanes share two adjacent carbon atoms, and the two rings are said to be **fused**.

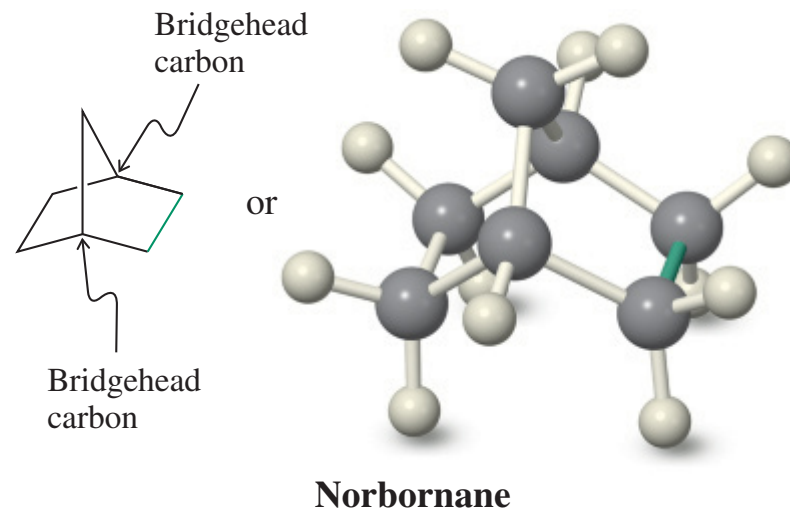
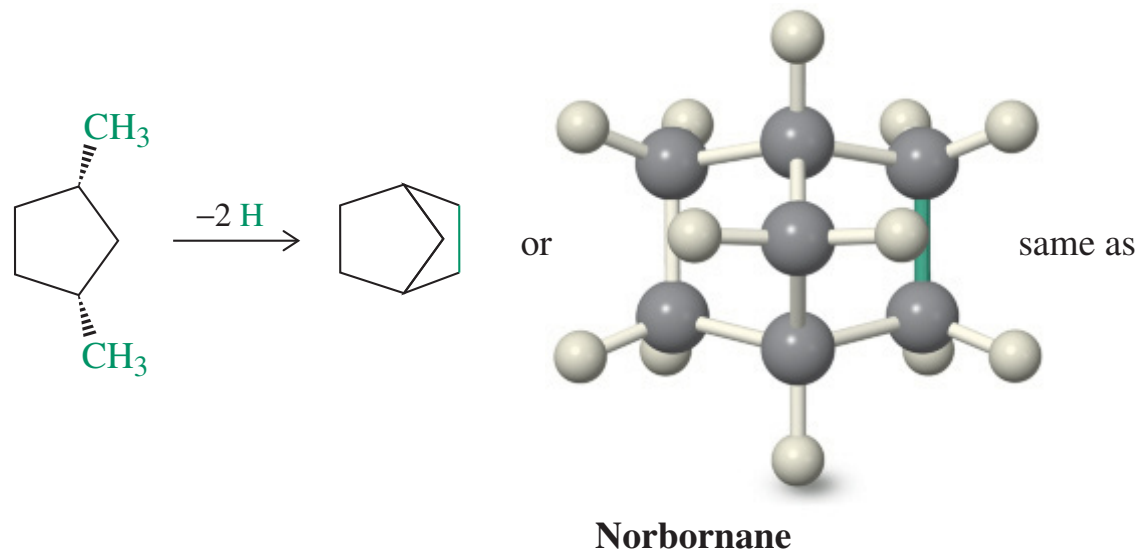
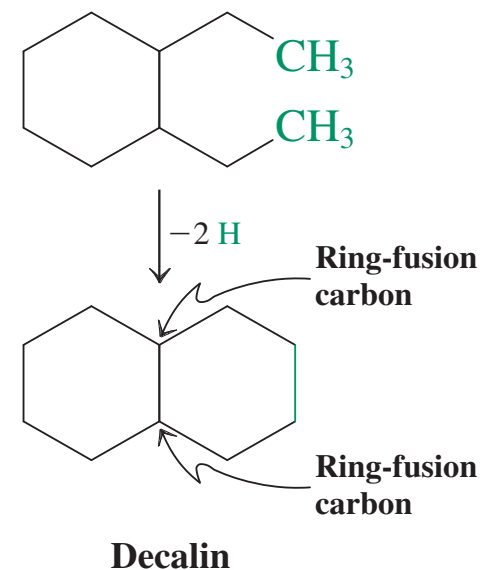
Compounds constructed in this way are called **fused bicyclic** ring systems and the shared carbon atoms are called the **ring-fusion carbons**.

Groups attached to ring-fusion carbons are called **ring-fusion substituents**.



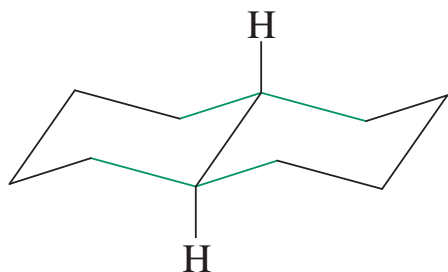
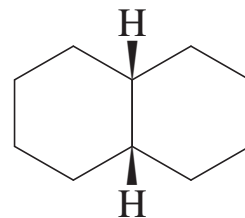
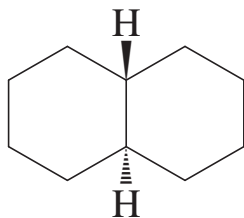
When we treat a molecular model of *cis*-1,3-dimethylcyclopentane in the same way, we obtain another carbon skeleton, that of norbornane.

Norbornane is an example of a **bridged bicyclic** ring system. In bridged bicyclic systems, two nonadjacent carbon atoms, the **bridgehead** carbons, belong to both rings.



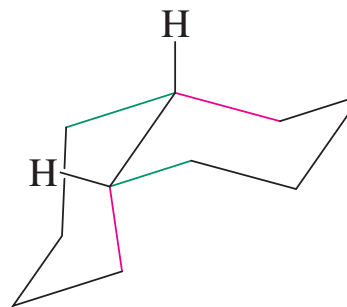
If we think of one of the rings as a substituent on the other, we can identify stereochemical relations at ring fusions. In particular, bicyclic ring systems can be *cis* or *trans* fused.

The stereochemistry of the ring fusion is most easily determined by inspecting the ring-fusion substituents. For example, the ring-fusion hydrogens of *trans*-decalin are *trans* with respect to each other, whereas those of *cis*-decalin have a *cis* relation.



Equatorial C–C bonds

trans-Decalin



Axial C–C bonds

Equatorial C–C bonds

cis-Decalin