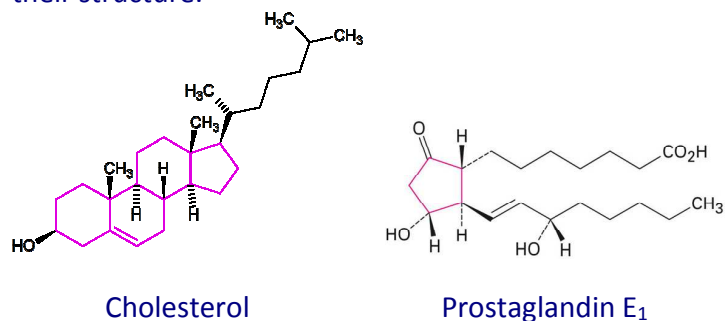


Chapter 4: Cycloalkanes and their stereochemistry

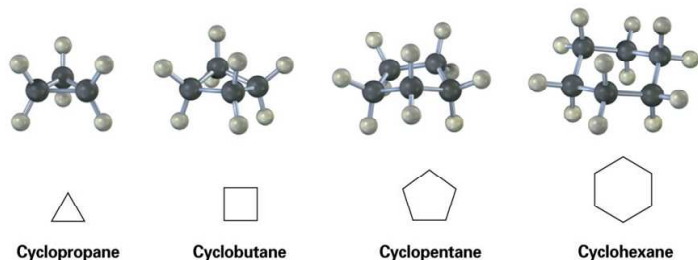
There are specific consequences to having functional groups in a ring as opposed to an open chain.

Many biological molecules contain one or many rings in their structure.



Cycloalkanes: saturated cyclic hydrocarbons

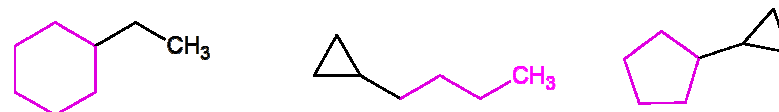
- General formula $(CH_2)_n$ - made of CH_2 units
- Drawn as polygons in line structures



4.1 Naming cycloalkanes

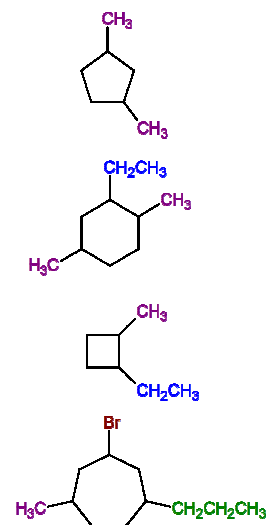
1. Find the parent

- In alkyl-substituted cycloalkanes the parent is the ring if the ring and alkyl group have same # C
- Compound is cycloalkyl-substituted alkane if alkane has longer chain of carbons



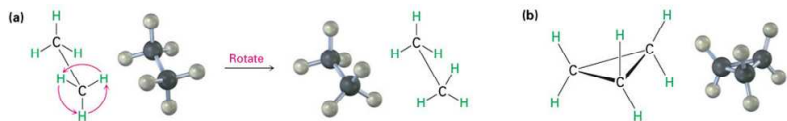
2. Number the substituents

- With one group starting at 1, make the other numbers as **small** as possible
- Give alphabetical priority when there's a tie
- Treat halogens as alkyl groups



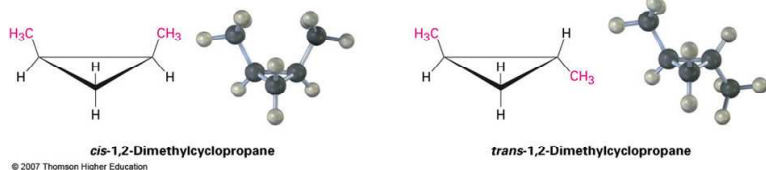
4.2 Cis-trans isomerism in cycloalkanes

sp^3 bonds rotate freely in open-chain alkanes, but have much less rotational freedom in cycloalkanes.



Cycloalkanes have a "top face" and a "bottom face" when viewed from the side.

There are two isomers of 1,2-dimethylcyclopropane:



cis: two groups are pointed towards the same face of a cyclic molecule.

trans: two groups are pointed towards opposite faces of a cyclic molecule

Stereoisomers

Stereoisomers: atoms are connected in same order, but differ in three-dimensional orientation

recall... **Constitutional isomers**: same formula but atoms connected differently

Constitutional isomers
(different connections between atoms)

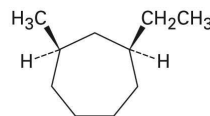
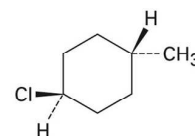
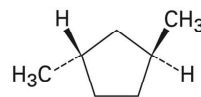


Stereoisomers
(same connections but different three-dimensional geometry)



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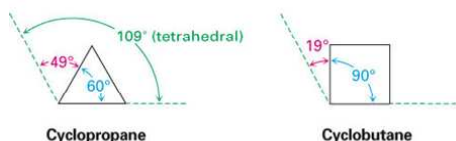
Name the following molecules, and draw one stereoisomer of each molecule.



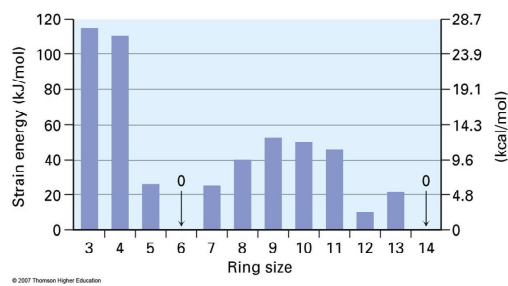
4.3 Ring strain

sp^3 carbons have an optimal bond angle of 109.5° .

In small rings like cyclopropane and cyclobutane, it is impossible to obtain the optimal bond angle due to the geometry of the ring.



Ring strain energy: measure of instability caused by the ring geometry.



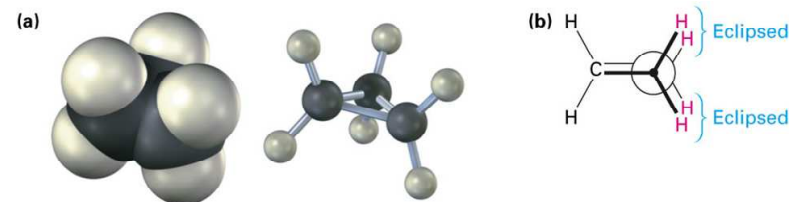
Ring strain comes from a combination of factors:

- **Angle strain:** deviation from ideal bond angle
- **Torsional strain:** from eclipsing bonds on neighboring atoms
- **Steric strain:** repulsive interaction when atoms approach each other too closely

4.4 Conformations of cycloalkanes

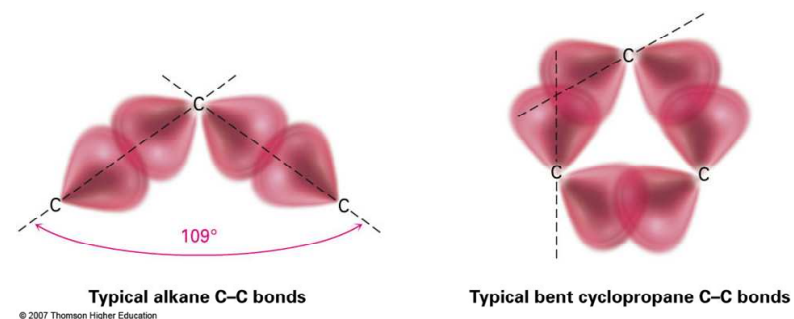
Cyclopropane: highly strained 3-carbon ring:

- **Angle strain:** 3 planar carbon atoms, 60° bond angles (optimally 109.5°)
- **Torsional strain:** all hydrogens eclipsed



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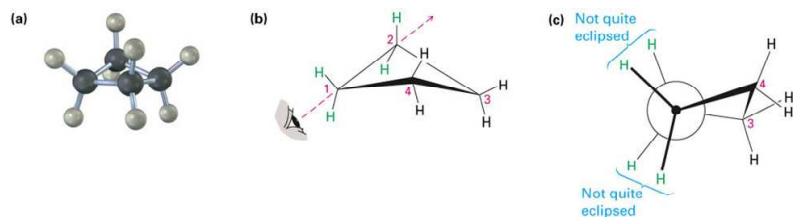
How are 60° bonds even able to form?
They are special **bent** bonds that have less orbital overlap than normal σ bonds.



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Cyclobutane and cyclopentane

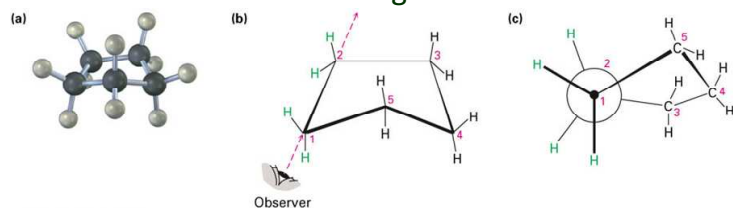
Cyclobutane: would have 90° bond angles if it were flat, but the actual structure is slightly puckered:



The ring is not quite planar. It is slightly bent so that one carbon is about 25° above the plane of the other 3.

- **Torsional strain:** reduced since it is bent - the H's are not quite eclipsed like in cyclopropane
- **Angle strain:** bending the ring increases angle strain a bit, but it gives the molecule the most stable overall conformation

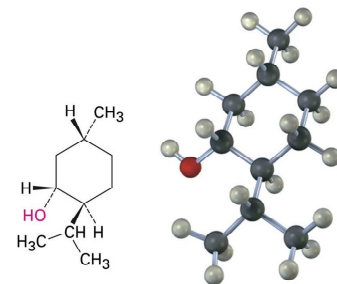
Cyclopentane: planar cyclopentane would have considerable torsional strain, so it is also puckered to strike a balance between angle and torsional strain:



Four atoms are in a plane, and one is above the plane. The hydrogens are nearly staggered (very little torsional strain).

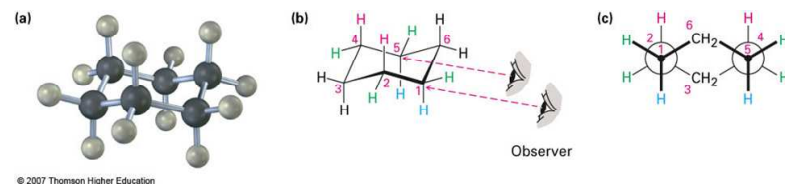
4.5 Conformations of cyclohexane

Substituted cyclohexanes are very common in nature.



Menthol

Cyclohexane is the only common cycloalkane that adopts a **strain-free conformation** (just as stable as an open-chain alkane). It is able to do this by forming a **chair conformation**.

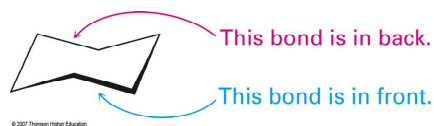
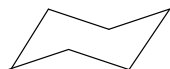
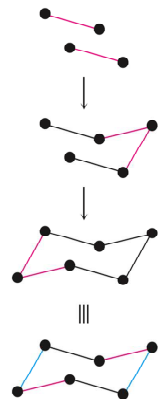


- All C-C bonds are nearly 109.5° (*no angle strain*)
- All neighboring C-H bonds are staggered (*no torsional strain*)

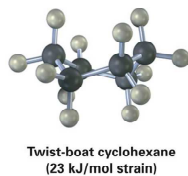
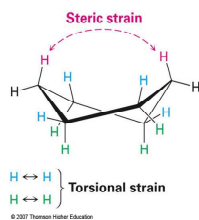
Please build a model of cyclohexane. It will be difficult to visualize otherwise.

Drawing the cyclohexane chair conformation

- Step 1** Draw two parallel lines, slanted downward and slightly offset from each other. This means that four of the cyclohexane carbons lie in a plane.
- Step 2** Place the topmost carbon atom above and to the right of the plane of the other four, and connect the bonds.
- Step 3** Place the bottommost carbon atom below and to the left of the plane of the middle four, and connect the bonds. Note that the bonds to the bottommost carbon atom are parallel to the bonds to the topmost carbon.



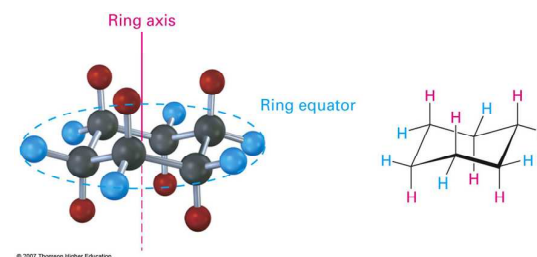
The **twist-boat** is another conformation of cyclohexane, but it has some strain.



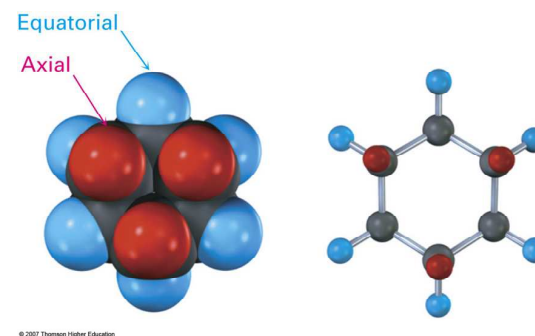
4.6 Axial and equatorial bonds in cyclohexane

Because of the chair conformation, there are two kinds of positions for substituents on the ring:

- **Axial** positions are perpendicular to the ring and parallel to the ring axis (pointed straight up and down)
- **Equatorial** positions are in the approx. plane of the ring, around the ring's equator.



Each carbon in cyclohexane has **one axial** and **one equatorial** hydrogen. Looking at the ring from the top, you will see alternating axial and equatorial hydrogens.



Drawing axial and equatorial hydrogens

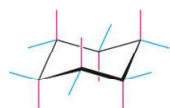
Axial bonds: The six axial bonds, one on each carbon, are parallel and alternate up-down.



Equatorial bonds: The six equatorial bonds, one on each carbon, come in three sets of two parallel lines. Each set is also parallel to two ring bonds. Equatorial bonds alternate between sides around the ring.



Completed cyclohexane

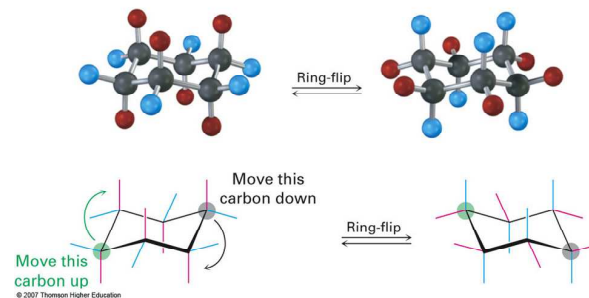


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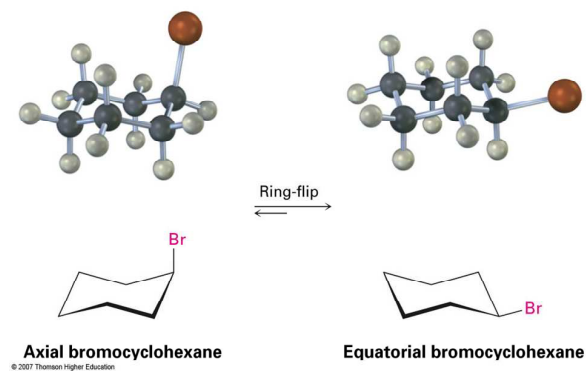
Ring-flip

Even though there are two possible positions on a cyclohexane ring there is only one primary conformation of methylcyclohexane or bromocyclohexane, etc.

This is because the positions can convert when the chair performs a **ring flip** - a conformational interchange that makes all axial positions equatorial and vice-versa.



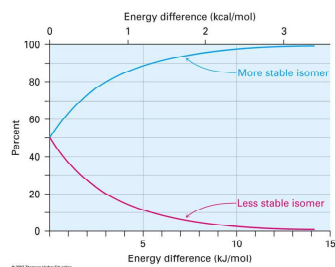
The two ring-flipped conformers are in rapid equilibrium and the more stable conformer is favored.



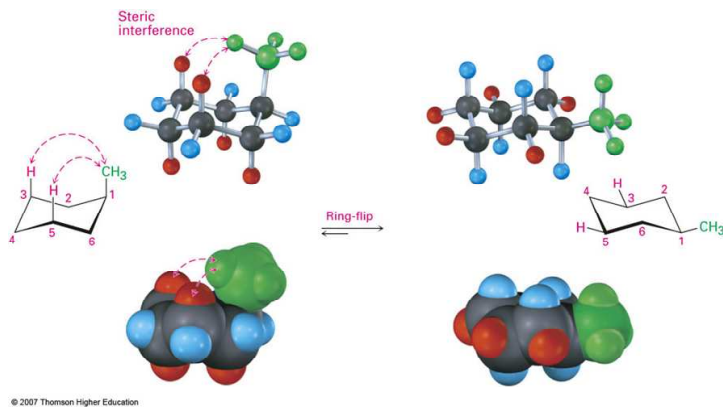
4.7 Conformations of monosubstituted cyclohexanes

The conformer that is lower in energy will be favored in the equilibrium mixture.

Recall $\Delta G = -RT \ln K$; if there's an energy difference of 10 kJ/mol, $K = 55/1$ which is a 98% to 2% mixture.

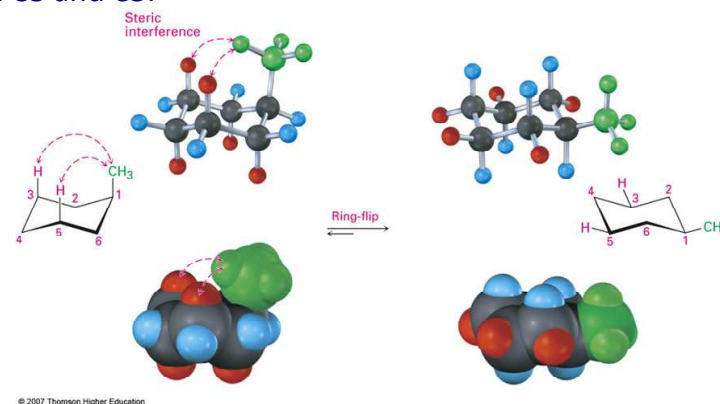


The equatorial conformer of methylcyclohexane is 7.6 kJ/mol more stable than the axial conformer.



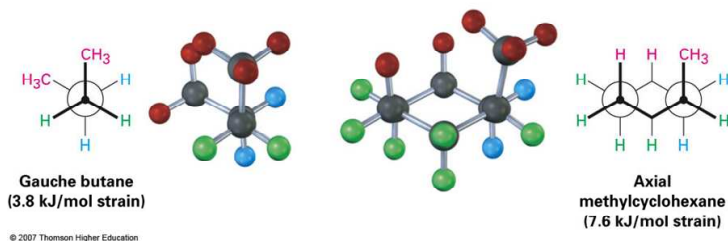
Steric strain: 1,3-diaxial interactions

The reason the axial methylcyclohexane is unstable is because of the 1,3-diaxial interactions. One hydrogen on the axial methyl group is too close to the axial hydrogens on C3 and C5.



In general, anything other than a H in an axial position will cause 1,3-diaxial interactions (unfavorable steric strain).

The 1,3-diaxial interaction is the same slightly unfavorable interaction that's in the **gauche** conformation of butane:



Steric strain energies

The amount of steric strain in an axial position depends on the size of the substituent:

Table 4.1 Steric Strain in Monosubstituted Cyclohexanes

Y	1,3-Diaxial strain	
	(kJ/mol)	(kcal/mol)
F	0.5	0.12
Cl, Br	1.0	0.25
OH	2.1	0.5
CH ₃	3.8	0.9
CH ₂ CH ₃	4.0	0.95
CH(CH ₃) ₂	4.6	1.1
C(CH ₃) ₃	11.4	2.7
C ₆ H ₅	6.3	1.5
CO ₂ H	2.9	0.7
CN	0.4	0.1

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What's the difference in energy between the axial and equatorial conformations of chlorocyclohexane?

t-butylcyclohexane?

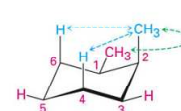
4.8 Conformations of disubstituted cyclohexanes

Monosubstituted (one group attached to the ring) cyclohexanes are always more stable in the equatorial position. Disubstituted cyclohexanes are more complex.

In ***cis*-1,2-dimethylcyclohexane**, there are two equal-energy conformations.

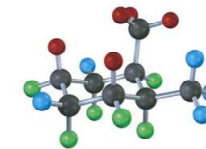
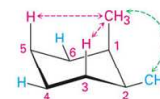
***cis*-1,2-Dimethylcyclohexane**

One gauche interaction (3.8 kJ/mol)
Two CH₃ ↔ H diaxial interactions (7.6 kJ/mol)
Total strain: 3.8 + 7.6 = 11.4 kJ/mol



Ring-flip

One gauche interaction (3.8 kJ/mol)
Two CH₃ ↔ H diaxial interactions (7.6 kJ/mol)
Total strain: 3.8 + 7.6 = 11.4 kJ/mol

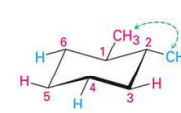


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In ***trans*-1,2-dimethylcyclohexane**, there are two conformations with different energies because the methyl groups are either both axial or both equatorial:

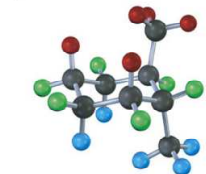
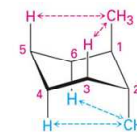
***trans*-1,2-Dimethylcyclohexane**

One gauche interaction (3.8 kJ/mol)



Ring-flip

Four CH₃ ↔ H diaxial interactions (15.2 kJ/mol)



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Disubstituted cyclohexanes

Rule of thumb: in the most stable conformation, the **larger** group(s) should be equatorial - this avoids unfavorable 1,3-diaxial interactions.

On the exam, the groups will either be the same, or one group will clearly be larger than the other. No need to memorize energies.

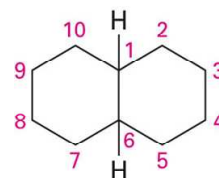
The *t*-butyl group is almost **never** in an axial position.



Draw the most stable conformation of *cis*-1-ethyl-2-methylcyclohexane.

4.9 Conformations of polycyclic molecules

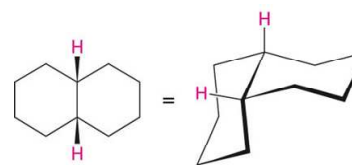
Polycyclic molecules have two or more rings fused together along a common bond.



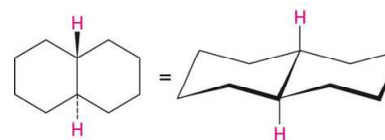
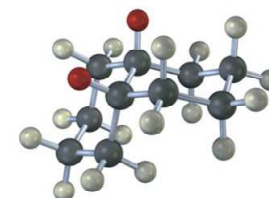
Decalin—two fused cyclohexane rings

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cis and *trans* decalin are stereoisomers - the name comes from the relationship of the two hydrogens on the bridgehead carbons (C1 and C6 - the carbons in common between the rings).

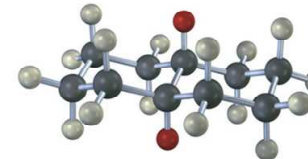


cis-Decalin



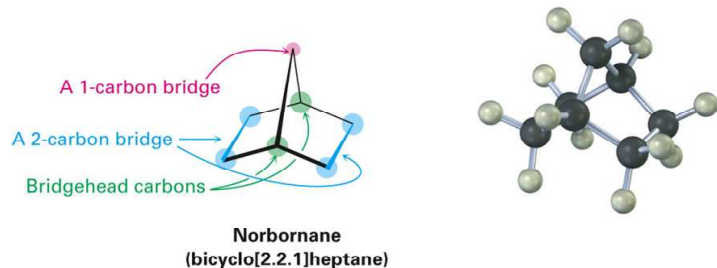
trans-Decalin

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Naming polycyclic molecules

Norbornane is an important common ring system in biological molecules. It consists of two 2-carbon and one 1-carbon bridges connecting the two bridgehead carbons.



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Polycyclic molecules can be named systematically:

- Start the name with **bicyclo**
- Write inside [square brackets] the number of carbons in each of the bridges (in descending order, separated by dots).
- End the name with an alkane name that shows the total number of carbons in the ring system.

