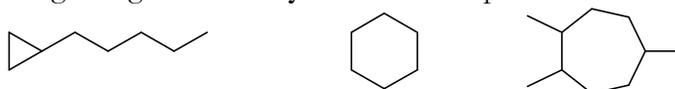


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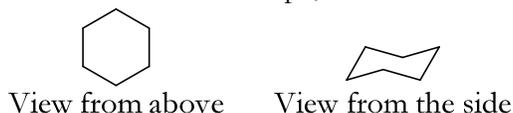
Compounds with a single ring are **monocyclic**. For example:



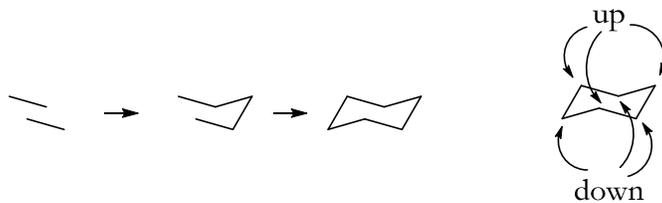
Assuming they have no double or triple bonds, they each have one degree of unsaturation. This means that their formulas follow the pattern C_nH_{2n} . This can be treated as some number of methylene groups, $n \cdot (CH_2)$, which is useful because it means each cycloalkane can be considered in terms of heat of formation per CH_2 group, given as $(\Delta H_f/n)$.

N	Name	$(\Delta H_f/n)$ in kcal/mol
3	Cyclopropane	+4.25
4	Cyclobutane	+1.7
5	Cyclopentane	-3.7
6	Cyclohexane	-4.95
7	Cycloheptane	-4.0
8	Cyclooctane	-3.7

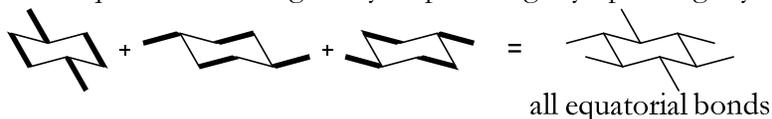
This shows that cyclopropane is by far the least stable, followed by cyclobutane. Cyclohexane is the most stable – in fact, it turns out to have the same energy per CH_2 group as an average linear, unbranched alkane. Since cyclohexane is the most stable, it shows up the most frequently in molecules (followed closely by cyclopentane). For this reason, it's worthwhile to take a closer look at how cyclohexane arranges itself in space – its conformation. Although cyclohexane is often shown in a top-down view, that's not how it exists in space. It's puckered into a chair-like shape, which is called chair cyclohexane.



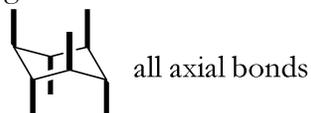
It's easiest to draw this molecule (and any variations) as sets of parallel lines. Draw the front and back bonds first, then the corners at either side. Each atom in this ring is pointing either "up" or "down" – they alternate around the ring.



Since each carbon atom in a cycloalkane is tetrahedral, it also has another two bonds. One is parallel to some other part of the ring – these are called the **equatorial** bonds, since they're arranged around the equator of the ring. They all point slightly up or slightly down.



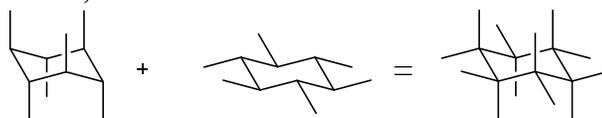
The other is vertical, either straight up or straight down. These are **axial**, since they point along the rotational axis of the ring.



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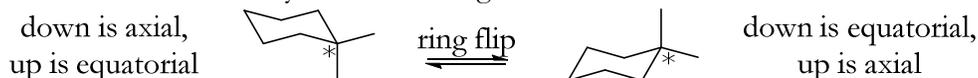
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If you show all bonds at once, it looks like this:



all axial bonds all equatorial bonds all total bonds

Note that the “up” carbons in the ring have up axial and down equatorial bonds, while the “down” carbons have down axial and up equatorial bonds. However, the ring is not locked into this position. It can convert between two different chair forms by doing a ring flip (also called chair flip or chair interconversion). During this conversion, the up carbons interconvert with down carbons, and axial positions interconvert with equatorial positions. This is easiest to see if we only focus on a single carbon.



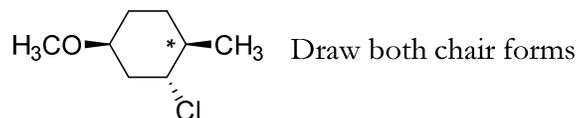
To do a chair flip, first one corner of the ring will fold up, briefly creating a high-energy conformation called “boat” or “twist-boat”. This will then convert to the new chair type. This interconversion is rapid (about 10^5 times per second for cyclohexane), so axial and equatorial hydrogens swap places rapidly and can’t be distinguished.



Now we can start attaching other substituents to the ring and looking at how the molecule behaves. The rules to follow are:

- Anything that’s shown with a bold bond in the top-down view is up or slightly up in the chair view.
- Anything that’s shown with a dashed bond in the top-down view is down or slightly down in the chair view.
- Anything that’s straight up or down is axial.
- Anything that’s slightly up or slightly down is equatorial.
- Cis and trans refer only to the comparison between bold and dashed. If both groups you’re comparing are bold or both are dashed, they’re cis to each other. If you have one bold and one dashed, they’re trans. Axial and equatorial don’t matter at all here.
- Doing a ring flip converts anything equatorial to an axial position, and vice-versa, but it doesn’t change what’s bold or dashed. If a group is up, then it should always be up (unless you’re flipping the entire object upside-down).

Here’s an example of how to use these rules:

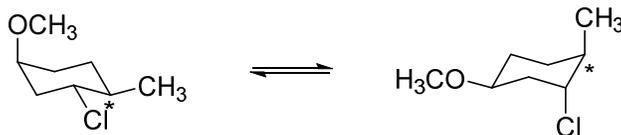


You can label one of the carbons in the top-down view with a star, and arbitrarily put the same label on any of the carbons in the chair view. Then you can fill in the groups. CH₃ is on the starred carbon and bold, so put it there coming upwards. Cl is on the first carbon moving clockwise from the starred carbon and it’s dashed, so put it there pointing down. The OCH₃ is two carbons further along in the clockwise direction on a bold bond, so it

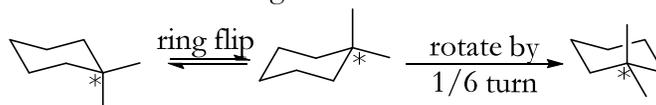
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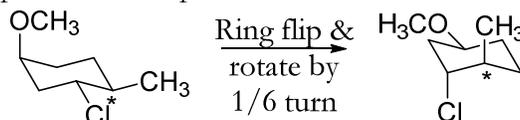
points up. No matter what, the CH₃ and the OCH₃ are always up or slightly up, and the Cl is always down or slightly down. The ring flip just swaps axial for equatorial.



Where it can get a bit confusing is in the fact that a lot of the time, people prefer to show just a single type of chair: either the leftmost carbon of the ring is always pointing up for them, or it's always pointing down. To achieve this, they combine a ring flip with a simultaneous rotation of the ring by 1/6 of a turn. In this example, the starred carbon still converts from down to up, but if the ring is rotated by a 1/6 turn then the starred carbon is no longer the rightmost carbon in the ring.



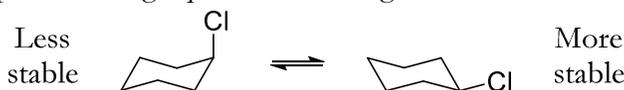
We can apply this to the previous example.



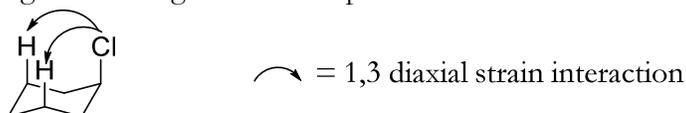
No matter which chair we show in which orientation, the CH₃ and OCH₃ are always cis to each other, while the CH₃ and Cl are trans to each other.

Relative Stability of Chair Forms

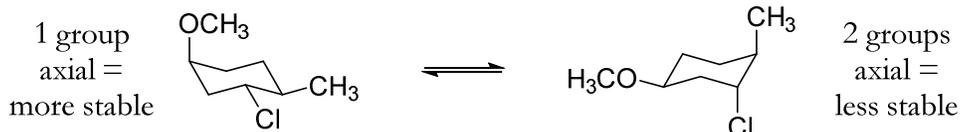
Almost every group prefers being equatorial to being axial.



If a group is axial, it experiences 1,3-diaxial strain from bumping against the two other groups that are axial and pointing in the same direction. This is another example of steric strain – groups trying to cram together into a space that is too small.



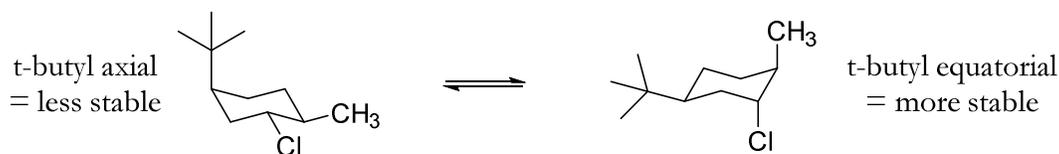
Each type of group has a particular energy cost for being axial (its A-value). For most groups we'll see, these values are close enough to equal that the ring is usually under majority rule: the chair conformation with the most groups equatorial is the most stable.



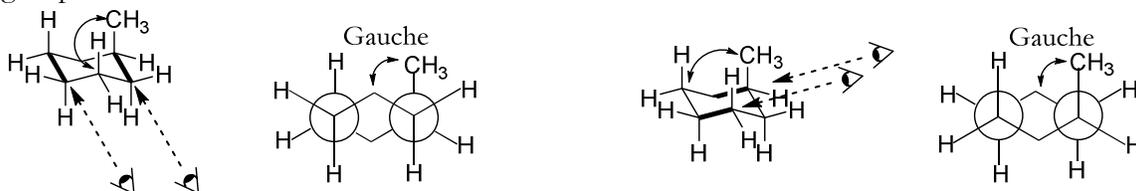
The one big exception is the tert-butyl group. It costs ~5 kcal/mol to place a t-butyl group in the axial position, so it will usually prefer to be equatorial even if this means that several other groups have to be axial as a result.

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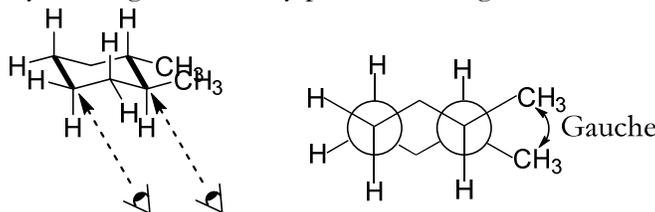
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Why does this preference exist? We can explain it using Newman projections. Just like for alkanes, we choose a bond to sight along. The ring is made up of parallel lines, though, so we're actually sighting along two bonds simultaneously. We can do this along either of the two bonds attached to the carbon that has the group of interest on it. When we do, it becomes apparent that the biggest difference between being axial or equatorial is gauche interactions. Being axial means that a group has two more gauche interactions than it otherwise would, with part of the ring itself. Which part of the ring appears gauche depends on which two bonds we sight along, but in reality both parts are gauche all the time that the group is axial.



When a ring has two groups on adjacent atoms, it's also possible for them to be gauche to each other even if they're not gauche to any part of the ring.

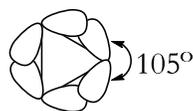


Smaller Rings

Cyclopentane is almost as stable as cyclohexane. It folds into an “envelope” shape, where four atoms are roughly coplanar and one atom folds up out-of-plane, like the flap of an envelope. Any one of the five atoms can do this and it can fold up or down, so there are at least 10 major conformations compared to 2 for cyclohexane. For this reason, we don't get into cyclopentane as much.



Cyclobutane and cyclopropane should have bond angles of 90° and 60° respectively, which is very far from the 109.5° preferred by tetrahedral carbons. This creates **angle strain**. Cyclopropane adjusts for this a little by having “bent bonds,” where the orbitals do not overlap head-on but at an angle. This allows the bond angles at each carbon to relax to 105° which is much closer to the ideal than 60° is, but it pays for this with the cost of much weaker bonds due to poor orbital overlap. This is why the heat of formation is highest for cyclopropane.

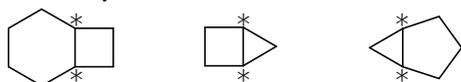


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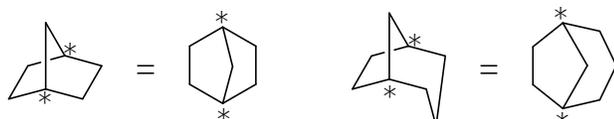
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Bicyclics & Polycyclics

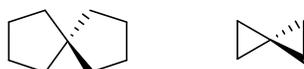
There are three different ways for rings to be joined to each other. Any atom that's part of multiple rings is called a **bridgehead atom** (marked with * below). In **fused bicyclics** the bridgeheads connect to each other directly. In **bridged bicyclics** they are separated by at least one atom. In **spirocyclics** there is only one atom shared between rings. Spirocyclics are not considered true bicyclics.



Fused bicyclics

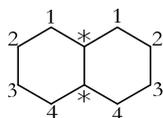


Bridged bicyclics

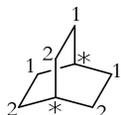


Spirocyclics

To name fused or bridged bicyclics, find the bridgeheads and count the number of atoms separating them along each path. List these in square brackets, separated by periods, in descending order. The beginning of the name gets changed to “bicyclo” instead of “cyclo”, and the parent chain is named after an n-alkane with the same number of carbons.

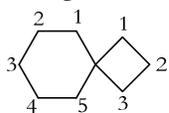


Ten C atoms total = bicyclo....decane
Bridgeheads are separated by 4, 4, and 0 atoms
bicyclo[4.4.0]decane



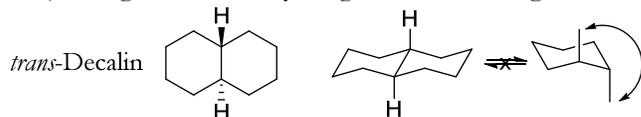
Eight C atoms total = bicyclo....octane
Bridgeheads are separated by 2, 2, and 2 atoms
bicyclo[2.2.2]octane

Spiro compounds are named similarly, but both routes start and end on the single shared atom. The prefix is “spiro” instead of “bicyclo” and the numbers are in ascending order.

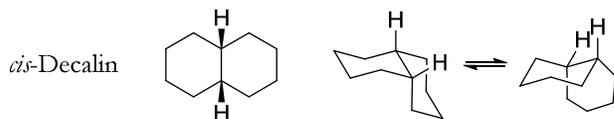


Nine C atoms total = spiro....nonane
Paths around rings contain 3 and 5 atoms
spiro[3.5]nonane

Fused rings can join in multiple different stereochemical ways. Bicyclo[4.4.0]decane (a.k.a. decalin) resembles two cyclohexane rings joined along one edge, but there are two options for joining them: the hydrogens at the bridgeheads can either be *cis* or *trans*.



These atoms are too far apart to be in a six-membered ring, so no interconversion is possible



Both of these chair forms are possible, but both of them have some steric strain due to a carbon on one ring being axial to the other ring.

Alkenes in Rings

There are only two rules to remember here.

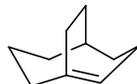
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1. In bridged compounds (but not fused), a bridgehead atom can't be sp^2 -hybridized (so, for example, it can't be part of a double bond) if all of the rings containing it are seven atoms or fewer. The angle strain is just too high for an sp^2 -hybridized carbon, which wants bond angles of 120° . This is called **Bredt's Rule**.



Largest ring has 6 Cs
Not allowed



Largest ring has 8 Cs
Allowed

2. Rings can't contain *trans* double bonds if they have seven atoms or fewer. This is because there just aren't enough other atoms to connect the two ends of the bond.



Six atoms
Not allowed

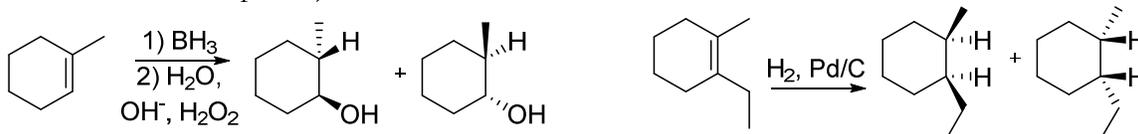


Eight atoms
Allowed

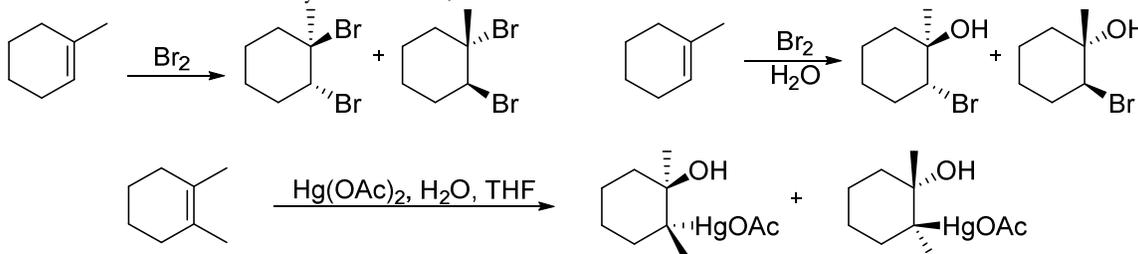
Stereochemistry of Alkene Addition Reactions

The reactions that we saw in Ch. 4 and 5 can be broken down into three categories, based on the stereochemistry of the two new groups that are added to the molecule.

1. Syn addition: both groups always add to the same face. This means that so long as you draw the skeleton of the molecule in the same orientation/conformation for both the starting material and product, then both new groups should be bold, or both should be dashed. During the reaction, both groups are added at the same time, from the same direction – in other words, this is a **concerted mechanism**. Reactions in this category are hydrogenation and hydroboration-oxidation (hydroboration is the step that determines stereochemistry; the oxidation just swaps the B for an OH without changing the direction it points).



2. Anti addition: the groups add to opposite faces. So long as you draw the skeleton of the molecule in the same orientation/conformation for both the starting material and product, then one group will be bold and one will be dashed. A common factor among the mechanisms we've seen is a three-membered ring that gets popped open, but this won't always be the case. Reactions in this category include halogenations, halohydrin formation, and oxymercuration (but not reduction – that's a separate deal, since the mercury gets replaced with an H that could be pointing either direction at random). Note that **anti addition is not the same thing as anti-Markovnikov**! Hydroboration is an anti-Markovnikov-style addition, but it's not an anti addition.

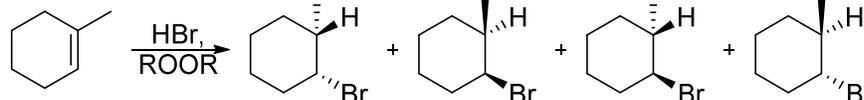


3. Random addition: sometimes they add to the same face and sometimes they add to opposite faces. This category includes anything that goes by a carbocation or carbon radical mechanism, since both these carbons go sp^2 and lose all their stereochemical

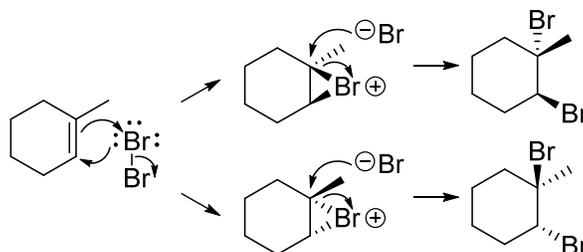
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information (this is called “scrambling” or “loss of stereochemistry”). Reactions in this category include acid-catalyzed hydration and HX addition, with or without peroxides.

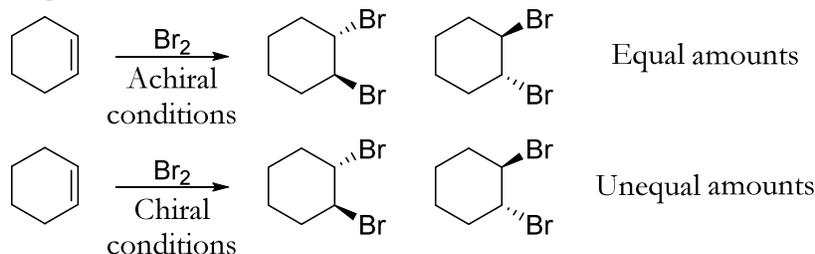


Here’s an example of how these reactions might look with stereochemistry shown. The bromonium ring can form on either side, but the bromide will always attack it from the opposite direction.



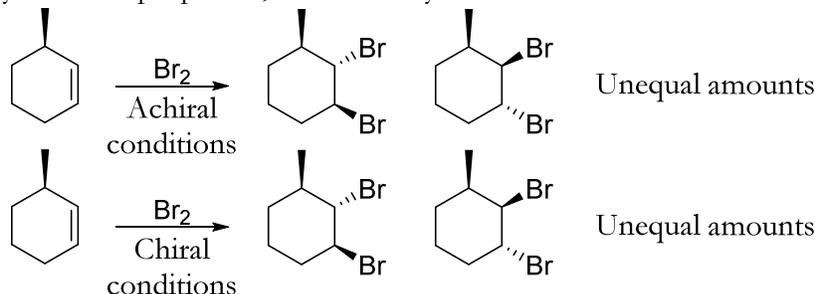
Stereochemistry and Reaction Outcomes

We already know that enantiomers have the same physical properties as each other, and diastereomers have different physical properties from each other. This extends to reaction outcomes too. Two enantiomers will be formed in equal amounts, provided there are no chiral compounds interacting with them during the reaction (in other words, if they are formed in an **achiral environment**). However, if they are in a chiral environment, then they will form in unequal amounts.



This is because the two enantiomers interact differently with chiral molecules – maybe one of them binds more tightly to a chiral catalyst, or forms a crystal more efficiently by packing together with the other chiral molecule. This also means they interact differently with biological molecules, which are almost always chiral. This is why enantiomers will often smell or taste different from each other; it’s because they interact differently with the chiral receptors in your nose.

Diastereomers are always formed in unequal amounts. This is because they have fundamentally different properties, whether they’re in a chiral environment or not.



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An overall way to sum up these rules is “optically inactive in, optically inactive out.” If the starting materials and environment are either fully achiral or racemic (so they don’t start with a bias towards one handedness or the other), then the products will be too. You could also list the opposite as “optically active in...probably optically active out unless there’s loss of stereochemistry.” Whether this happens or not is up to the details of the particular reaction.