

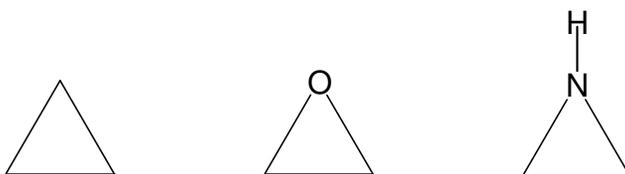
ALICYCLIC AND NON-AROMATIC HETEROCYCLIC CHEMISTRY (Ed Smith) II Year

Reference to the books noted in the synopsis will provide background reading to this course.

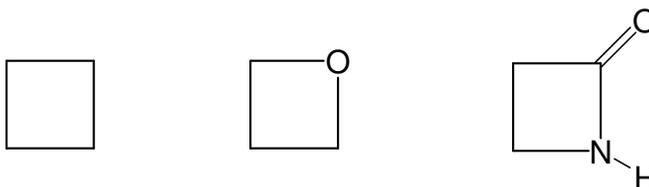
What does “Alicyclic” mean? The “Ali” comes from aliphatic i.e. we are NOT going to discuss aromatic compounds. The “cyclic” seems obvious but one should note that it refers to carbocyclic compounds i.e. those in which the atoms of the ring are only carbon. In contrast “Heterocyclic” means cyclic compounds in which one or more of the ring atoms is not carbon i.e. is a heteroatom such as O, N, S, P etc.

The classes of compounds which will be discussed in these lectures are

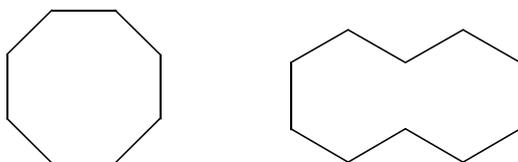
- 3-membered rings: cyclopropanes, epoxides (oxiranes) and aziridines



- 4-membered rings: cyclobutanes, oxetanes and β -lactams (azetidin-2-ones)



- 8-membered and 10-membered rings: cyclooctanes and cyclodecanes



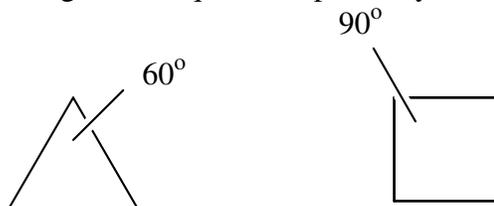
What distinguishes alicyclic and non-aromatic heterocyclic molecules from their non-cyclic counterparts, the acyclic molecules? Two phenomena, which are present in acyclic molecules, become predominant in saturated ring chemistry, namely, STRAIN and CONFORMATIONS.

Ring Strain

There are three types of strain in rings: angle strain, torsional strain and transannular strain.

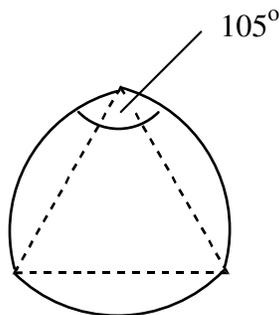
1. Angle (Baeyer) Strain (3- and 4-membered rings):

In acyclic molecules the tetrahedral angle of 109° about sp^3 hybridised carbons is preferred. In three- and four-membered rings this cannot be achieved if we represent them as equilateral triangles and squares respectively:



This raises the energy of the molecule relative to an acyclic one and this excess energy is called the angle (or Baeyer, who first defined it) strain.

Cyclopropanes, in particular, can overcome this strain to some extent as follows. If the carbon-carbon σ bonds did not form along the internuclear axis but rather bent outwards then an interbond angle of 105° can be achieved:



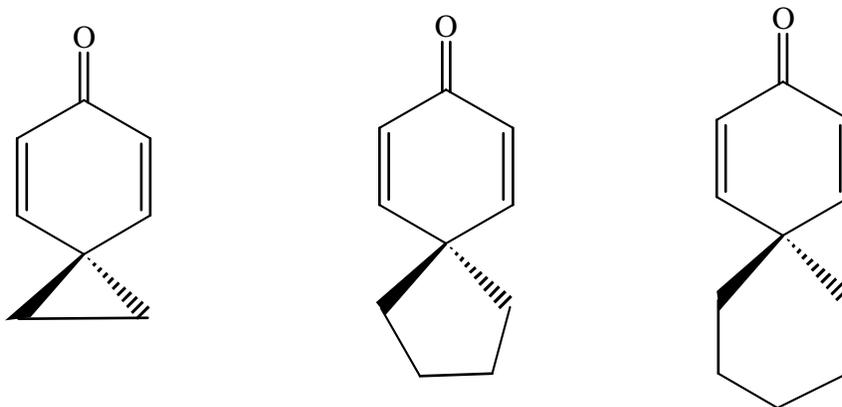
How is this done? Since p-orbitals project electron density above and below the internuclear axis, e.g. when forming π -bonds, an increase in p-orbital character in the σ -bonds should result in this bending. This extra p-orbital character in the ring C-C bonds is achieved at the expense of a lower p-orbital character in the exocyclic C-H bonds. Thus we get a rehybridisation of the orbitals on each carbon roughly as follows:



A consequence of this is that the C-C bonds are weaker and more π -like than the corresponding acyclic ones and the C-H bonds are stronger with greater s-character. The evidence for this rehybridisation comes from numerous techniques some of which are:

(a) C-C bond more π -like: (i) Ultra-violet-Visible Spectroscopy:

Cyclopropane σ -orbitals can overlap with adjacent π -systems because of their partial π -character to give extra conjugation not found in other rings:

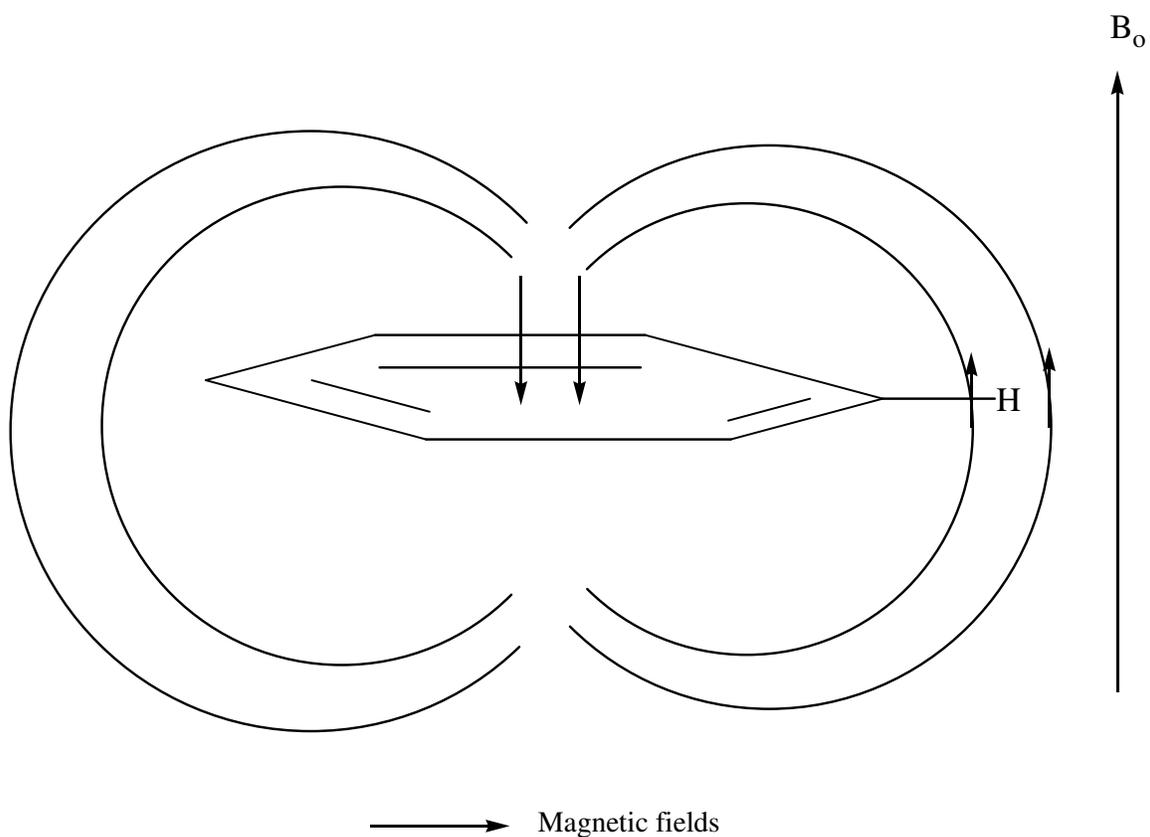


$\lambda_{\text{max}}(\text{nm})$ 274

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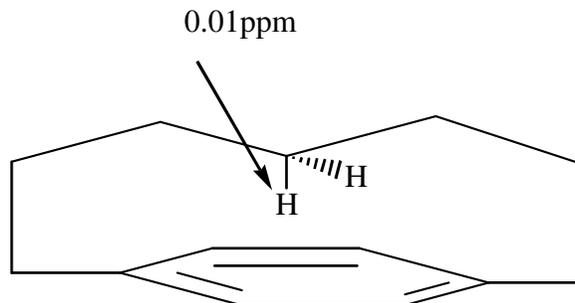
(ii) ^1H NMR Spectroscopy:



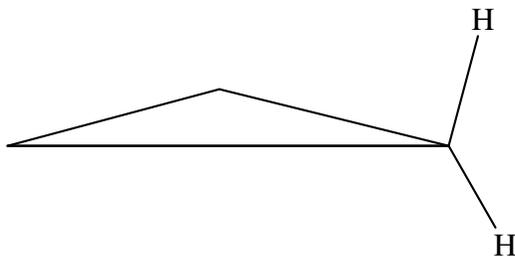
The usual explanation for the appearance of aromatic protons at low field (7-8 ppm) in their ^1H nmr spectra is because of a **ring current** caused by a pair of π -electrons circulating the ring thereby creating a toroidal magnetic field at right angles to that circulation which enhances the external field of the magnet in the region of the exocyclic

protons. Thus those protons experience a stronger field and resonate consequently downfield of aliphatic protons.

Note that if we had a proton above the ring, where the ring current magnetic field opposes the external magnetic field, it should shift in the opposite direction i.e. upfield. The following compound illustrates this effect:



Applying this thinking to cyclopropane we see that the σ -framework has some π -like character and, therefore, should show a weak ring current. Since the hydrogens on cyclopropane lie above and below the ring they should be in the shielding zone of this ring current:



and hence should appear upfield compared to a similar acyclic molecule, as indeed they do:

	cyclopropane	propane (CH ₂)
δ (ppm)	0.22	1.1

(b) C-H stronger with more s-character: (i) Microwave and IR spectroscopies:

These two techniques measure bond length and strength respectively. We can see the shorter and stronger C-H bond in cyclopropane clearly in comparison with other molecules of different hybridization:

	—	=	△	≡
Bond length (Å):	1.10	1.086	1.08	1.057
Bond strength (cm ⁻¹):	2960	3010-3060	3010-3040	3300

(ii) C-H Acidity (pKa):



Removal of a proton is easier from bonds with greater s-character because the electron pair of the resultant carbanion is held closer to the nucleus in such orbitals i.e. is more stabilized. This is reflected in the following pKa values:

				
pK _a :	42	39	36.5	25

(iii) ¹³C NMR Spectroscopy:

¹³C-H coupling constants are very sensitive to the local electronic state of the C-H bonds and because coupling between nuclei is transmitted by the electrons those orbitals which have a high electron density close to the nuclei, i.e. electrons in s-orbitals, will cause the transmission of the coupling to be more effective. Therefore, the greater the s-orbital character, the larger is the coupling constant as the following show:

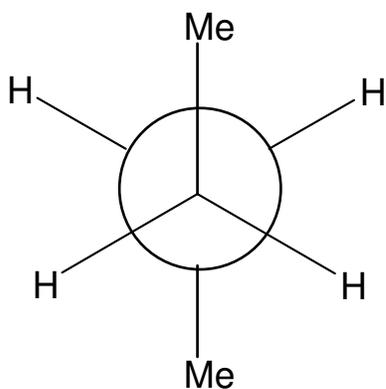
				
J _{CH} (Hz):	125	157	161	248

This technique is sufficiently sensitive that it enables us to see that some rehybridisation also occurs in cyclobutanes because J_{CH}(cyclobutane) = 134Hz.

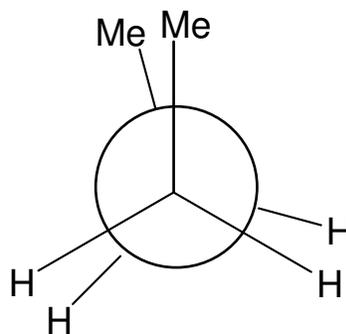
Although this discussion has been restricted to cyclopropanes, J_{CH} values for aziridines (168 Hz) and for epoxides (176 Hz) suggest that these molecules also show the same bonding effects.

2. Torsional (Pitzer) Strain (3- and 4-membered rings)

Torsional (or Pitzer, who defined it) strain occurs during rotation (torsion) about carbon-carbon single bonds. The case which we discussed in the first year is that of n-butane:



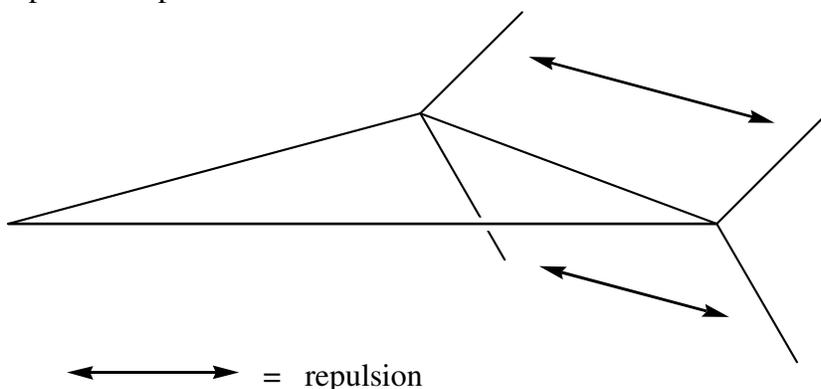
Staggered



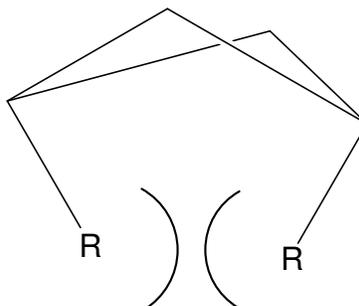
Eclipsed

n-Butane exists largely in the staggered conformation so as to avoid the repulsive forces, bond electron-bond electron and nucleus-nucleus (especially Me-Me), in the eclipsed form. Any molecule which is forced to adopt an eclipsed conformation is said to suffer from torsional strain because it cannot rotate to relieve those repulsive forces.

Cyclopropane, which is necessarily planar, is just such a molecule where all the external bonds and groups are eclipsed:



Planar cyclobutanes suffer in the same way, but some cyclobutanes can reduce this problem by adopting a puckered conformation in which the groups and bonds are slightly off-eclipsed. This is achieved by carbons opposite one another on the ring moving out of the plane; this movement can only proceed so far otherwise groups cis to one another (R in the diagram) on those two carbons come within their van der Waals radii:



The energy difference between planar and puckered forms is often quite small.