

1 CONFORMATIONS OF RINGS

1.1 INTRODUCTION

- In 1885 Adolf von Baeyer proposed that if carbon prefers to have a tetrahedral geometry with bond angles of 109.5 degrees, then ring sizes other than 5 and 6 may be too strained to exist. The basis for this proposal was that all ring systems are planar, clearly this is not the case. Ring systems can adopt many different conformations just as easily as acyclic compounds do.
- The Cambridge Structural Database is a unique resource providing a wealth of information on the preferred conformations of rings. Indeed, the database has been used extensively to map the conformational space of medium ring-sized cyclic and heterocyclic compounds (*Acta Cryst.*, B49, 910, 1993) and of macrocyclic ether and thioether ligands (*Acta Cryst.*, B53, 241, 1997).
- By examining crystal structures we can and understand why the observed conformations are adopted in terms of the strain present in these systems

1.2 OBJECTIVES

- To investigate and understand the reason for angle strain in fully saturated planar carbocyclic rings.
- For cyclohexane, determine the angle strain in actual compounds by analysing experimental crystal structure data.
- To compare the predicted angle strain (in planar rings) against that observed in actual compounds and account for the differences.
- To closely examine the conformations of 3- to 6-membered carbocyclic rings and understand why these conformations are adopted in terms of the strain present in these systems.

1.3 GETTING STARTED

- Open the interactive WebCSD teaching database by going to the following URL:

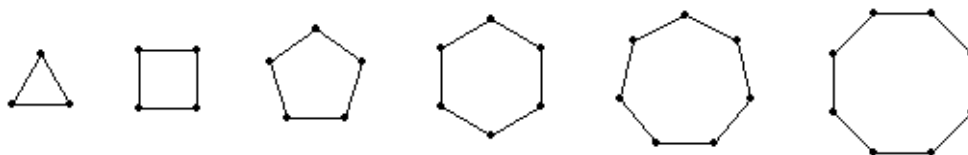
http://webcsd.ccdc.cam.ac.uk/teaching_database_demo.php

- This demo version of WebCSD allows you to browse all 500 entries in the teaching subset of the Cambridge Structural Database.
- Reference codes (refcodes) of the structures in the teaching set will appear in a list on the left hand side of the WebCSD page. Only those refcodes beginning with “A” are displayed initially. To show those refcodes starting with “B” click on the > button.
- To view a structure select the corresponding refcode in the list by left-clicking on it. Alternatively, you can type a refcode in the **Entry** box above the structure list.

1.4 STEPS REQUIRED

1.4.1 Investigate angle strain in planar rings.

- Ideally the sp^3 hybridised carbon atoms of fully saturated carbocyclic rings would adopt bond angles of 109.5 degrees. However, in planar rings the internal bond angles will depend on the number of atoms in the ring.



- The table below gives values for the internal angles for the regular planar polygons shown above and an indication of angle strain per carbon atom due to deviation from the ideal sp^3 angle of 109.5 degrees.

No. atoms in ring	Internal angle in planar ring (degrees)	Measure of angle strain abs(internal angle - 109.5)
3	60	49.5
4	90	19.5
5	108	1.5
6	120	
7	128.5	
8	135	

- Complete the table above by calculating the angle strain (angle strain = internal angle - 109.5) for 6- to 8-membered rings.
- This data is best presented as a graph. Plot the predicted angle strain against ring size (for three- to eight-membered planar rings). What conclusions can you draw?
- Strain is predicted to be largest for three-membered rings but rapidly decreases and reaches a minimum for a five-membered ring. In fact, a planar five-membered ring is predicted to be virtually free of angle strain. After the minimum at five, angle strain increases steadily as the rings get larger.

1.4.2 Calculating angle strain in actual compounds

- So far we only have a predicted value of angle strain in planar rings. We need a measure of angle strain in actual compounds, so that we can compare this to the predicted values.
- The preferred angle in actual compounds can be determined, for an n-membered carbocyclic ring, by taking the average internal angle across a large number crystal structures. Angle strain can then be calculated as the difference between this average internal angle and the ideal sp^3 angle of 109.5.
- Calculate, from crystal structure data, the actual angle strain in cyclohexane. For this task you are provided with 5 structures each containing a cyclohexane ring (refcodes: *BAVLOZ*, *CAFROR*, *CCXAPT*, *CLCHTF* and *CYCHEX*). To display a structure type it's reference code (refcode) in the **Entry** box above the structure list on the left hand side of the WebCSD page:

This interactive demo allows you to browse through all 500 entries in the new CSD Teaching Database using the standard WebCSD interface.

File Filter Help

Entry

Entry

BAFNIG
BAHSUY
BALGUQ10
BARBAD01
BATLAJ01
BAVLOZ
BAZGOY
BAZSUR
BCABOR10
BDMIUP
BECYIR
BEJFIF
BEJKUW
BENZAC02
BENZEN02
BERTOH01

36 'R' Entries

100%

Stop Search

Entry loaded

BAVLOZ (1R,2S,5R)-2-Isopropyl-5-methyl-cyclohexanol
R Bombicz, J Bushmann, P Luger, Nguyen Xuan Dung, Chu Ba Nam, Z Kristallogr. (1999), 214, 420

Hide Visualiser

Diagram Details Viewer Export Options Help

Ball and Stick [No Labels]

Hydrogens Disorder

Launch External Viewer

Identifier	BAVLOZ
Author(s)	R Bombicz, J Bushmann, P Luger, Nguyen Xuan Dung, Chu Ba Nam
Reference	Z Kristallogr. (1999), 214, 420
Formula	C ₁₀ H ₂₀ O
Compound	(1R,2S,5R)-2-Isopropyl-5-methyl- cyclohexanol
Synonym	(-)-Menthol
Space Group	P 3 ₁
Cell Lengths	a 21.262(10) b 21.262(10) c 5.984(5)
Cell Angles	α 90 β 90 γ 120
Cell Volume	2342.77
Z, Z'	Z 9 Z' 3
R-Factor (%)	4.93
Reduced Cell Lengths	a 5.984 b 21.262 c 21.262
Reduced Cell Angles	α 120 β 90 γ 90
Reduced Cell Volume	2342.77
Temperature (K)	143
Density (CCDC)	0.997
Average Sigma (C-C)	0 <= sigma <= 0.005
Radiation Probe	x-ray
Source	Mentha arvensis Linner
Habit	spherical
Recrystallisation Solvent	sublimation
CCDC Number	CCDC 112473

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- Complete the table below by measuring, for each structure, all six internal C-C-C angles, then calculate the average internal angle of that structure and the overall average across the set of 5.

To measure geometric parameters in the 3D viewer:

1. Select the type of measurement you wish to make by right-clicking within the 3D viewer and selecting **Measure**, followed by either **Distances**, **Angles** or **Torsions**
2. Geometrical measurements (intramolecular or intermolecular) can now be made by clicking on e.g., two atoms for a distance, three atoms for an angle or four atoms for a torsion angle.
3. To remove all geometrical measurements from the display right-click within the 3D viewer and select **Measure**, followed by either **Clear distances**, **Clear angles** or **Clear torsions**.

Refcode	Internal C-C-C Angles	Average Internal C-C-C Angle
BAVLOZ	Angle 1:	
	Angle 2:	
	Angle 3:	
	Angle 4:	
	Angle 5:	
	Angle 6:	
CAFROR	Angle 1:	
	Angle 2:	
	Angle 3:	
	Angle 4:	
	Angle 5:	
	Angle 6:	
CCXAPT	Angle 1:	
	Angle 2:	
	Angle 3:	
	Angle 4:	
	Angle 5:	
	Angle 6:	
CLCHTF	Angle 1:	
	Angle 2:	
	Angle 3:	
	Angle 4:	
	Angle 5:	
	Angle 6:	

Refcode	Internal C-C-C Angles	Average Internal C-C-C Angle
CYCHEX	Angle 1:	
	Angle 2:	
	Angle 3:	
	Angle 4:	
	Angle 5:	
	Angle 6:	
Average internal C-C-C angle over whole set:		

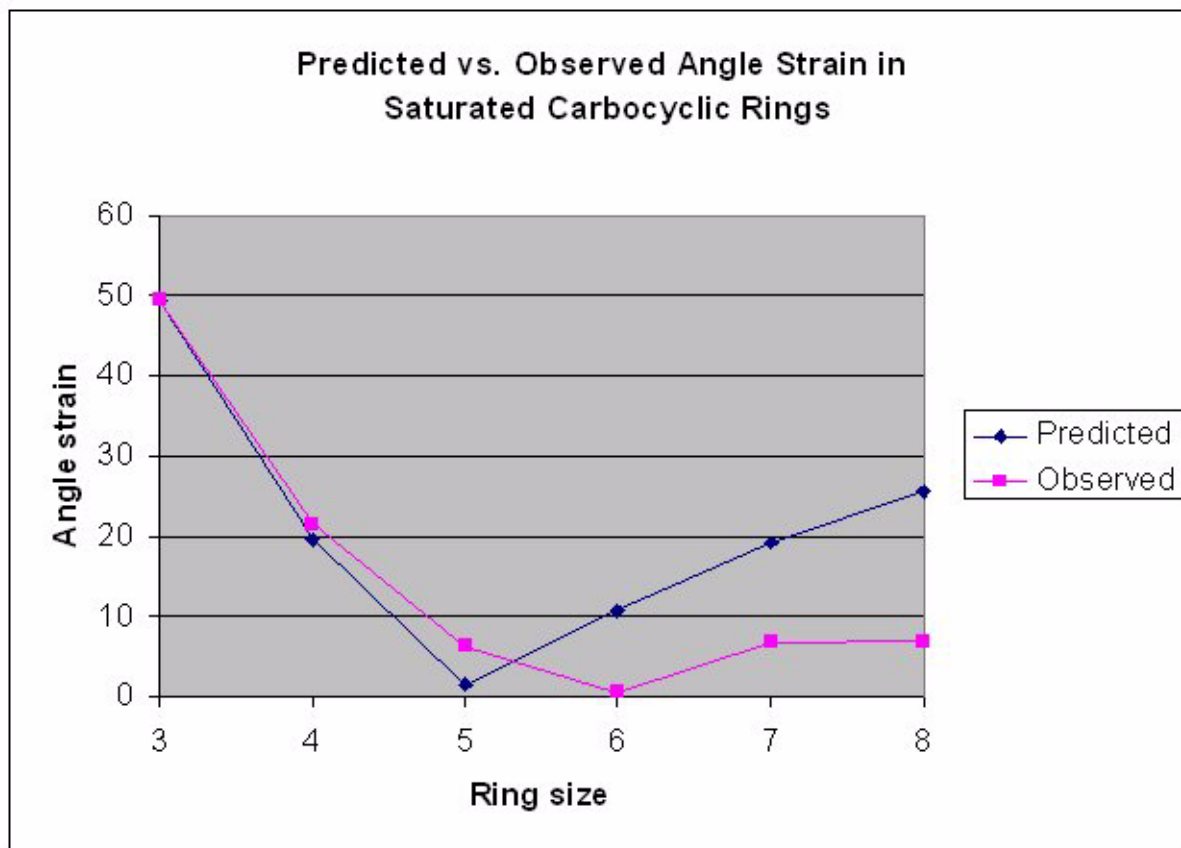
- Note: For the purpose of this task only a small number of representative structures are provided. However, if you have full access to the Cambridge Structural Database (CSD) the average internal angle can be calculated across a large number of cyclohexane fragments (see SUPPLEMENTARY MATERIAL: DETERMINING THE PREFERRED INTERNAL BOND ANGLE IN CYCLOHEXANE USING THE FULL CSD, page 45).*

1.4.3 Compare predicted angle strain against that calculated from actual compounds

- The table below shows both the predicted angle strain (in planar rings) and the angle strain calculated from actual compounds.
- Complete the table by entering the angle strain in cyclohexane calculated from actual compounds. Angle strain = average internal angle across all 5 structures - 109.5. Your answer should be close to zero.

No. Atoms in Ring	Measure of Angle Strain (internal angle - 109.5)	
	Predicted (in planar rings)	Calculated (crystal structure data)
3	49.5	49.5
4	19.5	21
5	1.5	6
6	10.5	
7	19	6.5
8	25.5	7

- Add the angle strain data calculated from actual compounds to the graph we plotted previously. This will allow us to easily compare the predicted angle strain against that observed in actual compounds.



Plot comparing predicted angle strain in planar rings against that calculated from actual compounds

- Compare the two data series. What conclusions can we draw?
- The observed angle strain is greatest in cyclopropane. Angle strain then decrease rapidly with ring size but reaches a minimum for cyclohexane, not cyclopentane (as predicted for the planar structure). Angle strain then increases again but not nearly as quickly as predicted.
- Why are six-membered rings essentially free of angle strain? and why is there some angle strain in five membered rings even though the bond angles in the planar structure are almost 109.5 degrees?
- The answer, at least to the first question, is that rings in actual compounds are not planar, they can adopt many different conformations just as easily as acyclic compounds do. To help answer the second question, let's look at some ring conformations in more detail.

1.4.4 Examine the conformation of cyclopropane

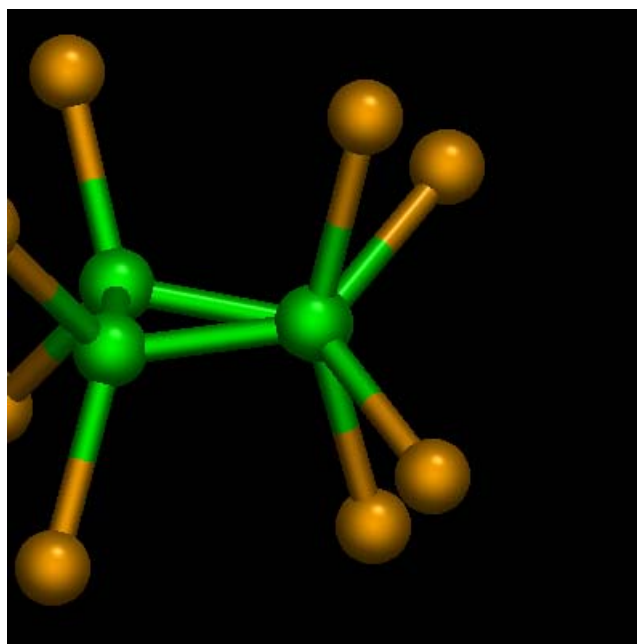
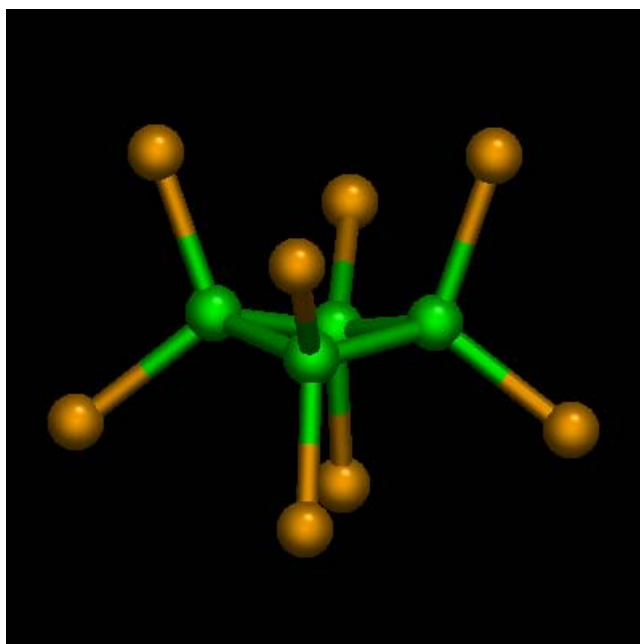
- Display the structure of cyclopropane by typing *QQQCIS01* in the **Entry** box above the structure

list on the left hand side of the WebCSD page.

- Examine the structure. The three carbon atoms of cyclopropane lie in a plane. Three membered rings must be planar since it is always possible to draw a plane through any three points.
- We know already that there is considerable angle strain in this planar molecule. This is due to the bond angles deviating from the ideal tetrahedral value of 109.5 degrees. However, there is a further cause of strain in cyclopropane. Can you identify what this is? (*hint*: it may help to view along one of the C-C bonds).
- All the C-H bonds in cyclopropane are eclipsed. This is energetically unfavourable and any rotation would lead to a more stable conformation. However, C-C bond rotation is impossible and so all the C-H bonds are forced to eclipse their neighbours. The strain resulting from eclipsed conformations is called *Pitzer* strain.

1.4.5 Examine the conformation of cyclobutane

- Display the structure of octachlorocyclobutane (refcode *CLCBUT*).
- Examine the structure. In octachlorocyclobutane the ring distorts from a planar conformation in order to reduce the eclipsing interactions, even though this increases the angle strain. Octachlorocyclobutane therefore adopts a *wing-shaped* conformation, with an angle between the C-C-C planes of about 26 degrees (measurements involving planes can be performed using the free visualiser *Mercury*).
- View along one of the C-C bonds in order to see how this deviation from planarity relieves the C-Cl eclipsing interactions.

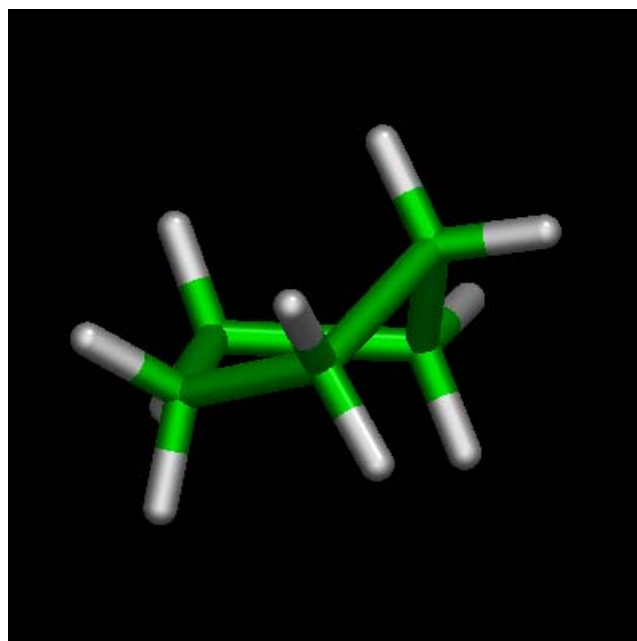
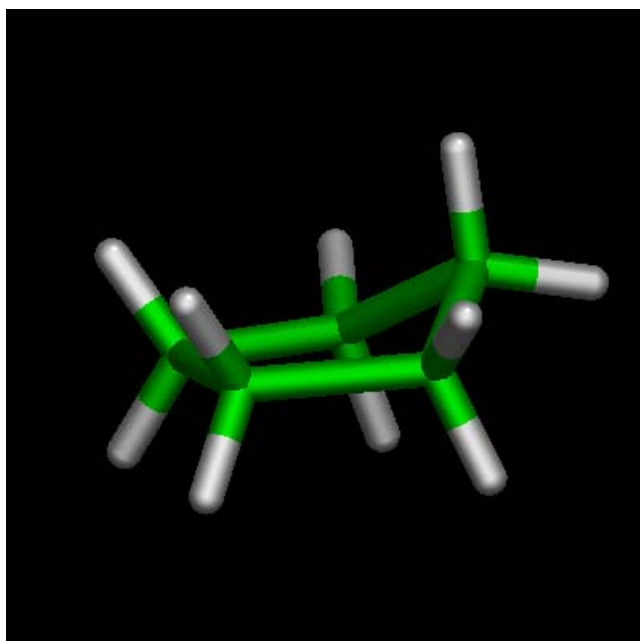


wing-shaped conformation of octachlorobutane (CLCBUT), this wing-shaped conformation relieves the C-Cl eclipsing interactions.

- By comparison, oxetane (*CIVXIO10*), in which eclipsing is less, is closer to planarity. If you have access to Mercury, then measure the distance between the two C-C-C planes in oxetane.

1.4.6 Examine the conformation of cyclopentane

- This eclipsing effect explains why there is some angle strain in five-membered rings even though the bond angles in the planar structure are almost 109.5 degrees.
- We now know that in the planar molecule there would be considerable strain caused by eclipsing of adjacent C-H bonds. Therefore the ring distorts (as in cyclobutane) to reduce these eclipsing interactions, but this increases the angle strain. Whatever happens there will always be some strain present. The minimum energy conformation adopted is therefore a balance of the two opposing types of strain.
- There are two puckered conformations of cyclopentane, the *envelope* (*IHIPOE*, *ACUHUB*) and the *half-chair* (*LISLOO*, *ABIKUR*). There is little energy difference between the two forms and many five-membered ring systems adopt conformations somewhere between the two.

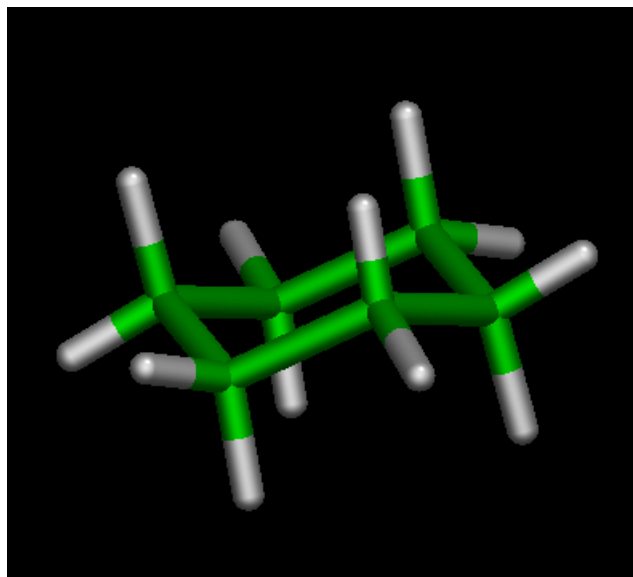
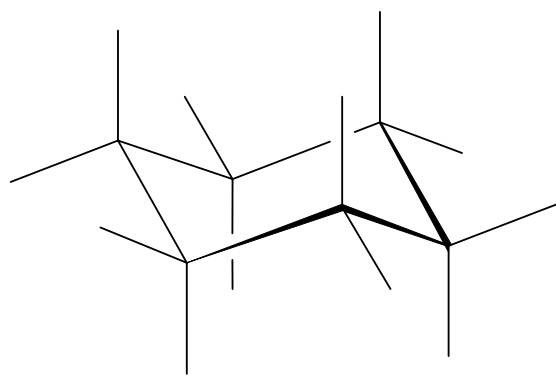


conformations of cyclopentane, left: *envelope* (*IHIPOE*); right: *half-chair* (*LISLOO*)

1.4.7 Examine the conformation of cyclohexane

- Display the structure of cyclohexane by entering the refcode *CYCHEX*.
- From our analysis of crystal structure data we have determined that six-membered rings are essentially free of angle strain. Inspect the structure of cyclohexane and explain why this is.
- Cyclohexane adopts a puckered conformation that relieves all strain. This conformation is called the *chair*.

- In the *chair* conformation of cyclohexane all bond angles are close to the ideal tetrahedral angle of 109.5 degrees. In addition, viewing along any of the C-C bonds clearly shows that there are no eclipsing C-H interactions. All bonds are fully staggered, i.e. in a *gauche* arrangement, giving the lowest possible energy. This is why cyclohexane is essentially strain-free.
- In the vast majority of compounds containing a cyclohexane ring, the molecule exist almost entirely in the *chair* form. However, other cyclohexane conformations are know.



Chair conformation of cyclohexane (CYCHEX)

1.5 SUMMARY OF KEY CONCEPTS

- Angle strain can occur in cycloalkanes due to deviation from the ideal sp^3 angle of 109.5 degrees.
- Strain can also occur when neighboring bonds are forced to be eclipsed, or partially eclipsed. The strain resulting from eclipsed conformations is called *Pitzer* (or *torsional*) strain.
- Cyclopropanes are forced to be planar and are highly strained because of both angle strain and the eclipsing of C-H bonds.
- Cyclobutanes adopt a *wing-shaped* conformation. This deviation from planarity occurs in order to relieve the eclipsing of neighboring bonds.
- Cyclopentanes are not planar even though the bond angles in the planar structure would be almost 109.5 degrees. Again, this distortion occurs in order to relieve eclipsing of adjacent C-H bonds. The minimum energy conformation adopted is therefore a balance between the two opposing types of strain.
- Cyclohexane is strain free because of its puckered *chair* conformation, in which all bond angles are close to 109.5 degrees and all neighboring C-H bonds are staggered. Cyclohexane rings are the most important of all ring sizes because of there wide occurrence.

