Determination of Position of Conformational Equilibrium of a *Trans* 1,2-disubstituted Cyclohexane by NMR


Introduction:

NMR spectroscopy is very useful in characterizing unknown compounds, but it can also be useful in determining the conformation of ring structures. Often, this is done by using the Karplus equation, which relates the H-C-C-H dihedral angle with the spin-spin coupling constant observed by NMR.

![Karplus equation](image)

\[ J = (7.76)\cos^2 \theta - (1.1)\cos \phi + 1.4 \]

This equation predicts that two axial hydrogens in a substituted cyclohexane would have a coupling constant of about 10 Hz (angle approximately 180 degrees). It also predicts that two equatorial hydrogens would have a coupling constant of about 3 Hz (angle approximately 60 degrees). This difference would allow one to distinguish between two different molecular conformations.

In this experiment, the ratio of molecules in each of these conformations will be determined. The relevant reaction is the following:
The product can take either conformation 3aa where both substituents are axial and their related hydrogens are equatorial or conformation 3ee where both substituents are equatorial and the hydrogens are axial.

An additional purpose of this experiment is to determine the effects of a relatively non-polar solvent (CDCl$_3$) as compared to a polar solvent (CD$_3$CN).

Prelaboratory Exercises:

This prelaboratory exercise should be completed with your Prelab section and turned in to your TA before starting the lab work.

1) Write a mechanism for the addition of o-nitrobenzenesulfenyl chloride to cyclohexene.

2) Use the mechanism you already described to explain why only the trans product is formed.

Cautions:

The o-nitrobenzenesulfenyl chloride is corrosive and moisture sensitive. Wear gloves when handling and do not leave out in the air for an extended period of time. Cyclohexene is a flammable liquid. Keep away from any flame.

Synthesis:

In a reaction tube, add 7.6 mg o-nitrobenzenesulfenyl chloride to 0.4 mL CDCl$_3$. In a different reaction tube, add 0.1 mL cyclohexene to 0.4 mL CDCl$_3$. To a clean, dry NMR tube, add the entire volume of the sulfenyl chloride solution and 0.4 mL of the cyclohexene solution.

Repeat the above procedure using CD$_3$CN as a solvent. Obtain the deuterated acetonitrile from the stockroom.

Shake both capped NMR tubes vigorously and allow to stand for 30 minutes.

Analysis:

Run $^1$H NMR analysis on each sample. Identify the peaks for H$_a$ and H$_b$ as shown in the introduction (They should appear at 4.1 and 3.6 ppm, respectively.). Determine the overall coupling constant, W, of each multiplet, i.e. find the change in Hz from one end of the multiplet to the other. This value is the sum of the coupling constants for each of the three adjacent protons for both H$_a$ and H$_b$. Use this information for the Final Report section.

Cleaning Up:

Both NMR tubes should be emptied into the halogenated waste containers.
Final Report:

Using the Karplus equation, calculate the theoretical coupling constant for Ha and Hb. Use the following values for dihedral angles (175˚ for axial-axial, 55˚ for axial-equatorial, and 65˚ for equatorial-equatorial). Record these values in the table below. Remember that the theoretical width of the multiplet for one hydrogen is the sum of the three individual coupling constants.

<table>
<thead>
<tr>
<th>Conformer</th>
<th>Proton</th>
<th>Neighbor</th>
<th>Dihedral angle</th>
<th>Calculated coupling constant (Hz)</th>
<th>Calculated width of the multiplet, W (Hz)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3aa</td>
<td>H_a</td>
<td>H_b</td>
<td>H-C-H (ax)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>H-C-H (eq)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3aa</td>
<td>H_b</td>
<td>H_a</td>
<td>H-C-H (ax)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>H-C-H (eq)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3ee</td>
<td>H_a</td>
<td>H_b</td>
<td>H-C-H (ax)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>H-C-H (eq)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3ee</td>
<td>H_b</td>
<td>H_a</td>
<td>H-C-H (ax)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>H-C-H (eq)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Since the flip in conformation from ax-ax to eq-eq occurs faster than the timescale of the NMR instrument, the observed W is actually a weighted average of the coupling constants in pure 3aa and 3ee. The average is shown below:

\[ W_{nmr} = x W_{ee} + (1-x) W_{aa} \]

The value x is the mole fraction of 3ee and (1-x) is the mole fraction of 3aa.

Use this equation to determine the mole fraction of each conformer for both solvents and speculate why the results may be different. (Hint: The eq-eq conformation should be more preferred in the acetonitrile than in the chloroform.)