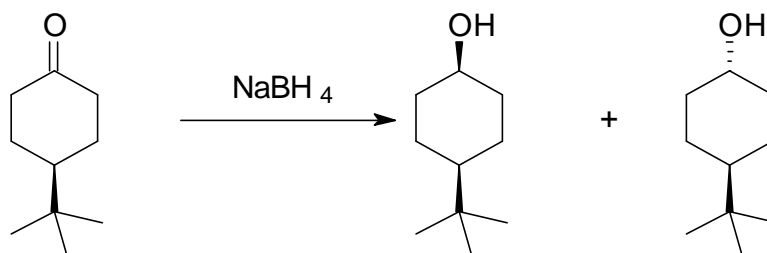


NaBH₄ Reduction of 4-*t*-Butylcyclohexanone

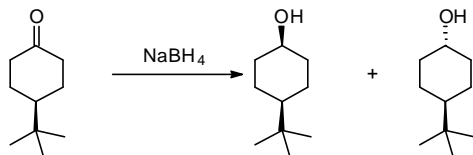


Reduction of this 4-substituted *cyclohexanone* with sodium borohydride (NaBH₄) can lead to the diastereomers, *trans*-4-*t*-butylcyclohexanol and/or *cis*-4-*t*-butylcyclohexanol. The reaction can be carried out quickly and easily and we will isolate only a crude product. Chromatography and various forms of spectroscopy can be used to analyze the product.

Experimental

Obtain approximately 1.54 g (0.01 mole) of 4-*t*-butylcyclohexanone and place it in a 50 mL Erlenmeyer flask. Use around 5-10 mL of methanol to dissolve the ketone. In a separate flask, place around 100 mg (0.1 g) of NaBH₄. Dissolve this in 5 mL of methanol and add a small amount of sodium methoxide. Pour the NaBH₄ mixture into the solution of the ketone in methanol. Swirl the reaction occasionally during the next 5 minutes.

Place some ice and about 50 mL of water in a beaker. To this add 2-3 mL of dilute HCl (10%). Pour the reaction mixture onto the ice-water-acid mixture and stir. Transfer the suspension to a separatory funnel (using some ether to complete the transfer). Extract the reduction product into ether, and separate from the aqueous layer. Dry the ether layer with anhydrous Na₂SO₄. Decant the ether from the drying agent, and evaporate the ether. Weigh the residue. Various instruments will be available for analyzing the product.

NMR Analysis of 4-*t*-Butyl-Cyclohexanols

The reduction of 4-*t*-butyl-*cyclo*-hexanone by NaBH₄ is expected to yield 2 products which are diastereomers. The reaction gives approximately a 4-5:1 mixture of the two alcohols. Chromatographic analysis does yield this information although unreacted ketone seems to have the same retention time as the *cis*- alcohol under the conditions used in the laboratory. Infrared spectroscopy can show any residual ketone (peak at ~1710 cm⁻¹). Unreacted ketone is also detected by a peak in the ¹³C NMR at ca. 212 ppm.

¹³C NMR shows that the product is a mixture because there are 10-12 observable peaks. There should be 6 peaks for each pure isomer. In particular, the signals at 65.85 δ and 71.17 δ which come from the carbon bearing the OH group in the *cis*- and *trans*-isomers, respectively, have intensities of 4 and 18 (1:4.5).

¹H NMR is particularly informative. There are two complex signals, one centered near 4.05 δ and the other near 3.5 δ. The areas under these complex signals integrate as 0.85:3.66 or 1:4.3. A detailed analysis of the coupling patterns for these hydrogens allows one to decide whether the major component is the *cis*-isomer or the *trans*-isomer.

Molecular Modeling (PCModel) can be used to produce a prediction of the most stable conformation of each isomer. From the calculated structure, one can determine the dihedral angles between the H on the carbon bearing the OH group (H1) and the H's on the adjoining carbons (H2_{ax}, H2_{eq}, H6_{ax} and H6_{eq}). From the dihedral angles, *J*-values can be predicted. In Figure 1, the predicted conformation of *trans*-4-*t*-butyl-*cyclo*-hexanol is shown. Since the OH is equatorial, H1 is axial and large coupling is expected for H1 with H2_{ax} and H6_{ax}. In fact, *J* is predicted to be 11.24 Hz for a dihedral angle of 174 degrees. H1 is also coupled to H2_{eq} and H6_{eq}. Here *J* is predicted to be

4.56 Hz for the 57° dihedral angle. Using a computer program, the partial NMR spectrum can be predicted (Figure 2). The observed partial nmr spectrum is shown in Figure 3.

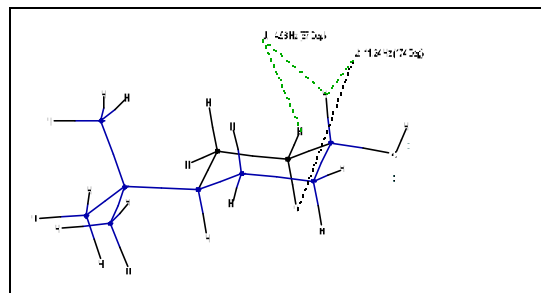


Figure 3 Conformation of *trans*-isomer from PCModel.

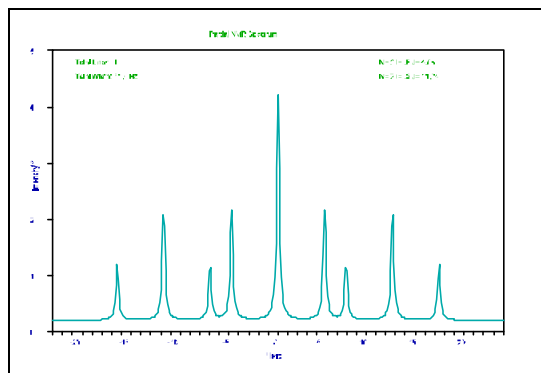


Figure 4 Predicted (partial) NMR spectrum of *trans*-isomer.

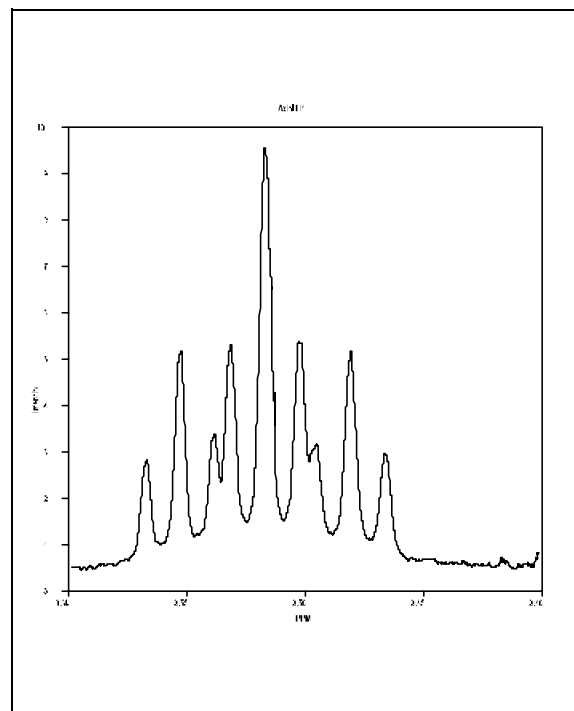


Figure 2 Experimental NMR Spectrum of *trans*-isomer.

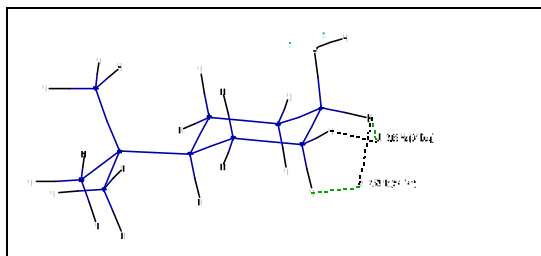


Figure 4 Conformation of *cis*-isomer from PCModel.

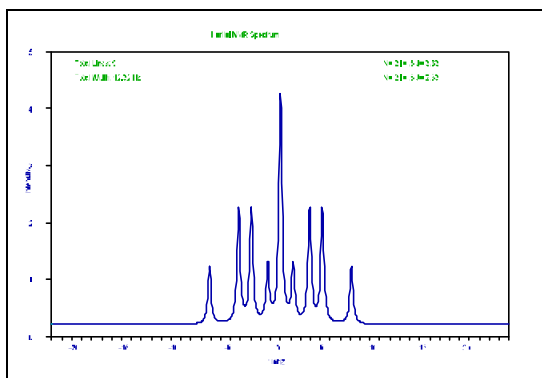


Figure 5 Predicted (partial) NMR spectrum of *cis*-isomer.

Figure 4 shows the predicted conformation of the *cis*-4-*t*-butylcyclohexanol with the H1 proton in the equatorial position. The predicted coupling constants (*J* values) are 3.63 Hz for the 61° dihedral angle between H1 and H2_{eq} or H6_{eq} and 2.53 Hz (54° dihedral angle for H1 and H2_{ax} or H6_{ax}). The calculated partial ¹H NMR spectrum is shown in Figure 5 with the experimentally determined spectrum in Figure 6.

At first glance, the calculated spectrum for the *cis*- and *trans*-isomers may look somewhat similar. On closer inspection note that the total width of the signal pattern for the *trans*-isomer is more than 30 Hz while it is around 16 Hz for the *cis*-isomer. Experimentally, the NMR instrument does not show all the separated peaks that come from the calculation. The peaks are actually too close together to be seen as separate peaks in the measured spectrum. Specifically, counting from left to right, the second and third peaks run together, the 4th, 5th and 6th peaks run together as do the 7th and 8th. In fact, there is little separation (on the scale used for the measurement) between peak #1, peaks 2-3, peaks 4-5-6, peaks 7-8 and peak #9. What we can clearly see is that the *trans*-isomer is

predicted to have a broad signal with a clearly defined *triplet of triplets* which it does have while the *cis*-isomer is predicted to have a much narrower signal, approaching a 5-line pattern.

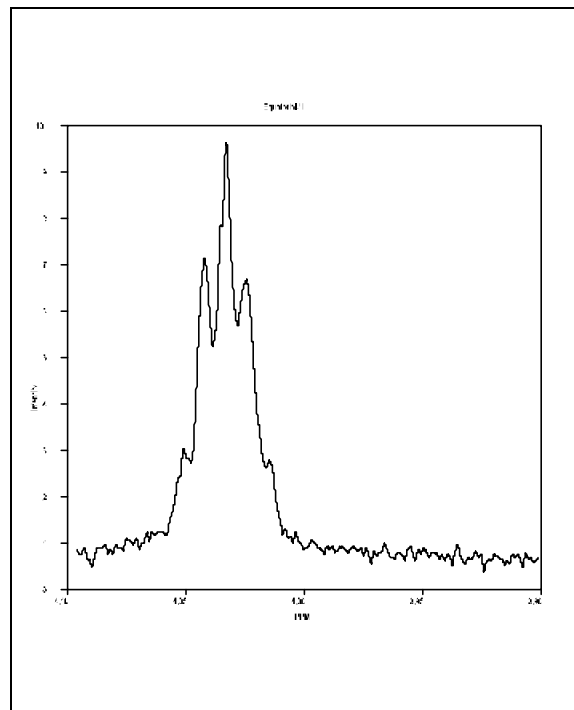


Figure 6 Experimental NMR Spectrum of *cis*-isomer.