EXPERIMENT 5
OXIDATION REDUCTION REACTIONS IN ORGANIC CHEMISTRY: THE INTERCONVERSION OF 4-tert-BUTYLCYCLOHEXANOL AND 4-tert-BUTYLCYCLOHEXANONE

OUTLINE AND GOALS OF THE PROJECT:

This is a 4 week project that will evaluate the stereochemistry of the oxidation-reduction interconversion of 4-tert-butylcyclohexanol and 4-tert-butylcyclohexanone. Week 1 you will oxidize the commercially available 4-tert-butylcyclohexanol, which is mixture of the siC and trans stereoisomers. Week 2 you will use sodium borohydride to reduce the ketone you made week 1. Weeks 3 and 4 you will use IR and NMR spectroscopy to evaluate the outcome of both reactions and determine and compare the diastereomeric ratios of the 4-tert-butylcyclohexanol you started with and the one you obtained after the oxidation reduction sequence.

OXIDATION

In this experiment, we will explore the oxidation of a secondary alcohol to a ketone using an oxidizing reagent, sodium hypochlorite, which is a readily available and commonly used household cleaning product. We will use thin layer chromatographic (TLC) technique to monitor the progress of oxidation reaction.

Sodium hypochlorite solutions (approximately 2 M) sold as liquid bleach are often described as having 11.5-12.5% available chlorine. The term “available chlorine” compares the oxidizing capacity of the solution relative to that of the same weight of chlorine, Cl₂. Sodium hypochlorite solutions are used extensively in swimming pool sanitation, and as bleach in the pulp and textile industries. A less-concentrated product (5% available chlorine) is used in laundry and as household bleach. It is reported that 210,000 tons of sodium hypochlorite were consumed in the United States in 1982. The reaction described in this experiment illustrates the use of liquid bleach as an oxidizing agent in the organic laboratory.

Sodium hypochlorite is prepared commercially by passing chlorine gas through a solution of aqueous sodium hydroxide (eq 1). In acidic condition, a rapid equilibrium is established between hypochlorite anion and hypochlorous acid (HOCl) which produces the Cl⁺ ion (eq 2).

\[
\text{Cl}_2 + \text{NaOH} \rightarrow \text{NaOCl} + \text{NaCl} \quad \text{(eq 1)}
\]
The actual oxidizing agent in the present experiment is believed to be $[\text{Cl}]^+$ which is reduced in the reaction to chloride ion ($\text{Cl}^-$). The alcohol acts as a reducing agent, and thus becomes oxidized to a ketone. The most likely operating mechanism is shown below.

This oxidation procedure is more efficient than the chromic acid-amberlite procedure, which is a heterogeneous solid-liquid reaction that proceeds poorly due to the requirement of very efficient agitation.

**REDUCTION**

In this experiment, we will explore the reduction of a ketone using sodium borohydride ($\text{NaBH}_4$) a mild reducing reagent. We will use TLC to monitor the progress of the reaction.

Sodium borohydride is a reagent commonly used for the reduction of ketones and aldehydes. Other reducing reagents such as lithium aluminum hydroxide react violently with water and alcohols to produce hydrogen gas while $\text{NaBH}_4$ reactions are commonly run in methanol or ethanol as solvent as $\text{NaBH}_4$ is significantly less basic and the acid base reaction is much slower. The mechanism of the reduction of 4-tert-butylcyclohexanone is shown below:
STEREOCHEMICAL CONSIDERATIONS

Tert-butylcyclohexane has two conformations: one where the tert-butyl group is equatorial and the other where it is axial. Most substituted cyclohexane rings will rapidly interconvert between the two conformations so at any given time the solution will be a mixture of both conformers. When the substituent is small like in the case of deuterium the two conformers are almost equal in energy so it is practically a 50:50 mixtures of the axial and equatorial conformers. The bigger the substituent, however, the more high energy the axial conformer becomes and therefore the ratio of equatorial to axial increases. When the substituent is a tert-butyl group the axial conformer has severe steric interactions that make it very high energy and therefore very unfavorable. In the case of tert-butylcyclohexane, the axial conformation is practically not observed and the cyclohexane ring is “locked” into a single conformation with the tert-butyl group equatorial.

Analogous, 4-tert-butylcyclohexanone is locked in the conformation with the tert-butyl group equatorial and thus the two faces of the carbonyl group become non-equivalent. This means that when the hydride source (from sodium borohydride) attacks the ketone it will result in the formation of two different diastereomers of product, depending on which face of the carbonyl it attacks. Also, since the two faces of the molecule will be different, the less sterically hindered one will presumably be the one that gets attacked more often. Therefore one can expect to see stereoselectivity in the reduction, meaning one diastereomers will be more prevalent than the other.
SPECTROSCOPY

Weeks 3 and 4 of the project we will use IR and NMR spectroscopy to analyze your products. The literature IR spectra are shown below. You will compare yours to the ones below to determine how successful your reactions were and that you have indeed made the correct compounds.

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<th>HIT-NO-1137</th>
<th>SCORE: 1</th>
<th>SUBS-NO-818</th>
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<td>4-TERT-BUTYLCYCLOHEXANONE</td>
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<tr>
<td>C_{10}H_{12}O</td>
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![IR Spectrum of 4-TERT-BUTYLCYCLOHEXANONE](image1)

<table>
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<tr>
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</tbody>
</table>

![IR Spectrum of 4-TERT-BUTYLCYCLOHEXANOL](image2)
You will also obtain an NMR spectrum of the 4-tert-butylcyclohexanol that you obtained after the reduction. The proton spectrum will give you information about the ratio between the cis and trans diastereomers. In the trans isomer, the methine proton on the carbon that is bound to the hydroxyl group (the one in blue) appears around 3.5 ppm. In the cis isomer that proton is equatorial and therefore shifted slightly downfield to 4.03 ppm.

You can easily calculate the cis:trans diastereomers ratio by using the integration on your $^1$H NMR spectrum.

$$\% \text{ cis isomer} = \frac{\text{area of 4.03 ppm signal}}{\text{area of 4.03 ppm + area of 3.5 ppm signals}} \times 100$$

You will then compare the % cis in the commercial sample of 4-tert-butylcyclohexanol to that in the product of your reduction. This way you will be able to determine whether sodium borohydride preferentially attacks one side of the ketone, and if so, which one it is.