

Chemistry 212 Laboratory

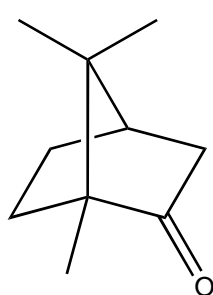
Preparation and Stereochemistry of Bicyclic Alcohols

Pre-lab Question:

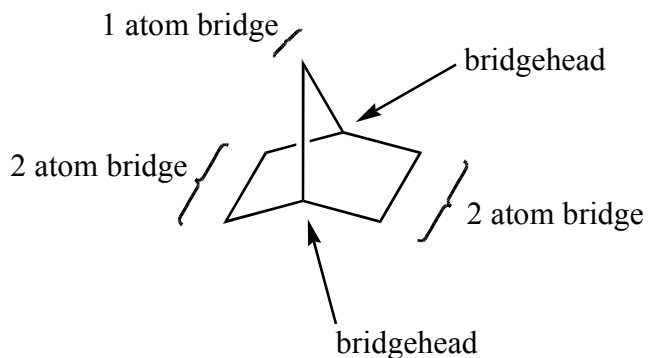
1. Draw the mechanism for each of the following reactions:
(1) Camphor \rightarrow Isoborneol
(2) Camphor \rightarrow Borneol
Predict which mechanism will be really occurring in this experiment.
2. In the lab you will be asked to build a model of camphor and a model of norcamphor. Be prepared.

Reactions and interconversions of compounds in the monoterpene series have been of great importance in studying the mechanism of carbocation rearrangements and the stereoselectivity of various reagents and synthetic reactions. Typical monoterpenes are the ketone camphor and the corresponding epimeric alcohols borneol and isoborneol.

In this experiment, you will reduce camphor, a naturally occurring ketone, using sodium borohydride. Camphor is an example of a bridged bicyclic molecule: a molecule with multiple rings that share non-adjacent atoms called bridgeheads. Camphor is a substituted bicyclo[2.2.1]heptane. The enclosed numbers represent the size of the "bridges" that are attached to the bridgeheads. The parent name is determined by adding the total number of carbons in the rings.



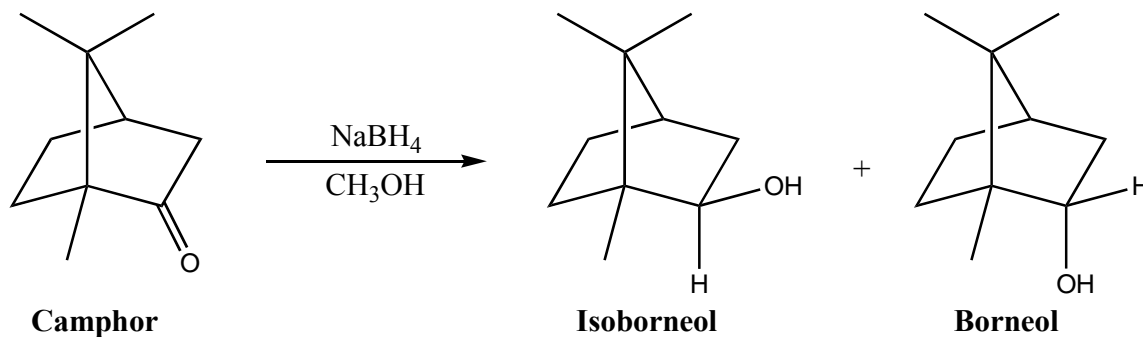
Camphor



There are many reagents that are useful for the reduction of various carbonyl compounds. The complex hydrides NaBH_4 and LiAlH_4 are among the most useful reagents available for the conversion of carbonyl compounds to alcohols. Sodium borohydride is the less reactive of the two; for example, esters and acids are not affected. Sodium borohydride is very convenient to use, since reactions can be carried out in aqueous or alcoholic solutions. The reduction of bicyclic ketones such as camphor and

norcamphor with these hydrides is quite stereoselective, with one of the two diastereomeric alcohols being formed in over nine times the amount of the other.

During the reduction of camphor, the reducing agent can approach the carbonyl face with a one carbon bridge (termed exo attack) or the face with a two carbon bridge (termed endo). The two product stereoisomers are called borneol (from exo attack) and isoborneol (from endo attack). The percentage of each of the isomeric alcohols in the mixture can be determined by gas chromatography (GC) analysis. IR analysis, unfortunately, does not allow this.



In rigid cyclic compounds such as camphor and norcamphor, the stereochemistry of the reaction is controlled by the shielding of one side of the carbonyl group from attack by the reagent. In camphor, the methyl groups on the one-carbon bridge screen the approach of the hydride from the “top” or exo side of the two-carbon bridge, and the hydrogen atom is added to the endo side, giving the exo alcohol isoborneol. Later on the lab report, you will be asked to predict the major isomeric alcohol formed by the hydride reduction of norcamphor.

Safety:

- METHANOL is toxic to the optic nerve.
- SODIUM BOROHYDRIDE (NaBH_4) is a flammable solid. It is especially dangerous when wet. (Its reacting with water will produce NaOH and H_2 .)

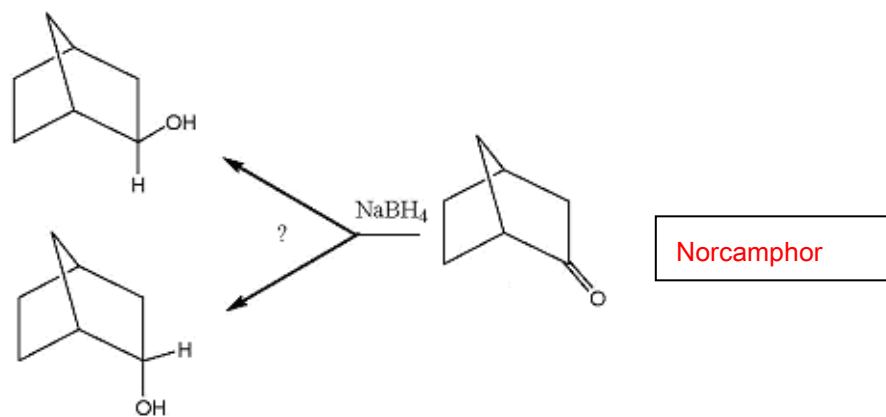
Procedure:

1. In a 5 mL conical vial with a spin vane, dissolve 100 mg of camphor in 1 mL of methanol.
2. Weigh out 100 mg of NaBH_4 , and add this in four portions to the camphor solution over the course of five minutes, stirring the reaction mixture during the addition.
3. Attach an air condenser and gently reflux the mixture for 5 min.
4. After cooling the reaction mixture to room temperature, carefully add 3.5 mL of ice-cold water.

5. Collect the crude product by vacuum filtration. Allow the vacuum to pull for about 10 minutes to dry the solid.
6. Dissolve the solid in 4 mL of dichloromethane and dry the solution over Na_2SO_4 .
7. Transfer the solution to a small E. flask. Remember to rinse the drying agent and the original container with a small amount of dichloromethane and also filter this into the beaker.
8. Gently evaporate the solvent on a hot plate under the hood.
Note: Watch the progress of evaporation carefully and as soon as a solid appears, remove the flask from the heat source immediately; otherwise the product may sublime and be lost. Lay the warm flask on its side under the hood and roll around to allow the solvent vapors to escape.
9. Determine the weight of the dry solid.
10. Determine the melting point by adding a small amount of your sample to a melting point capillary tube and sealing the top with parafilm.
11. Obtain an IR spectrum of your product.
12. Determine the percentage of each of the isomeric alcohols in the mixture by Gas Chromatography (GC) analysis.

For your report:

1. Calculate the percent yield of your product (or the product mixture).
2. Analyze the melting point and IR.
3. Include the chromatographic data with GC analysis parameters attached. Note the presence of any unreduced starting material in the product and tell how you determined this.
4. Calculate the percent composition of your product (i.e. percentage of each of the isomeric alcohols in the mixture).
5. Discuss why, according to the prediction, the major product of this reduction is isoborneol and not borneol.
6. Based on your results, identify the product as either the endo or exo product. Determine whether the hydride added by exo- or endo- attack to the carbonyl group. Did your result satisfy predictions made on the basis of the stereochemistry of camphor? Explain.
7. Questions to answer:
 - a. This reduction reaction has planar component (ketone), yet is stereoselective. Normally planar substances have no stereoselectivity. What causes the stereoselectivity in this reaction?
 - b. Predict the major isomeric alcohol formed by the hydride reduction of norcamphor (see below). Explain why.



- c. *Borneol* and *isborneol* are diastereomers. Starting from *borneol*, provide a multi-step synthesis that would form *isborneol*.