Reduction of Camphor to Borneol using Sodium Borohydride

Introduction:

Camphor and its reduction products, borneol and isoborneol, come from a bicyclic family called terpenes.[1] Terpenes are hydrocarbon terpenoids that contain double bonds. To further classify, camphor is a monoterpene, a 10-carbon compound derived from two isoprene units.[2] The properties of camphor have been used in embalming fluid to preserve and prevent decomposition of cadavers and for medicinal purposes such as relieving pain, itching or swelling caused by irritations, treating fungal infection of the toenail, warts, hemorrhoids, minor burns etc. Other uses would be used as an antimicrobial, essential oils, and insect repellents.[3] As for borneol, its properties have been used to help the digestive system, improve circulation, treat bronchitis, coughs and colds, reducing pain, swelling, and stress, etc. Also, has been used as an insect repellent.

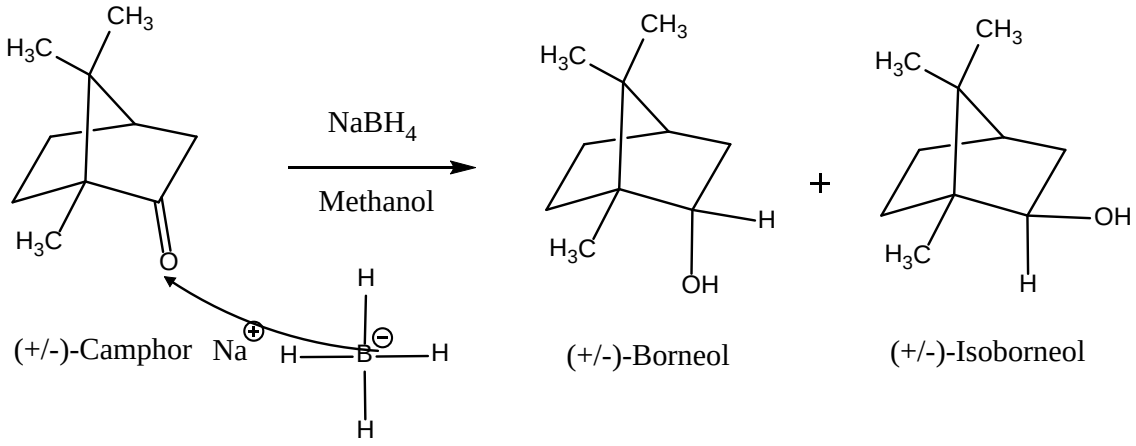
Oxidation-reduction reactions, also referred to as redox reactions, are important in organic chemistry because the utility of the reaction occurs in everyday processes such as rust, generating energy from natural resources, reactions occurring in living organisms, etc. Also, the oxidation reaction of an alcohol to an aldehyde and ketone and the reduction of aldehyde and ketone back to an alcohol is a very common reaction in organic chemistry.[4]

Alcohols are formed from the reduction of carbonyl compounds. Popular reducing agents used in organic chemistry are lithium aluminum hydride ($LiAlH_4$), diisobutylaluminum hydride (DIBAL), and sodium borohydride ($NaBH_4$). Comparing lithium aluminum hydride and sodium borohydride, $LiAlH_4$ is more reactive than $NaBH_4$. $LiAlH_4$ is able to reduce aldehydes, ketones, carboxylic acids and its derivatives, and nitriles. $NaBH_4$ is only capable of reducing aldehydes and ketones. In this experiment, the reducing agent used is $NaBH_4$.

The reduction of camphor using the reducing agent sodium borohydride resulted in the formation of two isomers, borneol and isoborneol, as shown in Scheme 1: Reduction of Camphor. In a methanol solvent, the sodium borohyride attacks the bottom side, the less sterically hindered side, of the camphor

structure to reduce the carbonyl and with the addition of water forms an alcohol group. Out of the two isomers formed, one is termed the endo-product and the other is termed the exo-product. Borneol is the endo-product meaning the dimethyl group is above the plane of the ring while the hydroxyl group is below the plane. As for isoborneol it is the exo-product meaning the dimethyl group and the hydroxyl group are both above the plane of the ring.[5]

The isomer that should form in the greater amount should be isoborneol because stereochemically isoborneol is less sterically hindered than borneol. Borneol is sterically hindered because for the reaction to occur the reducing agent would need to attack from the topside, but the dimethyl groups is hindering the top. Therefore, in order for borneol to be formed there would need to be an additional step taken. On the other hand, for isoborneol to form the reducing agent would need to attack the bottom side where it is less sterically hindered making it easier for the reducing agent to attack without requiring any other additions steps.



Scheme 1: Reduction of Camphor

The purpose of this experiment was to reduce camphor using the reducing agent sodium borohydride to form isoborneol as the major isomer and borneol as the minor isomer. An IR, 60 MHz ^{1}HNMR, GC, and GC-MS were ran to confirm the structure of the product formed.

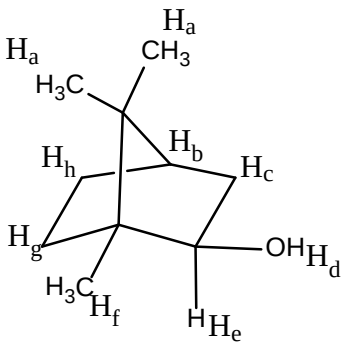
Experimental:

Isoborneol/Borneol. Added methanol (10.0 mL) and camphor (0.202 g, 1.32 mmol) into round-bottom flask and stirred. Cautiously and intermittently added sodium borohydride (0.121 g, 3.20 mmol) into the solution. Refluxed and heated solution via sand bath for 30 minutes. Upon completion, allowed to cool and then poured slowly into ice water (25 mL). Isolated solid via vacuum filtration (0.05 g, 0.324 mmol) and allowed to dry. IR (FTR) y_{max} (cm^{-1}) 3389.8, 2945.8, 2875.5; ^{1}H NMR (60 MHz, $CDCl_3$,): **δ** (ppm) 0.822-1.020 (m, 9H), 1.530-1.753 (m, 4H), 2.040 (s, 1H); GC (Isoborneol/Borneol, 40°C to 150°C at 10°C per min) RT 12.208 min; GC-MS (Isoborneol/Borneol, 40°C to 150°C at 10°C per min) RT 13.19 min, 95.06 m/z, RT 13.34 min, m/z 95.04.

Results and Discussion:

In this experiment, camphor was reduced to form two isomers, borneol and isoborneol, using the reducing agent sodium borohydride. This reaction helps understand the importance and utility of oxidation-reduction reactions. The reduction reaction reduces camphor into borneol, while the oxidation of borneol will yield back camphor.

From the results, the percent yield for isoborneol was about 46.1%. After purification by recrystallization the percent recovery came out to be about 53.2%. The percent yield is relatively low because of the two isomers that were formed from the reduction reaction. From the GC, the percent composition was 100% of isoborneol. However, analyzing the GC-MS there was a percent composition of about 85% isoborneol and 15% borneol. According to literature values for GC-MS, the reduced products came out to be 84% isoborneol and 16% borneol along with some presence of camphor.[1] To confirm whether or not the product formed an IR, 60 MHz ^{1}HNMR, GC, and GC-MS were ran to analyze the structure (Figure 1, Structure of Isoborneol).



(+/-)-Isoborneol

Figure 1: Structure of Isoborneol

From the IR analysis (Figure 2, Supplemental Information), there are two main peaks of interest; one at 3389.8 cm^{-1} that confirms the presence of a hydroxyl, this peak is the most important peak because it shows that carbonyl group reduced to an alcohol group and can confirm the structure of the product formed. The second peak of interest came at 2875.5-2945.8 cm^{-1}, which indicates a C-H stretch. There is a peak at 1735.7 cm^{-1} that indicates that there is a presence of a carbonyl group meaning that there is some starting material left in the product.

From the 60 MHz ^{1}HNMR (Figure 3, Supplemental Information), there are three main peaks of interest. The first peak of interest is a multiplet at 0.822-1.020 ppm ($H_{a, f}$) that indicates the presence of nine hydrogen protons coming from the tri-methyl groups. The second peak of interest is also a multiplet at 1.530-1.753 ppm ($H_{b, c, e, g, h}$) that should indicate 8 hydrogen protons coming off the ring. However, since only a 60 MHz ^{1}HNMR was ran not all of the hydrogen protons can be seen from the analysis because of the structure of the product and the formation of isomers. The third peak of interest is the most important peak, a singlet at 3.579 ppm (H_d) that indicates the presence of a hydroxyl group that confirms that product formed from the reduction reaction. There is also an impurity peak at 2.040 ppm and the solvent used $CDCl_3$ is indicated at 7.261 ppm.

A GC and GC-MS were ran to analyze the two isomers that were formed from the reduction of camphor. From the GC (Figure 4, Supplemental Information), there were two retention peaks that formed, the first peak did not have a retention time, but the second peak that formed had a retention peak

at 12.208 min with a percent composition of 100%. Analyzing the GC-MS (Figure 5, Supplemental Information) there are two peaks, one that formed at 13.19 min and another that formed at 13.34 min. The first peak that formed was at 13.19 min that indicated the formation of isoborneol with a percent composition of 84.8% according to the comparison of the GC-MS data and the library GC-MS data and the second peak that formed was at 13.34 min indicated the formation of borneol with a percent composition of 15.1% according to the comparison of the GC-MS data and the library GC-MS data.

In conclusion, the reduction of camphor was a success and the data analysis confirms the structure of the products formed with a percent recovery of 53.2% with a percent composition of 85% isoborneol and 15% borneol. The product wasn't completely pure; according to the IR there is a presence of a carbonyl group indicating that there is still starting material in the product. A possible source of error is the reduction not going to completion. Further improvements that can be made for future experiments would be monitoring the reflux of the reaction solution by TLC or another technique to observe whether or not the reduction of camphor has gone to completion.

Reference:

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3. Zuccarini, Paolo. "Camphor: Risk and Benefits of a Widely Used Natural Product." *J. Appl. Sci. Mang*. **2009**, *13(2)*, 69-74.

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5. Singh, G.; "Chemistry of Terpenoids and Carotenoids." Discovery Publ. House; New Delhi, **2007**; pp 63-64.

Supplemental Information:

Figure 1: Structure of Isoborneol

Figure 2: IR of Isoborneol/borneol

Figure 3: ^{1}HNMR of Isoborneol/borneol

Figure 4: GC of Isoborneol/borneol

Figure 5: GC-MS of Isoborneol/borneol