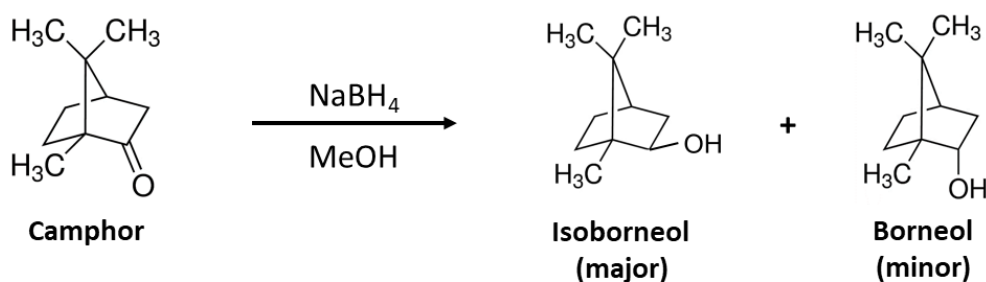


Elevating an Undergraduate Lab with Green Chemistry Principles: Reduction of Camphor

The awareness and implementation of Green Chemistry practice has been on the rise within the last few decades in the chemistry community in contribution to the global sustainability movement¹. Institutions and organizations have started the adaptation of Green Chemistry principles to their day-to-day practice with the intention of eliminating intrinsic hazard itself, rather than focusing on reducing risk by minimizing exposure. The Principles of Green Chemistry comprise of a set of practices and emerging research². They are 1) *Prevent waste*; 2) *Maximize atom economy*; 3) *Design less hazardous chemical syntheses*; 4) *Design safer chemicals and products*; 5) *Use safer solvents and reaction conditions*; 6) *Increase energy efficiency*; 7) *Use renewable feedstocks*; 8) *Avoid chemical derivatives*; 9) *Use catalyst, not stoichiometric reagents*; 10) *Design chemicals and products to degrade after use*; 11) *Analyze in real time to reduce pollution*; 12) *Minimize the potential for accidents*³. In this blog post, we will discuss how the use of the Spinsolve benchtop NMR spectrometer can incorporate the principles of Green Chemistry into undergraduate organic chemistry laboratory.

The transformation between camphor and isborneol/borneol is a well-utilized experiment in undergraduate organic chemistry laboratory. The lab may involve a reduction of camphor to isborneol/borneol mixture using a reducing agent (i.e. NaBH₄), or an oxidation of isborneol/borneol using greener reagents such as bleach or oxone⁴. After the isolation and purification of products, students are often instructed to analyze their isolated products with analytical techniques which include melting point determination, IR spectroscopy, GC or GC-MS, and NMR.



Scheme 1. Reduction reaction of camphor to form isborneol and borneol

Experimental Set-up

The procedure of the reduction of camphor often involves the addition of NaBH₄ to a solution of camphor in methanol. The reaction mixture is stirred for 30 minutes, then water is added to this solution, which results in the precipitation of the products. This reaction produces a mixture of isborneol and borneol products from the two different approaches in which NaBH₄ can interact with camphor (**Scheme 1**). The product mixture can be isolated through filtration and might be further cleaned up to remove the residual water. The product mixture is then analyzed through different analytical techniques, most often melting point determination and IR spectroscopy.

NMR Data & Discussion

While the data obtained from melting point analysis and IR can confirm the presence of isoborneol and borneol, they cannot determine the diastereomeric ratio between isoborneol and borneol in the product mixture without the physical separation and purification of each isomer. Gas chromatography (GC) can be used to separate the two isomers and analyze the diastereomeric ratio. However, GC requires the use of carrier gases with longer measurement time which increases the waste production of the lab overall. NMR analysis of the product mixture with benchtop NMR spectrometers allows for the structural verification of isoborneol and borneol, as well as their diastereomeric ratio with short measurement time. Benchtop NMR spectrometers do not require liquid cryogenics, or carrier gas; therefore, it reduces the waste generated from analytical instrumentations during the lab (*Principle 1 of Green Chemistry*).

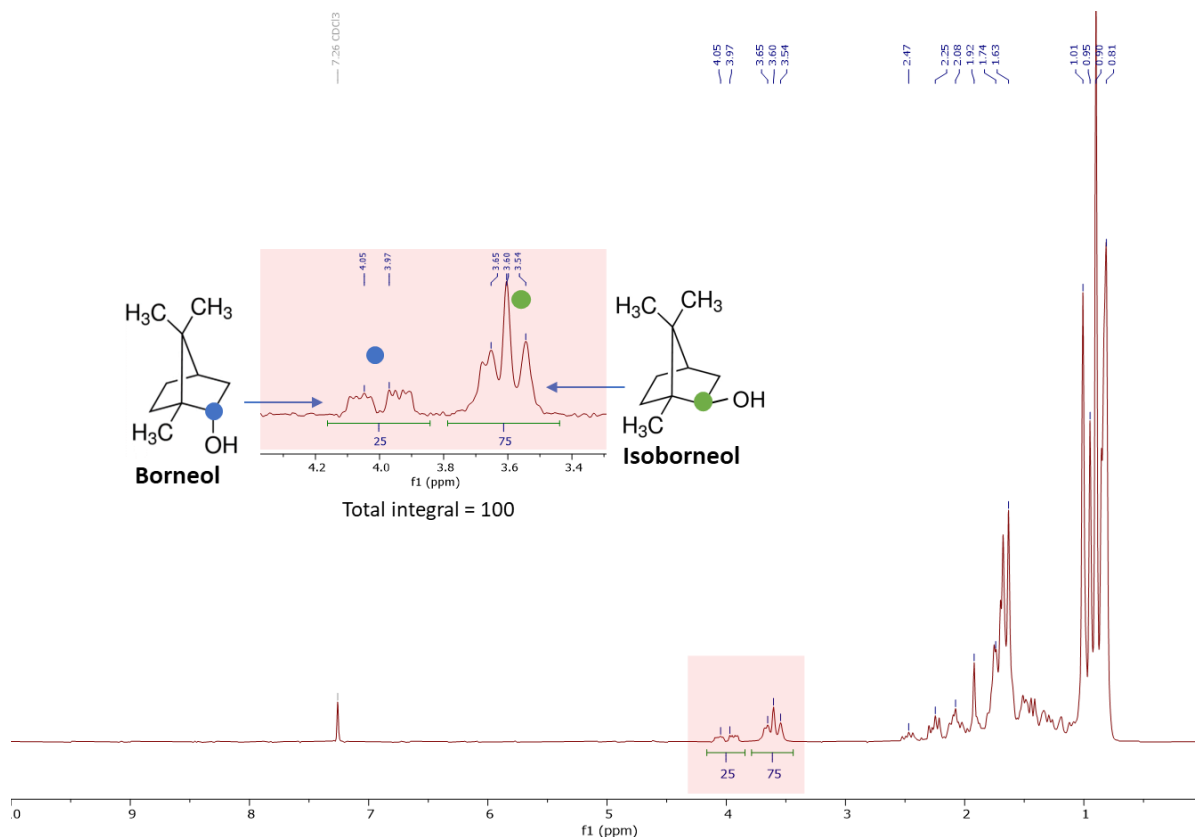


Figure 1. 1D ^1H spectrum of isoborneol-borneol mixture in CDCl_3 (concentration: 30 mg/mL; measurement time: 1 minute).

Figure 1 presents the 1D ^1H spectrum of the isolated product mixture from the camphor reduction reaction in CDCl_3 , collected on Spinsolve 80 Carbon ULTRA. The structure of both isomers can be verified through the analysis of the NMR signals. The diagnostic signal for isoborneol can be observed as a multiplet at 3.6 ppm; whereas the signal for borneol can be observed as another multiplet at 4.0 ppm. Since each signal corresponds to 1 proton, when the total integral is normalized to 100, the integral for each signal reflects the percentage of each product in the mixture. For this product mixture, the diastereomeric ratio of isoborneol:borneol can be determined to be 75:25.

The Spinsolve Benchtop NMR spectrometer, with the superior lineshape of the ULTRA model, can analyze samples in protonated solvent with the effective implementation of WET solvent suppression technique. For the reduction of camphor lab, students can simply transfer an aliquot (0.5 mL) of the reaction mixture in methanol to an NMR tube at the end of the 30-minute period reaction time. This can eliminate the work-up procedure, which cuts down on waste generated (*Principle 1 of Green Chemistry*), use safer solvents (*Principle 5 of Green Chemistry*), and allow the analysis to happen in real time to prevent pollution (*Principle 11 of Green Chemistry*). The reaction aliquot can be analyzed directly using NMR with WET solvent suppression. The 1D ^1H spectra of the reaction mixture acquired with and without solvent

suppression are shown in **Figure 2**. In the ^1H spectrum collected without solvent suppression (red trace), the diagnostic signal for isborneol can be observed heavily overlapped with the methanol signal. The diagnostic signal for borneol, even though is well separated from the methanol signal, also experiences an elevated baseline due to the tail of the methanol peak. This affects the calculation of diastereomeric ratio of the products. The 1D ^1H spectrum (with ^{13}C decoupling) collected with WET solvent suppression shows a clear resolution of the isborneol signal at 3.25 ppm from the residual methanol signal at 3.09 ppm. Even though the chemical shift separation between these two signals is 0.16 ppm (or 12.8 Hz at 80 MHz field strength), the calculated diastereomeric ratio of the two product remains the same as 75:25 (isborneol:borneol). This efficient implementation of WET solvent suppression with high selectivity on the Spinsolve ULTRA spectrometers allows for the accurate and quantitative analysis of mixtures in protonated solvents.

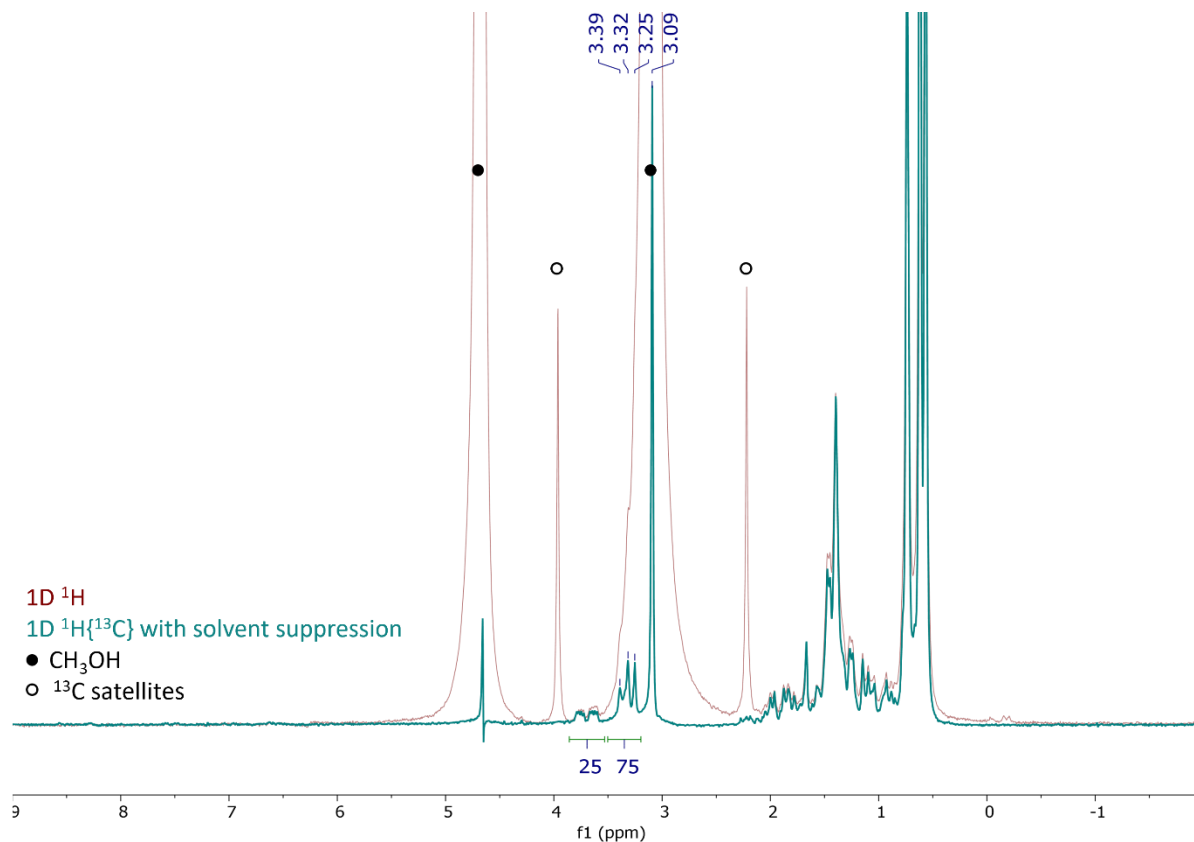


Figure 2. 1D ^1H spectrum (with ^{13}C decoupling) of isborneol-borneol mixture in protonated methanol collected without solvent suppression (red trace) and with solvent suppression (cyan trace). (concentration: 30 mg/mL; measurement time: 1 minute)

Conclusions

As highlighted in this blog post, the Spinsolve spectrometer can be easily incorporated in undergraduate organic lab exercises. With the rising awareness and practice of Green Chemistry, the Spinsolve enables the implementation of different green chemistry principles to the existing labs with the capability to work with protonated solvents to reduce waste and enable real-time data analysis of the reaction process. This will help the students to have a good understanding of green chemistry implementation, along with gaining practical experience for their professional careers after graduation.

References

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