

Experiment 13

Oxidation of Alcohols: Oxidation of Borneol to Camphor

Reading: Handbook for Organic Chemistry Lab, sections on Extraction (Chapter 8), Drying Organic Solutions (Chapter 11), and Solvent Removal (Chapter 15). Organic Chemistry by Marc Loudon, 6th ed., pp. 476-485 (10.6-10.7).

Compounds containing the ketone or aldehyde functional group are important in organic chemistry. They are common in nature and are often key intermediates in organic synthesis. Despite numerous methods for preparation, the single most important method for preparation of both ketones and aldehydes is the oxidation of alcohols. Alcohols are among the most readily available organic compounds, and therefore, this method for preparation of aldehydes and ketones is extremely useful.

Primary and secondary alcohols are oxidized to the corresponding aldehydes and ketones by various oxidizing agents, a few of which are listed in the table below. Aldehydes derived from primary alcohols can be further oxidized to carboxylic acids by some of these oxidizing agents (including HOCl), while the ketones derived from secondary alcohols are stable to further oxidation.

<i>Common Oxidants</i>	<i>Chemical Formula</i>	<i>Notes</i>
Chromic acid	H ₂ CrO ₄	Carcinogenic, very toxic, corrosive
Sodium dichromate	Na ₂ Cr ₂ O ₇	Carcinogenic, very toxic, corrosive
Potassium permanganate	KMnO ₄	Harmful, environmental risk
Nitric acid	HNO ₃	Toxic, highly corrosive
<i>tert</i> -Butyl hypochlorite	(CH ₃) ₃ COCl	Moderately expensive, mild, low toxicity
Hypochlorous acid	HOCl	Inexpensive, mild, low toxicity, unreliable results, requires heating
Oxone™ (Potassium peroxydisulfate)	2KHSO ₅ •KHSO ₄ •K ₂ HSO ₄	Inexpensive, safe, environmentally benign, reliable results, room temperature

Historically, one of the most widely used oxidizing agents has been chromic acid, which is prepared by mixing sodium dichromate with sulfuric acid. Chromium salts, however, are suspected mutagens, carcinogens, and highly corrosive. Strict EPA regulations exist for the handling and disposal of chromium compounds.

Oxone, an alternative oxidizing agent, is readily available, inexpensive, safe, and environmentally benign compared to chromium reagents. Oxone is a triplet salt of 2KHSO₅•KHSO₄•K₂HSO₄. The active oxidizing agent of the triplet salt is the potassium peroxydisulfate, KHSO₅, which forms hypochlorous acid through the reaction with catalytic amounts of chloride ion (Figure 13-1).

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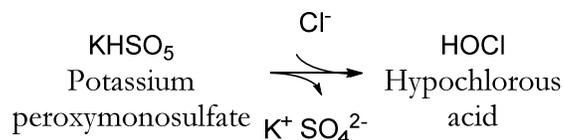


Figure 13-1: Hypochlorous acid can be prepared from potassium peroxysulfate and catalytic amounts of sodium chloride.

In this experiment¹, hypochlorous acid will be used to prepare camphor from borneol (Figure 13-2). (You can draw this compound by selecting the template tool in ChemDraw, and going to the bicyclics menu.)

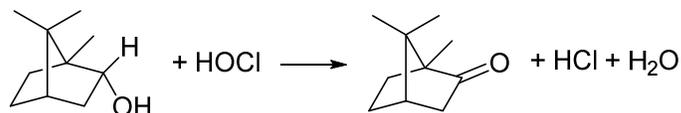


Figure 13-2: In this experiment, you will oxidize borneol to camphor.

The mechanism for this reaction has not been fully established, although the mechanism shown in Figure 13-3 seems likely. In this mechanism, the oxygen of the alcohol group eventually becomes the oxygen of the carbonyl. (Another possibility is that the alcohol oxygen gets protonated and leaves the molecule entirely, and then the oxygen atom from water becomes the carbonyl oxygen.)

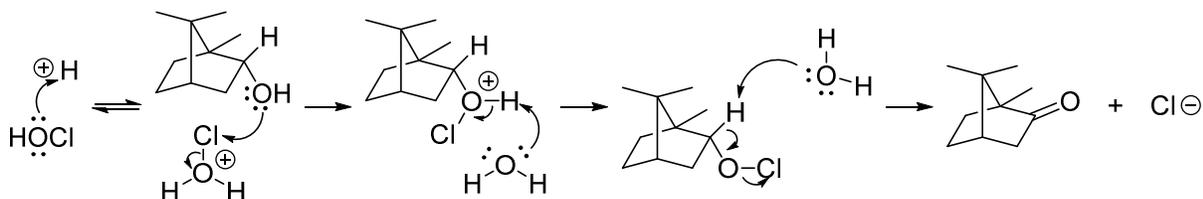


Figure 13-3: One possible mechanism for oxidation of borneol to camphor.

In order for the reaction of hypochlorous acid and borneol to go to completion, the hypochlorous acid must be in excess during the reaction. To generate the hypochlorous acid, you will use 0.6 molar equivalents of Oxone (which equates to 1.2 molar equivalents of the active oxidizing agent, KHSO_5). The presence of hypochlorous acid must be established by a chemical test, the potassium iodide-starch test. This test employs paper impregnated with iodide ions and starch (KI-starch test paper); a drop of the reaction mixture is placed on the paper. If hypochlorous acid is present, it oxidizes the iodide ion in the test paper to iodine, which in turn forms a blue-black complex with the starch in the test paper (Figure 13-4).

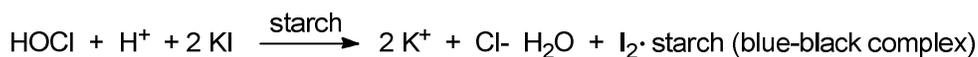


Figure 13-4: The reaction that occurs in starch-iodide paper will allow you to test whether your reaction still contains hypochlorous acid.

At the end of the reaction period, any excess oxidizing agent must be destroyed. This is accomplished by the addition of sodium bisulfite (NaHSO_3) which reduces excess oxidant (Figure 13-5).



¹ The procedure for this experiment is taken from Lang, P. T., Harned, A. W., Wissinger, J. E. Oxidation of Borneol to Camphor Using Oxone and Catalytic Sodium Chloride: A Green Experiment for the Undergraduate Organic Chemistry Laboratory. *J. Chem. Educ.*, **2011**, *88*, 652-656.

Figure 13-5: The reaction between hypochlorous acid and sodium bisulfite.

To determine if enough bisulfite has been added, the reaction mixture is again tested with KI-starch test paper. This time, the *absence* of hypochlorous acid is the desired result.

After neutralization with sodium bisulfite, the camphor is “salted out” by adding solid NaCl. Salting out is a common organic chemistry practice, based on the principle that dissolved inorganic salts decrease the solubility of most organic compounds in water. The camphor is extracted into ethyl acetate and the resulting solution treated with drying agent. Then, the mixture of solvent and product is decanted off from the drying agent, and the solvent is removed by rotary evaporation to yield the crude product.

To purify the product, you will use the technique of sublimation. This is sometimes used for compounds that have a direct solid-to-vapor phase transition, i.e., compounds which **sublime** or **sublimate** (both terms are used interchangeably). Sublimation is similar to distillation: you will heat up the compound you wish to purify and then cool down the vapors that form, hopefully leaving the impurities behind. During a normal, liquid-to-vapor distillation, the cooling would be done by a condenser, and you would collect the purified liquid that dripped out of the condenser. This will not work for this experiment, however: you would develop a large amount of camphor crystals inside your condenser, which would be hard to collect. For this reason you will instead use the setup shown below in Figure 13-6. The crude product will be placed in a small beaker, with a crystallizing dish placed upside-down over the top of it. Another beaker of ice water will be placed on top to cool the vapors. As the crude product is heated, it will slowly transform into vapor and then reform as crystals underneath the crystallizing dish (and possibly on the upper inside walls of the beaker containing the crude product). Any impurities will be left behind.

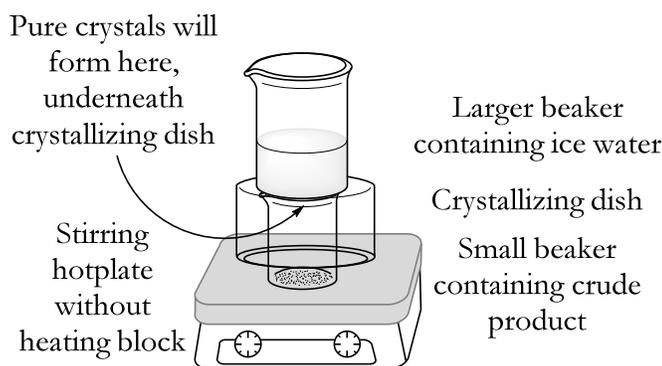


Figure 13-6: The apparatus you will use for sublimation.

You will run an IR, MP, and ^1H NMR of your product; this will indicate both the identity and the purity of your camphor.

Drawing the Product in ChemDraw

The product of this reaction is somewhat difficult to draw correctly in ChemDraw. You can make things easier by using a template. To do this, go to the tool that looks like a rubber stamp – a menu should pop out to the right (Figure 13-7). Select “Bicyclics”, and then select the compound that looks like the one selected below.

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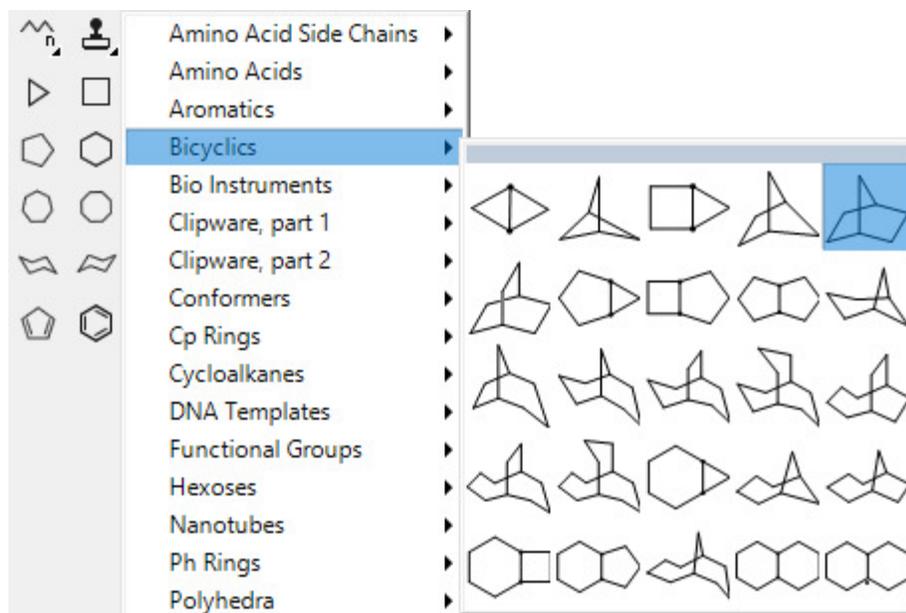


Figure 13-7: Selecting a template to modify into your product structure.

Click in the drawing area to create the structure. From here, you can make modifications until the structure looks like the product of the reaction you will perform today.

Safety Precautions

Oxone is corrosive to the skin; do not breathe the dust. If you get any of this reagent on you, wash the affected area well with water. Ethyl acetate is highly flammable; wear gloves and protective clothing. Borneol and camphor are irritants – avoid skin contact.

Procedure

You will perform this lab in pairs, but each of you will submit your own individual NMR sample.

Clamp a 50-mL round bottom flask to a ring stand and position a magnetic stirrer beneath it. Place a stir bar in the flask and add 1.0 g (6.5 mmol) of (1S)-borneol. Add 4 mL ethyl acetate and begin stirring to dissolve the borneol. Add 2.4 g (3.9 mmol) of Oxone (which corresponds to 7.8 mmol of KHSO_5) to the flask with continued stirring. Then add 0.08 g (1.4 mmol) NaCl, followed by 1.5 mL of deionized water. Allow the reaction to stir at room temperature for 15 minutes. Note any changes in color or temperature during the entire procedure.

While you are waiting for the reaction to proceed, clean an NMR tube with acetone and allow it to dry upside-down in a beaker or Erlenmeyer. Also clean out a vial and a vial cap, and allow them to dry – you will use them to make up your NMR sample.

By the end of this time the oxidation should be complete and excess oxidant can be destroyed. Add 15 mL of deionized water to the reaction and continue stirring to dissolve most of the salts. Slowly add a small amount (approximately a spatula-tip full) of solid sodium bisulfite to reduce the oxidants that remain. Test the aqueous layer (not organic) by dipping a glass rod into it and then touching a piece of starch-iodide paper, rather than dipping the paper directly into the reaction. By doing this, you can reuse a strip of test paper several times if you touch a different spot each time. A blue-black color (positive test) indicates the presence of excess oxidant; add small amounts of sodium bisulfite if the aqueous layer tests positive, until a negative test is achieved (no color change).

Carefully transfer contents to a separatory funnel. Add 1 to 2 mL of ethyl acetate to the reaction flask, swirl, and add this wash to the separatory funnel as well. Shake and invert the separatory funnel and separate the layers by draining the aqueous layer from the bottom. Pour the organic layer out of the top into a clean Erlenmeyer flask. Extract the aqueous layer twice more, with 5 mL of ethyl acetate each time. Return the combined organic phases to the separatory funnel and wash three times with 5 mL portions of saturated aqueous sodium chloride solution (brine). Pour the organic phase into a clean Erlenmeyer flask and dry over sodium sulfate.

Decant the solution into a tared round bottom flask and use the rotary evaporator to remove the ethyl acetate solvent. Record a crude mass before purifying. Because the rotovapped crude product is likely to be a goopy liquid instead of a solid, it's easiest to transfer out of the round-bottom flask by dissolving in the smallest possible amount of DCM, then pouring this solution into a small beaker. A small amount of DCM mixed with the crude product will not affect the sublimation process – it is volatile enough to be driven off by the heat.

Prepare a sublimation apparatus with your crude material in the bottom beaker, capped with an inverted evaporating dish, and cooled with a beaker of ice water on top. Heat the stirring hotplate on a medium power – after a few minutes, you should start to see crystals growing from the underside of the crystallizing dish. Crystals of product may also be deposited higher up the walls in the beaker containing the crude product – in this case, they can still be scraped carefully off later on.

Once the crystal growth stops, or once the amount of remaining crude product in the beaker is small, turn off the heat. Flip the crystallizing dish right-side-up and carefully scrape the sublimed product into a tared vial. Determine a mass of the purified product.

To prepare an NMR sample, transfer a small amount (10-20 mg) of sample into the vial that you cleaned earlier. Add 0.5 mL of CDCl_3 , cap the vial and swirl to dissolve as much of the sample as you can. After a few minutes, use a clean pipet to transfer this solution into the cleaned NMR tube and submit your own individual sample for ^1H NMR.

With your partner, analyze the purified product by IR and MP. Be aware that some of the material will sublime while taking a melting point; use enough and record the onset point and the meniscus point in your observations.

Wastes

Aqueous Waste: Aqueous layer remaining after ethyl acetate extraction.

Organic Waste: Reaction product

Solid Chemical Waste: Used drying agents

Lab Report

Your conclusions should include:

- An analysis of your ^1H NMR and IR spectra, including a comparison of your spectra to the literature spectra for borneol and camphor. If your sublimated product contains both starting material and product, what is the molar ratio between them? (Note: the full name for the isomer of borneol used in this experiment is (1S-endo)-borneol, and the camphor is (+)-camphor. This might help you find these compounds in a spectral database.) You might have a hard time picking out an isolated peak to use for camphor, but if you're careful about assigning the three methyl groups around 0.9 ppm on each compound, you should be able to use those. Also, since the two

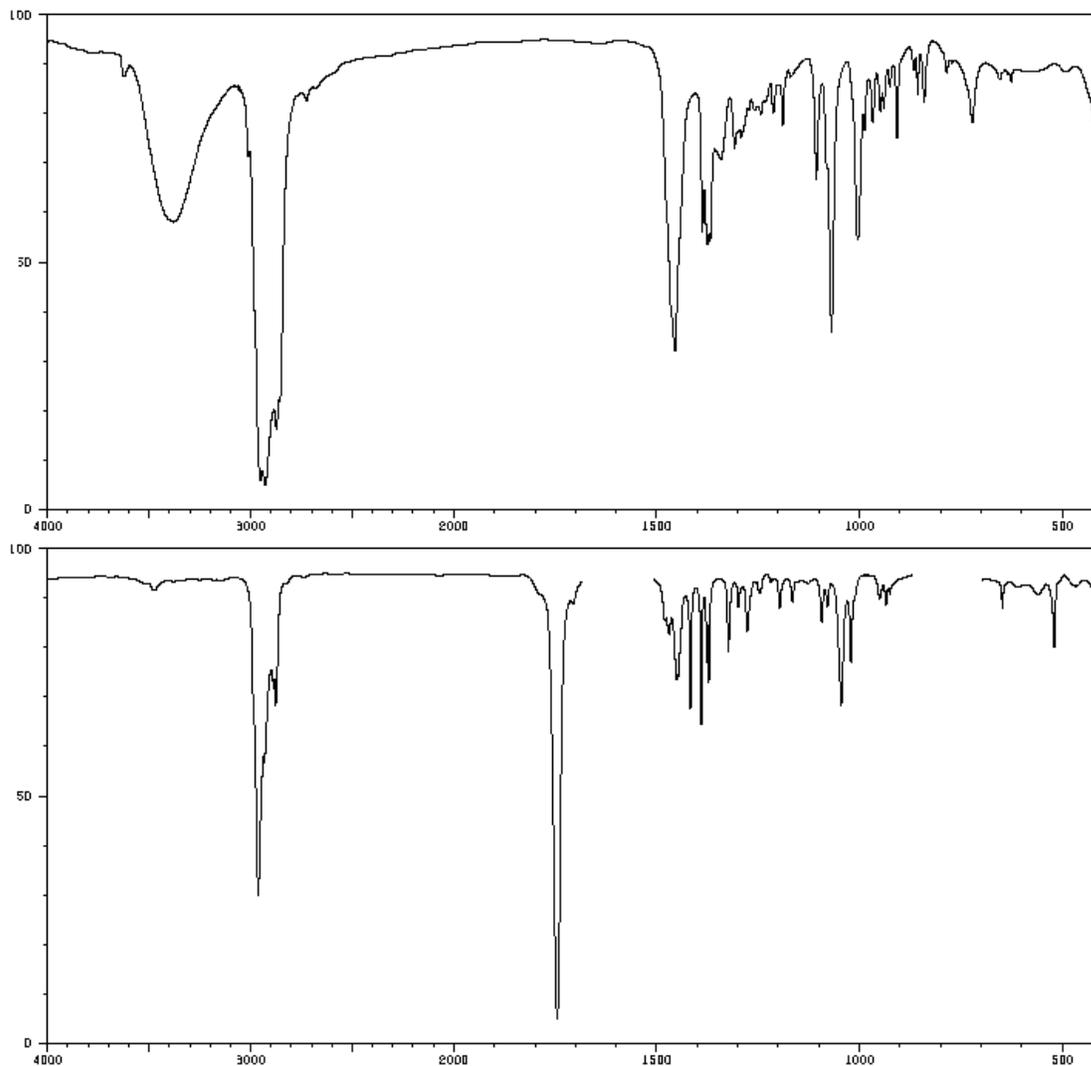
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methyl groups at the top of the structure appear to be symmetrical, MestreNova might try to incorrectly assign both of them to the same peak. You can avoid this by going to Analysis → Assignments → Options and turning off “Always assign together the symmetrical atoms”.

- Analysis of melting point.
- Calculation of yields (crude and sublimed).

Study Questions

- 1) The IR spectra of borneol and camphor are shown below (taken from SDBS). Identify which spectrum belongs to which compound and assign the bands to rationalize your choice.



- 2) Each of the compounds below is treated with hypochlorous acid (HOCl). For each compound, give the structure of the product of the reaction or, if no reaction occurs, write “No Reaction.” Assume that conditions are chosen so that no carboxylic acid is formed at any point.

