Honors Cup Synthetic Proposal

Section: 270
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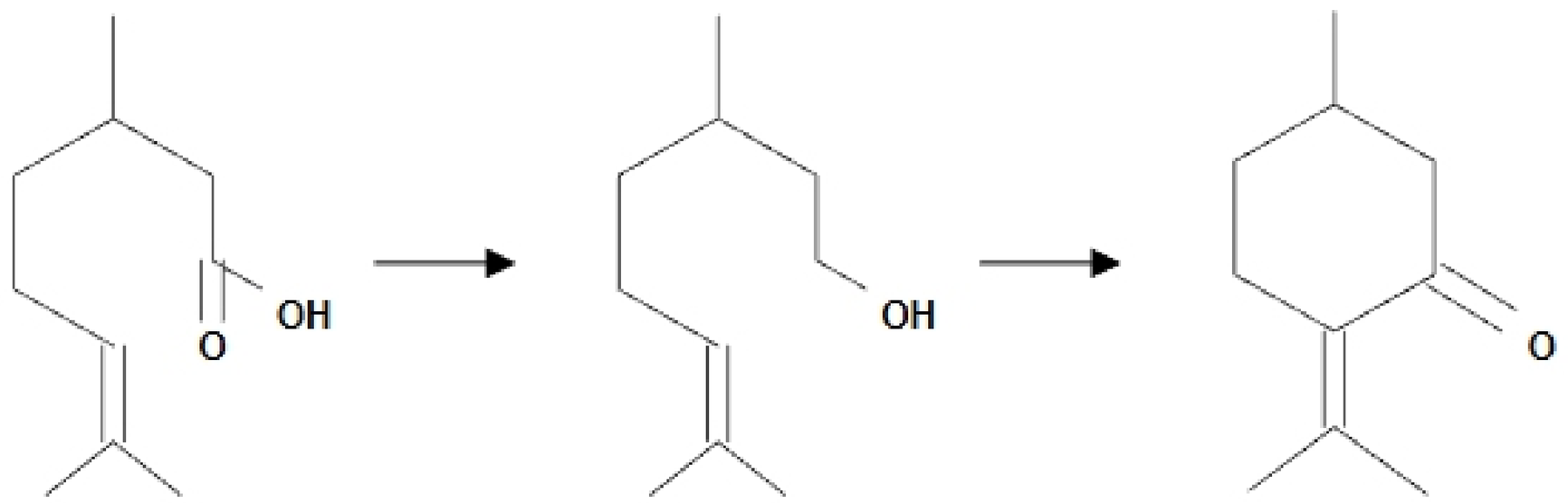
Title: Synthesis of Menthone

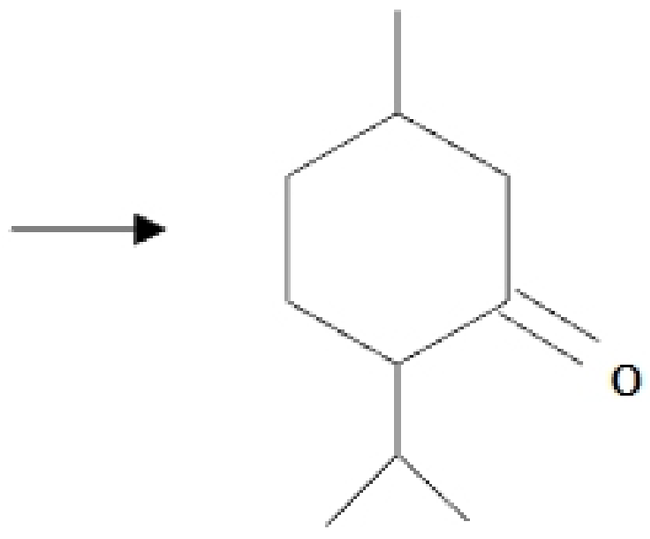
Introduction:

The target molecule menthone is the ketone form of the commonly known acid, menthol. This synthesis was done in three steps: the starting material, citronellic acid, was synthesized into citronellol, then into pulegone, and then finally, using hydrogenation, into menthone.

Physical characteristics of menthone include its colorless appearance, a boiling point of 210°C, and a distinct mint/peppermint odor. Since menthone is very closely related to menthol, many of its interesting aspects are along the same line as menthol, in their wide-range commercial use. For example, menthol is found in topical pain and itching relievers, it is responsible for the tingling sensation felt after the application of after shave and suntan lotion, and it can even be used as a local anesthetic for sore throats and muscle aches. However, menthol is most heavily used as a mint flavoring agent in products like medicine, tobacco, cough drops, tooth paste, ice cream and perfumes.

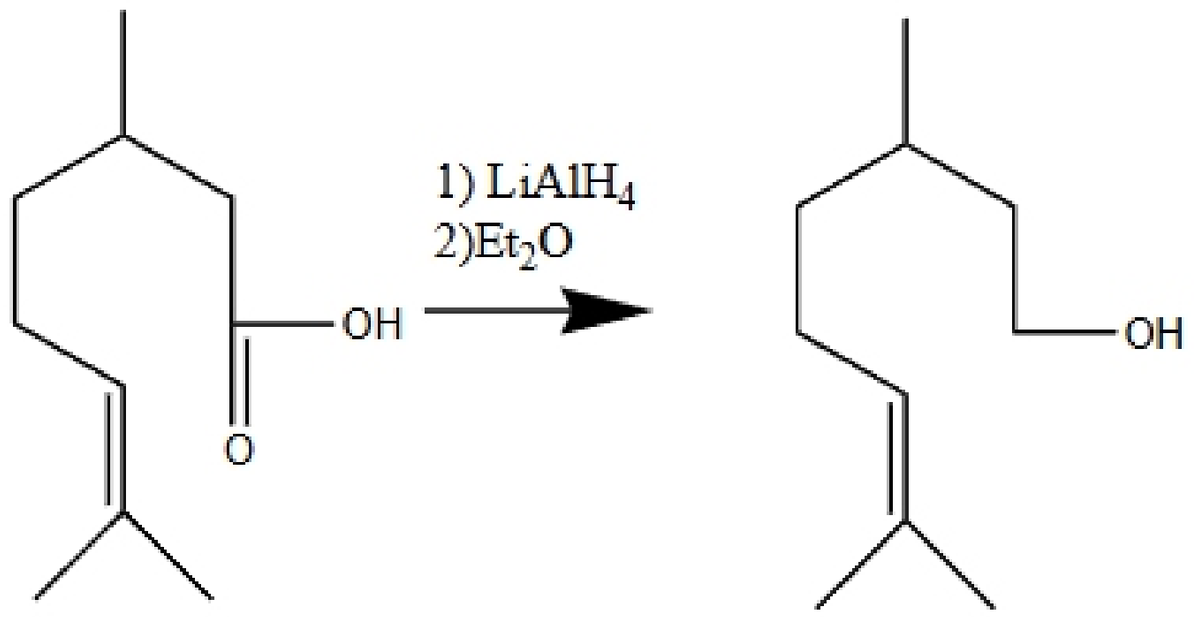
Overall synthetic reaction scheme: (a Chemdraw or similar drawing of all three steps)





Step 1

Synthetic transformation 1: (Chemdraw picture of first transformation)



Experimental 1 (notes if this transformation is not exactly the one reported in literature (e.g. on a different scale) and how it was modified):
A solution of citronellic acid (51.2g, 0.30 mol) in diethyl ether (200 ml) was gradually added to a magnetically stirred suspension of $LiAlH_4$ (16.0 g, 0.30 mol) in diethyl ether (2000 mL) that was kept under N_2. Then the mixture was stirred for 5 hours at room temperature. Water (100 mL) was slowly added to the mixture. The resulting mixture was filtered with suction and the filter cake was washed with ethyl acetate. After drying (using $MgSO_4$) and evaporation of the solvent the resulting oil was distilled.

Note 1: In order to achieve 40 grams of the product obtained from step one, twice the amount of citronellic acid, the dry ether (diethyl ether), $LiAlH_4$, and water was used.

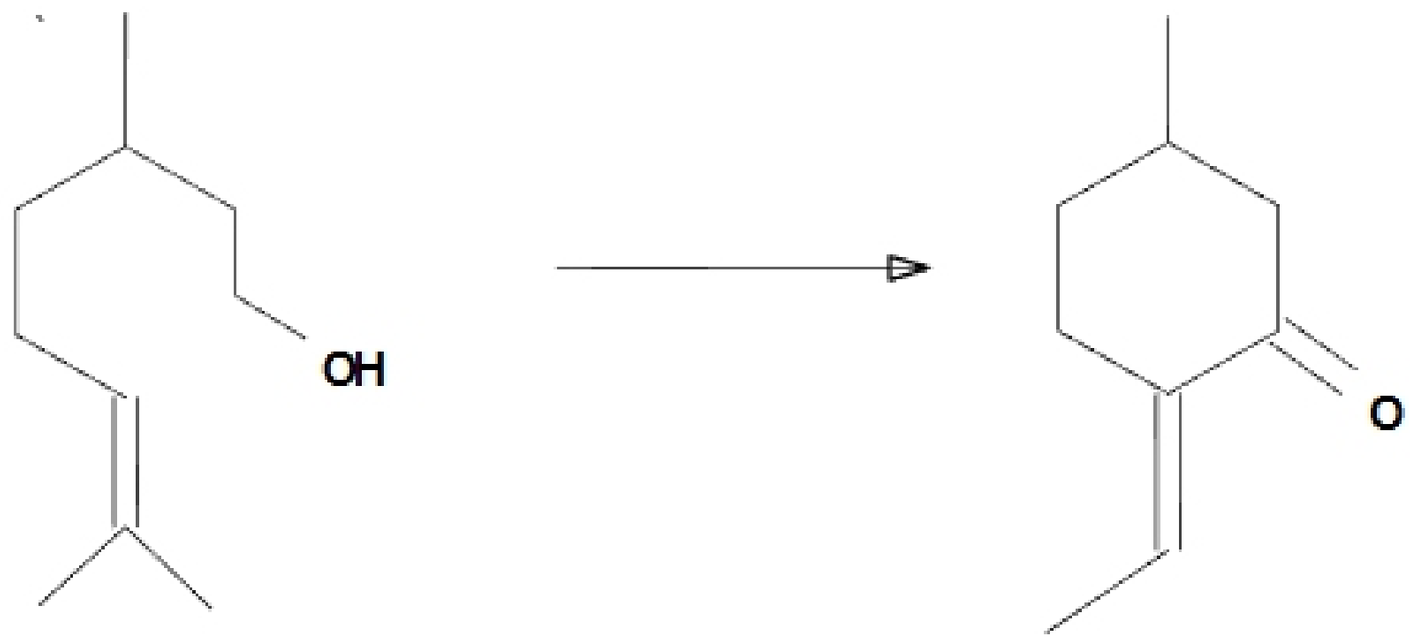
Note 2: Step two was the most complex of the three, so it was kept exactly the same in amounts and procedures as the reference article's, in order to minimize any unpredictable errors from making changes. Consequently, the other steps' chemical amounts were altered to fit the step two's needs.

Expected yield: 90 % 42.4 g

Safety, disposal and green issues 1:
Water is to be added slowly to the mixture that was gradually stirred for five hours to keep $LiAlH_4$ from reacting with water violently. $LiAlH_4$ is an inflammable compound, especially when it is in an ether solution. Thus, adding water to a solution of $LiAlH_4$ and ether must be done slowly and with great caution.

Step 2

Synthetic transformation 2: (Chemdraw picture of second transformation)



Reactant **Product**

Experimental 2 (notes if this transformation is not exactly the one reported in literature (e.g. on a different scale) and how it was modified):

To a suspension of 160g (0.8mol) of pyridinium chloromate (PCC) in 1 L of dry methylene chloride was added 40.0g (0.26 mol) of (–)-citronellol. The slurry was stirred at 25 degrees for 36 hours. The mixture was filtered through Celite and the solids were washed thoroughly with methylene chloride. The solution was evaporated to ca. 500mL and washed with 10% hydrochloric acid, 10% sodium bicarbonate, and water. The methylene chloride solution was evaporated to give a mobile oil (43g). The oil was taken up in 300mL of ethanol and treated with 600mg (!5mmol) of sodium hydroxide. The solution was heated for 1 hr, then the ethanol was evaporated under redued pressure and the residue was partitioned between 200mL of diethyl ether and 100mL of water. The diethyl ether was washed with 10% hydrochloric acid and then brine. Evaporation of the solvent and distillation of the residue gave 28g (0.184 mol, 71%) of (–)-pulegone.

Expected yield: 71 % , 28 g

Safety, disposal and green issues 2:
PCC is toxic by inhalation and irritable to skin, so it must not be touched with bare skin. It can also have adverse effects on aquatic orgnisms or environment, so it must be disposed as hazardous wastes. Celite must not be inhaled because inhalation of it is health hazard. Diethyl ether is flammable, so no smoking is allowed and the lab must be kept well-ventilated.

Step 3