

Honors Cup Synthetic Proposal

Section: 231

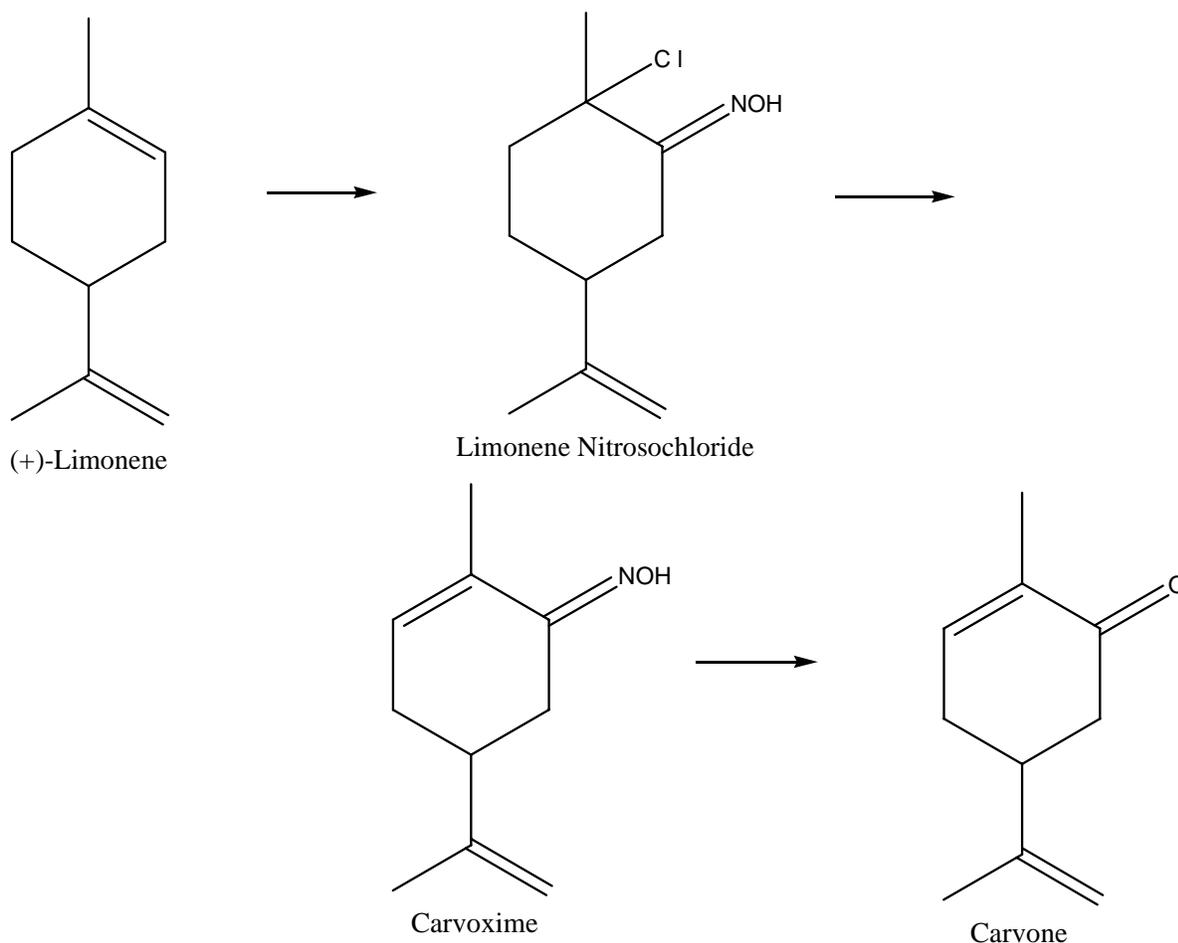
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Title: Synthesis of Carvone from Limonene

Introduction:

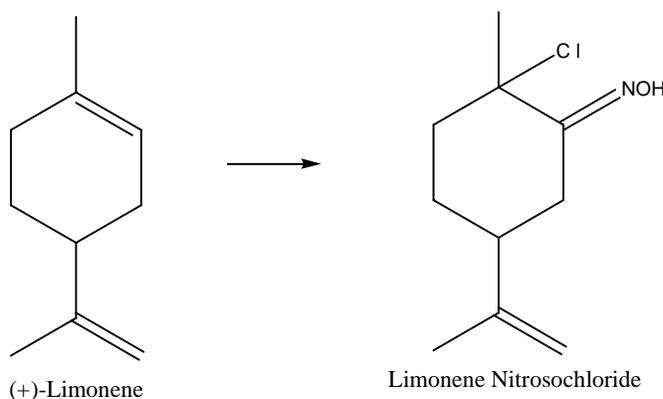
This process converts *d*-limonene to *l*-carvone (also known as *s*-carvone). *D*-limonene constitutes about 95% of orange and grapefruit oils. *l*-carvone can be extracted from spearmint oils. It is the conjecture of this article that this process can be used to provide a substitute or partial replacement for the natural oil of spearmint. Our group found it very interesting that fruit oils would yield spearmint oils through a chemical process. We were also surprised to see that both of the given chemicals have industrial uses. *D*-limonene is used as an orange fragrance and flavoring. *L*-Carvone is also used as a spearmint flavor. Both of these chemicals have enantiomers that have different fragrances which we also found significant. The three step synthesis also appealed to us as the process contained many steps that we are familiar with from CHEM 210 and 215.

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):

Make a solution of 1.27* g (0.00934* moles) of (+)-limonene in 1.25* mL of isopropyl alcohol and cool to below 10° C. Make a solution of 3.75* mL of concentrated hydrochloric acid in 2.5 mL of isopropyl alcohol and a concentrated aqueous solution of 0.65* g (0.00934* moles) sodium nitrite. Then add these simultaneously through separate dropping funnels to the (+)-limonene solution. Adjust the addition rate in order to maintain the temperature below 10° C. Stir the mixture for an additional 15 minutes and allow it to stand in the refrigerator for 1 hour. Then isolate the solid by filtration and wash with enough cold ethanol to make a thick slurry which provides a water white product. Repeat this step with the liquid from the previous filtration and combine the solids. A total of 5* grams (0.25* moles) (80.7% of theoretical yield) of limonene nitrosochloride should be obtained.

*These values were adjusted in order to reduce the yield from 161.4 grams to 5 grams.

Expected yield: 80.7 % 5 g

Safety, disposal and green issues 1:

Isopropyl alcohol:

This reagent is flammable and irritant. It is also irritating to the eyes. For safety issues it is recommended to keep the container highly closed and keep it away from the sources of ignitions – No smoking. To avoid contact with skin and eyes is also advised. In case of contact with eyes, it is recommended to rinse immediately with plenty of water and seek medical advice.

Hydrochloric acid:

This reagent is corrosive. It causes burns and it is irritating to the respiratory system. For safety issues it is recommended to wear suitable protecting clothing, gloves and eyes/face protection. In case of accident or if the person feels unwell, seek medical

attention immediately. In addition, in case of contact with eyes, rinse immediately with plenty of water and seek medical advice.

Sodium Nitrite

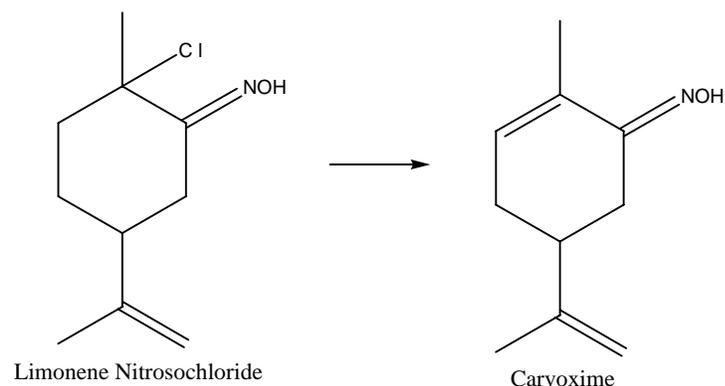
This reagent is oxidizing, toxic, and dangerous for the environment. When in contact with combustible material this chemical may cause fire. It is toxic if it appears swallowed. It is also very toxic to aquatic organisms. It is recommended to avoid contact with the eyes and to avoid the release to the environment of this chemical.

Ethanol

This reagent is highly flammable. It is recommended to keep the container tightly closed and keep the reagent away from sources of ignition –no smoking.

Step 2

Synthetic transformation 2: (Chemdraw picture of second transformation)



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):

Boil 4* grams of limonene nitrosochloride (product from the previous step) with 2* mL of dimethylformamide for 30 minutes under reflux in 12.5* mL of isopropyl alcohol. Pour the product into 75* mL of cracked ice and water, stir vigorously, and filter after the ice has melted. Wash the resulting solid three times with 5* mL of cold water and once with 1.5* mL of cold isopropyl alcohol. The dry product should weigh 2.74* g (83.5% of theoretical yield).

*These values have been cut in half in order to reduce the yield from 5.47 grams to 2.74 grams, which will in turn reduce the final yield of carvone from 18.6 grams to 9.3 grams.

Expected yield: 83.5 % 2.74 g

Safety, disposal and green issues 2:

N-N-Dimethylformamide This chemical is toxic. It may also cause harm to the unborn child. It is harmful by inhalation and in contact with the skin. It is also irritating to the

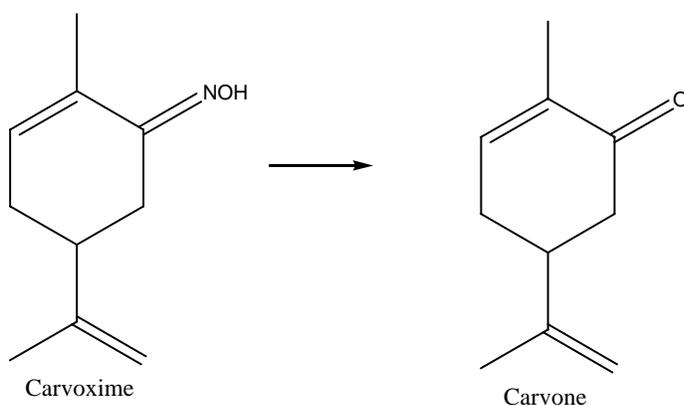
eyes. It is recommended to avoid exposure to this reagent and obtain special instruction before use. In case of accident, seeking medical advice immediately is emphasized.

Isopropyl alcohol:

This reagent is flammable and irritant. It is also irritating to the eyes. For safety issues it is recommended to keep the container highly closed and keep it away from the sources of ignitions – No smoking. To avoid contact with skin and eyes is also advised. In case of contact with eyes, it is recommended to rinse immediately with plenty of water and seek medical advice.

Step 3

Synthetic transformation 3: (Chemdraw picture of third transformation)



Experimental 3 (notes if this transformation is not exactly the one reported in literature (e.g. on a different scale) and how it was modified):

On a 500* mL three-necked flask, one neck was fitted with a pH meter,** another had a separation funnel and the third neck was fitted for distillation. As we are preparing for distillation everything must be sealed to no gas escapes. In the flask, 350* mL of water was brought to boiling and the pH was adjusted to .8 with 3N sulfuric acid(1.5 mol, about 20* mL of acid was required). First the solid oxime was melted in the separation funnel, using an infrared lamp. The carvoxime was added dropwise from the sep funnel, forming an azeotrope product with the water (meaning they stay mixed in the liquid and gaseous state). Evolution of carvone (to the gaseous state) was nearly instantaneous and the addition was so regulated that the carvone in the still pot would be voided within 5 min. The addition took about 1.25 hours. Dilute sulfuric acid was added as needed to maintain the pH at .7-.9. The product was isolated using distillation (in a continuous separator). The condensate water returned to the still pot.

*These values have been cut in half in order to reduce the yield from 5.47 grams to 2.74 grams, which will in turn reduce the final yield of carvone from 18.6 grams to 9.3 grams.

**The article specifies a Beckman high temperature glass electrode.

Expected yield: 83 % 9.3 g

Safety, disposal and green issues 3:

Sulfuric Acid

This chemical is corrosive and it causes severe burns. It is crucial to never add water to this product. In case of contact with eyes, rinse immediately with water and seek medical attention. Also seek medical advice in case of accident or feeling unwell.

Overall budget:

Chemical	Supplier	Cost	Amt. Needed	Total
N,N-Dimethylformamide (anhydrous, 99.8%)	Sigma-Aldrich	\$0.017 / g \$0.016 / mL	2 ml	\$0.03
Sodium Nitrite ($\geq 99.99\%$)	Sigma-Aldrich	\$0.582 / g	0.65 g	\$0.38
(R)-(+)-Limonene (97%)	Sigma-Aldrich	\$0.106 / g \$0.090 / mL	1.27 g	\$0.13

Total costs per synthesis: \$0.54

References (include at least two different sources for your experimentals):

For all three steps:

Reitsema, R. H. *J. Org. Chem.* **1958**, *23*, 2038-2039.

Bordenca, C.; Allison, R. K. *Ind. Eng. Chem.* **1951**, *43*, 1196-1198.

Royals, E. E.; Horne, S. E. Jr. *J. Am. Chem. Soc.* **1951**, *73*, 5856-5857.

For the third step:

Murugan, R.; Reddy, B. S. R. *Chem. Lett.* **2004**, *33*, 1038-1039.