Experimental Procedures

Experiment: 5 | **Date: 03/04/2020;**

Lab No: 4 | **Time: 9:00a.m. to 1:00p.m.**

Alkyne Hydrolysis

The hydrolysis has traditionally been performed with protic acids. Recently, however, transition metals have been used to facilitate the reaction. Frequently, with internal alkynes, a mixture of regioisomeric ketones are formed.

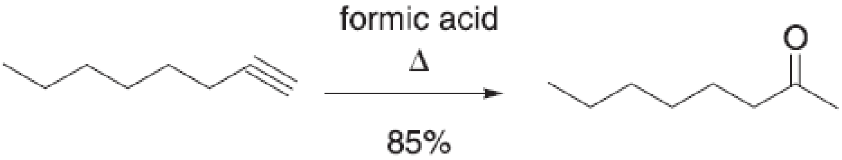

Figure 1 synthesis of 2-octanone

Procedure:

1-Octyne (7.5 g) and formic acid (100 mL) were heated in an oil bath at 100 ºC until all starting material was consumed. The progress of the reaction was monitored by GC analysis of the reaction solution. Quantitative GC analysis at the end of the reaction (6 h) indicated 92% yield of 2-octanone. The cooled reaction mixture was taken up with CH_2Cl_2 (170 mL), and the solution was washed with water, sodium carbonate solution, and water, dried over $MgSO_4$, and evaporated in vacuo. The residue was distilled (bp 171–173 ºC) to give 2-octanone.

Reference: Menashe, N.; Reshef, D.; Shvo,Y. *J. Org. Chem.* **1991**, *56*, 2912–2914.

Yield: 7.42 g, 85%

Experiment: 6 **Date: 07/04/2020;**
Lab No: 5 **Time: 9:00a.m. to 1:00p.m.**

Fischer Esterification

The Fischer esterification is one of the oldest and most reliable methods of converting an acid to an ester. The reaction requires acid catalysis, elevated temperatures, and frequently the removal of the water by-product. As long as the remainder of the starting acid can withstand these requirements, the Fischer esterification deserves consideration.

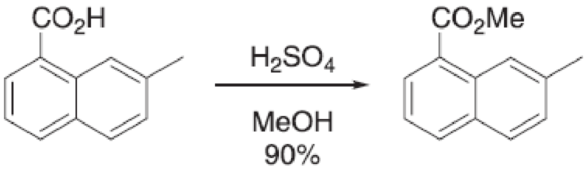

Figure 2 synthesis of amide derivatives

Procedure:

To methanol (40 mL) cooled to 0 ºC (ice/water) was added dropwise concentrated H_2SO_4 (12 mL). To the resulting clear solution was added immediately the carboxylic acid (10 g, 56 mmol), and the mixture was refluxed for 3 h, at which time TLC indicated the reaction to be complete. The resulting yellowish emulsion was cooled to room temperature, and the solvent was evaporated as much as possible. The residue was partitioned between CH_2Cl_2 and water. The collected organic layer was washed with saturated $NaHCO_3$ (aqueous), collected, dried (Na_2SO_4), and decanted. The solvent was concentrated and the resulting brownish oil was subjected to vacuum distillation to afford the ester as a yellowish oil.

Reference: Kolotuchin, S. V.; Meyers, A. I. *J. Org. Chem.* **1999**, *64*, 7921–7928.

Yield: 10 g, 90%

Experiment: 7 **Date: 10/04/2020;**
Lab No: 4 **Time: 9:00a.m. to 1:00p.m.**

Base Promoted Hydrolysis to Amide

The base promoted conversion of nitrile to amide is sometimes catalyzed by addition of hydrogen peroxide. Because of safety concerns with peroxides, a procedure without this additive has been selected.

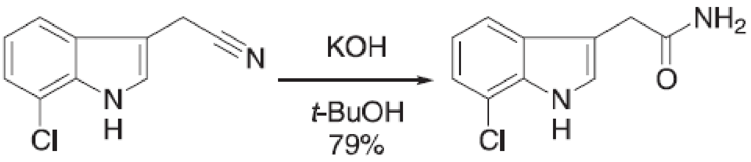

Figure 3 synthesis of amide

Procedure:

A solution of the nitrile (2.77 g, 14.5 mmol) and powdered 85% KOH (7.66 g, 116 mmol) in *t*-butyl alcohol (30 mL) was heated at reflux for 1.5 h. The reaction mixture was then cooled to room temperature, diluted with water (30 mL), and acidified with 1 N HCl (116 mL, 116 mmol) to give a slurry that was filtered and rinsed with water and then Et_2O (40 mL). The solid was dried in a vacuum oven at 40 ºC to give 2.39 g (79%) of the amide.

Reference: Faul, M. M.; Winneroski, L. L.; Krumrich, C. A. *J. Org. Chem.* **1999**, *64*, 2465–2470.

Yield: 2.39 g, 79%

Experiment: 8 **Date: 14/04/2020;**
Lab No: 5 **Time: 9:00a.m. to 1:00p.m.**

Piperonyl Alcohol to Piperonal

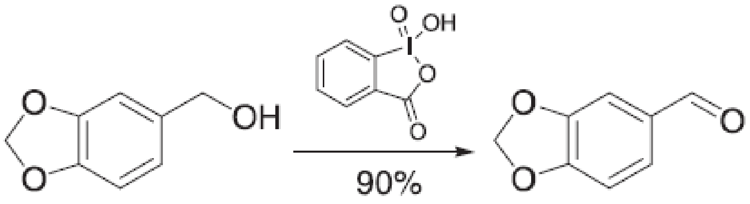

Figure 4 synthesis of piperonal

Procedure:

Piperonyl alcohol (0.15 g, 1.00 mmol) was dissolved in EtOAc (7 mL, 0.14 M final concentration), and 1-hydroxy-1,2,benziodoxol-3(1*H*)-one (IBX 0.84 g, 3.00 mmol) was added. The resulting suspension was immersed in an oil bath set to 80 °C and stirred vigorously open to the atmosphere. After 3.25 h (TLC monitoring), the reaction was cooled to room temperature and filtered through a medium glass frit. The filter cake was washed with 3 × 2 mL of EtOAc, and the combined filtrates were concentrated to yield 0.14 g (90%, > 95% pure by 1H NMR) of piperonal as a waxy solid.

Reference: More, J. D.; Finney, N. S. *Org. Lett.* **2002**, *4*, 3001−3003.

Yield: 0.14 g, 90%