

Honors Cup Synthetic Proposal

Section: 230-IV

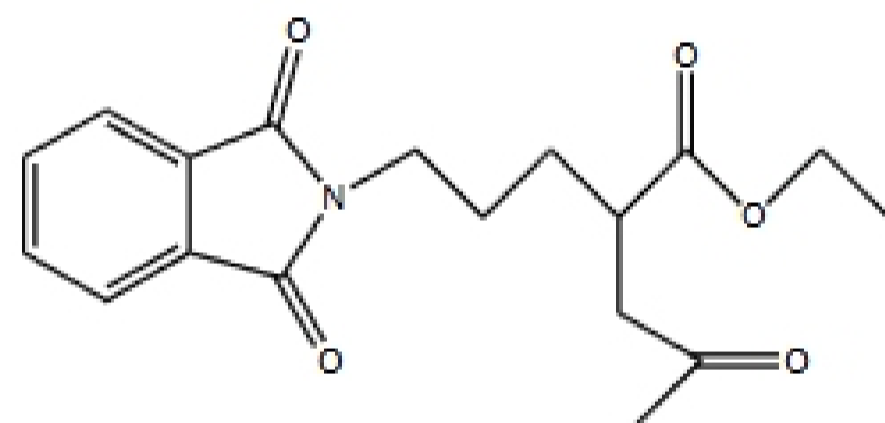
Group Members: Alex Hyla, Lauren Heath, Sahar Rahmani

Title: Synthesis of Melatonin from 3-(3-phthalimidopropyl) ethyl acetate using Green Chemistry

Introduction: Melatonin (5-methoxy-N-acetyltryptamine) is a neurohormone naturally synthesized in the brain by the pineal gland. It is a hormone found in all living creatures and thus proved to have a profound impact on life in various ways. The primary role it serves is the regulation of the body's circadian rhythm. Much research has gone into developing drugs containing melatonin that can be used to treat various sleep disorders. Interestingly, research suggests that Melatonin also has strong antioxidant properties and can be used as a part of the treatment of a multitude of serious disorders: cancer, immune disorders, cardiovascular diseases, depression and sexual dysfunction. Melatonin can be formed synthetically from 3-(3-phthalimidopropyl) ethyl acetate, as shown in the following set of reactions.

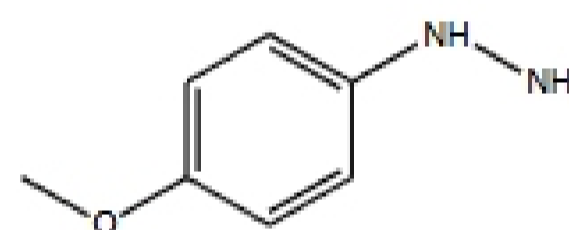
Overall synthetic reaction scheme:

1)



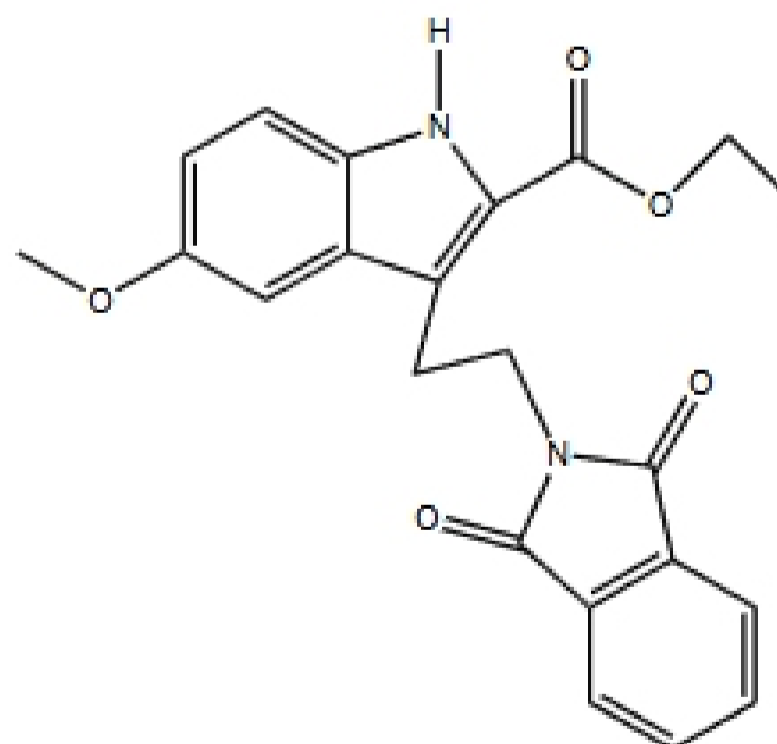
3-(3-phthalimidopropyl) ethyl acetate

+

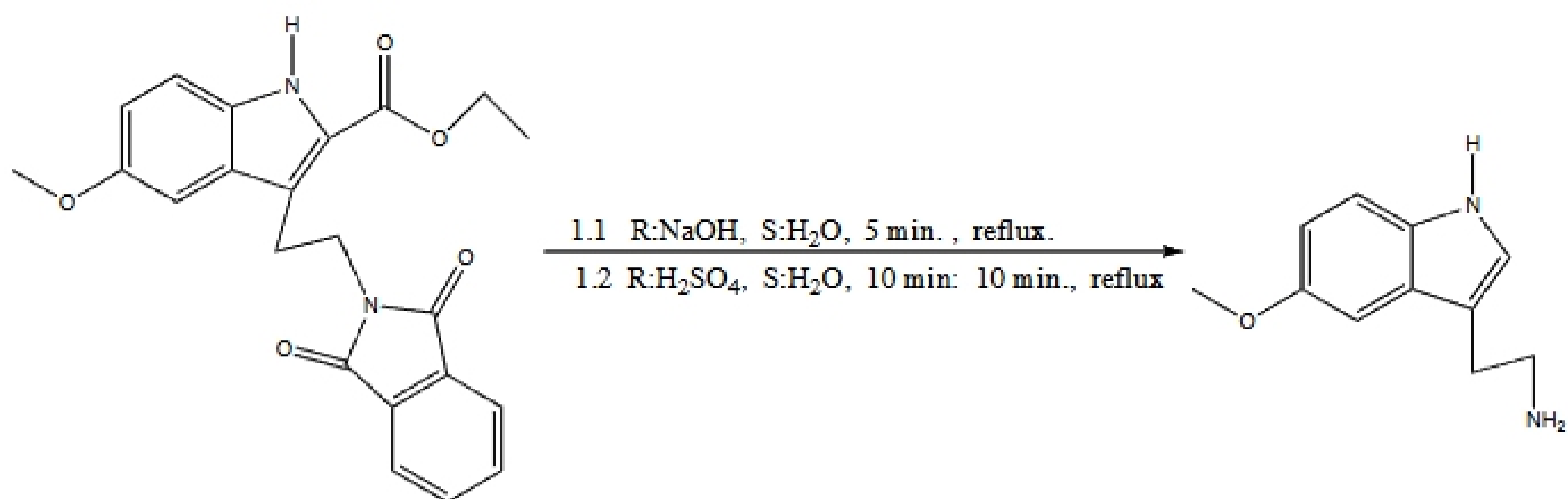


4-methoxyphenyl hydrazine

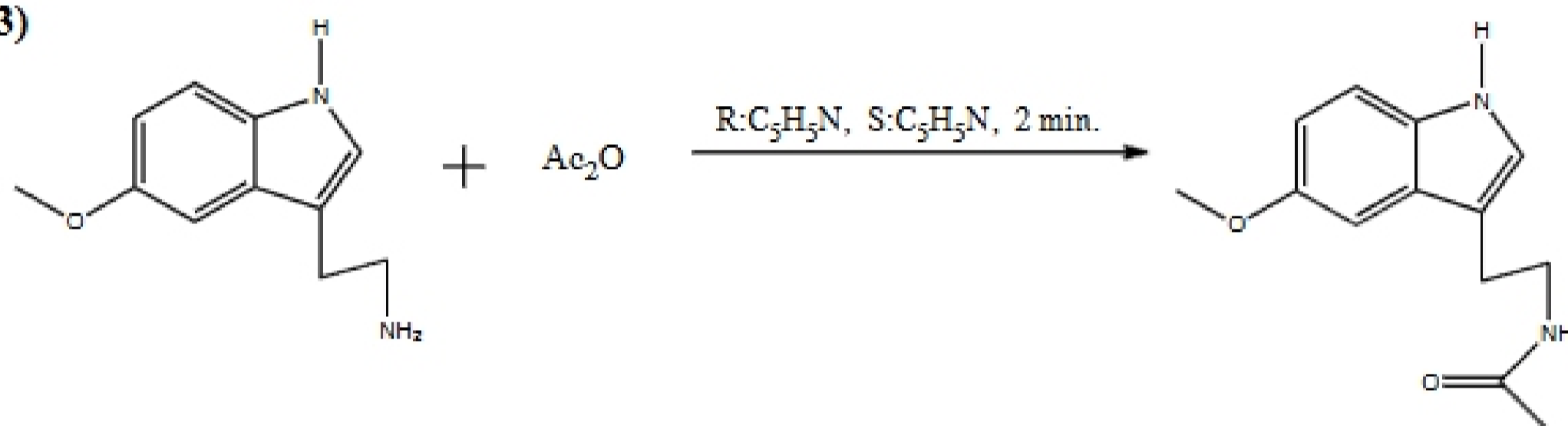
R: HCl, S: BuOH, S:H₂O, 15 min, reflux; overnight



2)

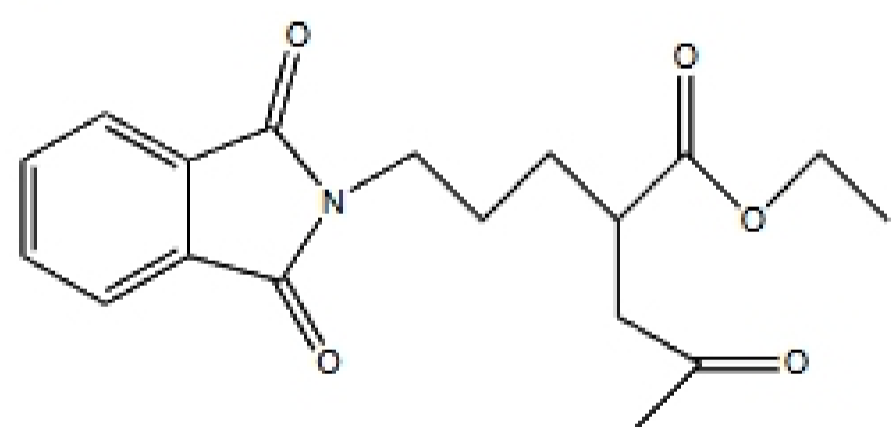


3)



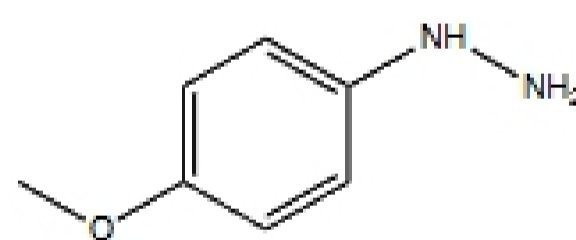
Step 1

Synthetic transformation 1:



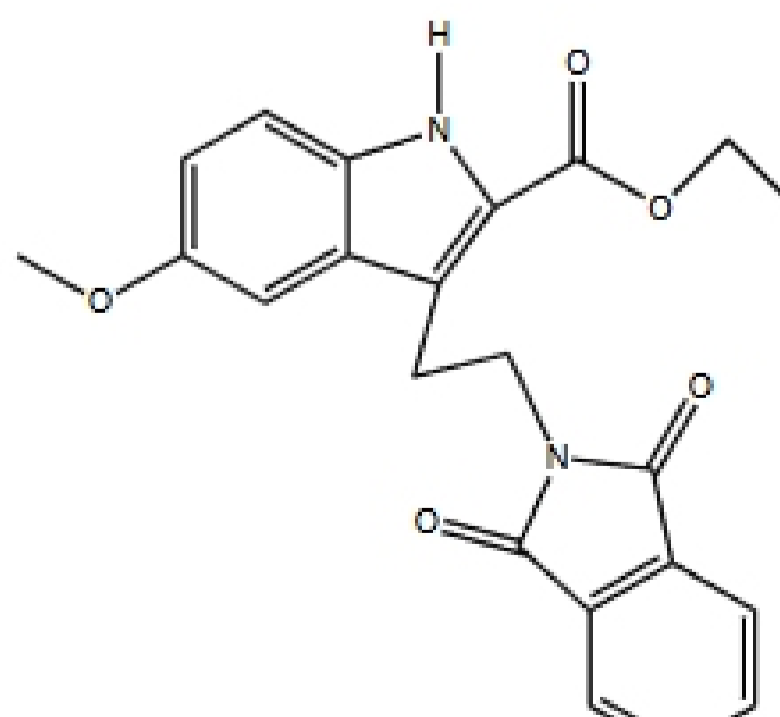
3-(3-phthalimidopropyl) ethyl acetate

+



4-methoxyphenyl hydrazine

R: HCl, S: BuOH, S:H₂O, 15 min, reflux; overnight



Citations:

He, W.; Li, X.; Zhang, B.; Li, Z. *Disi Junyi Daxue Xuebao*. 2000, 21, 949-951.

He, L.; Li, J.L.; Zhang, J.J.; Su, P.; Zheng, S.L.; *Synth. Commun.* 2003, 5, 741-747

Experimental 1:

This step in the literature calls for a large amount of starting material to be used. Our synthesis will not need to create as much as the synthesis in the article created, so we are only using 1.58g of the starting material instead of the recommended 9.5g. We also scaled down the amount of reagents based on the scale needed to create the desired amount of product.

Add 1.7 mL of n-butanol dropwise with a solution of hydrochloride acid to a solution of 4-methoxyphenyl hydrazine (0.664g) and 3-(3-phthalimidopropyl) ethyl acetate (1.577g) in 11.6 mL of n-butanol (0.2 mol acetochloride + n-butanol). Reflux the mixture under microwave irradiation for 15 min, then let cool and put in refrigerator overnight. Collect the resulting yellow solid by filtration and recrystallize the solid from ethanol.

Expected yield: 80 % 1.26g

Safety, disposal and green issues 1:

n-Butanol can cause minor irritation if it comes in contact with your skin. Wash the area thoroughly with water. It can be disposed of in the non halogenated waste container.

Acetochloride and n-butanol should be disposed of in the halogenated organics container.

4-methoxyphenyl hydrazine should be disposed in the non-halogenated waste container.

The use of microwaves is a green issue because it cuts down on time needed for reactions and requires less energy to complete.

Step 2

Synthetic transformation 2:

