

An Interesting Electrophilic Aromatic Substitution: The Preparation of Ethyl *o*-Nitrobenzoate from Acetophenone

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Abstract The preparation of ethyl *o*-nitrobenzoate from acetophenone, a three-step synthesis project, is described. The *o*-nitration of acetophenone is an unusual reaction since the acetyl group ($-\text{COCH}_3$ electron-withdrawing group), is a meta-directing substituent. Nevertheless, students performed the electrophilic aromatic nitration twice under mild conditions and obtained the *o*-nitroacetophenone product in yields ranging from 21 – 23 %. The *o*-nitroacetophenone product was then oxidized to provide *o*-nitrobenzoic acid in 74 % yield. Fisher esterification gave ethyl *o*-nitrobenzoate in 81 % yield.

Keywords Aromatic nitration, Green oxidation, Fischer esterification

1. Introduction

As an option to the original organic chemistry II synthesis project published earlier, [1] undergraduate students taking the second semester of organic chemistry (Chemistry 2212K) at Georgia Gwinnett College engage in a semester-long URCE synthesis project in the laboratory. [2] Although this project can be carried out by individual students, instructors usually will have students work in small teams to conduct the synthesis project to encourage collaborative learning. The URCE project, adapted from Stradling and Gage [3], involves the preparation of methyl *m*-nitrobenzoate from acetophenone. See Figure 1.

The project offers three synthesis pathways from which the students may choose:

1: acetophenone $\rightarrow$ benzoic acid $\rightarrow$ *m*-nitrobenzoic acid $\rightarrow$ methyl *m*-nitrobenzoate

2: acetophenone $\rightarrow$ *m*-nitroacetophenone $\rightarrow$ *m*-nitrobenzoic acid $\rightarrow$ methyl *m*-nitrobenzoate

3: acetophenone $\rightarrow$ benzoic acid $\rightarrow$ methyl benzoate $\rightarrow$ methyl *m*-nitrobenzoate

Before this synthesis project was incorporated into the Organic Chemistry II lab curriculum, each pathway was tested by an instructor team to assess the overall ease of the synthesis pathway and identify possible areas of difficulty with isolation and purification of the intermediate and final products. For all pathways, the nitration reaction was the least efficient in terms of yield (usually $< 50\%$) with meta nitrated product accounting for more than 80% of the total

yield. The oxidation and esterification reactions typically gave much higher conversions (70 – 80 %). Pathways 1 or 2 required very simple product isolation methods - filtration and recrystallization. On the other hand, pathway 3 required distillation of the methyl benzoate intermediate product to ensure purity. Once the project was introduced to the students, because of these findings, instructors recommended pathways 1 or 2 as the best options.

This green chemistry-based synthesis project provides students with three advantages. First, students gain an appreciation for key types of reactions covered during the organic chemistry II course where instructors link the reactions conducted in the laboratory with those covered in class. Second, and equally important, students understand the advantages of reactions carried out in an environmentally responsible manner using small reactant and reagent quantities, benign solvents, heavy-metal free oxidizing agents such as 5 % NaOCl (bleach), simple, aqueous workup procedures and straightforward isolation processes. Finally, the research-like laboratory experience students receive prepares them for success when conducting upper-level green chemistry, independent undergraduate research projects and our integrated laboratory course sequence later in their academic program. [1,4-8]

This work describes a variation of synthesis pathway 2, which is outlined in blue in Figure 1. As Scheme 1 shows, students nitrated acetophenone (**1**) obtaining and isolating *o*-nitroacetophenone (**2**) as the first intermediate product via column chromatography, along with *m*-nitroacetophenone (**3**) and *p*-nitroacetophenone (**4**). Compounds **3** and **4** were also isolated via column chromatography and identified by melting point and proton NMR but were not taken forward in the synthesis. Students then oxidized *o*-nitroacetophenone to prepare *o*-nitrobenzoic acid (**5**) and finally prepared the ethyl ester of *o*-nitrobenzoic acid (**6**) by Fisher esterification.

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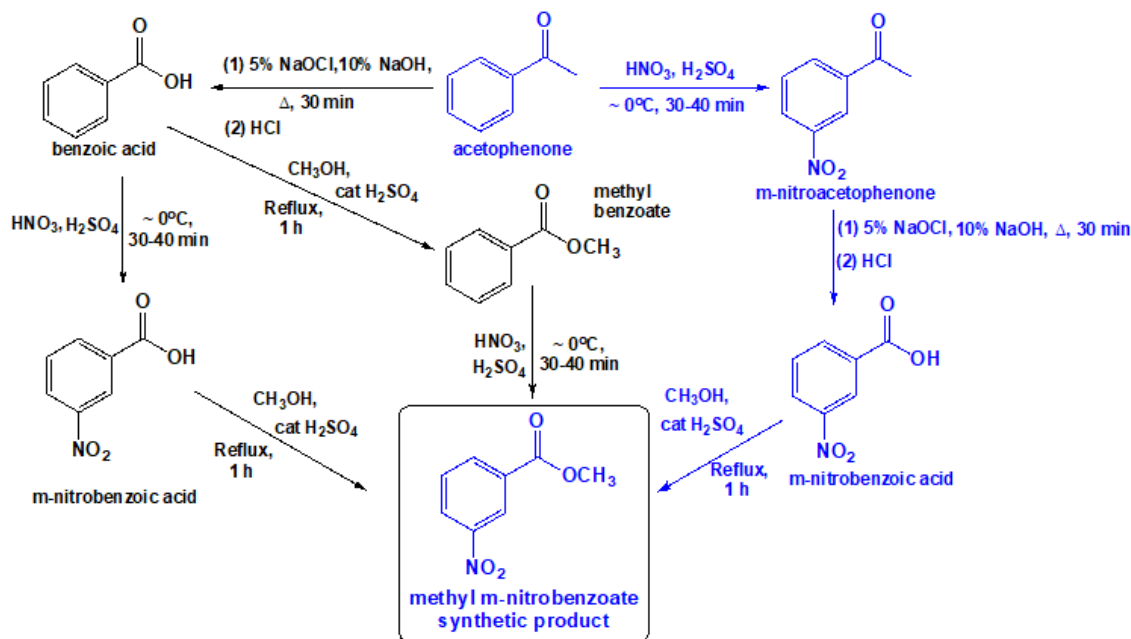
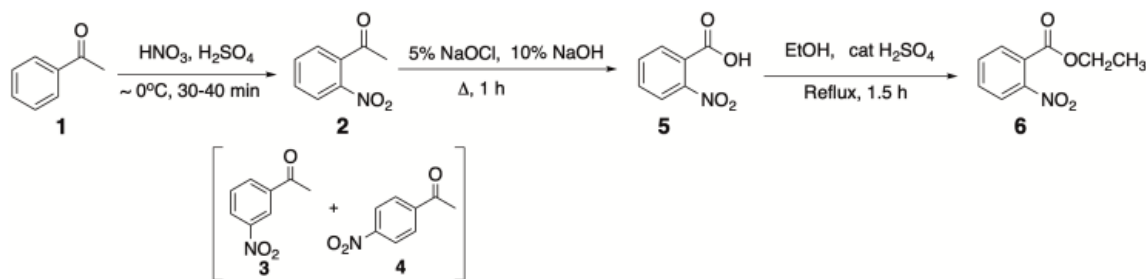


Figure 1. Chemistry 2212K Organic Synthesis Project

Scheme 1. Synthesis of ethyl *o*-nitrobenzoate

2. Materials and Instrumentation

The materials and instrumentation used for this experiment include:

- Experimental Instructions (contained in the addendum to the on-line Laboratory Text – Chemistry 2211K/2212K). [2]
- Acetophenone, concentrated HNO_3 and H_2SO_4 , 6 M HCl, 50 % NaOH (aq) (v:v), Methanol, Ethanol, Acetone, household bleach ($\sim 5\%$ NaOCl), distilled, deionized water.
- 2.5 cm $\times$ 7.5 cm, plastic-backed, silica gel coated G_F 254 TLC plates, eluted with 3:1 hexanes:diethyl ether.
- 120 mesh silica gel for flash chromatography.
- Buchi Rotary Evaporator.
- UV-Visible lamp
- Digimelt-45 apparatus for melting point analysis (uncorrected).
- Perkin-Elmer FTIR (Zn/Se ATR) for IR analysis with resolutions of 2 cm^{-1} .
- Anasazi-90 NMR operating at 90.51 MHz for ^1H spectroscopy.
- Shimadzu QP 20105 GC-MS for GC/MS analysis

equipped with a DB-5ms column (30 m $\times$ 0.25 mm i.d., 0.25 μm film thickness) in scan mode to identify the acetophenones. Helium was used as the carrier gas at a constant pressure of 150.5 kPa. A 1.0 μL aliquot of the sample in methylene chloride was injected in splitless mode at an injector temperature of 280°C . The GC oven temperature was initially held at 110°C for 1 min, increased to 300°C at a rate of $15^\circ\text{C}/\text{min}$, and then held at 300°C for 10 min. The GC-MS interface and MS ion source temperatures were maintained at 280 and 230°C , respectively. Mass spectra were acquired in electron ionization (EI) mode at an electron energy of 70 eV over a mass range of m/z 40–370.

- Drying Lamp.
- Kontes 2" chromatography column (0-100 % Ethyl Acetate: Hexanes)

3. Experimental Procedure

3.1. Preparation for the Synthesis Project

During the first laboratory session, students receive a presentation by the instructor on the project parameters and

laboratory tasks students are expected to accomplish during the semester. [9] Students then form small teams and select which synthesis pathway they plan to pursue. Next, students prepare a synthesis plan briefing (ppt format) which they present orally to the instructor at the next laboratory session.

The synthesis plan briefing includes the following items:

- The overall reaction pathway scheme,
- Balanced chemical equation for each step of the synthesis – all teams start with 2.0 grams of acetophenone,
- Mole table for the first reaction in the synthesis plan,
- General procedure for each synthesis step – adapted from [3],
- Tentative timeline for completion of the project.

Following feedback from the instructor and approval of their plan, students prepare their laboratory notebooks in accord with the GGC Organic Chemistry laboratory manual [2] for the first reaction in their synthesis plan and commence laboratory operations the following session.

3.2. Laboratory Synthesis Activities

3.2.1. Synthesis of *o*-nitroacetophenone (2)

Preparation of nitrating mixture. A 25 mL Erlenmeyer flask equipped with a thermometer and stir bar was placed into a salt-ice water bath and charged with HNO₃ (1.33 mL, 12 M) and H₂SO₄ (2.0 mL, 18.8 M). The mixture was stirred and temperature monitored to ensure the mixture temperature was maintained within a narrow range of -5 °C - 0 °C.

Preparation of *o*-nitroacetophenone. A 50 mL beaker equipped with a thermometer and stir bar was placed into a salt-ice water bath (ca. 0-5 °C) and charged with acetophenone (1) (2.00 g, 0.0166 mol) and concentrated H₂SO₄ (5.0 mL, 18.8 M) with continuous stirring. To the resulting solution was added the cold nitrating mixture dropwise slowly to prevent rapid temperature change over a 20-minute period. The temperature was observed to rise to ~10 °C during the administration of the nitrating mixture. The reaction was stirred for an additional 20 min once addition of the nitrating agent was complete while ensuring the low temperature (≤ 10 °C) was maintained. Then, the reaction mixture was slowly poured over an ice-water mixture (approximately 20 g ice and 20 mL distilled water) with stirring. When the ice was melted, the solution was filtered and approximately 0.51 g of *m*-nitroacetophenone was obtained. The filtrate was added to a separatory funnel, extracted with three 10 mL aliquots of EtOAc. The organic layers were combined, washed with 2 × 5 mL portions of distilled water, dried over Na₂SO₄ and the mixture separated via column chromatography. Upon concentration of the fractions under reduced pressure, a pale yellowish, semisolid product was obtained, *o*-nitroacetophenone (2) (run 1: 0.57 g, 21.0 % yield; run 2: 0.63 g, 23.1 % yield). TLC: R_f = 0.20. Melting range: 24-27 °C [lit m.p. 25-28 °C] [10]. IR (cm⁻¹): 3090 (Ar-H), 2950 (sp³ C-H), 1710 (C=O), 1616 (Ar C=C), 1530, 1355 (NO₂). ¹H NMR (ppm, CDCl₃): δ 8.08 (d, 1H, J=8.0 Hz), 7.82 – 7.27 (m, 3H), 2.52 (s, 3H). GC/MS (m/z): 165 (M⁺, 2 %); 150

(M⁺ - CH₃, 75 %); 91 (10 %); 76 (45 %); 43 (CH₃CO⁺, 100 %). Additional fractions, containing 3-nitroacetophenone (3) (run 1: 0.60 g + 0.51 g*, 40.5 % yield; run 2: 0.62 g + 0.55 g*, 42.7 % yield) and 4-nitroacetophenone (4) (run 1: 0.34 g, 12.3 % yield; run 2: 0.30 g, 11.1 % yield) were also obtained, but were not carried forward in the synthesis.

*Obtained during initial filtration.

3.2.2. Synthesis of *o*-nitrobenzoic acid (5)

A 125 mL beaker, equipped with a stir bar, was charged with 2 (1.10 g, 0.0066 mol), household bleach (5 % NaOCl, 80 mL), 10 % NaOH (5 mL) and heated to ~ 80 - 85 °C with stirring. The reaction was allowed to proceed for 1 h. The reaction mixture was allowed to cool to room temperature and ~ 4 mL acetone added to destroy any remaining NaOCl. Then, 6 M HCl was added slowly to the solution with stirring until a pH of 2-3 was reached. The cloudy suspension was then placed in an ice bath for 15 min. The cold solution was subjected to vacuum filtration. The crude product was washed with 2 × 5 mL portions of distilled water and dried under a heat lamp. Recrystallization from hot water afforded 5 (0.82 g, 74 % yield) as a pale, yellow solid. TLC: R_f = 0.11. Melting range: 150-152 °C [lit m.p. 146 - 148 °C] [11]. IR (cm⁻¹): 3260-2520 (COO-H), 1680 (C=O), 1630 (Ar C=C), 1537, 1362 (NO₂), 1290 (C-O). ¹H NMR (ppm, CDCl₃): δ 12.40 (1H, bs), 7.88-7.78 (m, 2H), 7.75-7.64 (m, 2H).

3.2.3. Preparation of ethyl *o*-nitrobenzoate (6)

A 25 mL round-bottomed flask, equipped with a stir bar, was charged with 5 (0.80 g, 0.0048 mol), ethanol (6.5 mL, 95 %) and concentrated H₂SO₄ (0.33 mL, 18.8 M). A reflux condenser is affixed to the flask and the reaction mixture refluxed for 1.5 h with stirring. The resulting reaction mixture was allowed to cool to room temperature and then placed into a separatory funnel, extracted with 3 × 5 mL aliquots of EtOAc and the organic layers combined. The organic layer was washed with 3 × 5 mL saturated NaHCO₃ and dried over Na₂SO₄. The solvent was removed under reduced pressure to afford 6 (0.76 g, 81 % yield) as a pale, yellow liquid that solidified upon cooling in an ice bath. TLC: R_f = 0.36. Melting range: 26 - 30 °C [lit m.p. 26-29 °C] [12]. IR (cm⁻¹): 3060 (Ar-H), 2950 (sp³ C-H), 1735 (C=O), 1630 (Ar C=C), 1550, 1350 (NO₂), 1290 (C-O-C). ¹H NMR (CDCl₃): δ 7.92 (d, 1H, J=7.5 Hz) 7.77-7.61 (m, 3H), 4.38 (q, 2H, J = 7.1 Hz), 1.39 (t, 3H, J = 7.1 Hz).

4. Results and Discussion

4.1. Synthesis

The synthesis plan undertaken is depicted in Scheme 2.

The nitration of acetophenone usually results in *m*-nitroacetophenone as the majority product. However, *o*-nitration and *p*-nitration of acetophenone may also occur if the reaction temperature exceeds 0 °C. [3,13,14] In this work, as the students administered the nitrating mixture to the

sulfuric acid-acetophenone reaction mixture over a 20 minute period, the temperature was observed to rise to as high as 10 °C and the solution became dark in color. Filtration of the reaction mixture in accord with Stradling and Gage [3] gave approximately 600 mg of *m*-nitroacetophenone solid. The filtrate was placed into a separatory funnel and extracted with three 10 mL aliquots of ethyl acetate. Following drying of the organic layer with sodium sulfate and filtration, the solvent was removed under reduced pressure to afford a mixture of the *o*, *m*, *p*-nitroacetophenones, 2 - 4, as a reddish, oily solid. Because isolation of the *o*-nitroacetophenone and *p*-nitroacetophenone could not be effected via filtration, column chromatography was performed. The students then conducted another run to see if their initial findings were reproducible. In the second run, the administration of the chilled nitrating mixture was done more slowly so that the temperature of the reaction mixture did not rise above 5 °C. Once again, however, a complex mixture was obtained, and a chromatographic separation was required. Overall, the nitrations were very effective, with the average yield for the two runs exceeding 75 %. Following purification and analysis, the *o*-nitroacetophenone from runs 1 and 2 were combined and used in the oxidation to the benzoic acid.

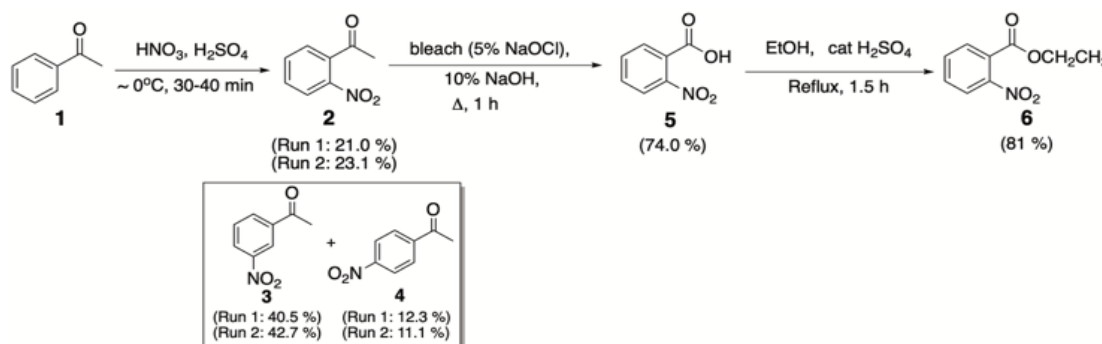
The green oxidation of *o*-nitroacetophenone was

conducted using the method described by Stradling and Gage. [3] The reaction time was lengthened to 1 h to account for the likely lower reactivity due to the steric effect of the adjacent nitro group to the acetophenone methyl moiety. The crude product, obtained as a pale, yellow solid, was recrystallized from boiling water to give 5 as a yellow microcrystalline solid in 74 % yield, which was of satisfactory purity for further analysis.

The Fischer esterification of *o*-nitrobenzoic acid was modified by preparing the ethyl ester instead of the methyl esterification typically performed. [3] Preparation of the ethyl ester was conducted instead of the methyl ester since the ethyl ester product is nominally a solid at room temperature. The reaction time was lengthened to 1.5 h to account for the lower nucleophilicity of the ethanol versus methanol in the Fischer esterification. Following isolation, the product, 6, was obtained in sufficient purity for analysis.

4.2. Characterization

For each of the products in the three-step synthesis, experimental IR and ¹H NMR spectra were obtained and compared with reported literature spectroscopic data. In all cases, spectral results from compounds 2, 5 and 6 were found consistent with previously reported data. See Tables 1 and 2.



Scheme 2. Synthesis of ethyl *o*-nitrobenzoate

Table 1. Key IR Functional group wavenumbers for 2, 5 and 6

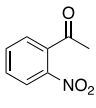
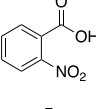
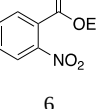
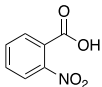
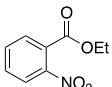
Compound	Functional Group	Experimental IR Spectral Wavenumbers ^a (cm ⁻¹)	Literature IR Spectral Wavenumbers (cm ⁻¹)	Ref.
 2	Ar-H sp ³ C-H C=O Ar C=C NO ₂	3090 2950 1710 1616 1530, 1355	3100 2955 1715 1620 1540, 1365	15
 5	O-H C=O Ar C=C NO ₂ C-O	3260-2520 1680 1630 1537, 1362 1290	3250-2550 1681 1630 1533, 1366 1293	16
 6	Ar-H C=O Ar C=C NO ₂ C-O-C	3060 1735 1630 1550, 1350 1290	3065 1737 1625 1540, 1350 1291	17

Table 2. Proton Chemical Shifts for **2**, **5** and **6**

Compound		Experimental ¹ H NMR	Literature ¹ H NMR	Ref.
		δ (ppm)	δ (ppm)	
 2	Ar-H -CH ₃	8.08 (d, J=8.0 Hz, 1H) 7.82 – 7.27 (m, 3H) 2.52 (s, 3H)	8.10 (d, J=8.1 Hz, 1H) 7.85 – 7.30 (m, 3H) 2.55 (s, 3H)	15
 5	O-H Ar-H	12.4 (bs, 1H) 7.88-7.78 (m, 2H) 7.75-7.64 (m, 2H)	12.5 (bs, 1H) 7.90-7.80 (m, 2H) 7.75-7.65 (m, 2H)	16
 6	Ar-H CH ₂ CH ₃	7.92 (d, 1H, J=7.5 Hz) 7.77-7.61 (m, 3H) 4.38 (q, 2H, J=7.1 Hz) 1.37 (t, 3H, J=7.1 Hz)	7.93 (d, 1H, J=7.6 Hz) 7.77 (d, 1H, J=7.2 Hz) 7.72-7.62 (m, 2H) 4.40 (q, 2H, J=7.2 Hz) 1.36 (t, 3H, J=7.2 Hz)	18

5. Conclusions

This modification of the synthesis project represents an alternative pathway that students may follow in the event the nitration of acetophenone yields a substantial proportion of *o*-nitroacetophenone in addition to the usual *m*-nitroacetophenone. The ability to use this product instead of discarding it was in keeping the value of scientific inquiry as well as with the green chemistry principle of waste minimization. Subsequent oxidation to *o*-nitrobenzoic acid was accomplished using the procedures set forth by Stradling and Gage. [3] The final esterification step to prepare ethyl *o*-nitrobenzoate was the second modification to ensure a solid product is obtained. All products were satisfactorily characterized, and spectral results were found to be in good agreement with the scientific literature. Yields for the individual reactions with the modifications were also satisfactory, giving an overall reaction sequence yield of 13.2 %. The students conducting the experiments found that the synthesis, isolation and analysis of the intermediate and final products were interesting and challenging. They also enjoyed learning additional isolation and purification techniques while undertaking a synthesis pathway that resulted in different organic products.

ACKNOWLEDGEMENTS

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REFERENCES

- [1] Coppock, P., Park, S. H., Pennington, R., Pursell, D., Rudd, G., Sloop, J., Tsoi, M. "Enhancing Research Skills and Attitudes in Undergraduate Organic Chemistry with a Course-embedded Undergraduate Research Experience (CURE) via Green Organic Synthesis," *J. Lab. Chem. Educ.*, 2017, 5(3), 41-47. <https://10.5923/j.lce.20170503.01>.
- [2] Sloop, J., Pennington, R., Tsoi, M., Paredes, J., Pursell, D., Coppock, P., Giles, G. Laboratory Text for Chem 2211K/2212K Organic Chemistry, edited and compiled by J. C. Sloop, 2012. <https://10.13140/RG.2.1.3353.7448>.
- [3] Stradling, S.; Gage, C. "And the Winner Is...A Multistep Synthesis for the Introductory Organic Course," *J. Chem. Educ.*, 1985, 62(12), 1116-1117. <https://10.1021/ed062p1116>.
- [4] Mordacq, J.; Drane, D.; Swarat, S.; Lo, S. "Development of Course-Based Undergraduate Research Experiences Using a Design-Based Approach," *J. Coll. Sci. Teach.*, 2017, 46(4), 64-75. <https://doi.org/10.1155/2023/1295987>.
- [5] Wilczek, L.; Clarke, A.; Martinez, M.; and Morin, J. "Catalyzing the Development of Self-Efficacy and Science Identity: A Green Organic Chemistry CURE," *J. Chem. Educ.*, 2022, 99(12), 3878-3887. <https://10.1021/acs.jchemed.2c00352>.
- [6] Haining, R., Sloop, J. "A New Model for Advanced Undergraduate Chemistry Laboratory Courses: A Two-semester Integrated Laboratory Experience," *J. Lab. Chem. Educ.*, 2018, 6(2), 24-30. <https://10.5923/j.lce.20180602.02>.
- [7] Sloop, J., Awong-Taylor, J., Mundie, T. "Raising Student Awareness of Research Opportunities at Georgia Gwinnett College," *CUR Quarterly on the Web*, 2012, 33(2), 3-8. https://www.researchgate.net/publication/233911416_Raising_Student_Awareness_of_Research_Opportunities_at_Georgia_Gwinnett_College.

- [8] Bindewald, J.; Dobiesz, G.; Medrano-Cervantez, I.; Moody, K.; Rockey, T.; Sloop, J. C.; Taza, J.; Woodbridge, C. M. "The Preparation of *meso*-Stilbene Dibromide: Scaffolding Green Chemistry Principles via an Electrophilic Addition Reaction," *J. Lab. Chem. Educ.*, 2023, *11*(2), 15-19. <https://10.5923/j.jlce.20231102.01>.
- [9] Instructor briefing slides are available as supplemental material.
- [10] 2-Nitroacetophenone m.p.: <https://www.fishersci.com/shop/products/o-nitroacetophenone-95-thermo-scientific/AC128320025>. Accessed 18 Feb 2026.
- [11] 2-Nitrobenzoic acid m.p.: https://www.chemsrc.com/en/cas/552-16-9_587973.html. Accessed 18 Feb 2026.
- [12] Ethyl 2-nitrobenzoate m.p.: <https://www.chembk.com/en/chem/Ethyl%202-nitrobenzoate>, Accessed 18 Feb 2026.
- [13] Barkenbus, C.; Clements, J. "The Nitration of α -Chloro and α -Bromoacetophenone," *J. Amer. Chem. Soc.*, 1934, *56*(6), 1369-1370. <https://10.1021/ja01321a041>.
- [14] Leonard, N.; Boyd Jr. S. "Cinnolines. I. Synthesis of Aminoacetophenones and Aminopropiophenones," *J. Org. Chem.*, 1946, *11*(4), 405-418. <https://10.1021/jo01174a018>.
- [15] 2-nitroacetophenone IR & ^1H NMR: https://www.chemicalbook.com/SpectrumEN_577-59-3_1HNMR.htm, Accessed 4 March 2026.
- [16] Samsonowicz, M.; Wisłocka, R. S.; Regulska, E.; Lewandowski, W. Experimental and Theoretical IR, Raman, NMR Spectra of 2-, 3-, and 4-Nitrobenzoic Acids, *J. Quant. Chem.*, 2007, *107*(2), 480–494. <https://10.1002/qua.21085>.
- [17] Ethyl 2-nitrobenzoate IR: <https://webbook.nist.gov/cgi/inchi?ID=C610344&Type=IR-SPEC&Index=1#IR-SPEC>. Accessed 4 Mar 2026.
- [18] Islam, S.; Ghosh, K.; Roy, A.; Molla, R. Polymer supported Pd catalyzed carbonylation of aryl bromides for the synthesis of aryl esters and amides, *RSC Adv.*, 2014, *4*(73), 38986-38999. <https://10.1039/C4RA05365F>.