

# A Nitration Reaction Puzzle for the Organic Chemistry Laboratory

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To enhance the critical thinking and problem-solving skills of chemistry students, our second-semester organic chemistry laboratory course incorporates a number of guided-inquiry structure elucidation exercises. In each exercise, students, following provided instructions, synthesize an unknown product whose structure is determined from an analysis of infrared and  $^1\text{H}$  NMR spectral data and any other data students deem relevant. This *Journal* has published numerous articles (1–15) that have inspired the majority of exercises performed in the course. One such exercise is an adaptation of a nitration experiment in which phenylacetic acid is treated with fuming (90%) nitric acid (16). In our adaptation, half the class performs the nitration of phenylacetic acid using fuming (90%) nitric acid while the other half of the class uses concentrated (70%) nitric acid.

During the course of the reaction, the two groups of students are encouraged to engage in discussions among themselves. Based on the presence of a carboxyl group in the starting material, students need to verify the acidity of their nitration product and to determine its neutralization equivalent. On the basis of melting point and neutralization equivalent data, students compile a list of nitration product possibilities. Infrared spectroscopy is then utilized in an attempt to determine the nature of benzene ring substitution that has resulted from nitration. Lastly, students obtain a  $^1\text{H}$  NMR spectrum of their nitration product and assign structure. The class is asked to compare and contrast the products synthesized in the two nitration runs.

## Experimental Procedure

In a well-ventilated fume hood, 2.5 g of phenylacetic acid was slowly added to a 50 mL round-bottom flask containing 25 mL of either 90% or 70% nitric acid. During the addition process, the temperature of the reaction mixture was maintained between 25–35 °C. When all the phenylacetic acid had been added to the nitric acid, the reaction mixture was heated at reflux for approximately one hour. The reaction mixture was then cooled to room temperature, after which, the contents of the round-bottom flask were poured into 35–40 mL of ice-water. The precipitated product (crystallization may need to be induced) was collected via suction filtration, washed with a minimum quantity of cold water, and allowed to air dry in the suction funnel for at least 15–20 minutes.

## Instrumentation

Infrared spectra were taken on a Thermo Electron Corporation Nicolet 380 infrared spectrophotometer.  $^1\text{H}$  NMR spectra were taken on an Anasazi Instruments EFT-60 NMR spectrometer.  $^1\text{H}$  NMR samples are 2–5% (wt/v)  $\text{CDCl}_3$ - $\text{DMSO}-d_6$  solutions. GC–MS analyses were carried out on a Hewlett-Packard 5890 GC–5973 MS instrument controlled by a Hewlett-Packard ChemStation.

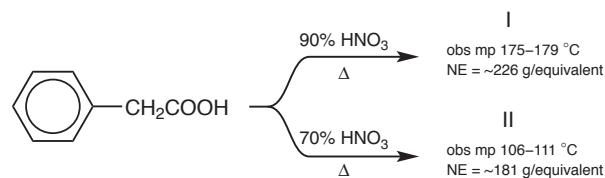
## Hazards

Both 90% and 70% nitric acid are powerful oxidizing agents and highly corrosive liquids capable of causing serious injury to the eyes, skin, and respiratory tract. Students should exercise extreme caution by wearing gloves and eye protection at all times when working with nitric acid. The nitration products of phenylacetic acid obtained in this experiment are considered to be irritants. Phenylacetic acid is an eye, skin, and respiratory irritant and a possible teratogen that has a particularly objectionable odor that clings to clothing, skin, and hair. To minimize an individual's exposure, phenylacetic acid must be weighed, transferred, and kept in a fume hood. Likewise, the generation of toxic fumes during the course of the nitration reaction makes it imperative that this experiment be performed in a well-ventilated fume hood. Dispose of hazardous waste according to local, state, and federal regulations.

## Results and Discussion

The nitration experiment described herein illustrates fundamental electrophilic aromatic substitution concepts while posing an interesting structure elucidation puzzle for organic chemistry students. The nitration of phenylacetic acid requires students to ponder the directing ability of the carboxymethyl group. Given that nitric acid is a powerful oxidizing agent, students must also ponder whether the carboxymethyl group is subject to oxidation under the reaction conditions employed. Lastly, students must determine what impact, if any, the concentration of the nitric acid used will have on the structures of the nitration products obtained. This is an important consideration because a nitric acid to phenylacetic acid mole ratio in excess of 20:1 is employed in the nitration reaction using 90% nitric acid as well in that using 70% nitric acid.

The reaction of 90% nitric acid and phenylacetic acid yields **I**, a yellow solid with an observed melting point of 175–179 °C (Scheme I). As Southam (16) points out, product **I** is consistent with being 2,4-dinitrophenylacetic acid (mp 179–180 °C) or 2,4-dinitrobenzoic acid (mp 183 °C). Acid–base titration of product **I** leads to a neutralization equivalent (NE) of approximately 226 g/equivalent and to the tentative conclusion that product **I** is 2,4-dinitrophenylacetic acid. The presence of



Scheme I. Nitration reaction of phenylacetic acid.

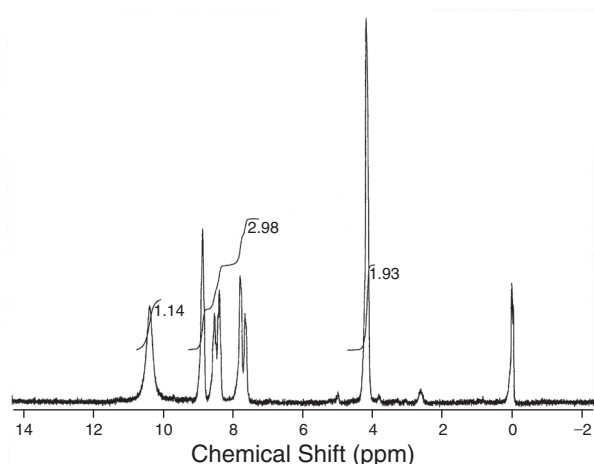
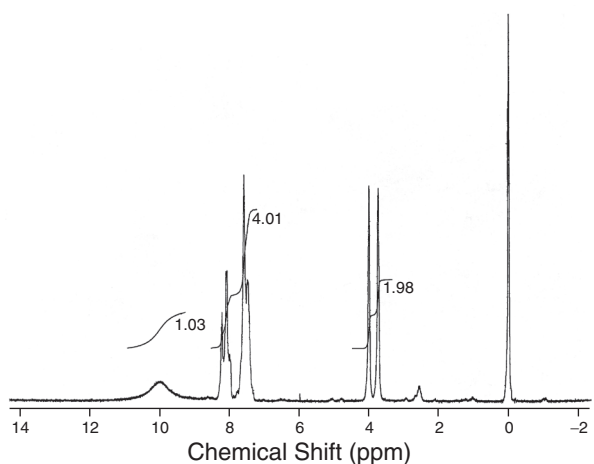
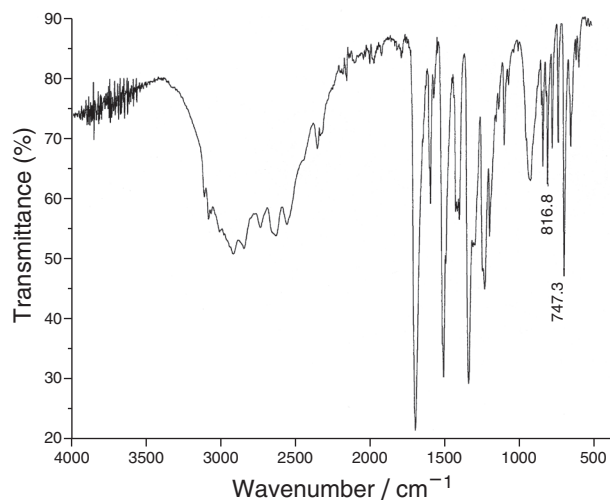
Figure 1. 60 MHz  $^1\text{H}$  NMR spectrum of product I.Figure 2. 60 MHz  $^1\text{H}$  NMR spectrum of product II.

Figure 3. Infrared spectrum of product II.

a methylene singlet at  $\delta$  4.1 ppm in the  $^1\text{H}$  NMR spectrum of I (Figure 1) strongly supports this conclusion. GC–MS analysis<sup>1</sup> confirms that product I is 2,4-dinitrophenylacetic acid based on a direct comparison with a known sample.

The reaction of 70% nitric acid and phenylacetic acid yields II, a pale yellow solid with an observed melting point of 106–111 °C (Scheme I). Acid–base titration of product II leads to a neutralization equivalent of approximately 181 g/equivalent that students quickly note correlates with nitrophenylacetic acid. Of the three structurally isomeric nitrophenylacetic acids, the para-isomer has a mp of 152 °C (17), the ortho-isomer has a melting point of 141 °C (17), and the meta-isomer has a melting point of 120 °C (17).

At this point in their analysis, students must reconcile the following conflicting facts. If product I is 2,4-dinitrophenylacetic acid, then the carboxymethyl group of phenylacetic acid must be an ortho–para director. Yet the observed melting point of product II correlates best with that of *m*-nitrophenylacetic acid. Examination of the  $^1\text{H}$  NMR spectrum of II (Figure 2) further confuses the issue for students. Two methylene singlet signals are present at  $\delta$  3.7 ppm and  $\delta$  4.0 ppm. However, none of the three nitrophenylacetic acid isomers should have a  $^1\text{H}$  NMR spectrum in which two methylene signals are present.

Whereas the semester's synthesized products and unknowns have heretofore been pure substances, students are invariably challenged to discern that product II is a mixture of *ortho*- and *para*-nitrophenylacetic acid. An infrared spectrum of product II (Figure 3) shows characteristic peaks at 747.3  $\text{cm}^{-1}$  and 816.8  $\text{cm}^{-1}$  that are indicative of *ortho*- and *para*-substituted benzene derivatives, respectively. GC–MS analysis<sup>1</sup> of product II confirms its identity as a mixture of *ortho*- and *para*-nitrophenylacetic acid based on a direct comparison with the commercially available *ortho*- and *para*-compounds.

## Summary

The nitration reaction exercise described reinforces electrophilic aromatic substitution concepts. It requires students to analyze and integrate spectral and chemical data to reach a valid conclusion and, most importantly, provides an opportunity for students to “think outside the box”. It is a relatively straightforward experiment that is capable of being performed in a four-hour laboratory period. Although unintended, it also affords organic chemistry students the opportunity to learn how to minimize the dangers of working with noxious substances.

## Note

1. GC–MS analysis of the nitration product is performed as a demonstration for our second-semester organic chemistry students and is not an integral component of the experiment. Such analyses are performed by students enrolled in our instrumental analysis course.

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