

Gold(III)-Catalyzed Hydration of Phenylacetylene

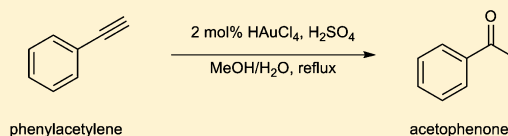
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S Supporting Information

ABSTRACT: A guided inquiry-based experiment exploring the regioselectivity of the hydration of phenylacetylene is described. The experiment uses an acidic gold(III) catalyst in a benign methanol/water solvent system to introduce students to alkyne chemistry and key principles of green chemistry. The experiment can be easily completed in approximately 2 h, and is suitable for use in introductory organic chemistry laboratories. The experiment is versatile and amenable to many lab settings, as it requires no specialized glassware, and the crude product can be analyzed via gas chromatography, infrared spectroscopy, or nuclear magnetic resonance spectroscopy.

KEYWORDS: Second-Year Undergraduate, Laboratory Instruction, Organic Chemistry, Inquiry-Based/Discovery Learning, Aldehydes/Ketones, Alkynes, Catalysis, Green Chemistry, Spectroscopy



Relatively few experiments for an introductory undergraduate organic chemistry lab demonstrate addition reactions to alkynes,¹ despite the fact that this topic is typically covered extensively in a corresponding lecture class. Recent research into the hydration of alkynes has focused on the use of less toxic and more reactive transition metal catalysts such as gold(I), gold(III), platinum(II), and palladium(II).² Of these alternate catalysts, the use of gold complexes seems to be taking a prominent role.³ For this experiment, HAuCl₄ was selected as the gold(III) catalyst, and an electron-rich aryl alkyne was selected as the substrate to ensure the reaction could be completed rapidly and reliably within the constraints of a typical 3–4 h lab class. Catalytic activity of the gold(III) catalyst is improved by the addition of H₂SO₄ as an acidic cocatalyst.⁴

As most organic chemistry textbooks^{5,6} include only the classic Hg²⁺-catalyzed Kucherov⁷ conditions for alkyne hydration, the use of a gold(III) catalyst presented an excellent opportunity to write the experiment in a discovery-based fashion.⁸ If water adds in an anti-Markovnikov fashion, the product will be phenylacetaldehyde; if it adds in a Markovnikov fashion, the product will be acetophenone (Scheme 1). The two possible products are easily differentiated using gas chromatography (GC), infrared (IR) spectroscopy, and ¹H or ¹³C nuclear magnetic resonance (NMR) spectroscopy. From the product obtained, students are challenged to make general predictions regarding the regioselectivity of the addition reaction, and to apply their knowledge by predicting the

major products of gold(III) catalyzed hydrations of other terminal alkynes in a postlab assignment (Supporting Information).

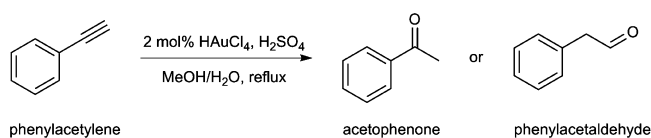
EXPERIMENTAL SECTION

Students work in groups of two and utilize a procedure^{9,10} that can be completed in approximately 2 h. Students dissolve phenylacetylene (220 μL, 2.0 mmol) in methanol (3.0 mL), add an aqueous solution of the HAuCl₄ catalyst (400 μL, 0.10 M, 2.0 mol %), and add 1 or 2 drops of concentrated H₂SO₄ (~100 μL). The reaction mixture is stirred at, or near, reflux temperature for 20–30 min, until metallic gold can be observed precipitating from the solution. The reaction mixture is neutralized with aqueous sodium bicarbonate solution (saturated, 3.0 mL), and the product is extracted with diethyl ether (2 × 3.0 mL). The ether solution is washed with brine solution (saturated, 2 × 3.0 mL) and dried over sodium sulfate before filtering through a short silica gel column. A sample of the ether solution is used for GC analysis. Evaporation of the remaining ether under a stream of air affords the crude product as a pale yellow liquid that is suitable for IR analysis. Students are provided with representative ¹H and ¹³C NMR spectra (Supporting Information).

HAZARDS

Gloves should be worn while manipulating the reagents for this experiment. Phenylacetylene is harmful and flammable. Hydrogen tetrachloroaurate and sulfuric acid are both corrosive. Phenylacetaldehyde and acetophenone are harmful. Methanol and diethyl ether are both flammable and toxic. Sodium bicarbonate, sodium chloride, sodium sulfate, and silica gel are nonhazardous.

Scheme 1. Potential Products from the Hydration of Phenylacetylene



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DISCUSSION

This experiment has been performed by ~150–180 students per year for the past five years. The experiment has been included near the end of the term of a first-semester introductory undergraduate organic chemistry course that is required of all chemistry, biochemistry, forensic science, and B.S. biology majors. At the point in the semester that this experiment is introduced, students have already been exposed to GC, IR, and NMR spectroscopy.

Typical student yields ranged from ~40–80%. Percent conversion to the acetophenone product was generally high, ~80–98%, as calculated by GC. In the cases where incomplete conversion (~50–70%) to product was observed, it was suspected that temperature played a role. If the solution was refluxed too vigorously, metallic gold could be observed precipitating from the solution earlier in the reaction, which was correlated with a lower conversion to product and a lower percent yield.

An IR spectrum (Supporting Information) of the product clearly showed the absence of alkyne peaks (3288 and 2107 cm^{-1}) and the presence of a conjugated carbonyl at 1675 cm^{-1} that was assigned to acetophenone. Analysis of a sample ^1H NMR spectrum of the product (Supporting Information) clearly showed the singlet corresponding to the methyl ketone ($\delta = 2.50$ ppm) of acetophenone and the absence of an aldehydic proton signal ($\delta = 9.90$ ppm) that would be expected if the hydration reaction proceeded via the anti-Markovnikov pathway to yield phenylacetaldehyde. From a sample ^{13}C NMR spectrum of the product (Supporting Information), the aliphatic carbon signal ($\delta = 26$ ppm) was assigned to the methyl carbon of acetophenone.

GREEN CHEMISTRY

The 12 principles of green chemistry¹¹ are heavily emphasized throughout the sequence of laboratory experiments that students complete. The student handout for the experiment (Supporting Information) includes the 12 principles and highlights those that pertain to this experiment: prevention of waste, atom economy, less hazardous chemical syntheses, and catalysis. After completing the experiment, students analyzed the greenness of the reaction and suggested ways in which the procedure could be improved to increase the greenness of the reaction.

SUMMARY

An experiment was described that effectively demonstrated an alkyne hydration reaction without the use of a toxic mercury salt. The experiment was straightforward and can be completed in approximately 2 h, requiring no specialized glassware or inert conditions. The product of the hydration reaction was analyzed using GC, IR, and NMR spectroscopy. As any one of these techniques can be used as a stand-alone method of analysis, this experiment is easily adaptable to many lab settings, depending on equipment availability and the instructors' discretion. Presentation of the experiment in a discovery-based format enriches the experience for the students by engaging their critical thinking skills. The reaction is an excellent example to introductory organic chemistry students of many key principles of green chemistry.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available on the ACS Publications website at DOI: 10.1021/acs.jchemed.5b00628.

A student handout, consisting of a prelaboratory worksheet, an introduction to the experiment, full experimental details, postlaboratory questions, and notes for instructors; representative GC-FID chromatograms (student generated) and IR and ^1H and ^{13}C NMR spectra (instructor generated) (PDF, DOCX)

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Notes

The authors declare no competing financial interest.

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