JOURNAL OF CHEMICAL EDUCATION

Laboratory Experiment

pubs.acs.org/jchemeduc

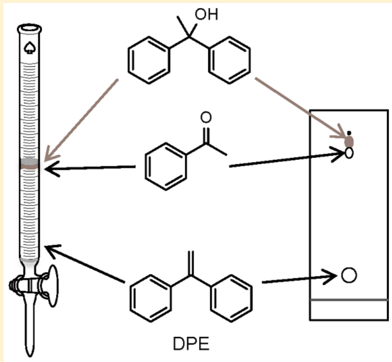
Synthesis of 1,1-Diphenylethylene (DPE): The Marriage of a Grignard Reaction and a Column Chromatography Experiment

Lisa T. Alty,* Marcia B. France, Isaac G. Alty,† Christine A. Saber,‡ and Donna M. Smith

Department of Chemistry and Biochemistry, Washington and Lee University, Lexington, Virginia 24450, United States

Supporting Information

ABSTRACT: The synthesis of 1,1-diphenylethylene (DPE) via a Grignard reaction, followed by an acid-catalyzed dehydration reaction, yields a mixture of compounds. DPE is a high boiling liquid that cannot be purified using simple distillation. However, it is easily separated from the more polar starting material and intermediate alcohol using both thin layer and column chromatography. Second-semester organic chemistry laboratory students learn the techniques of running reactions under anhydrous conditions and of column chromatography. In addition, the experiment demonstrates clearly the relationship between thin layer and column chromatography.

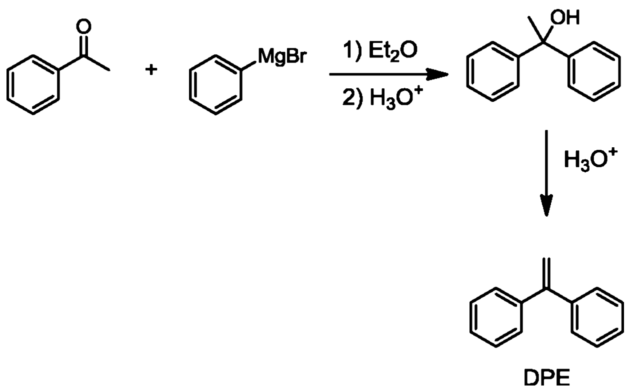


KEYWORDS: *Second-Year Undergraduate, Laboratory Instruction, Organic Chemistry, Hands-On Learning/Manipulatives, Grignard Reagents, Elimination Reactions, Thin Layer Chromatography, Chromatography*

■ INTRODUCTION

Both the Grignard reaction and the technique of column chromatography remain standards in the second-year organic chemistry laboratory lexicon;[1] column chromatography is often employed in the biochemistry laboratory when separating mixtures of proteins. The experiment serves as an introduction to (1) the anhydrous reaction techniques necessary for a successful Grignard reaction, (2) column chromatography, and (3) a refresher in thin layer chromatography (TLC) in a second-semester introductory organic chemistry laboratory course. It combines these techniques in the synthesis of 1,1-diphenylethylene (DPE), a colorless alkene product (Scheme 1).[2,3] The high boiling point of DPE makes distillation impractical as a means of purification, so column chromatography is employed. Because both the reactants and the products of the reaction are colorless, students are unable to visualize the separation process during chromatography. Students utilize TLC to monitor the two reactions, as well as the column chromatography purification process. Unlike typically employed TLC and column chromatography experiments that separate colored organic molecules,[4,5] dyes,[6] or pigments from plant sources,[7−9] this experiment requires students to evaluate the column separation *after* it has occurred using TLC. Because many organic and biomolecules are colorless in solution, this column chromatography experiment most resembles a research laboratory experience in separation science and results in a pure product.

Scheme 1. Synthesis of DPE



The goals of this experiment are as follows:

(1) Students will achieve competency with anhydrous reaction techniques as evidenced by production of a Grignard product.
(2) Students will achieve competency in column chromatography technique, as evidenced by separation of DPE from other reaction compounds, as well as responses in the laboratory reports and prelab quizzes.
(3) Students will follow the progress of a reaction using TLC, and predict and determine the results of a colorless column chromatography separation using TLC, as evidenced by responses in the laboratory report and prelab quizzes.
(4) Students will demonstrate knowledge of the mechanism of the Grignard reaction, the mechanism of the

DOI: 10.1021/acs.jchemed.5b00212
J. Chem. Educ. XXXX, XXX, XXX−XXX

elimination reaction, and infrared (IR) characterization of alkenes, as evidenced by responses in the laboratory reports.

In this *Journal*, DPE has been used as a substrate in organic chemistry laboratories for bromination reactions[10,11] and in fluorescence kinetics experiments.[12] DPE as a monomer has attracted significant interest from both academia and industry. It has been used as an additive to initiate (with a free-radical initiator) and control radical polymerizations in the synthesis of block copolymers.[13] "DPE can undergo copolymerization by living anionic polymerization but is incapable of forming a homopolymer due to steric hindrance."[14]

■ EXPERIMENTAL OVERVIEW

The experiment has multiple parts: the Grignard addition and workup, the dehydration reaction and workup, and the purification of DPE by column chromatography. As presented, the experiment requires three laboratory periods: one for the Grignard reaction (3 h), one for the dehydration (2 h), and another for the column chromatography experiment (2.5 h). Students conduct the Grignard reaction and dehydration in pairs; students divide the crude product and purify DPE using column chromatography individually.

Grignard Reaction

The glassware setup is dried using a heat gun; drying tubes are placed to maintain dryness in the reaction vessel and addition funnel. A solution of phenyl magnesium bromide in THF (1.0 M; 1.8 equiv) is added slowly over a 5 min period to a stirred solution of acetophenone (1 equiv) in diethyl ether at 0 °C. A precipitate forms during the addition. After the addition is complete, the solution is allowed to warm to room temperature with stirring over a period of 25 min. The solution is chilled to 0 °C again, and water and dilute hydrochloric acid are added dropwise to quench any remaining Grignard reactant and to release the product, 1,1-diphenylethanol. The product mixture is extracted into diethyl ether, and the progress of the reaction is examined using TLC. The solvent is removed by rotary evaporation to yield a pale yellow oil.

Dehydration Reaction

The oil is dissolved in a cold (4 °C) solution of concentrated acetic acid and concentrated sulfuric acid (4:1 v/v). After addition of cold water, the product is extracted into diethyl ether to isolate crude DPE. The solvent is removed by rotary evaporation to yield a brown oil.

Column Chromatography

The column is prepared using the slurry method. Silica gel (60−200 μm, 7.5 g) and hexane/dichloromethane (DCM) (2:1 v/v, 75 mL), the eluting solvent, are mixed and poured into a buret (1 cm i.d., 50 mL). The product mixture (0.25 g or less) is applied to the silica gel column (16.0 cm high), and eight test tubes containing 3 mL of eluent are collected. TLC conditions: plates, Silica Gel GHLF, Analtech, Cat. no. 21521; eluent, hexane/DCM (2:1 v/v); visualization, UV light, followed by iodine chamber. R_f values for the reaction components are the following: acetophenone, 0.10; 1,1-diphenylethanol, 0.07; 1,1-diphenylethylene, 0.72. Fractions containing DPE are combined and the solvent is removed by rotary evaporation. Analysis is conducted using IR spectroscopy.

Full details are available in the Supporting Information.

■ HAZARDS

Appropriate personal protection (safety glasses, gloves, lab coat) should be worn at all times. All reactions and chromatography should be carried out in a fume hood. Diethyl ether is an extremely flammable liquid that causes serious eye irritation and is harmful if swallowed or inhaled. Acetophenone is a combustible liquid that causes serious eye damage and is harmful if swallowed. Tetrahydrofuran is a highly flammable liquid, causes serious eye irritation, may cause respiratory irritation, and is suspected of causing cancer. Phenylmagnesium bromide causes severe skin burns and eye damage. Hydrochloric acid causes severe skin burns and serious eye damage, may cause respiratory irritation, and may be corrosive to metals. Sulfuric acid causes severe skin burns and serious eye damage and may be corrosive to metals. Acetic acid is a flammable liquid and causes severe skin burns and eye damage. Hexane is a highly flammable liquid that causes skin irritation and may be fatal if swallowed and enters airways. It is suspected of damaging fertility or the fetus and may cause damage to the nervous system through prolonged or repeated exposure if swallowed. DCM causes skin irritation and serious eye irritation and may cause respiratory irritation. DCM is a suspected carcinogen; it may cause damage to the liver, blood or central nervous system through prolonged or repeated exposure if swallowed or inhaled. DPE and 1,1-diphenylethanol are not hazardous substances, but should be handled using standard precautions. Silica gel powder is not a hazardous substance, but it should not be inhaled; take precautions when pouring/measuring. Iodine vapor is a skin and eye irritant and should not be inhaled.

■ RESULTS AND DISCUSSION

By coupling Grignard and dehydration reactions to column chromatography, students had a satisfying experience with both procedures. Students isolated and characterized a pure product from the Grignard reaction and appreciated column chromatography as a useful purification technique. This experiment also served as an introduction to anhydrous reaction procedures. As this experiment was employed at the beginning of a second-semester introductory organic chemistry course, students were reacquainted with liquid−liquid extraction, use of a rotary evaporator, and thin layer chromatography.

At the end of the Grignard reaction workup, TLC revealed acetophenone, 1,1-diphenylethanol, and DPE, in roughly equal amounts. At the end of the dehydration reaction, TLC revealed mostly DPE with small amounts of acetophenone, 1,1-diphenylethanol, and trace amounts of two other unidentified impurities. At this stage, the average student yield of crude product was 0.72 g (65%), with a standard deviation of 0.33 g, n = 100. Column chromatography of this crude product yielded an average student recovery of pure DPE of 63%, with a standard deviation of 25%, n = 104. TLC analysis of the eluent test tubes against the product standard solution revealed pure DPE in test tubes numbered 3−6 (Figure 1).

This experiment has been performed by six sections of approximately 20 second-semester introductory organic chemistry students each, without difficulty. Only two of 50 pairs of students did not generate a Grignard product; those students were given crude product mixture to run the column. All students separated and isolated DPE from acetophenone and 1,1-diphenylethanol using column chromatography. Laboratory reports and prelab quizzes required students to draw out the

DOI: 10.1021/acs.jchemed.5b00212
J. Chem. Educ. XXXX, XXX, XXX−XXX

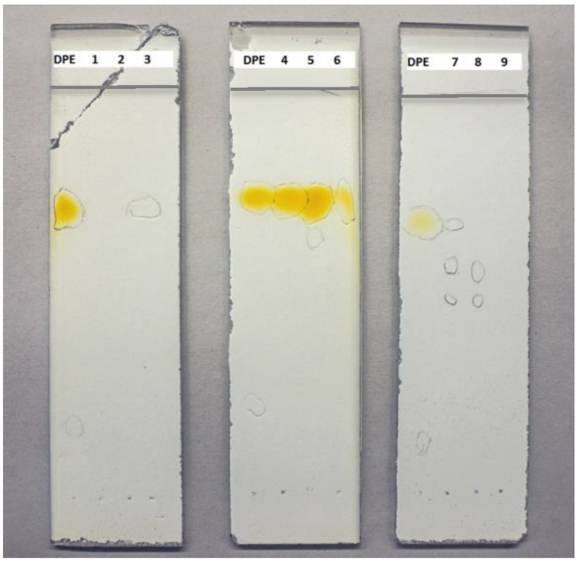


Figure 1. TLC analysis of fractions is shown after UV visualization and development in an iodine chamber. DPE standard is the first lane on each plate; fraction numbers are indicated above the solvent front line. DPE is in fractions 3−6; a small amount of DPE is in fraction 7, along with other impurities. Neither acetophenone nor 1,1-diphenylethanol is eluted.

complete reaction mechanism, calculate R_f values, attempt to identify the impurities in the TLC analysis, explain the ease of the dehydration reaction, answer general questions about chromatography, and identify specific IR stretching and bending modes in DPE. Students' yields, as well as the quality of their reports, demonstrated that the goals of the experiments were met. The mean scores on these assignments were the following: prelab quiz, Grignard reaction and dehydration (81%); prelab quiz, column chromatography and TLC (91%); Grignard reaction and dehydration report (87%); column chromatography report (87%); IR interpretation report (88%).

Students characterized DPE using IR spectroscopy; they identified and labeled the peaks for sp^2 C−H stretches, C═C stretches, vinyl ═C−H out-of-plane bend, and aromatic ═C−H out-of-plane bends. IR spectra showed the lack of C═O (from acetophenone) and the lack of OH (from the alcohol), as well as the presence of aromatic C═C and sp^2 C−H stretches. Characterization using GC/MS, and ^{1}H NMR and ^{13}C NMR spectroscopy can also be utilized, and conditions are described and spectra provided in the Supporting Information.

One of the unexpected outcomes of this experiment was students' understanding of the relationship between TLC and column chromatography. For some students, making the connection between what was happening within the column and what had happened on the TLC plate was confusing: in TLC, the solvent moves *up* the plate, and in column chromatography, it moves *down* the column. Several students also voiced concern when the yellow/brown layer of impurities did not move through the column; it stayed at the top where the mixture was applied. When student's TLC plates were turned upside down next to the column, students immediately understood the correlation. Students noted that the brown oil initially added to the column became a colorless oil after purification by column chromatography.

■ PEDAGOGICAL ENHANCEMENTS

Synthesis of an alkene in the second-semester organic chemistry course provided an opportunity to revisit the mechanism of acid-catalyzed dehydration of an alcohol. A question on the report sheet was as follows: "Normally a dehydration reaction requires heating <u>and</u> removal of water as it forms during the reaction in order to drive the dehydration in the forward direction. However, this particular dehydration takes place readily, even at lower temperatures. Explain." Students identified the reaction intermediate as a benzyl cation, much more stable and of lower energy than alkyl cations, following a different reaction path with a lower activation energy barrier for the forward reaction. They also recognized that the newly formed alkene is in conjugation with the adjacent phenyl rings, providing stability for the product.

This reaction also reviewed the synthesis of alcohols using a Grignard reagent and previewed the reactivity of ketones with strong nucleophiles, which commonly is covered later in a second-semester organic chemistry course.

References to and descriptions of enhancements describing the use of DPE in polymer chemistry and experiments using DPE in an introductory organic chemistry sequence are in the Supporting Information.

■ CONCLUSION

The coupling of a Grignard addition and dehydration reaction to column chromatography enhanced students' appreciation for column chromatography as a purification technique. By monitoring the colorless chromatography procedure using TLC, students comprehended the correlation between the two chromatographic techniques. Placement of this experiment at the beginning of the second semester of a two-semester organic chemistry sequence allowed for review of elimination mechanisms and alkene chemistry, previewed nucleophilic addition to carbonyl compounds, and can provide an opportunity to discuss alkene polymerization reactions.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available on the ACS Publications website at DOI: 10.1021/acs.jchemed.5b00212.

Student handouts (laboratory manual pages, report sheets and quizzes), instructor notes with added enhancements, and experimental data and spectra (IR, ^{1}H NMR, ^{13}C NMR, GC/MS) (PDF, DOCX)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: altyl@wlu.edu.

Present Addresses

†Isaac G. Alty is a student in the Department of Chemistry, College of William and Mary, Williamsburg, VA 23187.
‡Christine A. Saber is now in the Department of Chemistry, Gannon University, Erie, PA 16541.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

Financial support was provided by the Department of Chemistry and Biochemistry at Washington and Lee University. We thank Steve Desjardins for his help with photographs.

■ REFERENCES

(1) See, for example: (a) Pavia, D. L.; Kriz, G. S.; Lampman, G. M.; Engel, R. G. *A Microscale Approach to Organic Laboratory Techniques*, 5th ed.; Cengage: Stamford, CT, 2013; pp 52−55, *790−809*, 305−315. (b) Gilbert, J. C.; Martin, S. F. *Experimental Organic Chemistry: A Miniscale & Microscale Approach*, 6th ed.; Cengage: Stamford, CT, 2015; pp *189−195*, 716−740.

(2) Tiffeneau, M. Carbures Benzéniques a chaine latérale pseudo-allylique: Méthovinylbenzène et ses homologues. Étude de quelques migrations moléculaires. *Ann. Chim. Phys.* **1907**, *10*, 322−378.

(3) Chen, Z.; Su, W.; Jing, L.; Huang, S.; Chen, J.; Liang, X. Mild and simple method for preparation of 1,1-diphenylethylene. Chinese Patent 103755516, Dec 27, 2013.

(4) Hwa, R.; Weizman, H. Revisiting the Separation of Ferrocene and Acetylferrocene by Adsorption Chromatography: Adding a Third Component. *J. Chem. Educ.* **2007**, *84* (9), 1497−1498.

(5) Heumann, L. V.; Blanchard, D. E. Colorful Column Chromatography: A Classroom Demonstration of a Three-Component Separation. *J. Chem. Educ.* **2008**, *85* (4), 524−526.

(6) Clark, D. D. Analysis and Identification of Acid−Base Indicator Dyes by Thin-Layer Chromatography. *J. Chem. Educ.* **2007**, *84* (7), 1186−1187.

(7) Valverde, J.; This, H.; Vignolle, M. Quantitative Determination of Photosynthetic Pigments in Green Beans Using Thin-Layer Chromatography and a Flatbed Scanner as Densitometer. *J. Chem. Educ.* **2007**, *84* (9), 1505−1507.

(8) McCullagh, J. V.; Ramos, N. Separation of the Carotenoid Bixin from Annatto Seeds Using Thin-Layer and Column Chromatography. *J. Chem. Educ.* **2008**, *85* (7), 948−950.

(9) Johnston, A.; Scaggs, J.; Mallory, C.; Haskett, A.; Warner, D.; Brown, E.; Hammond, K.; McCormick, M. M.; McDougal, O. M. A Green Approach To Separate Spinach Pigments by Column Chromatography. *J. Chem. Educ.* **2013**, *90* (6), 796−798.

(10) Jarret, R. M.; New, J.; Karaliolios, K. Reactions of Bromine with Diphenylethylenes: An Introduction to Electrophilic Substitution. *J. Chem. Educ.* **1997**, *74* (1), 109−110.

(11) McGowens, S. I.; Silversmith, E. F. Organic Reactions Involving Bromine: Puzzles for the Organic Laboratory. *J. Chem. Educ.* **1998**, *75* (10), 1293−1294.

(12) Poulsen, L.; Zabala Ruiz, A.; Uttrup Pedersen, S.; Ogilby, P. R. Characterizing the Behavior and Properties of an Excited Electronic State: Electron-Transfer Mediated Quenching of Fluorescence. *J. Chem. Educ.* **2003**, *80* (7), 819−921.

(13) Wieland, P. C.; Nuyken, O.; Heischkel, Y.; Raether, B.; Strissel, C. New Concepts for Controlled Radical Polymerization: The DPE System. In *Advances in Controlled/Living Radical Polymerization*; Matyjaszewski, K., Ed.; ACS Symposium Series 854; American Chemical Society: Washington, DC, 2003; pp 619−630.

(14) Hutchings, L. R.; Brooks, P. P.; Parker, D.; Mosely, J. A.; Sevinc, S. Monomer Sequence Control via Living Anionic Copolymerization: Synthesis of Alternating, Statistical, and Telechelic Copolymers and Sequence Analysis by MALDI ToF Mass Spectrometry. *Macromolecules* **2015**, *48* (3), 610−628.

DOI: 10.1021/acs.jchemed.5b00212
J. Chem. Educ. XXXX, XXX, XXX−XXX