

Microwave-Assisted Synthesis of Solvatochromic Dye and Analysis of Solvent Polarity in Undergraduate Organic Chemistry Laboratory

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Cite This: *J. Chem. Educ.* 2024, 101, 3384–3389



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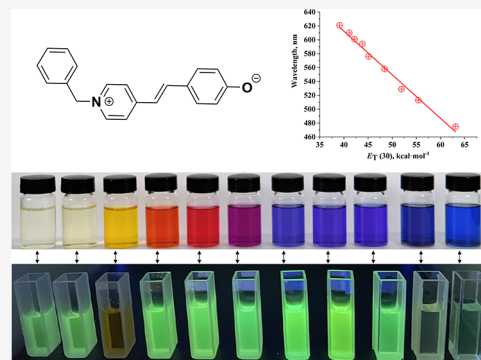
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Supporting Information

ABSTRACT: Brooker's merocyanine (MOED), a solvatochromic dye, was initially suggested as a visual indicator of solvent polarity. However, its synthesis is hindered by the use of iodomethane, a raw material with a low boiling point and high toxicity. To address these issues, benzyl bromide was employed as a substitute for iodomethane, leading to the synthesis of the MOED analogue 1-benzyl-4-[(oxocyclohexadienylidene)ethylidene]-1,4-dihydropyridine (BNOED). However, the lengthy reaction time of 26 h limits its practicality in a standard organic chemistry laboratory teaching. A microwave-assisted method reported in this text successfully reduced the reaction time to 18 minutes. BNOED exhibits solvatochromic properties, with its maximum absorption wavelength in various solvents showing a linear relationship with the solvent's Reichardt polarity parameter $E_T(30)$. Consequently, the synthesis of the solvatochromic dye BNOED is highly suitable for organic chemistry laboratory instruction at the undergraduate level. Through UV–vis and fluorescence spectroscopy, ^1H NMR spectroscopy, and visual observation, students are guided to deeply explore the principles of solvatochromism. This experiment encompasses classic organic chemistry concepts, including N-alkylation and condensation reactions. It primarily assists students in investigating the properties of the synthesized product through visual observations and data from UV–vis, fluorescence, and NMR spectroscopy. This approach encourages students to think critically and analytically, enhancing their ability to address problems in an organic chemistry laboratory course.

KEYWORDS: Solvatochromism, Microwave-Assisted Synthesis, Organic Chemistry, UV–Vis Spectroscopy, Fluorescence Spectroscopy, ^1H NMR Spectroscopy, Solutions/Solvents



INTRODUCTION

Solvatochromism is the phenomenon where a solution changes color upon dissolving a solute in different solvents.^{1,2} A solvatochromic dye, 4-(2-(1-methylpyridin-4(1H)-ylidene)ethylidene)cyclohexa-2,5-dienone (MOED), also known as Brooker's merocyanine, has been integrated into undergraduate laboratory courses, as reported in this *Journal*.^{3,4} In various solvents, MOED exhibits a range of colors. These color changes reflect alterations in the molecular electronic structure and energy levels due to solvation effects, providing students with both a visual experience and a basis for contemplating the nature of electromagnetic spectroscopy. The preparation of MOED (Scheme 1) involves N-methylation of 4-methylpyridine (salt I), followed by condensation with 4-hydroxybenzaldehyde in ethanol/piperidine and subsequent dehydration and deprotonation with gentle heating in aqueous potassium hydroxide.³ However, the N-methylation step using iodomethane, with its low boiling point and high toxicity, presents challenges in a laboratory setting. Its volatile nature and the lengthy 26 hour reaction time limit the experiment's feasibility for junior undergraduate students. To address these issues, our students successfully synthesized the related compound 1-benzyl-4-

[(oxocyclohexadienylidene)ethylidene]-1,4-dihydropyridine (BNOED) employing microwave conditions, replacing the original synthesis method (Scheme 2),⁵ and studied its fluorescence and solvatochromic behavior. Similar to MOED, BNOED exhibits solvatochromic properties, with its maximum absorption wavelength in different solvents linearly correlating with the solvent's Reichardt polarity parameter $E_T(30)$, effectively illustrating solvatochromic behavior. Microwave-assisted synthesis, an environmentally friendly and highly selective method with rapid reaction times, has been introduced into undergraduate laboratories.^{6–9} After two sessions of laboratory teaching involving 180 students, the entire process, including reaction and postprocessing to obtain pure BNOED, took only 2.5 class hours and gave yields of about 40–56%. This efficiency makes the BNOED synthesis experiment suitable for

Received: December 25, 2023

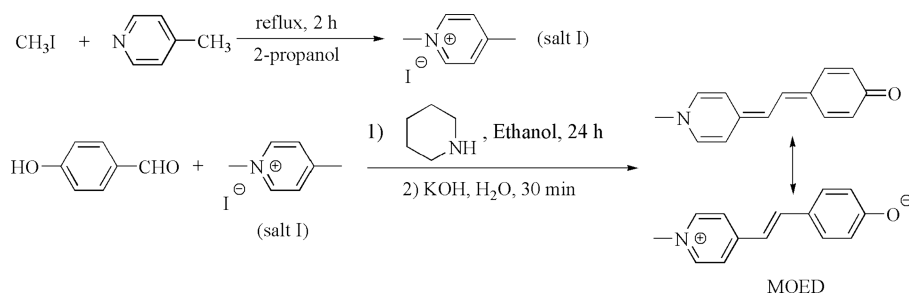
Revised: July 15, 2024

Accepted: July 17, 2024

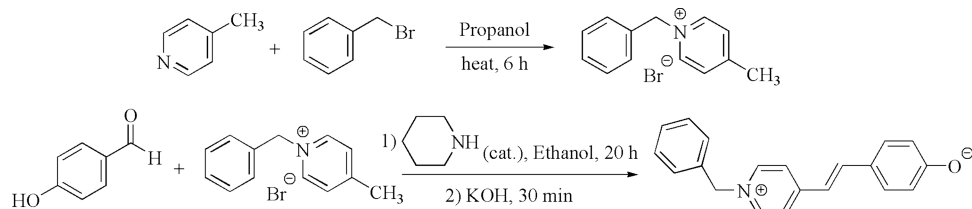
Published: July 26, 2024



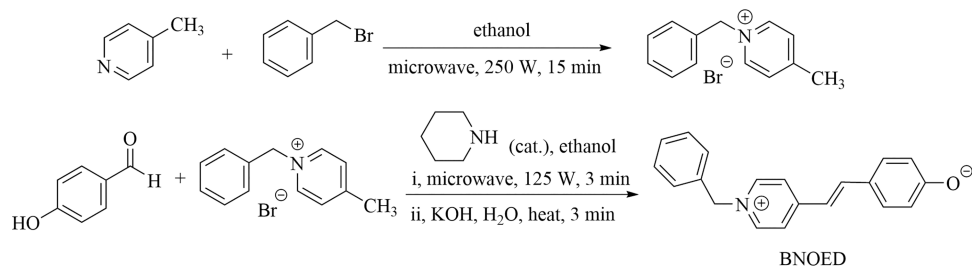
Scheme 1. Reported Synthesis Procedure for MOED



Scheme 2. Reported Synthesis Procedure for BNOED



Scheme 3. Synthesis Procedure for BNOED



general organic laboratory teaching for undergraduates. After completing the synthesis, students spend 1.5 hours comparing the colors and fluorescence of BNOED in different solvents, observing visual fluorescence under a 365 nm UV lamp. They also scan electronic absorption spectra in various solvents by using UV–vis spectroscopy. For more advanced experiments, fluorescence spectroscopy and NMR analysis can be conducted to further examine the effect of solvent polarity on the spectra. In our laboratory, students are provided with known fluorescence spectra and NMR data for their analysis.

LEARNING OBJECTIVES

This experiment not only teaches students about specific organic chemical concepts but also fosters skills in independent thinking, problem-solving, and data analysis. The use of color change as a visual indicator adds an element of excitement and engagement to the learning process, enhancing students' interest and motivation in the subject matter. The overall learning objectives of this experiment are as follows: (1) Learn the basic methods of microwave synthesis and purification. (2) Understand and describe reaction mechanisms. (3) Operate UV–vis absorption spectrophotometers and analyze data. (4) Observe fluorescence emission using a UV lamp. (5) Understand fluorescence spectra and ^1H NMR spectra of dyes in different solvents.

EXPERIMENTAL OVERVIEW

This experiment is a half-day (4 hour) class activity. It has been conducted by 10 groups, totaling 180 students, in a first-year or second-year chemistry class over two sessions. A prelab

assignment requires students to read about N-alkylation and condensation reactions, microwave synthesis technology, and NMR, UV–vis, and fluorescence spectroscopies as well as to gain a general understanding of previous research on solvatochromic dyes and their applications (see the [Supporting Information](#)). During the experiments, students work in pairs and complete the two reactions in a one-pot synthesis (Scheme 3). The chemical reactions proceed very quickly. If higher purity is desired, the BNOED product can be recrystallized by 1:3 ethanol/water. The reactions are complete within 2.5 hours, with an average yield of 49%. Due to the time constraints of the class, the fluorescence and NMR data can be demonstrated by the teacher in the last 30 minutes. It is noteworthy that the fluorescence of BNOED in different solvents can be easily observed under a 365 nm UV lamp. Subsequently, students scan UV–vis absorption spectra to examine the relationship between the maximum wavelength and solvent polarity, a process that takes about 1 hour. This step is conducted in small groups of 4–6 students, enabling an exploration of the solvatochromism effects. Each student tests 1–2 solvents. Finally, students discuss the observed solvatochromic phenomena of BNOED within their groups. After the class, students use Microsoft Excel or Origin software to process the experimental data and complete their experimental reports. Overall, this experiment consists of three main steps: preparation and purification (lasting 2.5 hours), solution preparation (lasting 0.5 hours), and UV–vis spectral analysis and observation of fluorescence (lasting 1 hour). The complete procedure for the experiment is detailed in the [Supporting Information](#).

HAZARDS

Reagents used in this experiment include 4-methylpyridine, benzyl bromide, *p*-hydroxybenzaldehyde, piperidine, potassium hydroxide (KOH), sodium bicarbonate, dimethylformamide (DMF), methanol, dichloromethane (DCM), trichloromethane (TCM), propan-2-ol, dimethyl sulfoxide (DMSO), ethanol, and acetone.

Benzyl bromide is a potent lachrymator and can intensely irritate the skin and mucous membranes. It can cause irritation of the nose and throat upon inhalation; severe exposure may lead to pulmonary edema. Liquid contact can burn the eyes, and skin contact may cause irritation. Ingestion can irritate the mouth and stomach.

Piperidine is toxic if inhaled, swallowed, or absorbed through the skin. Prolonged or repeated exposure may lead to more serious health effects, including respiratory problems, skin sensitization, and damage to internal organs. It can cause burns upon contact with the skin or eyes and may corrode materials such as aluminum, steel, and copper. Proper protective equipment, such as gloves and goggles, should be worn when handling piperidine to prevent skin and eye contact. Piperidine can contaminate water sources and harm aquatic life. Proper disposal methods should be followed to minimize the environmental impact.

DMF, DCM, and TCM are known for their potential carcinogenic properties. KOH is dangerously corrosive, and its solutions are severe irritants to the skin and other tissues. Ingestion, inhalation, or skin absorption of methanol and propan-2-ol can cause poisoning and should be strictly avoided. Methanol, ethanol, isopropyl alcohol, and acetone are highly flammable. Direct contact with all of these chemicals should be absolutely avoided. Detailed information about these chemicals is provided in Table S3.

In the prelab assignments, it is crucial to ensure that students are fully aware of the potential hazards associated with this experiment. Therefore, all experiments should be conducted in fume hoods to ensure safety. Students are required to wear goggles, gloves, and protective clothing while performing the experiment.

RESULTS AND DISCUSSION

Synthesis of BNOED

BNOED was synthesized by reacting benzyl bromide with 4-methylpyridine in ethanol under 250 W microwave irradiation for 15 minutes. This process did not require the separation of the product, which was then directly reacted with *p*-hydroxybenzaldehyde and the catalyst piperidine under 125 W microwave irradiation for an additional 3 minutes. Subsequent dehydration and deprotonation were conducted with gentle heating in aqueous potassium hydroxide. Then the mixture was gradually poured into sodium bicarbonate solution in an ice bath, stirring continuously until the oily substance disappeared to allow the product to fully precipitate. The product was filtered off, washed with a small amount of ice-water, and dried to obtain the BNOED product. The more-purified BNOED can be recrystallized using 1:3 ethanol/water, achieving an average yield of 49%. The purity of BNOED was verified using melting point analysis, thin-layer chromatography, mass spectrometry, and ¹H NMR and FT-IR spectroscopy, as detailed in the Supporting Information.

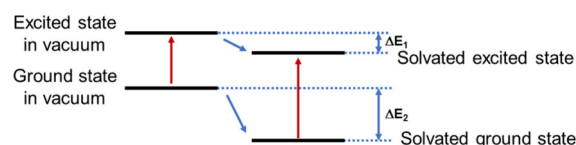
The synthesis of BNOED entails two key steps under microwave conditions, as outlined in Scheme 3. The first step is

the N-benylation reaction of 4-methylpyridine, which involves a nucleophilic substitution reaction with benzyl bromide, resulting in the formation of a pyridinium salt. This reaction can proceed via either an S_N1 or S_N2 mechanism given the unique structure of the benzyl group. In the subsequent condensation step, *p*-hydroxybenzaldehyde, activated by piperidine, forms an iminium ion, thereby increasing its electrophilicity. The pyridinium salt, under the influence of the piperidine base, loses a proton, creating a nucleophilic site. This site then attacks the iminium ion. The process is completed under microwave conditions with the removal of the piperidine catalyst, leading to the formation of BNOED.

Solvatochromism of BNOED

Solvatochromic molecules, whose absorption energy changes based on the solvent's nature, are categorized into two main types: positive and negative.³ Positive solvatochromic molecules are characterized by having a neutral form in the ground state and a charge-separated form in the excited state. This results in a bathochromic shift in their UV-vis absorption spectra when they are in polar solvents, indicating that the excited state is more stabilized in such environments. Conversely, negative solvatochromic molecules possess a charged ground state and a neutral excited state. In polar solvents, this leads to a hypsochromic shift in their UV-vis absorption spectra, as the ground state becomes more stable, as shown in Scheme 4. This

Scheme 4. Mechanism for Negative Solvatochromism



negative solvatochromism suggests that the ground-state dipole moment (μ_{GS}) is greater than that of the excited state (μ_{ES}) because polar solvent molecules selectively stabilize the electronic state with the larger dipole moment. The MOED dye is an example of a molecule that exhibits negative solvatochromism, which is attributed to the transformation of its π -electron distribution from a zwitterionic (charged) form in polar solvents to a neutral form in nonpolar solvents.¹⁰

Similar to MOED, BNOED in its ground state exhibits two stable resonance forms, as illustrated in Figure 1. Resonance

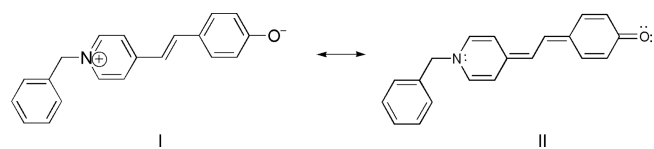


Figure 1. Two stable resonance forms of BNOED in the ground state.

form I is characterized by a higher degree of polarization, whereas resonance form II exhibits a lower degree. During the electronic excitation process of BNOED, there is a significant transfer of π electrons, resulting in changes in the charge distribution. The degrees of polarization in BNOED's ground and excited states differ, leading to varied interactions with the solvent and, consequently, different degrees of energy reduction. In the ground state, resonance form I, being more polar, is the dominant contributor. As a result, the degree of polarization in the ground state is greater than that in the excited state. With an

increase in solvent polarity, the energy of the solvated ground state decreases more compared to the excited state. This means the energy difference between the ground and excited states increases, resulting in a blue shift of the absorption peak.

Furthermore, the oxygen anion in resonance form I of BNOED can interact with protons through hydrogen bonding, which stabilizes the system and further lowers the energy of the solvated ground state. This interaction results in a blue shift of the absorption peak. Consequently, both hydrogen bonding and solvent polarity significantly influence the UV–vis absorption spectrum of BNOED. Therefore, when analyzing the effect of the solvent on BNOED's UV–vis absorption spectrum, it is crucial to consider these two factors in conjunction.

BNOED displays a range of colors in various solvents. Comparative analyses were conducted using aqueous, alcoholic, and nonprotic solvent solutions. The results show that BNOED appears light yellow in water, light red in methanol, bright red in ethanol, light purple in propan-2-ol, blue in DMSO and DMF, and dark blue in acetone, dichloromethane, and trichloromethane, as depicted in Figure 2.

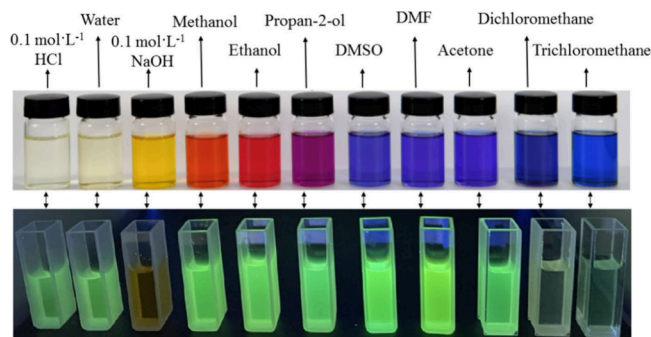


Figure 2. (top) Colors of BNOED in different solvents and (bottom) its green fluorescence (under a 365 nm lamp) in different solvents, except for the yellow fluorescence in 0.1 mol·L^{−1} NaOH solution.

As the polarity of the solvent increases or its proton-donating ability rises, a blue shift in the absorption peak of BNOED is observed. To further investigate the solvatochromism of BNOED, UV–vis absorption spectroscopy was employed to determine the maximum absorption wavelength in different solvent solutions, as detailed in Figure S1 and Table S1. The absorption peak of BNOED varies with the solvent's polarity. From trichloromethane to pure water, as the solvent polarity increases, the absorption peak at the long wavelength progressively blue-shifts from 621 to 475 nm. As illustrated in Figure 3, the absorption wavelength in different solvents correlates linearly with the solvent's Reichardt polarity parameter $E_T(30)$; the equation of the regression line is $\lambda = 863 - 6.27E_T$ with the correlation coefficient $R = 0.995$.^{11–15} The observation confirms that BNOED is a negative solvatochromic dye with $\mu_{GS} > \mu_{ES}$. This is further substantiated by observing the fluorescence of BNOED in various solvents under 365 nm UV light, as shown in Figure 2. The fluorescence spectra of BNOED in different solvents are shown in Figure S3. BNOED exhibits a consistent bright-green fluorescence in different solvents, though with slightly weaker intensity in less polar solvents such as dichloromethane and trichloromethane. The notably different fluorescence of BNOED in sodium hydroxide solution is attributed to the deprotonated BNOED. The yellow fluorescence originates from the anion of BNOED in 0.1 mol·L^{−1} sodium hydroxide solution. Additionally, the absorption

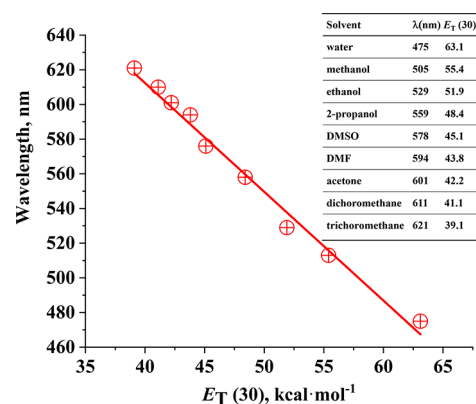


Figure 3. Linearity of absorption maximum wavelength of BNOED in different solvents with $E_T(30)$. ^aData from ref 14.

spectra of BNOED were measured in different pH buffer solutions, and it was determined that the pK_a of BNOED is 8.4, as shown in Figure S4.

¹H NMR Characterization of BNOED

¹H NMR spectra of BNOED were recorded in D₂O, methanol-*d*₄, and DMSO-*d*₆ solvents. The spectra are presented in Figure 4, with detailed data provided in the Supporting Information.

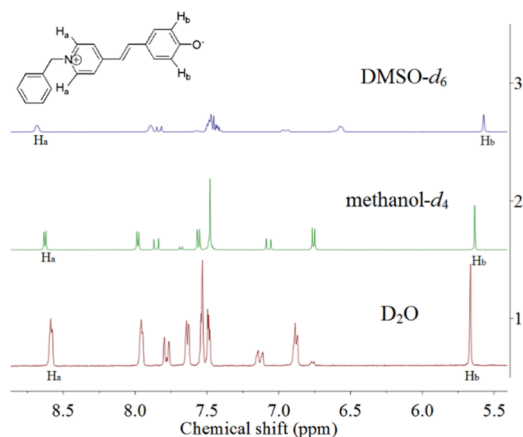


Figure 4. ¹H NMR spectra of BNOED in D₂O (1), methanol-*d*₄ (2), and DMSO-*d*₆ (3) solvents.

A comparison of the three spectra reveals variations in the chemical shifts of the protons on the pyridine ring (H_a), the phenoxide ring (H_b), and the inter-ring double bond. These changes indicate that the solvent affects the ¹H NMR peak positions of BNOED. In deuterated water and methanol, which are protic solvents, hydrogen bonding can occur with BNOED, leading to stabilization of tautomeric form I. In this form, BNOED predominantly exists with the N atom as N⁺, which enhances electron withdrawal from H_a. Simultaneously, the O atom, existing as O[−], donates electrons more effectively. The formation of hydrogen bonds with water and methanol reduces the electron density around H_b, causing its shift to a lower field, while the electron density around H_a shifts to a higher field. Conversely, in deuterated DMSO, a nonprotic solvent, the prevalence of BNOED in tautomeric form I is relatively reduced compared to water and methanol. This leads to the observed changes in the NMR spectra. These observations demonstrate that the electronic distribution state of BNOED in the ground state varies to some extent in different solvents.

ASSESSMENT OF LEARNING OUTCOMES

Since the main aim of this laboratory experiment is to help students understand fundamental organic chemical concepts such as N-alkylation reactions and condensation reactions as well as to interpret experimental phenomena using UV–vis spectroscopy, fluorescence spectroscopy, and NMR spectroscopy data, the pedagogic goals for the first- and second-year chemistry class groups are almost the same. We evaluated the experiment results from the following four aspects: (1) Target products: Students are expected to produce pure BNOED dye in satisfactory yields. The purity of the dye can be assessed using thin-layer chromatography or by determining its melting point (see Part 4 and Figure S5 in the Supporting Information). Full marks for this part total 30, with an average of 20. Students achieved an average yield of 49% with a standard deviation of 15%. (2) Operational section: The operational section's grade comprises three components: utilization of the microwave reactor, operation of the rotary evaporator, and handling the postreaction solution. Each segment is worth 5 points, with an average score of 4 points. (3) Preparation and absorption analysis of BNOED in different solvents: Students are tasked with preparing sample solutions to investigate the solvatochromic phenomenon. Full marks for this section total 15, with an average of 10. Students should analyze absorption using a UV–vis absorption spectrophotometer, ensuring alignment with Figures 2 and S1. (4) Lab reports: Students are required to submit their lab reports within 1 week after the experiment. These reports should consist of five sections: Experimental Goals, Principles, Results, Discussion, and Questions. The full marks and average marks for the Experimental Goals, Principles, and Results sections are 5 and 4, 5 and 4, and 10 and 6, respectively. In the Discussion section, which has full and average marks of 10 and 7, students should focus on explaining why BNOED exhibits solvatochromic properties. They are encouraged to use software such as Microsoft Excel or Origin to graphically represent the relationship between the maximum wavelength and the $E_T(30)$ data of different solvents. For the Questions section, with full and average marks of 10 and 7, instructors may choose five or six questions from Part 6 in the Supporting Information. More detailed criteria for evaluating students' learning outcomes is provided in Table S4.

Additionally, an optional and anonymous survey was administered to the students in class 2022 immediately following the completion of the experiment. The survey aimed to gather information about their understanding of laboratory techniques, perceptions of the laboratory, and curiosity about solvatochromism. A total of 66 students completed the survey. None of the students reported disinterest in this experiment after completing it. When students were asked about their interest in the experiment, more than 92% expressed interest in observing the intriguing experimental phenomena. The final section of the survey consisted of free responses, seeking their suggestions or comments on the experiment. They perceived the experiment's results as very good, with the color change being highly noticeable. Their feedback will help enhance future iterations of the experiment, confirming the achievement of the intended outcomes. The detailed survey can be found in the questionnaire document.

CONCLUSIONS

The experiment utilizes microwave-assisted synthesis for the preparation of BNOED, which is characterized by its short

reaction time and generally straightforward experimental operations. Additionally, the product displays a variety of colors and bright-green fluorescence in different solvents, providing a strong visual impact that significantly enhances students' interest and enthusiasm. BNOED offers vivid visual observations through its color changes and fluorescence emission, giving students an intuitive understanding of the solvation effects. This experiment merges organic synthesis with spectroscopic analysis, guiding students to comprehend the comprehensive solvent–solute interactions occurring in solutions. It aids in deepening students' insight into the intrinsic relationships between solvatochromism and molecular structures. Moreover, the synthesis and characterization experiment of BNOED possesses strong expandability. A variety of dyes can be synthesized in organic laboratory courses to study their solvatochromic properties. This half-day experiment is well-suited for laboratory teaching, particularly in general organic chemistry courses or as a comprehensive experiment depending on actual teaching requirements.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available at <https://pubs.acs.org/doi/10.1021/acs.jchemeduc.3c01337>.

Absorption spectra, fluorescence spectra, ^1H NMR spectra in different solvents, experimental details, characterization data for the dye, notes to the instructor, questions and answers, assessment of learning outcomes, and basic principles of solvatochromism of organic dyes (PDF, DOCX)

Student handout (PDF, DOCX)

Questionnaire with results (PDF, DOCX)

Visual observation of fluorescence (MP4)

Experimental procedures (MP4)

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<https://pubs.acs.org/10.1021/acs.jchemed.3c01337>

Author Contributions

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Notes

The authors declare no competing financial interest.

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ACKNOWLEDGMENTS

This work was supported by the Research Funds of National Program for Top Students Training in Basic Disciplines (20211038), Fujian Province College Education Research Funds (FBJG20200281 and FBJG20210279), and the fund of teaching reform research project of Xiamen University (2020, 2021). We express our gratitude to Professor Lin Min from the National Demonstration Center for Experimental Chemistry Education of Xiamen University for his discussion during the experiments and thank the 2021 and 2022 students of the College of Chemistry and Chemical Engineering, Xiamen University, for completing this experiment.

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