Greening the Organic Chemistry Laboratory: Comparing Synthetic and Purification Techniques in Organic Process Development

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Abstract

Two undergraduate experiments are introduced that teach important techniques common to many teaching labs, but keep the learning within the context of the 12 prinicples of Green Chemistry. In this study, an experiment is described for the undergraduate organic chemistry lab which compares microwave-induced organic reaction enhancement (MORE) to that of more traditional synthetic procedures. MORE and traditional reflux procedures for nucleophilic aromatic substitution reactions on 1-bromo-2,4-dinitrobenzene as well as characterization by ^{13}C NMR and mass spectrometry are described. We are also currently developing a series of process oriented guided inquiry learning (POGIL) experiments whereby organic compounds will be isolated from an unknown mixture by column chromatography as well as liquid-liquid extraction and then the environmental factor (E factor) and process mass intensity (PMI) metrics determined for each of the separation techniques. Oral presentations by the class (where distinct synthetic and separation procedures are consistently observed to be quicker, easier, result in higher yields and "greener") leads to a discussion of general synthetic and purification methods and provides the impetus for students to research alternative methods, the 12 principles of green chemistry and green chemistry metrics.

Keywords: *Chemical Education, Laboratory Instruction, Organic Chemistry, Green Chemistry;*

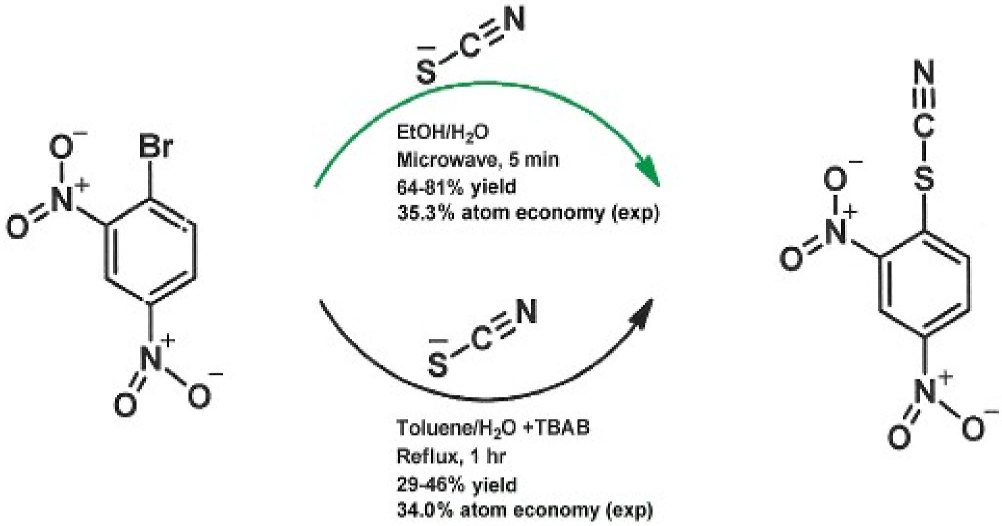
1. Introduction

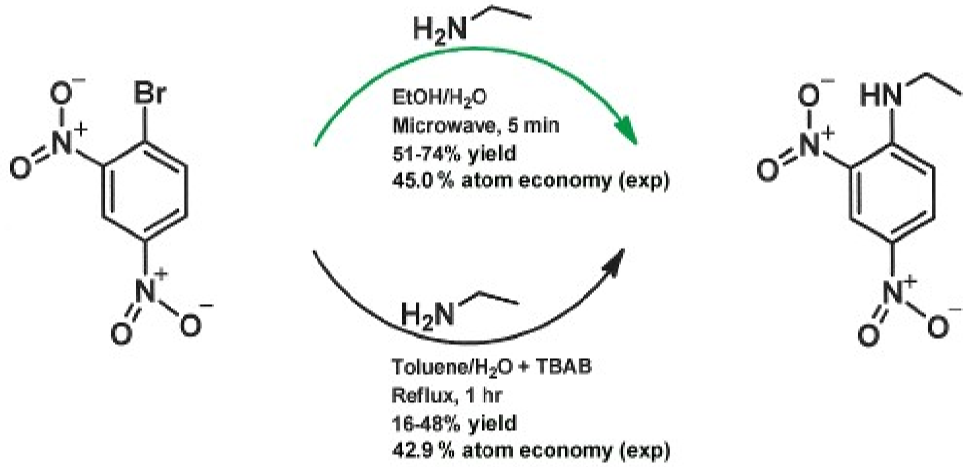
The development of novel organic processes requires sufficient chemical background, a methodical and committed work ethic, and often months or years of time on the part of the practicing chemist. Because of this, when the scientific problem has been solved, it is often tempting for the chemist to continue work developing only the route that was 'discovered' rather than continuing to find a more environmentally friendly alternative. In an editorial in the journal Green Chemistry Letters and Reviews,[1] Haack notes that laboratory methodology leading to greener results is critical to current educational practice. Future chemists will decide whether chemistry will develop with sustainability as part of the focus, but only if they have a strong foundation on sustainability issues and the meaning of making green chemistry development decisions. The third annual American Chemical Society Green Chemistry Summer School participants noted that incorporation of a general knowledge of green chemistry should begin at the undergraduate level and continue through graduate course work.[2] These curricular developments are greatly facilitated by the fact that contemporary laboratory students have come to expect to be educated in an environmentally sustainable fashion.[3] Further, it has been noted that, rather than developing new techniques, achieving greener chemistry in many cases will simply require a redirection of current techniques.[4] There are a number of published experiments that demonstrate alternative, greener practices to students. [5] [6]

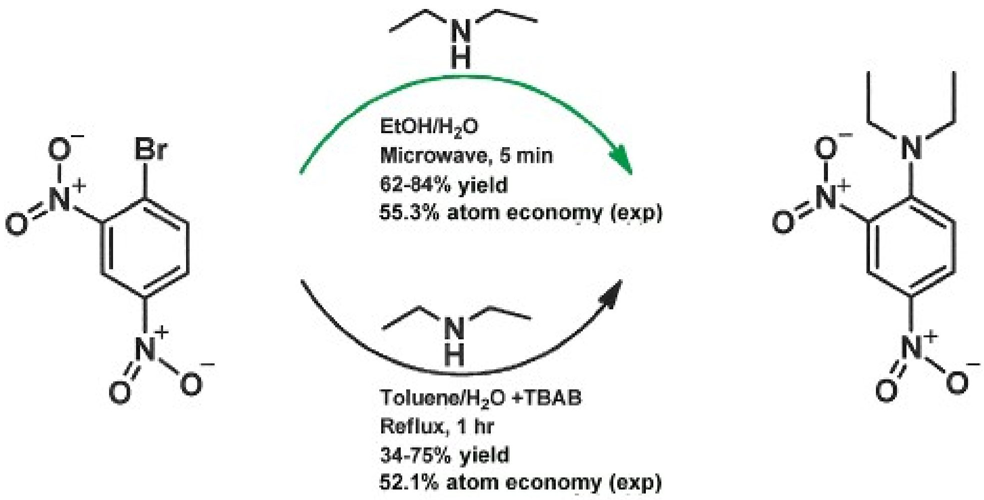
2. Curriculum development – organic synthesis

At the University of Winnipeg, we wanted to introduce our senior students to the modern synthetic technique of microwave heating and so we developed a nucleophilic aromatic substitution experiment which compares microwave heating to the traditional technique of reflux.[7] Table 1 shows average student results which demonstrates that microwave heating consistently gives greener results (higher yielding, greater atom economy, uses less power and less organic solvent) when compared to a traditional reflux synthesis .

Table 1: Nucleophilic aromatic substitution reaction using each of three nucleophiles (thiocyanate, ethylamine, and diethylamine) comparing microwave-assisted procedures to traditional reflux heating techniques.

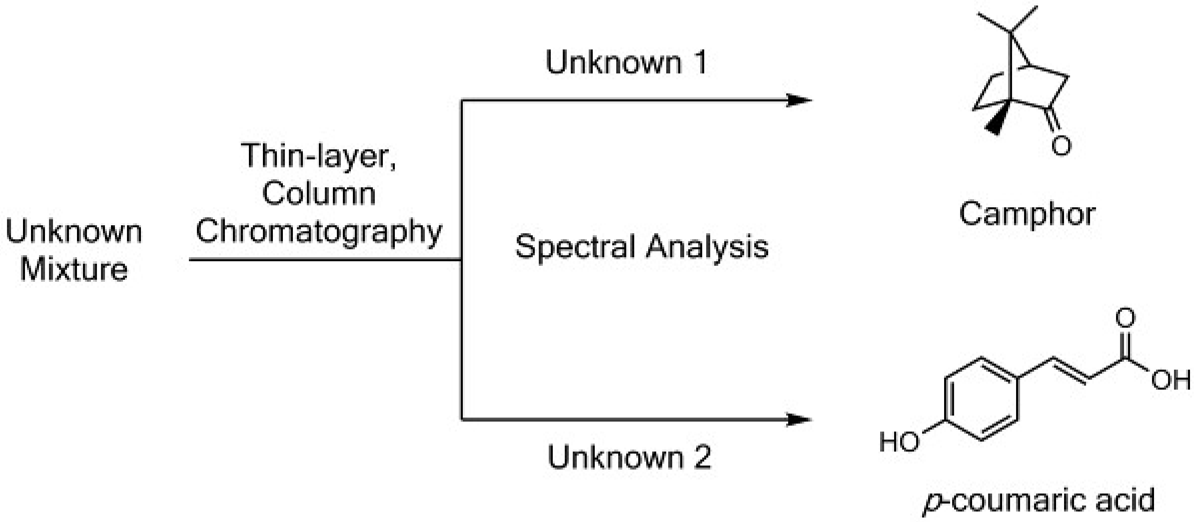






3. Curriculum development – organic mixture characterization

We have previously developed a guided-inquiry, upper-division undergraduate organic lab experiment which involves a complex separation as well as thoughtful NMR experiments and solvent selection.[8] The full characterization of the organic mixture in the figure below (85% camphor/15% *p*-coumaric acid) is relatively complex with a TLC visualization challenge (one of the components is observable under UV light while the other component requires a chemical visualization such as I_2 staining), column chromatography, as well as two different NMR challenges: (i) a complicated ^{1}H NMR and 10 carbon environments from ^{13}C NMR lead students to 2D COSY, HSQC and HMBC analyses to solve the structure of camphor, and (ii) after determining the basic structure of the second component, a ^{1}H NMR coupling constant analysis reveals that the E isomer of *p*-coumaric acid is present. We designed this experiment as a PBL exercise to ease the transition from the senior organic lab to the research lab environment.



We now propose a guided inquiry exercise that will demonstrate an alternate technique for the separation of the components of this mixture while using green chemistry metrics to show the importance of fully analyzing and comparing methodologies in choosing the best route in process chemistry development. The separation of the components is being investigated by liquid-liquid extraction under basic conditions (the *p*-coumaric acid will deprotonate to form a salt and thus become more hydrophilic while the camphor remains hydrophobic). Separation of aqueous and organic phases, neutralization of the aqueous *p*-coumaric acid salt solution followed by further organic extraction and work-up will yield the individual components. As a guided inquiry exercise, students will be challenged to develop an experimental scheme and then complete both the chromatographic and extraction separations of the unknown mixture in a prudent manner while recording a full inventory of all materials and energy expended as well as yields of purified products. Following full spectral characterization of all products, the concepts of environmental factor (E factor) and process mass intensity (PMI) metrics[9] will be introduced and determined for each of the separation techniques and students will then be guided to a discussion of all 12 principles of green chemistry.[10] For both green chemistry and economic reasons, it is estimated that PMI values are now used by over 67% of chemical companies while E factors are used by 48%.[11]

4. Conclusion

We introduce two experiments to the undergraduate organic lab that teach important techniques common to many teaching labs, but keep the learning within the context of the 12 prinicples of Green Chemistry. We propose that all chemistry labs be taught in this way. It is vitally important that chemistry students be familiar with green chemistry metrics since established journals such as *Organic Process Research and Development* now warn that "authors risk having papers rejected unless environmental impact and green chemistry principles are considered."[12] In order to change the mindset of the industry from economically driven development to sustainability driven development, new organic processes must develop in the hands of scientists that automatically put environmental considerations at the forefront.

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