RESEARCH LETTER

Facile synthesis of 4-nitro-N-substituted-1,8-naphthalimide derivatives using ultrasound in aqueous media

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(Received 19 November 2013; final version received 3 March 2014)

This study describes the ultrasound-assisted synthesis of 4-nitro-N-substituted-1,8-naphthalimide derivatives from 4-nitro-1,8-naphthalic anhydride and related amines by irradiating at 35 KHz in a sonic bath in aqueous media at room temperature. The results obtained by this method are comparable to those obtained by a common reflux method. The imidation reaction under ultrasound irradiation preceded 8 and 20 times faster than the common method and produced higher yields.

Keywords: ultrasound; aromatic amine; naphthalimide; imidation; common method

1. Introduction

Naphthalimide derivatives are a special class of environmentally sensitive fluorophores. Because of their strong fluorescence and good photostability, 1,8-naphthalimide derivatives have found applications in a number of areas such as in the coloration of polymer \cite{1,2} as laser-active media \cite{3}, fluorescent markers in biology \cite{4}, anticancer agents \cite{5}, light-emitting diodes \cite{6,7}, photoinduced electron-transfer sensors \cite{8,9}, fluorescence switchers \cite{10,11}, electroluminescent materials \cite{12,13}, liquid-crystal displays \cite{14,15}, and ion probes \cite{16}.

In the last few years, there has been a considerable increase in the application of ultrasound in synthetic organic chemistry. “Sonochemistry” is a new trend in organic chemistry, offering a versatile and facile pathway for a large variety of syntheses. A large number of organic reactions can be carried out under ultrasonic irradiation, resulting in high yields, short reaction times, and mild conditions \cite{17-21}. The imidation of naphthalimide derivatives is one of the most widely studied reactions and finds extensive application in the synthesis of a variety of fine chemicals \cite{22-27}. Based on our knowledge there are no report on sonic synthesis of aromatic amine derivatives of 1,8-naphthalimide and study the effect of reaction time and percentage of reactants on reaction yield. Currently, the study of organic reactions in water medium as a solvent is considered an important strategy for developing more environmentally friendly methodologies.

Herein, we report a rapid and facile procedure for the imidation of naphthalimide derivatives by treating various alkyl and aryl amines as imidation agents with 4-nitro-1,8-naphthalic anhydride using water as a solvent under ultrasound irradiation in aqueous media at room temperature and compare the results obtained from this method with those obtained from a common reflux method. The effect of reaction time and percentage of reactants on reaction yield was studied.

2. Experimental

All compounds used in this study were of analytical grade unless otherwise stated. The NMR spectra were recorded with a Bruker DRX AVANCE spectrometer operating at 500 MHz and 125 MHz for $^1$H NMR and $^{13}$C NMR, respectively, using a dual 5 mm probe head. The measurements were carried out in a deuterated dimethyl sulfoxide (DMSO-d6) solution under ambient conditions. The Fourier transform infrared spectroscopy (FTIR) were recorded on a Perkin-Elmer Spectrum One, and elemental analysis was performed on a Heraeus CHNO-Rapid analyzer. 5-Nitroacenaphthene and 4-nitronaphthalic anhydride were prepared using the method of Okazaki and Taniguchi, 4-nitro-N-substituted-1,8-naphthalimide was synthesized according to the modified method of Dangwu \cite{28}.

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2.1. General procedure for the preparation of naphthalimide derivatives

Ultrasound irradiation: A mixture of 0.03 mol 4-nitro-1,8-naphthalimide and 0.03 mol amine in 10 mL water was sonicated at 35 kHz in a sonic bath maintained at 25 °C. Thin-layer chromatography (TLC) was performed at the end of the reaction, and then the contents were filtered, and recrystallized in ethanol.

Common reflux method: First, 0.03 mol of 4-nitro-1,8-naphthalic anhydride was dissolved in 50 mL absolute water with stirring and heating. Then, the mixture was refluxed until TLC showed no remaining 4-nitro-1,8-naphthalic anhydride. Then, the mixture was filtered, and recrystallized in ethanol.

4-Nitro-N-methyl-1,8-naphthalimides

4-Nitro-N-ethyl-1,8-naphthalimides

4-Nitro-N-propyl-1,8-naphthalimides
7.31–7.33 (t, 2H, J = 7.2 Hz, 3′-H, 5′-H), 7.42–7.45 (d, 2H, J = 7.4 Hz, 2′-H, 6′-H), 7.47–7.49 (d, 2H, J = 7.5 Hz, 2′-H, 3-H), 7.55–7.57 (d, 1H, J = 7.8 Hz, 7-H), 7.59–7.62 (t, 1H, J = 8.1 Hz, 6-H), 7.74–7.78 (d, 1H, J = 7.7 Hz, 5-H), 13C NMR (CDCl₃) δ: 210.6, 200.0 (C=O ketone), 140.4, 135.83, 131.68, 130.85, 129.29, 122.8, 120.4, 119.9, 113.12 (Ar), Anal. Calcd. (%): C=68.46, H=3, N=8.4, Found (%): C=68.48, H=2.98, N=8.4.

3. Results and discussion

The condensation of 4-nitro-1,8-naphthalic anhydride with aryl and alkyl amines under ultrasonic irradiation in water at room temperature afforded products (2a–h) in high yields and shorter reaction time in comparison with conventional conditions (Scheme 1).

The results obtained are shown in Table 1. It has been observed that for various amines, alkylation under reflux required 4–16 h. However, when this reaction was performed with the same conditions under sonication, the reaction proceeded rapidly within 35–40 min. Various types of primary amines with electron-donating and -withdrawing groups were rapidly condensed with 1,8-naphthalic anhydride and afforded the corresponding 1,8-naphthalimides in excellent yields.

As seen in Scheme 2, the attack of the amine on the carbonyl group of naphthalimide (nucleophilic addition reaction) leads to ring opening, followed by a second nucleophilic attack on another carbonyl group. Then, the elimination of water and the closing of the ring form the substituted 1,8-naphthalimide. The nucleophilic behavior of primary amines is very important.

The results in Tables 1 and 2 show that by changing the nucleophilicity of the amine, the reaction time in the reflux method increased (2e, 2f: 12–16 h versus 2a–2d: 4–6 h). As expected, the reaction times for the ultrasonic method are not very different for different amines.

Tables 1 and 2 show that the ultrasound method reduced the reaction time from several hours to minutes and improved the yields from 72–85% (under conventional conditions) to 90–96%. The improvement induced by ultrasound can be attributed to the well-established theory of ultrasonic irradiation.

Ultrasonic irradiation differs from traditional energy sources (such as heat) in duration, pressure, and energy per molecule. Because of the extremely high temperatures and pressures and the extraordinary heating rate generated by cavitation bubble collapse, ultrasound provides an unusual mechanism (17) that results in decreased reaction times and increased yields.
The reaction shown in Tables 1 and 2 for this procedure were more productive and efficient than those previously reported (25) for ultrasonication. For example, compound 2a was previously prepared in 84% yield within 90 min under ultrasonication, whereas in this study, it was obtained in 90% yield in 35 min. The yield increased and the reaction time decreased. It seems that the higher solubility of reactants in water caused a higher yield and shorter reaction time.

The effect of change in the concentration of various reagents on the reaction system was also investigated and the results are presented in Table 3. It was observed that there was good agreement between the concentration of the reagents and the total products formed, a concentration of 15% showed the best results.

### 4. Conclusion

The synergistic effect of ultrasound has been successfully demonstrated to offer an environment friendly method and easy way for the synthesis of 1,8-naphthalimides in excellent yields in aqueous media at room temperature. The milder conditions, high reaction rates, excellent yields, and easy work up make this procedure an improved alternative to the conventional long thermal processes for imidation of 4-nitro-1,8-naphthalic anhydride with various alkyl and aryl amines.

### Acknowledgments

The authors are grateful to thank the Center of Excellence for Color Science and Technology, and Institute for Color Science and Technology for the financial support and providing us a good environment and facilities to complete this project.

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| Compounds | Sonic method | Products | t (min) | Y (%) | Mp (°C) | Lit. mp (°C) (ref.) |
|-----------|--------------|----------|---------|-------|---------|---------------------|
| 2a        | 35           | 90       | 210–211 | 211.02|
| 2b        | 35           | 93       | 192–193 | 193.53|
| 2c        | 35           | 92       | 138–139 | 138.18|
| 2d        | 35           | 96       | 105–106 | 105.25|
| 2e        | 40           | 95       | 197–198 | 196.22|
| 2f        | 40           | 94       | 196–197 | 196.75|
| 2g        | 40           | 96       | 166–167 | 168.23|
| 2h        | 40           | 94       | 214–215 | 215.43|

| Compounds | Naphthalimide:amine (mole ratio) | 1:1 | 1:5 | 1:10 | 1:15 |
|-----------|---------------------------------|-----|-----|------|------|
| 2a        | T (min)                         | 35  | 15  | 10   | 3    |
|           | %Y                              | 90  | 92  | 95   | 96   |
| 2b        | T (min)                         | 35  | 15  | 10   | 3    |
|           | %Y                              | 93  | 93  | 95   | 96   |
| 2c        | T (min)                         | 35  | 15  | 10   | 3    |
|           | %Y                              | 92  | 93  | 96   | 96   |
| 2d        | T (min)                         | 35  | 15  | 10   | 3    |
|           | %Y                              | 96  | 96  | 98   | 98   |
| 2e        | T (min)                         | 40  | 20  | 10   | 3    |
|           | %Y                              | 95  | 96  | 98   | 98   |
| 2f        | T (min)                         | 40  | 20  | 10   | 3    |
|           | %Y                              | 94  | 96  | 97   | 98   |
| 2g        | T (min)                         | 40  | 20  | 10   | 3    |
|           | %Y                              | 96  | 97  | 98   | 98   |
| 2h        | T (min)                         | 40  | 20  | 10   | 3    |
|           | %Y                              | 94  | 96  | 98   | 98   |
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