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Efficient Synthesis of 3-Phenylnaphtho[2,3-*b*]furan-4,9-diones in Water and Their Fluorimetric Study in Solutions

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A simple and efficient protocol has been developed for the synthesis of 3-phenylnaphtho[2,3-*b*]furan-4,9-diones by domino reaction of *α*-bromonitroalkenes to 2-hydroxynaphthalene-1,4-dione. With the optimal reaction conditions [NaOAc (120 mol%), water, 70 ℃, 7 h], the scope of the domino reaction was explored and the green approach provided the desired products in moderate to good yields at elevated temperature under aqueous-mediated conditions. A mechanistic rationalization for this reaction is also provided. The absorption characteristics of the compounds were examined by UV-Vis spectra and fluorescence spectroscopy. All compounds were fluorescent in solution emitting at blue light (432—433 nm), green light (512—536 nm), or yellow light (591 nm).

Keywords domino reaction, naphthoquinones, fluorescence, Michael addition, 2-hydroxynaphthalene-1,4-dione

Introduction

Naphthoquinones and their derivatives occur in various families of plants, fungi, bacteria and insects.[1] Many of these naturally occurring naphthoquinones and their synthetic analogues are important precursors for the synthesis of natural products and pharmaceuticals.[2] And naphthoquinone derivatives have been broadly explored for their anti-inflammatory,[3] antifungal,[4] trypanocida,[5] molluscicidal,[6] leishmanicidal[7] and antitumor biological activities.[4,8] Moreover, naphthoquinone derivatives owe their importance to their sufficient fluorescence in the visible yellow, large Stokes shift, high quantum yield of photoluminescence and reasonable solubility, which gives rise to one of the most extensively investigated and commercially significant organic dyes.[9] For example, 2-hydroxy-1,4-naphthoquinone (HNQ; Lawsone) is the principal natural dye in the leaves of Henna, *Lawsonia inermis*. In recent years, some semipermanent hair dyes containing Henna as well as its pure dye ingredient HNQ are widely used and have become increasingly popular due to their natural origin.[10] Many pigments (strepto-carpone, *α*-dunnione, dunniol and dunnione), which contain naphthoquinone skeleton, have been isolated and characterized from *Streptocapus dunnii*.[11] In view of their importance in pharmaceuticals and dyes, different approaches toward the synthesis of naphthoquinone derivatives have been reported.[12,13] Recently, the syntheses of quinones in water have also been reported.[14] In this paper we describe an efficient protocol for the synthesis of new 3-phenylnaphtho[2,3-*b*]furan-4,9-diones under mild conditions. In addition, it was revealed that 3-phenylnaphtho[2,3-*b*]furan-4,9-diones exhibit fluorescence in $CHCl_3$.

In the course of our investigations on the use of *α*-bromonitroalkenes in organic synthesis, this reagent turned out to be highly reactive and versatile.[15,16] Especially, the bromo or nitro group could behave as a better leaving group in the nucleophilic substitution reaction in comparison with bromoalkenes or nitroalkenes, *α*-bromonitroalkenes have become important intermediates in the synthesis of heterocycles. Organic solvents can cause significant air pollution, land contamination and water pollution in many synthetic organic processes, and the development of efficient synthetic methodologies for organic reactions, in the absence of organic solvents, is an important challenge toward reducing the amount of waste.[17,18] An ideal organic reaction would proceed in an environmentally benign solvent, such as water. Considering the above reports, the development of new and simple synthetic methods for the efficient preparation of heterocycles and new dyes containing nahthoquinone moiety is therefore an interesting challenge. Herein, we present a simple and efficient protocol for the synthesis of 3-phenylnaphtho[2,3-*b*]furan-4,9-diones[19] by domino reaction of *α*-bromonitroalkenes to 2-hydroxynaphthalene-1,4-dione under aqueous-mediated conditions and their fluorimetric study in solutions.

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Experimental

All reactants were commercially available and used without further purification. All melting points were uncorrected. Nuclear magnetic resonance spectra were recorded on Bruker DRX 400 and chemical shifts are expressed relative to TMS as an internal standard. ESI-HRMS spectra were measured with a Finnigan LCQ^{DECA} ion trap mass spectrometer. Absorption spectra were recorded on an Shimadzu UV-2550 spectrophotometer. Fluorescence spectra were obtained on a Perkin-Elmer LS55 spectrofluorometer. The widths of the excitation slit and the emission slit were both set to 10 nm with the scanning speed at 200 nm•min^{-1}.

General procedure for the synthesis of 3-phenylnaphtho[2,3-*b*]furan-4,9-diones (3a—3h)

To a solution of 2-hydroxynaphthalene-1,4-dione (26 mg, 0.15 mmol) and *α*-bromonitroalkene **2c** (77 mg, 0.3 mmol) in water (1 mL) was added NaOAc (15 mg, 0.18 mmol) and TBAB (tetrabutylammonium bromide) (10 mg, 0.03 mmol) at 70 ℃ for 7 h. The crude product was isolated by filtration, washed with water, and recrystallized from EtOAc to give naphtho[2,3-*b*]furan-4,9-dione (**3a**—**3h**).

3-Phenylnaphtho[2,3-*b*]furan-4,9-dione (3a) Yield 78%; yellow solid; m.p. 192—194 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.26—8.23 (m, 1H, ArH), 8.21—8.18 (m, 1H, ArH), 7.87 (s, 1H, CH=), 7.78—7.76 (m, 2H, ArH), 7.72—7.70 (m, 2H, ArH), 7.50—7.43 (m, 3H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 180.7, 174.0, 153.8, 145.5, 134.1, 133.8, 132.1, 128.9, 128.8, 128.7, 128.5, 127.6, 127.2, 127.0, 126.7; IR (KBr) *v*: 2922, 1675, 1585, 1194, 832 cm^{-1}; ESI-HRMS calcd for $C_{18}H_{10}O_3$+H 275.0708, found 275.0705.

3-*p*-Tolylnaphtho[2,3-*b*]furan-4,9-dione (3b) Yield 76%; yellow solid; m.p. 193—195 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.23 (dd, *J*=5.8, 3.1 Hz, 1H, ArH), 8.19 (dd, *J*=5.4, 3.6 Hz, 1H, ArH), 7.83 (s, 1H, CH=), 7.77 (d, *J*=3.6 Hz, 1H, ArH), 7.75 (d, *J*=3.2 Hz, 1H, ArH), 7.59 (d, *J*=7.9 Hz, 2H, ArH), 7.29 (s, 1H, ArH), 7.26 (s, 1H, ArH), 2.42 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 178.7, 173.2, 149.7, 135.0, 134.6, 133.4, 131.9, 130.2, 129.9, 128.2, 127.9, 127.6, 127.2, 125.6, 125.2, 29.7; IR (KBr) *v*: 2921, 1673, 1587, 1195, 838 cm^{-1}; ESI-HRMS calcd for $C_{19}H_{12}O_3$+H 289.0865, found 289.0865.

3-(4-Methoxyphenyl)naphtho[2,3-*b*]furan-4,9-dione (3c) Yield 64%; red solid; m.p. 214—216 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.24 (dd, *J*=5.8, 3.1 Hz, 1H, ArH), 8.20 (dd, *J*=5.5, 3.5 Hz, 1H, ArH), 7.83 (s, 1H, CH=), 7.78 (d, *J*=3.3 Hz, 1H, ArH), 7.76 (d, *J*=3.3 Hz, 1H, ArH), 7.67 (d, *J*=1.8 Hz, 1H, ArH), 7.66 (d, *J*=2.1 Hz, 1H, ArH), 7.02—7.00 (m, 2H, ArH), 3.88 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 180.8, 173.9, 160.1, 153.8, 145.0, 134.0, 133.9, 133.7, 132.1, 130.2, 127.4, 127.2, 126.9, 126.6, 121.0, 114.0, 55.4; IR (KBr) *v*: 2922, 1678, 1589, 1198, 836 cm^{-1}; ESI-HRMS calcd for $C_{19}H_{12}O_4$+H 305.0814, found 305.0813.

3-(4-Chlorophenyl)naphtho[2,3-*b*]furan-4,9-dione (3d) Yield 81%; yellow solid; m.p. 212—214 ℃; ^{1}H NMR (400 MHz, DMSO) *δ*: 8.59 (s, 1H, CH=), 8.13—8.07 (m, 2H, ArH), 7.88 (dd, *J*=5.6, 3.4 Hz, 2H, ArH), 7.80 (d, *J*=8.5 Hz, 2H, ArH), 7.54 (d, *J*=8.5 Hz, 2H, ArH); ^{13}C NMR (100 MHz, DMSO) *δ*: 180.9, 173.7, 153.9, 147.8, 134.8, 134.6, 133.8, 133.6, 132.1, 131.0, 128.8, 128.3, 127.2, 126.5, 125.5; IR (KBr) *v*: 2922, 1675, 1588, 1197, 835 cm^{-1}; ESI-HRMS calcd for $C_{18}H_9ClO_3$+H 309.0318, found 309.0317.

3-(4-Bromophenyl)naphtho[2,3-*b*]furan-4,9-dione (3e) Yield 83%; yellow solid; m.p. 228—230 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.25 (d, *J*=5.6 Hz, 1H, ArH), 8.19 (d, *J*=2.9 Hz, 1H, ArH), 7.87 (s, 1H, CH=), 7.79 (d, *J*=3.3 Hz, 1H, ArH), 7.78 (d, *J*=3.5 Hz, 1H, ArH), 7.61 (s, 4H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 180.7, 173.9, 153.9, 145.4, 134.2, 133.9, 133.7, 132.0, 131.7, 130.5, 127.7, 127.3, 126.8, 126.6, 123.1; IR (KBr) *v*: 2922, 1673, 1586, 1172, 839 cm^{-1}; ESI-HRMS calcd for $C_{18}H_9BrO_3$+H 352.9813, found 352.9811.

3-(4-Fluorophenyl)naphtho[2,3-*b*]furan-4,9-dione (3f) Yield 77%; yellow solid; m.p. 208—210 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.22 (dd, *J*=5.2, 3.7 Hz, 1H, ArH), 8.19—8.16 (m, 1H, ArH), 7.83 (s, 1H, CH=), 7.76 (dd, *J*=5.5, 3.5 Hz, 2H, ArH), 7.72—7.66 (m, 2H, ArH), 7.15 (t, *J*=8.7 Hz, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 180.7, 173.8, 164.3, 161.8, 153.8, 145.3, 134.1, 133.9, 133.7, 132.0, 130.8, 130.7, 127.2, 126.7, 126.7, 124.8, 115.7, 115.4; IR (KBr) *v*: 2921, 1677, 1589, 1167, 837 cm^{-1}; ESI-HRMS calcd for $C_{18}H_9FO_3$+H 293.0614, found 293.0614.

3-(2-Chlorophenyl)naphtho[2,3-*b*]furan-4,9-dione (3g) Yield 47%; yellow solid; m.p. 224—226 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.26—8.23 (m, 1H, ArH), 8.16—8.12 (m, 1H, ArH), 7.84 (s, 1H, CH=), 7.78—7.74 (m, 2H, ArH), 7.55—7.51 (m, 1H, ArH), 7.46 (dd, *J*=7.1, 2.0 Hz, 1H, ArH), 7.41—7.35 (m, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 180.3, 173.9, 153.0, 146.8, 134.0, 133.8, 133.5, 132.3, 131.7, 130.1, 129.8, 128.1, 127.1, 126.8, 126.6, 123.5; IR (KBr) *v*: 2923, 1675, 1581, 1196, 822 cm^{-1}; ESI-HRMS calcd for $C_{18}H_9ClO_3$ +H 309.0318, found 309.0316.

3-(2-Bromophenyl)naphtho[2,3-*b*]furan-4,9-dione (3h) Yield 54%; yellow solid; m.p. 215—217 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.26—8.23 (m, 1H, ArH), 8.15—8.11 (m, 1H, ArH), 7.83 (s, 1H, CH=), 7.78—7.74 (m, 2H, ArH), 7.72 (dd, *J*=7.4, 0.6 Hz, 1H, ArH), 7.41 (dd, *J*=8.4, 1.6 Hz, 2H, ArH), 7.34—7.29 (m, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 180.3, 173.9, 152.9, 146.7, 134.0, 133.8, 133.5, 133.0, 132.3, 131.7, 130.3, 130.2, 128.1, 127.2, 127.1, 126.8, 125.2, 124.2; IR (KBr) *v*: 2922, 1678, 1588, 1196, 822 cm^{-1}; ESI-HRMS calcd for $C_{18}H_9BrO_3$+H 352.9813, found 352.9812.

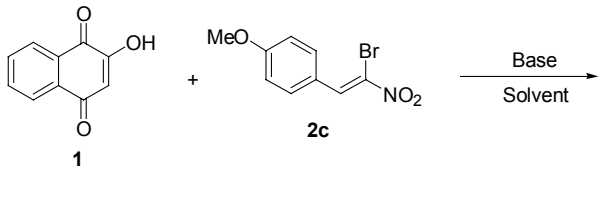
Results and Discussion

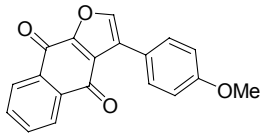
Synthesis of 3-phenylnaphtho[2,3-*b*]furan-4,9-diones (3)

We started our original studies by screening a series of bases for the domino reaction of *α*-bromonitroalkene **2c** with 2-hydroxynaphthalene-1,4-dione (**1**) in water. As shown in Table 1, various bases such as NaOH, DABCO, $NaHCO_3$ and Na_2CO_3, were screened and similar results were achieved when the reaction was carried out at room temperature (Table 1, Entries 1—5). When the base NaOAc was used as the catalyst, the yield of the desired product was higher than those by using NaOH, DABCO, $NaHCO_3$ and Na_2CO_3 as catalysts (Table 1, Entry 3). Subsequently, we evaluated the effects of solvent on the reaction. It was found that, various solvents such as CH_3CN, toluene and EtOH, were all tolerated to afford product **3c**, and H_2O was identified as the best solvent for this reaction (Table 1, Entries 3, 6—8). Finally, we investigated the effects of temperature and reaction time on the reactivity, and found out that the best yield was obtained at 70 ℃ after 7 h (Table 1, Entry 10). In fact, similar results were obtained when other bases were used at 70 ℃ (Table 1, Entries 12—14). However, when the stronger base NaOH, was used at 70 ℃, the reaction became very complicated and low yield was isolated (Table 1, Entry 11). When the reaction temperature was increased, the reaction became a little complicated, somewhat low yield was isolated (Table 1, Entry 15). Compared with TBAB, lower yield was obtained (only 17%) using SDS (sodium dodecyl sulfate) as PTC (Table 1, Entry 16).

With the optimal reaction conditions [NaOAc (120 mol%), water, 70 ℃, 7 h] in hand, the scope of the domino reaction of *α*-bromonitroalkenes **2** with 2-hydroxynaphthalene-1,4-dione (**1**) was explored. The results are summarized in Table 2. In general, the desired product can be prepared in moderate to good yields under standard conditions from the corresponding *α*-bromonitroalkenes **2** and 2-hydroxynaphthalene-1,4-dione (**1**). Good yields were obtained when there was electron-withdrawing group on *para* positions of aromatic ring of *α*-bromonitroalkenes **2** (Table 2, Entries 4—6). On the contrary, *α*-bromonitroalkenes **2** with electron-donating substituents on the *para* positions of aromatic ring afford 3-phenylnaphtho[2,3-*b*]furan-4,9-diones **3** with slightly inferior yields (Table 2, Entries 2—3). Only moderate yields were obtained with electron-withdrawing group on the *ortho* positions of aromatic ring of *α*-bromonitroalkenes **2** (Table 2, Entries 7—8).

Table 1 Optimizing reaction conditions[a]



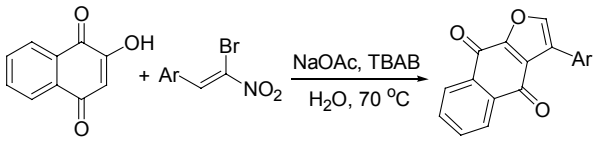


3c

Entry	Base	Solvent	Tem./℃	Time/h	Yield[d]/%
1[b]	NaOH	H_2O	25	24	30
2[b]	Na_2CO_3	H_2O	25	24	33
3[b]	NaOAc	H_2O	25	24	38
4[b]	DABCO	H_2O	25	24	28
5[b]	$NaHCO_3$	H_2O	25	24	36
6	NaOAc	CH_3CN	25	24	20
7	NaOAc	Toluene	25	24	27
8	NaOAc	EtOH	25	24	34
9[b]	NaOAc	H_2O	50	12	37
10[b]	NaOAc	H_2O	70	7	64
11[b]	NaOH	H_2O	70	7	21
12[b]	Na_2CO_3	H_2O	70	7	55
13[b]	DABCO	H_2O	70	7	64
14[b]	$NaHCO_3$	H_2O	70	7	62
15[b]	NaOAc	H_2O	100	7	44
16[c]	NaOAc	H_2O	70	7	17

[a] Unless otherwise noted, reactions were performed with 0.15 mmol of **1**, 0.3 mmol of **2c** in the indicated solvent (1 mL). [b] 20 mol% TBAB was added. [c] 20 mol% SDS was added. [d] Isolated yield.

Table 2 Reaction of 2-hydroxynaphthalene-1,4-dione (**1**) with different *α*-bromonitroalkenes **2**[a]



2 **3**

Entry	Ar	**2**	Prod. **3**	Yield[b]/%
1	C_6H_5	**2a**	**3a**	78
2	*p*-MeC_6H_4	**2b**	**3b**	76
3	*p*-$MeOC_6H_4$	**2c**	**3c**	64
4	*p*-ClC_6H_4	**2d**	**3d**	81
5	*p*-BrC_6H_4	**2e**	**3e**	83
6	*p*-FC_6H_4	**2f**	**3f**	77
7	*o*-ClC_6H_4	**2g**	**3g**	47
8	*o*-BrC_6H_4	**2h**	**3h**	54

[a] Unless otherwise noted, reactions were performed with 0.15 mmol of **1**, 0.3 mmol of *α*-bromonitroalkene, 20 mol% TBAB in 1 mL water at 70 ℃ for 7 h. [b] Isolated yield.

A mechanistic rationalization for this reaction is provided in Scheme 1. The domino reaction of *α*-bromonitroalkenes **2** with 2-hydroxynaphthalene-

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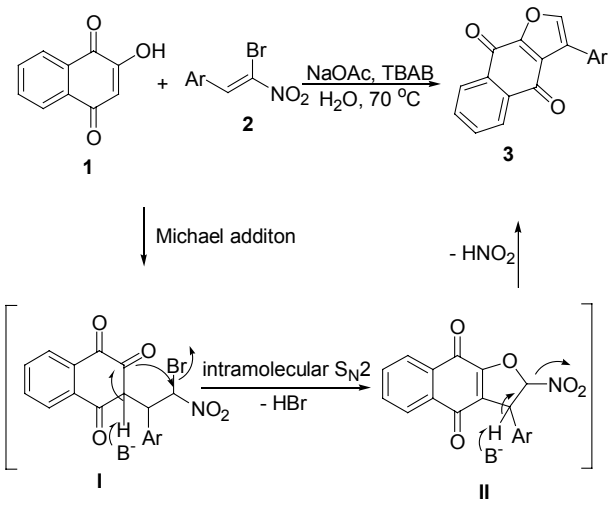
1,4-dione (**1**) gives the Michael addition product **I** catalyzed by NaOAc. Then, the enolate anion was formed under the basic conditions and the subsequent intramolecular nucleophilic displacement of **I** affords intermediate **II**. Subsequently, elimination of the nitro group leads to the formation of 3-phenylnaphtho[2,3-*b*]-furan-4,9-diones (**3**).

Scheme 1 Formation mechanism of 3-phenylna-phtho[2,3-*b*]-furan-4,9-diones (**3**)



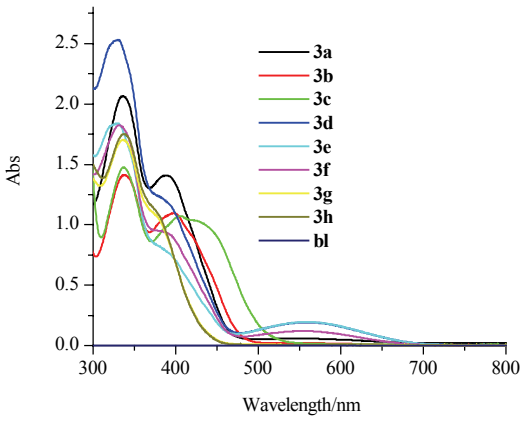


Figure 1 UV/Vis spectra of compounds **3** in $CHCl_3$ (4×10^{-4} mol/L).

Spectral properties

Compounds **3a**—**3h** are stable solids whose structures are fully supported by IR, ^1H and ^{13}C NMR spectroscopy and ESI-HRMS. Electronic absorption spectra of 4×10^{-4} mol/L solutions of **3a**—**3h** in chloroform were measured (Figure 1). Data are summarized in Table 3. All compounds **3a**—**3h** showed similar absorptions, with maximum wavelengths in the range of 328.5—405.5 nm and the substituents have little effect on the electronic absorption.

Fluorimetric properties

The fluorescence spectra of all compounds were measured in $CHCl_3$ (Figure 2) and the relevant data are listed in Table 4. As shown in Table 4, compound **3e** and **3g** are fluorescent in solution emitting at blue light. Compounds **3a**, **3b**, **3d**, **3f** and **3h** are fluorescent in solution emitting at green light. Compound **3c** presents a yellow emission of fluorescence. Although the fluorescence of these compounds is not very excellent. In the future, the structure of these compounds will be modified through the introduction of the different functional groups to improve the properties of fluorescence. We hope these can expand the range of the application in the field of fluorescent materials.

Table 3 UV/Vis data for compounds **3** in $CHCl_3$ (4×10^{-4} mol/L)

Entry	3	λ_{max}/nm	Molar absorptivity (log ε)
1	**3a**	335.5, 387.5	2.065, 1.409
2	**3b**	338.0, 397.0	1.411, 1.096
3	**3c**	337.0, 405.5	1.474, 1.073
4	**3d**	330.0, 388.0	2.532, 1.197
5	**3e**	328.5, 385.5	1.839, 0.798
6	**3f**	331.0, 385.0	1.826, 0.944
7	**3g**	336.0, 380.5	1.705, 1.038
8	**3h**	337.0, 380.0	1.752, 1.077

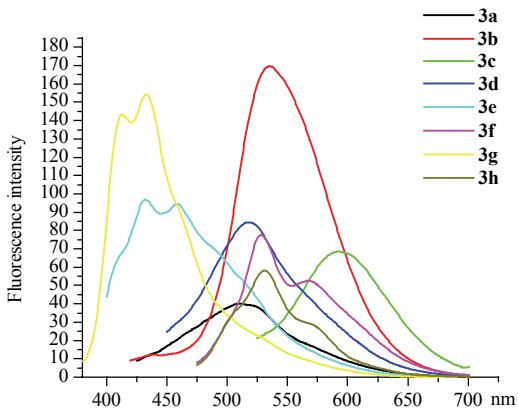


Figure 2 Emission spectra of selected compounds (2×10^{-4} mol/L in $CHCl_3$).

Table 4 Fluorescence data for compound in $CHCl_3$ (2×10^{-4} mol/L)

Entry	3	$\lambda_{ex,\ max}$/nm	$\lambda_{em,\ max}$/nm	Stoke's shift/nm
1	**3a**	400	512	112
2	**3b**	396	536	140
3	**3c**	398	591	193
4	**3d**	400	518	118
5	**3e**	376	432	56
6	**3f**	451	529	78
7	**3g**	366	433	67
8	**3h**	448	532	84

Conclusions

We have reported a simple and clean methodology for the synthesis of new 3-phenylnaphtho[2,3-*b*]furan-4,9-diones by domino reaction of α-bromonitroalkenes to 2-hydroxynaphthalene-1,4-dione under aqueous-mediated conditions. This green approach provided the desired products in moderate to good yields at elevated temperature. The absorption characteristics of the compounds were examined by UV-Vis spectra and fluorescence spectroscopy. All compounds were fluorescent in solution emitting at blue light (432—433 nm), green light (512—536 nm), or yellow light (591 nm).

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