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One-pot three-component regioselective synthesis of linear naphtho[2,3-*b*]-furan-4,9-diones

Mohammad Bagher Teimouri[a,*] and Hamid Reza Khavasi[b]

[a]*Petrochemical Department, Iran Polymer and Petrochemical Institute, PO Box 14965-115, Tehran, Iran*
[b]*Department of Chemistry, Shahid Beheshti University, PO Box 19396-4716, Tehran, Iran*

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Abstract—The regioselective three-component condensation reaction of 2-hydroxy-1,4-naphthoquinone with isocyanides in the presence of a variety of aldehydes offers an easy one-pot access to linear naphtho[2,3-*b*]-furan-4,9-dione derivatives. This method has the advantage of good yields, high regioselectivity, and uses readily accessible substrates and reagents. The elucidation of regiochemistry has been accomplished by X-ray determination of some representative compounds.

1. Introduction

The chemistry of quinone annulated heterocycles is largely dependent on the substituents being either on the quinonic or on adjacent rings.[1,2] Among various classes of heterocyclic quinones, naphthofuroquinones have attracted widespread interest in view of their presence in natural products, and for their pharmacological activities. A great number of naphthofuroquinones are natural products exhibiting a broad spectrum of biological activity. For example, some naphthofuroquinone derivatives as represented by avicequinones[2,3] and maturinones[4] have shown a diversity of biological activities of medical importance, such as anticancer, antibacterial, and anti-inflammatory activities.[5] Also, many synthetic naphthofuroquinones and their phytochemical analogs isolated from the inner bark of *Tecoma ipe Mart* show antitumor activity.[6] In addition, the chloroform extract of *Tabebuia ochracea ssp. neochrysanta* that contained six naphthofuroquinone derivatives has shown cytotoxicity against melanoma B16 cells, and antimalarial activity in vitro against strains of *Plasmodium berghei*.[7] Furthermore, because of their potent activity against the growth of human keratinocytes, some naphthofuroquinone compounds, in particular: naphtho[2,3-*b*]furan-4,9-diones, appear to be promising as effective antipsoriatic agents.[8] Finally, very recently, naphthofuroquinone were evaluated for inhibitory activities against receptor tyrosine kinases.[9] The diversity of their natural origins and biological activities have motivated efforts toward their syntheses or to find pathways to structural analogs.[10–22] The naphthofuroquinone derivatives have mainly been synthesized from 2,3-dichloro-1,4-naphthoquinone by base catalyzed condensation with 1,3-dicarbonyl compounds or from 2-hydroxy-1,4-naphthoquinone by different [3+2] annulation strategies, by thermal cyclization with enamines,[11] photochemical cycloaddition with alkenes and alkynes,[12] CAN mediated cycloaddition with alkenes and alkynes,[13,14] with 1,3-dicarbonyl compounds[15a] and 2,3-dimethoxy-1,3-butadiene,[15b] base promoted reaction with 3,4-dibromo-2-butanone,[16] and reaction with alkynyl(phenyl)iodonium tetrafluoroborate via tandem O-Michael-carbene insertion.[17] They have also been synthesized from 2-hydroxy-3-iodo-1,4-naphthoquinone or 3-phenyliodonio-1,2,4-trioxo-1,2,3,4-tetrahydronaphthalenides by palladium catalyzed heteroannulation with terminal alkynes,[18] from 2,3-dihydronaphtho[2,3-*b*]furan by formylation, oxidation, and dehydrogenation,[19] from benzofuranquinone by Diels–Alder cycloaddition with butadiene and subsequent dehydrogenation,[20] from thio-substituted 1,4-naphthoquinone by regioselective addition with enolate,[21] and from 2-lithiofuran by reaction with phthalic anhydride followed by intramolecular Friedel–Crafts acylation reaction.[22] Many of the synthetic protocols reported so far suffer from disadvantages, such as relying on multistep reactions,[10b,d,12a] difficulties in controlling regiochemistry,[10i,15a] generating by-products,[10f,16] low yields,[10g,16] and use of metal-containing reagents.[10e,13,14,15a,18] Therefore, the development of new, efficient methods for the preparation of linear naphtho[2,3-*b*]-furan-4,9-dione derivatives is still strongly desirable.

To the best of our knowledge, there are no reports concerning the synthesis of naphtho[2,3-*b*]-furan-4,9-dione ring systems by formation of three bonds. Following our recent

Keywords: Aldehyde; 2-Hydroxy-1,4-naphthoquinone; Isocyanide; Multicomponent reaction; Naphtho[2,3-*b*]-furan-4,9-dione.
* Corresponding author. Tel.: +98 21 44580000; fax: +98 21 44580032; e-mail: m.teimouri@ippi.ac.ir

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Table 1. Synthesis of linear naphtho[2,3-*b*]-furan-4,9-dione derivatives

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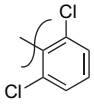
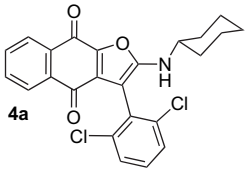
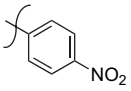
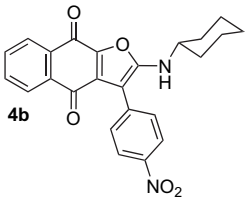
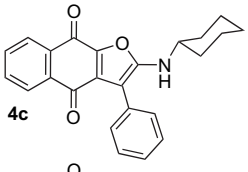
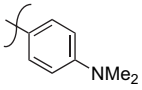
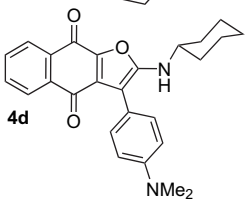
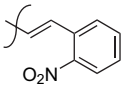
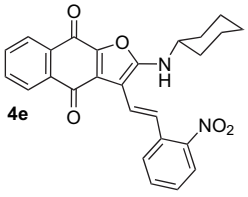
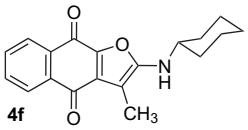
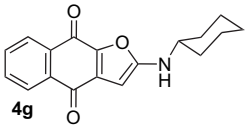
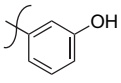
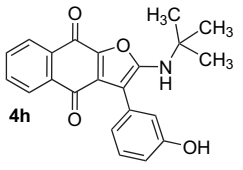
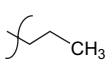
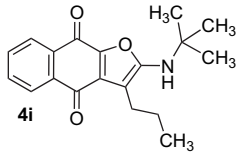
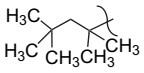
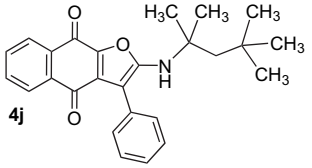
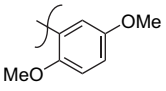
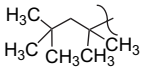
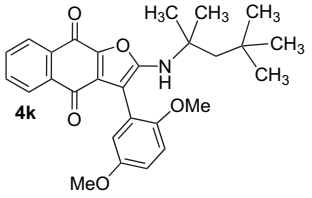
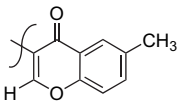
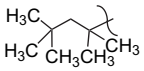
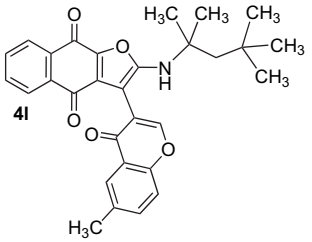
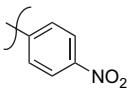
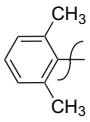
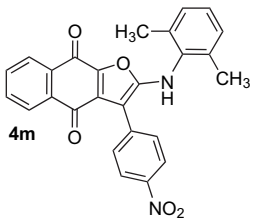
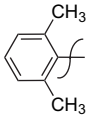
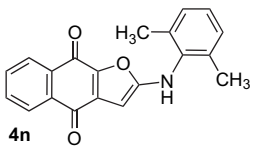
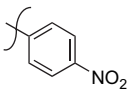
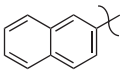
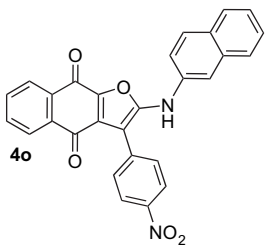
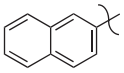
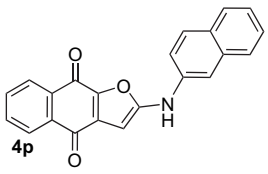
1			4	 **4a**	76
2			4	 **4b**	92
3			4	 **4c**	71
4			4	 **4d**	80
5			4	 **4e**	86
6	CH_3		4	 **4f**	75
7	H		4	 **4g**	81
8			4	 **4h**	65

(*continued*)

Table 1. (*continued*)

Entry	R	R′	Time (h)	Product	Yield (%)
9			4	 **4i**	81
10			4	 **4j**	74
11			4	 **4k**	76
12			4	 **4l**	84
13			48	 **4m**	19
14	H		48	 **4n**	15
15			48	 **4o**	14
16	H		48	 **4p**	17

works[23] on the application of isocyanide-based multicomponent reactions in heterocyclic synthesis, in the present work, we report on the use of 2-hydroxy-1,4-naphthoquinone in the formation of novel naphthofuroquinone derivatives incorporating naphtho[2,3-*b*]-furan-4,9-dione skeleton via a three-component condensation reaction of isocyanides with the formation of three bonds by a [3+1+1] furannulation strategy. 2-Hydroxy-1,4-naphthoquinone **1** and aldehydes **2** in the presence of isocyanides **3** undergo an addition reaction in refluxing toluene, to produce the linear naphtho[2,3-*b*]-furan-4,9-dione derivatives **4** in good yields. The reaction can be represented as in Table 1.

2. Results and discussion

The one-pot three-component condensation reactions of 2-hydroxy-1,4-naphthoquinone **1** with various aldehydes **2** in the presence of alkyl isocyanides **3** proceeded rapidly in refluxing toluene and were complete after 4 h to afford 2-(alkylamino)-3-alkyl or arylnaphtho[2,3-*b*]furan-4,9-diones **4** in good yields. ^{1}H and ^{13}C NMR spectra of the crude products clearly indicated the formation of fused naphthofuroquinone **4**. All the products were characterized by FTIR, ^{1}H and ^{13}C NMR spectra, and elemental analysis. Furthermore, the structure and regiochemistry of **4i** (regioselectivity of reaction) was established by an X-ray crystallographic analysis.[24] The molecular structure of **4i** is shown in Figure 1.

The scope of the reaction with respect to the aldehyde component was examined and it was found that aliphatic aldehydes, the substituted aromatic aldehydes containing electron-withdrawing groups and electron-donating groups, and α,β-unsaturated aldehydes can tolerate the reaction conditions with good yields. To explore the scope of this reaction with respect to isocyanides, we have examined five alkyl or aryl isocyanides. We have found that the reaction proceeds very efficiently with hindered alkyl isocyanides, but in the case of the reaction of aryl isocyanide (2,6-dimethylphenyl isocyanide and 2-naphthyl isocyanide) with 2-hydroxy-1,4-naphthoquinone in the presence of 4-nitrobenzaldehyde or formaldehyde, after refluxing for 48 h in toluene, the corresponding naphthofuroquinones **4m**, **4n**, **4o** and **4p** were isolated in 19, 15, 14 and 17% yields, respectively (entries 13–16).

Although we have not established the mechanism of the reaction between 2-hydroxy-1,4-naphthoquinone and aldehydes in the presence of isocyanides experimentally, the synthesis of linear naphtho[2,3-*b*]-furan-4,9-dione derivatives **4** can be rationalized by initial formation of a conjugated electron-deficient enone **5** by a Knoevenagel condensation of the cyclic 2-hydroxy-1,4-naphthoquinone **1** and the aldehyde **2**. The next step of this mechanism could involve a [4+1] cycloaddition reaction[25] of the electron-deficient heterodiene moiety of adduct **5** with the isocyanide to afford an iminolactone intermediate **6**. The subsequent isomerization of iminolactone **6** leads to formation of product **4** (Scheme 1).

In conclusion we have achieved an efficient process for the synthesis of biologically interesting functionalized linear naphtho[2,3-*b*]-furan-4,9-dione derivatives starting from readily available reagents. The reaction is very simple from the experimental point of view and allows the creation of a fused naphthofuroquinone ring with concomitant formation of two new C–C bonds and one C–O bond in a single operation.

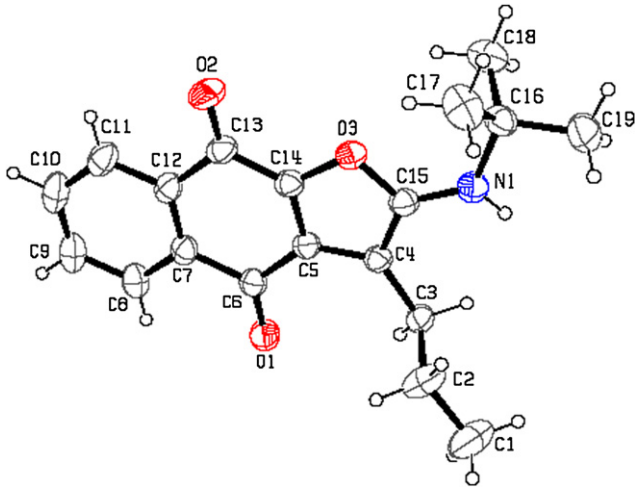
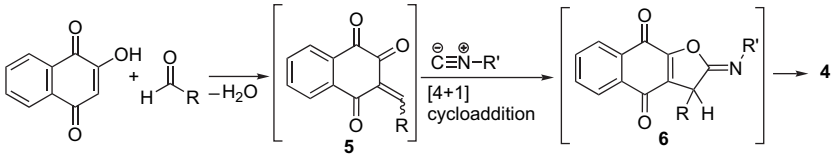


Figure. 1. Stereoscopic ORTEP plot of compound **4i**, showing the atomic numbering scheme.

3. Experimental

3.1. General

Melting points were measured on a Büchi 535 apparatus and are uncorrected. Elemental analyzes were performed using a Heraeus CHN-O-Rapid analyzer. FTIR spectra were recorded on a Bruker Equinox-55 spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DRX-400 Avance spectrometer at 400.13 and 100.77 MHz, respectively, with $CDCl_3$ as solvent. The solvents, aldehydes, and 1,1,3,3-tetramethylbutyl isocyanides used in this work were purchased from Merck, and the *tert*-butyl and 2,6-dimethylphenyl isocyanide were obtained from Fluka (Buchs, Switzerland). The 2-naphthyl isocyanide and 2-hydroxy-1,4-naphthoquinone were obtained from Aldrich chemical company. All reagents were used without further purification.



Scheme 1.

3.2. Typical procedure for preparation of 2-(cyclohexylamino)-3-(2,6-dichlorophenyl)naphtho[2,3-*b*]furan-4,9-dione (4a)

To a magnetically stirred solution of 2-hydroxy-1,4-naphthoquinone (0.174 g, 1.0 mmol) and 2,6-dichlorobenzaldehyde (0.175 g, 1.0 mmol) in toluene (25 mL) was added cyclohexyl isocyanide (0.110 g, 1.0 mmol) via a syringe and the mixture was heated to reflux for 4 h. The solvent was removed under reduced pressure, the residue was washed with toluene (5 mL) and recrystallized from diethyl ether/*n*-hexane (1:3) to give blue needles (0.336 g, 76%); mp 239–241 °C; FTIR (KBr) (ν_{max}, cm^{-1}): 3263 (N–H), 1648 (C=O), 1598 (C=C); δ_H (400.1 MHz, $CDCl_3$) 1.16–2.06 (10H, m, 5CH_2), 3.75 (1H, m, N–C*H*), 4.40 (1H, d, *J* 7.4 Hz, N*H*), 7.26–4.43 (3H, m, $C_6H_3Cl_2$), 7.58, 7.67, 7.96, and 8.16 (4H, 4m, C_6H_4); δ_C (100.7 MHz, $CDCl_3$) 181.50, 169.65, 158.48, 143.22, 137.05, 133.77, 133.38, 132.75, 132.67, 132.29, 130.17, 128.21, 126.33, 126.23, 92.65, 52.57, 34.04, 25.29, 24.79; Anal. Calcd for $C_{24}H_{19}Cl_2NO_3$ (440.31): C, 65.47; H, 4.35; N, 3.18%. Found: C, 65.50; H, 4.37; N, 3.17%.

3.2.1. 2-(Cyclohexylamino)-3-(4-nitrophenyl)naphtho[2,3-*b*]furan-4,9-dione (4b). Blue needles (0.384 g, 92%); mp 246–249 °C; FTIR (KBr) (ν_{max}, cm^{-1}): 3287 (N–H), 1678, 1645 (C=O), 1585 (C=C); δ_H (400.1 MHz, $CDCl_3$) 1.24–2.34 (10H, m, 5CH_2), 3.87 (1H, m, N–C*H*), 4.97 (1H, d, *J* 7.3 Hz, N*H*), 7.66 and 8.28 (4H, 2d, *J* 8.7 Hz, $C_6H_4NO_2$), 7.62, 7.70, 8.01, and 8.15 (4H, 4m, C_6H_4); δ_C (100.7 MHz, $CDCl_3$) 181.72, 169.92, 158.94, 146.41, 143.91, 137.68, 133.97, 133.01, 132.87, 132.67, 130.52, 129.88, 126.58, 126.24, 124.05, 96.18, 52.23, 33.83, 25.25, 24.71; Anal. Calcd for $C_{24}H_{20}N_2O_5$ (416.42): C, 69.22; H, 4.84; N, 6.73%. Found: C, 69.25; H, 4.79; N, 6.76%.

3.2.2. 2-(Cyclohexylamino)-3-phenylnaphtho[2,3-*b*]furan-4,9-dione (4c). Blue needles (0.264 g, 71%); mp 245–248 °C; FTIR (KBr) (ν_{max}, cm^{-1}): 3226 (N–H), 1676, 1640 (C=O), 1583 (C=C); δ_H (400.1 MHz, $CDCl_3$) 1.18–2.34 (10H, m, 5CH_2), 3.85 (1H, m, N–C*H*), 4.95 (1H, br s, N*H*), 7.15–7.50 (5H, m, C_6H_5), 7.58, 7.67, 8.00, and 8.15 (4H, 4m, C_6H_4); δ_C (100.7 MHz, $CDCl_3$) 181.91, 169.25, 159.15, 143.26, 133.67, 133.38, 133.22, 132.20, 131.20, 130.12, 129.33, 128.85, 127.68, 126.41, 126.08, 98.83, 52.30, 33.90, 25.33, 24.73; Anal. Calcd for $C_{24}H_{21}NO_3$ (371.42): C, 77.61; H, 5.70; N, 3.77%. Found: C, 77.55; H, 5.68; N, 3.80%.

3.2.3. 2-(Cyclohexylamino)-3-[4-(dimethylamino)phenyl]naphtho[2,3-*b*]furan-4,9-dione (4d). Blue prisms (0.332 g, 80%); mp 248–251 °C; FTIR (KBr) (ν_{max}, cm^{-1}): 3299 (N–H), 1636 (C=O), 1579 (C=C); δ_H (400.1 MHz, $CDCl_3$) 1.18–2.07 (10H, m, 5CH_2), 2.97 (6H, NMe_2), 3.85 (1H, m, N–C*H*), 4.96 (1H, d, *J* 8.3 Hz, N*H*), 6.77 and 7.34 (4H, 2d, *J* 8.7 Hz, $C_6H_4NMe_2$), 7.57, 7.65, 8.00, and 8.14 (4H, 4m, C_6H_4); δ_C (100.7 MHz, $CDCl_3$) 182.04, 168.48, 159.43, 149.84, 142.84, 133.75, 133.51, 133.32, 131.85, 131.24, 130.08, 126.32, 125.97, 117.10, 112.41, 99.93, 52.23, 40.37, 33.90, 25.37, 24.47; Anal. Calcd for $C_{26}H_{26}N_2O_3$ (414.49): C, 75.34; H, 6.32; N, 6.76%. Found: C, 75.28; H, 6.30; N, 6.81%.

3.2.4. 2-(Cyclohexylamino)-3-[2-(2-nitrophenyl)-1-ethenyl]naphtho[2,3-*b*]furan-4,9-dione (4e). Blue needles (0.342 g, 86%); mp 220–223 °C; FTIR (KBr) (ν_{max}, cm^{-1}): 3384 (N–H), 1647 (C=O), 1617 and 1588 (C=C); δ_H (400.1 MHz, $CDCl_3$) 1.30–2.16 (10H, m, 5CH_2), 3.96 (1H, m, N–C*H*), 5.59 (1H, d, *J* 7.7 Hz, N*H*), 7.14–8.16 (10H, m, arom. hydrogens and C*H*=C*H*); δ_C (100.7 MHz, $CDCl_3$) 182.87, 169.08, 159.77, 146.80, 142.61, 133.88, 133.65, 133.49, 132.81, 132.20, 130.30, 127.75, 126.23, 126.21, 125.23, 123.90, 123.42, 96.20, 52.71, 33.68, 25.25, 24.60; Anal. Calcd for $C_{26}H_{23}N_2O_5$ (442.46): C, 70.58; H, 5.01; N, 6.33%. Found: C, 70.65; H, 5.03; N, 6.31%.

3.2.5. 2-(Cyclohexylamino)-3-methylnaphtho[2,3-*b*]furan-4,9-dione (4f). Blue needles (0.232 g, 75%); mp 192–195 °C; FTIR (KBr) (ν_{max}, cm^{-1}): 3425 (N–H), 1642 (C=O), 1588 (C=C); δ_H (400.1 MHz, $CDCl_3$) 1.24–2.08 (10H, m, 5CH_2), 2.19 (3H, s, *Me*), 3.81 (1H, m, N–C*H*), 4.97 (1H, d, *J* 7.3 Hz, N*H*), 7.57, 7.66, 8.03, and 8.13 (4H, 4m, C_6H_4); δ_C (100.7 MHz, $CDCl_3$) 182.97, 164.60, 158.87, 146.36, 141.29, 134.10, 133.29, 131.52, 126.75, 126.01, 122.66, 96.12, 53.53, 33.54, 25.21, 24.78, 15.28; Anal. Calcd for $C_{19}H_{19}NO_3$ (309.35): C, 73.77; H, 6.19; N, 4.53%. Found: C, 73.82; H, 6.22; N, 4.51%.

3.2.6. 2-(Cyclohexylamino)naphtho[2,3-*b*]furan-4,9-dione (4g). Purple needles (0.240 g, 81%); mp 215–218 °C; FTIR (KBr) (ν_{max}, cm^{-1}): 3251 (N–H), 1668, 1639 (C=O), 1582 (C=C); δ_H (400.1 MHz, $CDCl_3$) 1.26–2.16 (10H, m, 5CH_2), 3.35 (1H, m, N–C*H*), 4.96 (1H, br s, N*H*), 5.57 (1H, s, =C*H*), 7.61, 7.66, 8.06, and 8.12 (4H, 4m, C_6H_4); δ_C (100.7 MHz, $CDCl_3$) 181.83, 162.20, 133.49, 133.82, 132.73, 132.22, 126.94, 126.44, 126.25, 80.49, 80.40, 80.31, 53.01, 32.99, 25.37, 24.54; Anal. Calcd for $C_{18}H_{17}NO_3$ (295.33): C, 73.20; H, 5.80; N, 4.74%. Found: C, 73.25; H, 5.81; N, 4.76%.

3.2.7. 2-[(*tert*-Butyl)amino-3-(3-hydroxyphenyl)naphtho[2,3-*b*]furan-4,9-dione (4h). Blue needles (0.236 g, 65%); mp 241–244 °C; FTIR (KBr) (ν_{max}, cm^{-1}): 3338 (N–H and O–H), 1689 and 1640 (C=O), 1585 (C=C); δ_H (400.1 MHz, $CDCl_3$) 1.45 (9H, s, CMe_3), 5.08 (1H, br s, N*H*), 7.33–7.41 (4H, m, C_6H_4OH), 7.57, 7.66, 7.97, and 8.15 (4H, 4 m, C_6H_4), 9.93 (1H, s, O*H*); δ_C (100.7 MHz, $CDCl_3$) 181.90, 169.12, 159.99, 156.76, 143.54, 137.80, 133.87, 132.33, 131.36, 130.30, 126.56, 126.17, 123.01, 122.12, 121.15, 116.50, 115.03, 100.57, 54.14, 29.85; Anal. Calcd for $C_{24}H_{21}NO_4$ (387.42): C, 74.40; H, 5.46; N, 3.62%. Found: C, 74.44; H, 5.45; N, 3.60%.

3.2.8. 2-(*tert*-Butylamino)-3-propylnaphtho[2,3-*b*]furan-4,9-dione (4i). Blue prisms (0.253 g, 81%); mp 197–199 °C; FTIR (KBr) (ν_{max}, cm^{-1}): 3344 (N–H), 1675 and 1640 (C=O), 1582 (C=C); δ_H (400.1 MHz, $CDCl_3$) 0.94 (3H, t, *J* 7.3 Hz, $CH_2CH_2CH_3$), 1.45 (9H, s, CMe_3), 1.58 (2H, m, $CH_2CH_2CH_3$), 2.54 (2H, t, *J* 7.3 Hz, $CH_2CH_2CH_3$), 4.28 (1H, br s, N*H*), 7.57, 7.65, 8.01, and 8.12 (4H, 4m, C_6H_4); δ_C (100.7 MHz, $CDCl_3$) 182.94, 168.82, 159.73, 143.73, 133.75, 133.62, 133.07, 131.97, 131.89, 126.15, 126.01, 101.77, 53.93, 30.17, 24.62, 22.61, 13.88; Anal. Calcd for $C_{19}H_{21}NO_3$ (311.37): C, 73.29; H, 6.80; N, 4.50%. Found: C, 73.35; H, 6.81; N, 4.48%.

3.2.9. 3-Phenyl-2-[(1,1,3,3-tetramethylbutyl)amino]-naphtho[2,3-*b*]furan-4,9-dione (4j). Blue needles (0.298 g, 74%); mp 262–264 °C; FTIR (KBr) (ν_{max}, cm^{-1}): 3287 (N–H), 1673 and 1643 (C=O), 1582 (C=C); δ_H (400.1 MHz, $CDCl_3$) 0.98 (9H, s, C*Me*$_3$), 1.52 (6H, s, C*Me*$_2$), 1.78 (2H, s, C*H*$_2$), 5.06 (1H, br s, N*H*), 7.46 (5H, m, C_6H_5), 7.58, 7.67, 8.00, and 8.15 (4H, 4m, C_6H_4); δ_C (100.7 MHz, $CDCl_3$) 181.90, 169.03, 159.40, 143.74, 133.66, 133.59, 133.45, 133.27, 132.14, 130.15, 129.38, 128.87, 127.76, 126.39, 126.03, 100.07, 57.67, 53.46, 31.44, 31.39, 30.26; Anal. Calcd for $C_{26}H_{27}NO_3$ (401.49): C, 77.78; H, 6.78; N, 3.49%. Found: C, 77.85; H, 6.80; N, 3.52%.

3.2.10. 3-(2,5-Dimethoxyphenyl)-2-[(1,1,3,3-tetramethylbutyl)amino]naphtho[2,3-*b*]furan-4,9-dione (4k). Blue prisms (0.352 g, 76%); mp 251–254 °C; FTIR (KBr) (ν_{max}, cm^{-1}): 3295 (N–H), 1666 and 1641 (C=O), 1573 (C=C); δ_H (400.1 MHz, $CDCl_3$) 0.97 (9H, s, C*Me*$_3$), 1.51 (6H, s, C*Me*$_2$), 1.80 (2H, s, C*H*$_2$), 3.77 and 3.79 (6H, 2s, 2O*Me*), 5.03 (1H, br s, N*H*), 6.89–6.98 (3H, m, $C_6H_3(OMe)_2$), 7.56, 7.65, 7.99, and 8.15 (4H, 4m, C_6H_4); δ_C (100.7 MHz, $CDCl_3$) 181.63, 168.71, 159.41, 153.61, 150.64, 144.01, 133.51, 133.36, 131.99, 131.33, 126.39, 125.95, 123.54, 119.63, 117.64, 114.61, 113.14, 97.05, 57.23, 56.63, 55.79, 53.66, 31.76, 31.43, 30.39; Anal. Calcd for $C_{28}H_{31}NO_5$ (461.54): C, 72.86; H, 6.77; N, 3.03%. Found: C, 72.90; H, 6.75; N, 2.99%.

3.2.11. 3-(6-Methyl-4-oxo-4*H*-chromene-3-yl)-2-[(1,1,3,3-tetramethylbutyl)amino]naphtho[2,3-*b*]furan-4,9-dione (4l). Blue prisms (0.406 g, 84%); mp 274–277 °C; FTIR (KBr) (ν_{max}, cm^{-1}): 3368 (N–H), 1645 (C=O), 1592 (C=C); δ_H (400.1 MHz, $CDCl_3$) 0.99 (9H, s, C*Me*$_3$), 1.55 (6H, s, C*Me*$_2$), 1.86 (2H, s, C*H*$_2$), 2.47 (3H, s, =C–C*H*$_3$), 6.54 (1H, br s, N*H*), 7.43–8.12 (7H, m, arom. hydrogens), 8.47 (1H, s, C=C*H*); δ_C (100.7 MHz, $CDCl_3$) 182.67, 176.94, 168.72, 161.11, 157.52, 154.16, 144.42, 135.65, 135.20, 133.80, 133.30, 133.26, 132.11, 129.93, 126.40, 126.01, 125.37, 123.43, 118.00, 114.57, 91.06, 57.14, 53.07, 31.45, 30.81, 30.30, 21.40; Anal. Calcd for $C_{30}H_{29}NO_5$ (483.55): C, 74.52; H, 6.04; N, 2.90%. Found: C, 74.48; H, 6.01; N, 2.90%.

3.2.12. 2-(2,6-Dimethylanilino)-3-(4-nitrophenyl)naphtho[2,3-*b*]furan-4,9-dione (4m). Violet prisms (0.084 g, 19%); mp 252–254 °C; FTIR (KBr) (ν_{max}, cm^{-1}): 3298 (N–H), 1677 (C=O), 1581 (C=C); δ_H (400.1 MHz, $CDCl_3$) 2.30 (6H, s, $C_6H_3Me_2$), 5.33 (1H, br s, N*H*), 7.03–7.06 (3H, m, $C_6H_3Me_2$), 7.75, 7.78, 8.28, and 8.32 (4H, 4m, C_6H_4), 8.06 and 8.34 (4H, 2d, *J* 8.5 Hz, $C_6H_4NO_2$); δ_C (100.7 MHz, $CDCl_3$) 181.48, 169.87, 161.43, 140.81, 140.05, 135.16, 134.88, 130.49, 130.12, 129.39, 128.45, 128.35, 127.31, 127.11, 126.58, 124.09, 123.89, 123.60, 113.49, 79.66, 18.25; Anal. Calcd for $C_{26}H_{18}N_2O_5$ (438.43): C, 71.23; H, 4.14; N, 6.39%. Found: C, 71.30; H, 4.17; N, 6.38%.

3.2.13. 2-(2,6-Dimethylanilino)naphtho[2,3-*b*]furan-4,9-dione (4n). Red prisms (0.048 g, 15%); mp 236–239 °C; FTIR (KBr) (ν_{max}, cm^{-1}): 3306 (N–H), 1654 (C=O), 1577 (C=C); δ_H (400.1 MHz, $CDCl_3$) 2.28 (6H, s, $C_6H_3Me_2$), 5.28 (1H, s, N*H*), 6.51 (1H, s, =C*H*), 7.12–7.16 (3H, m, $C_6H_3Me_2$), 7.61, 7.68, 8.05, and 8.14 (4H, 4m, C_6H_4); δ_C (100.7 MHz, $CDCl_3$) 181.52, 170.12, 161.10, 144.03, 135.82, 135.24, 134.17, 133.84, 133.24, 132.77, 132.51, 128.96, 127.92, 126.53, 126.34, 81.86, 18.09; Anal. Calcd for $C_{20}H_{15}NO_3$ (317.33): C, 75.70; H, 4.76; N, 4.41%. Found: C, 75.78; H, 4.80; N, 4.38%.

3.2.14. 2-(2-Naphthylamino)-3-(4-nitrophenyl)naphtho[2,3-*b*]furan-4,9-dione (4o). Blue prisms (0.065 g, 14%); mp 250–252 °C; FTIR (KBr) (ν_{max}, cm^{-1}): 3320 (N–H), 1669 (C=O), 1581 (C=C); δ_H (400.1 MHz, $CDCl_3$) 5.37 (1H, br s, N*H*), 7.10–8.21 (15H, m, arom. hydrogens); δ_C (100.7 MHz, $CDCl_3$) 181.44, 169.12, 162.25, 144.08, 136.13, 135.82, 135.24, 134.73, 134.17, 134.09, 133.76, 133.50, 133.24, 132.76, 132.63, 132.47, 131.11, 130.29, 128.90, 127.81, 127.46, 126.83, 126.48, 126.39, 126.15, 95.89; Anal. Calcd for $C_{28}H_{16}N_2O_5$ (460.44): C, 73.04; H, 3.50; N, 6.08%. Found: C, 73.10; H, 3.52; N, 6.01%.

3.2.15. 2-(2-Naphthylamino)naphtho[2,3-*b*]furan-4,9-dione (4p). Purple prisms (0.058 g, 17%); mp 233–236 °C; FTIR (KBr) (ν_{max}, cm^{-1}): 3343 (N–H), 1681, 1661 (C=O), 1582 (C=C); δ_H (400.1 MHz, $CDCl_3$) 5.23 (1H, br s, N*H*), 6.21 (1H, s, =C*H*), 7.13–8.20 (11H, m, arom. hydrogens); δ_C (100.7 MHz, $CDCl_3$) 180.21, 170.33, 161.76, 144.01, 136.10, 135.94, 135.73, 134.61, 134.22, 134.06, 133.90, 133.47, 133.17, 132.60, 132.44, 131.01, 130.53, 128.08, 127.15, 126.28, 126.11, 82.84; Anal. Calcd for $C_{22}H_{13}NO_3$ (339.34): C, 77.87; H, 3.86; N, 4.13%. Found: C, 77.91; H, 3.85; N, 4.11%.

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24. X-ray data for **4i**: ($C_{19}H_{21}NO_3$), M=311.37 g mol^{-1}, monoclinic system, space group $P2_1/c$, a=13.086(4) Å, b=9.1409 (18) Å, c=15.353(4) Å, β=113.136(19)°, V=1688.8 Å^3, Z=4, Dc=1.38 g cm^{-3}, μ(Mo Kα)=0.083 mm^{-1}, crystal dimension of 0.4×0.3×0.3 mm^3. The structure was solved by using SHELXS. The structure refinement and data reduction were carried out with SHELXL of the X-Step32 suite of programs.[26] The non-hydrogen atoms were refined anisotropically by full matrix least-squares on F^2 values to final R_1=0.0657, wR_2=0.1805, and S=1.134 with 213 parameters using 63,401 independent reflections. Hydrogen atoms were located from expected geometry and were not refined. Crystallographic data for **4i** have been deposited with the Cambridge Crystallographic Data Centre. Copies of the data can be obtained, free of charge, on application to The Director, CCDC 615113, Union Road, Cambridge CB2 1EZ, UK. Fax: +44 1223336033 or e-mail: deposit@ccdc.cam.ac.uk.
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