JOC The Journal of Organic Chemistry

Note

pubs.acs.org/joc

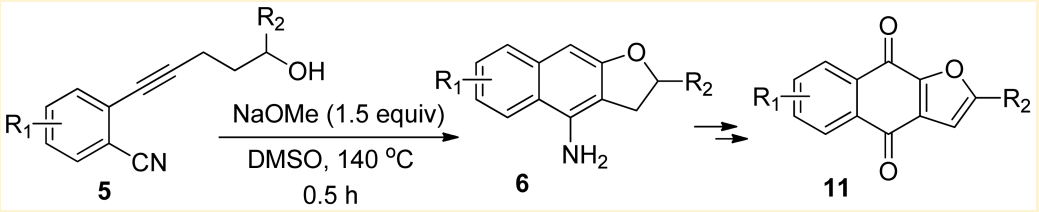
Base-Mediated Cyclization Reaction of 2-(5-Hydroxy-1-pentynyl)benzonitriles to 4-Amino-2,3-dihydronaphtho[2,3-*b*]furanes and Synthesis of Furanonaphthoquinones

Chih-Jyun Tsai,[†] Chin-Chau Chen,[†] Chih-Wei Tsai,[‡] and Ming-Jung Wu*[,†,‡]

[†]Department of Chemistry, National Sun Yat-sen University, Kaohsiung, Taiwan 804

[‡]Department of Medicinal and Applied Chemistry, Kaohsiung Medical University, Kaohsiung, Taiwan 807

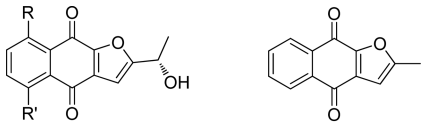
Supporting Information



ABSTRACT: An efficient transformation of 2-(5-hydroxy-1-pentynyl)benzonitriles **5** to furanonaphthoquinones **11** is presented. Treatment of **5** with 1.5 equiv of NaOMe in DMSO at 140 °C for 0.5 h gave **6** in good yields. Conversion of **6** to **11** was carried out by oxidation of **6** with Fremy's salt and KH_2PO_4 in acetone and water, followed by dehydrogenation using palladium on charcoal in diphenylether at reflux temperature.

Many naturally occurring or synthetic furanonaphthoquinones have been found to exhibit a broad spectrum of biological activities, in particular, antitumor activity.[1] For instance, kigelinone (**1**) was isolated by Inoue from the wood of *Kigelia pinnata* and showed good antitumor activity.[1a] Compounds **2** and **3** were isolated by Kingston from *Crescentia cujete* and exhibited high cytotoxicity against Vero cells.[1c] The synthetic compound FNQ3 (**4**) reported by Takegami was found to have good antiviral activity against the Japanese encephalitis virus (JEV)[1d] (Scheme 1). Because of the

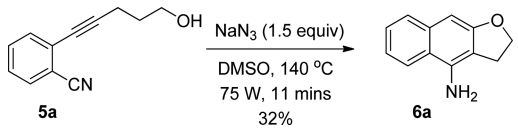
Scheme 1. Structures of Some Furanonaphthoquinones



importance of furanonaphthoquinones to drug development, several synthetic methods have been developed to construct this ring system.[2] Most of them suffer from either long synthetic sequences or limitations of using 2-hydroxy-1,4-naphthoquinone as the starting material. We herein report an efficient synthesis of furanonaphthoquinones by the cyclization of 2-(5-hydroxy-1-pentynyl)benzonitriles **5** to 4-amino-2,3-dihydronaphtho[2,3-*b*]furanes **6** followed by oxidation and dehydrogenation reactions.

The starting 2-(5-hydroxy-1-pentynyl)benzonitrile (**5a**) was prepared by the Sonogashira coupling reaction of 2-bromobenzonitrile and 4-pentyn-1-ol using palladium as the catalyst.[3] During our investigation of the reaction of internal alkynes with sodium azide to triazoles,[4] we found that reaction of **5a** with 1.5 equiv of NaN_3 gave compound **6a** in low yield (Scheme 2). Apparently, sodium azide reacts as a base in this

Scheme 2. Preliminary Result of the Cyclization Reaction



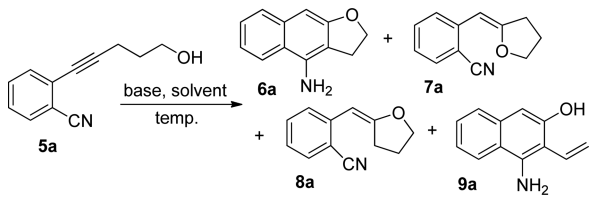
reaction with subsequent nucleophilic addition and subsequent cyclization reactions to give compound **6a**. We then anticipated that if a more suitable base was employed in this reaction, compound **6a** should be obtained in higher yield. Compound **6a** could further be oxidized to furanonaphthoquinones.

Six different bases were screened for this study, and the results are summarized in Table 1. It was found that reaction of **5a** with 1.5 equiv of NaOMe in DMSO at 140 °C for 0.5 h gave compound **6a** in 66% yield. Bases, such as NaOH, K_2CO_3, and Na_2CO_3, were not as efficient as NaOMe for the formation of **6a**. Using the stronger bases, such as KO*t*Bu and NaH,

Received: November 1, 2015
Published: April 5, 2016

DOI: 10.1021/acs.joc.5b02514
J. Org. Chem. 2016, 81, 3882−3889

Table 1. Screening the Base, Temperature, and Solvent Effects on the Cyclization Reactions of 5a



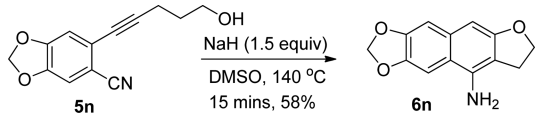
entry	base	solvent	temp (°C)	product/yield
1	NaOH	DMSO	140	**6a**/49; **7a**/40; **8a**/8
2	K_2CO_3	DMSO	140	**7a**/63; **8a**/10
3	Na_2CO_3	DMSO	140	**7a**/44; **8a**/9
4	NaH	DMSO	140	**6a**/16; **9a**/43
5	KO*t*Bu	DMSO	140	**6a**/8; **9a**/38
6	NaOMe	DMSO	140	**6a**/66
7	NaOMe	DMF	140	**6a**/18; **7a**/63; **8a**/12
8	NaOMe	NMP	140	**6a**/24; **7a**/61; **8a**/11
9	NaOMe	CH_3CN	140	**7a**/64; **8a**/11
10	NaOMe	1,4-dioxane	140	**7a**/36; **8a**/51
11	NaOMe	toluene	140	**7a**/55; **8a**/24
12	NaOMe	DMSO	120	**6a**/43; **7a**/22; **8a**/5
13	NaOMe	DMSO	100	**6a**/26; **7a**/53; **8a**/8

compound **9a** was obtained as the major product. Apparently, compound **9a** came from the further elimination reaction of product **6a**. Various solvents were also tested. The polar aprotic solvents, such as DMF and NMP, also provided compound **6a** but in lower yields, and the major product was **7a**. When the reaction was carried out in CH_3CN, 1,4-dioxane, or toluene, only **7a** and **8a** were obtained and no **6a** was formed. To summarize the screening study, the optimized reaction conditions for compound **6a** included treatment of **5a** with 1.5 equiv of NaOMe in DMSO at 140 °C for 0.5 h.

With the optimized reaction conditions in hand, cyclization reations of the other substrates[5] **5b–l** were carried out to give various 4-amino-2,3-dihydronaphtho[2,3-*b*]furanes **6b–l** in modest to good chemical yields. The results are summarized in Scheme 3. Compounds **5b–e** bearing primary hydroxyl groups gave the cyclization products **6b–e** in 70–77% yields. Compounds **5f–h** bearing secondary hydroxyl group and R_2 as an alkyl group also produced the cyclization products **6f–i** in good chemical yields. However, when R_2 is a vinyl or an aryl group, such as in **5j–m**, cyclization products **6j–m** were obtained in lower yields.

On the other hand, treatment of **5n** under the optimized reaction conditions gave a complex product mixture. Although we did not isolate any identified product, the acetal cleavage must take place under these reaction conditions. Therefore, we carried out the cyclization reaction of **5n** in DMSO at 140 °C using the less nucleophilic base, NaH, and the reaction time was reduced to 15 min; product **6n** was obtained in 58% yield (Scheme 4).

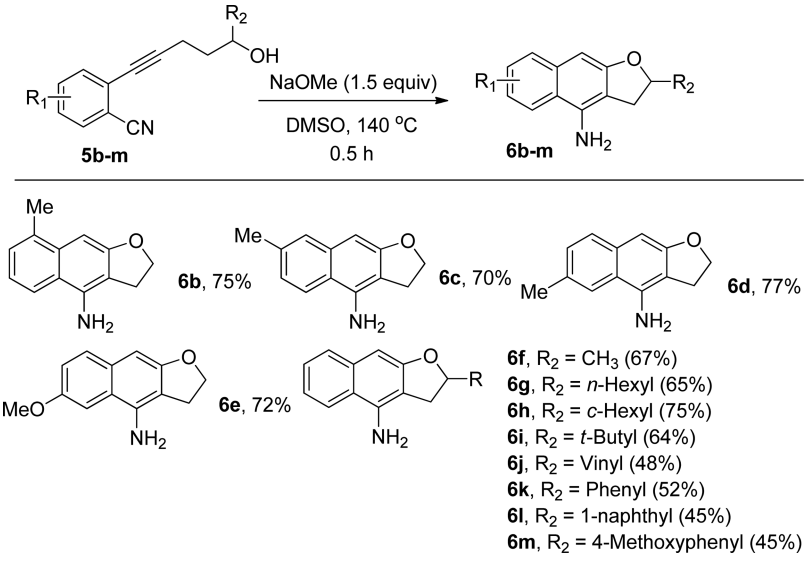
Scheme 4. Synthesis of 6n



The proposed mechanism for the cyclization of **5a** to **6a** is shown in Scheme 5. The first step is the deprotonation of **5a** with base to form alkoxide **I** that would undergo intramolecular 5-exo-dig cyclization to form the vinyl anions **7a**′ and **8a**′. The vinyl anions **7a**′ or **8a**′ could undergo direct proton transformation and equilibration to give anion **II** or protonation to give the intermediates **7a** and **8a**. Under the described reaction conditions, compounds **7a** and **8a** undergo equilibrium with each other. Further deprotonation of **8a** would also give anion **II** that could directly attack the cyano group to give the iminium ion **IV**[6] or undergoes tautomerization to form ketenimine anion **III** and then the electrocyclic ring closure reaction to give **IV**.[7] Finally, protonation of **IV** to give imine **V** and following the imine–enamine tautomerization converts the imine **V** to the final product **6a**.

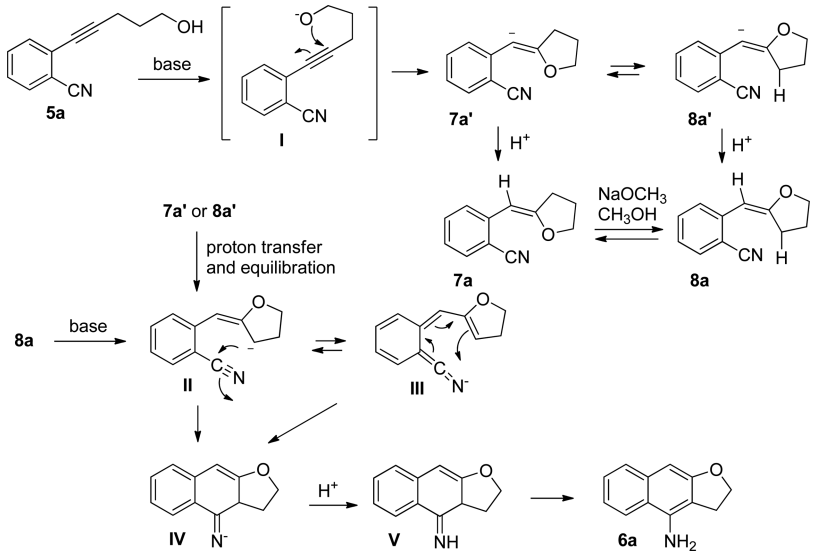
To understand more insight of the reaction mechanism, we carried out the experiments by recharging either compound **7a** or **8a** into the optimized reaction conditions, and both of them were converted to **6a** slowly. After being stirred for 24 h, only 52% of **6a** was obtained and isolated both the staring material

Scheme 3. Synthesis of 4-Amino-2,3-dihydronaphtho[2,3-*b*]furanes



DOI: 10.1021/acs.joc.5b02514
J. Org. Chem. 2016, 81, 3882–3889

Scheme 5. Proposed Mechanism for the Formation of 6a

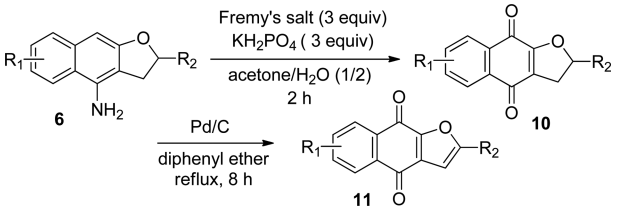


and its isomer. Compared to the one-pot reaction, conversion of **5a** to **6a** under the optimized reaction conditions requires only 0.5 h. We therefore conclude that the intramolecular proton transfer from **7a**′ or **8a**′ to anion **II** must be faster than the formation of **7a** and **8a**, and these two isomers can undergo equilibrium with each other under these reaction conditions.

The conversion of 4-amino-2,3-dihydronaphtho[2,3-*b*]-furanes **6** to furanonaphthoquinones **11** is summarized in Table 2. Oxidation of compounds **6a**−**k** and **6n** was carried out using Fremy's salt[8] and KH_2PO_4 in acetone and water to give dihydrofuranonaphthoquinones **10a**−**k** and **10n** in good yields except for compound **6b**. The low yield for the conversion of **6b** to **10b** could be due to the steric hindrance of the methyl group at the 8-position which prevents the oxidation from taking place at the 9-position. Finally, all of the dihydrofuranonaphthoquinones **10a**−**k** and **10n** were dehydrogenated using palladium on charcoal in diphenylether at reflux temperature[9] to give furanonaphthoquinones **11a**−**e**, **4**, **11g**−**i**, **11k**, and **11n** in 48−86% yields. Only compound **10j** gave a complex mixture of products under these reaction conditions.

In conclusion, we have developed an efficient synthesis of 4-amino-2,3-dihydronaphtho[2,3-*b*]furanes through the base-mediated cyclization of 2-(5-hydroxy-1-pentynyl)benzonitriles. The base, such as NaOMe, used in this transformation is readily available, easy to handle, and not expensive. The 4-amino-2,3-dihydronaphtho[2,3-*b*]furanes have been demonstrated to be easily converted to furanonaphthoquinones by oxidation and dehydrogenation.

Table 2. Oxidation and Dehydrogenation of 6 to Furanonaphthoquinones 11



compounds	products/yields (%)	
6a	**10a**/88	**11a**/75
6b	**10b**/46	**11b**/62
6c	**10c**/92	**11c**/77
6d	**10d**/92	**11d**/72
6e	**10e**/88	**11e**/68
6f	**10f**/92	**4**/65(80)[a]
6g	**10g**/81	**11g**/48
6h	**10h**/77	**11h**/38[b]
6i	**10i**/88	**11i**/86
6j	**10j**/93	**11j**/decomposed
6k	**10k**/84	**11k**/63
6n	**10n**/75	**11n**/52

[a]Value in parentheses was determined at a 1.85 mmol scale. [b]26% of **11k** was also obtained.

EXPERIMENTAL SECTION

General Procedure for the Preparation of Compound 5a (5a−e, 5n). To the solution of 2-bromobenzonitrile (10.0 g, 55.0 mmol) in THF (50 mL) were added $Pd(PPh_3)_4$ (0.50 g, 0.43 mmol), alkyne (66.0 mmol), CuI (0.521 g, 2.74 mmol), and Et_3N (6.65g, 65.93 mmol). The reaction mixture was stirred at room temperature for 8 h. The reaction mixture was quenched with saturated aqueous solutions of NH_4Cl and extracted with EtOAc. The combined organic extracts were dried over anhydrous $MgSO_{4(s)}$. After filtration and removal of solvent, the residue was purified by column chromatography to give compounds **5a**−**e** and **5n**.

*2-(5-Hydroxypent-1-ynyl)benzonitrile (**5a**):* Yield 9.04 g, 89%; a yellow oil; R_f = 0.48 (2:1 Hex/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.89 (quint, J = 6.5 Hz, 2H), 1.94 (br s, 1H), 2.62 (t, J = 6.5 Hz, 2H), 3.86 (t, J = 6.0 Hz, 2H), 7.34 (td, J = 8.0, 2.0 Hz, 1H), 7.41−7.52 (m, 2H), 7.60 (dd, J = 8.0, 0.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.0, 30.8, 61.1, 77.6, 97.0, 115.2, 117.9, 127.7, 127.9, 132.1, 132.3, 132.4; MS (70 eV) m/z (%) 185 (6) [M^+], 85 (85), 71 (100); HRMS (EI-MS) calcd for $C_{12}H_{11}ON$ 185.0841, found 185.0839.

*2-(5-Hydroxypent-1-ynyl)-3-methylbenzonitrile (**5b**):* Yield 2.38 g, 47%; a yellow oil; R_f = 0.43 (2:1 Hex/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.93−1.91 (m, 3H), 2.44 (s, 3H), 2.67 (t, J = 7.0 Hz, 2H), 3.88 (t, J = 6.0 Hz, 2H), 7.23 (t, J = 7.5 Hz, 1H), 7.40 (d, J = 7.5 Hz, 1H), 7.45 (d, J = 7.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.1, 20.8, 31.0, 61.2, 76.7, 100.9, 115.4, 118.3, 127.4, 127.4, 129.8, 138.4, 141.2; MS (70 eV) m/z (%) 199 (82) [M^+], 181 (88), 180 (100); HRMS (EI-MS) calcd for $C_{13}H_{13}ON$ 199.0997, found 199.0999.

*2-(5-Hydroxypent-1-ynyl)-4-methylbenzonitrile (**5c**):* Yield 4.51 g, 89%; a yellow oil; R_f = 0.44 (4:1 Hex/EtOAc); ^{1}H NMR (500 MHz,

DOI: 10.1021/acs.joc.5b02514
J. Org. Chem. 2016, 81, 3882−3889

$CDCl_3$) δ 1.91−1.87 (m, 3H), 2.37 (s, 3H), 2.62 (t, J = 7.0 Hz, 2H), 3.87 (br s, 2H), 7.15 (d, J = 5.0 Hz, 1H), 7.30 (s, 1H), 7.48 (d, J = 7.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.0, 21.6, 30.9, 61.2, 77.8, 96.3, 112.3, 118.2, 127.7, 128.7, 132.3, 132.7, 143.3; MS (70 eV) m/z (%) 199 (70) [M^+], 181 (93.63), 180 (100); HRMS (EI-MS) calcd for $C_{13}H_{13}ON$ 199.0997, found 199.0998.

*2-(5-Hydroxypent-1-ynyl)-5-methylbenzonitrile (**5d**):* Yield 4.56 g, 90%; a yellow oil; R_f = 0.47 (2:1 Hex/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.91−1.82 (m, 3H), 2.35 (s, 3H), 2.60 (t, J = 7.0 Hz, 2H), 3.87 (t, J = 6.0 Hz, 2H), 7.29 (dd, J = 8.0, 1.0 Hz, 1H), 7.37 (d, J = 8.0 Hz, 1H), 7.40 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.0, 21.0, 30.9, 61.2, 77.6, 95.9, 115.1, 118.0, 125.0, 132.0, 132.7, 133.3, 138.2; MS (70 eV) m/z (%) 199 (58) [M^+], 181 (94), 180 (100); HRMS (EI-MS) calcd for $C_{13}H_{13}ON$ 199.0997, found 199.0997.

*2-(5-Hydroxypent-1-ynyl)-5-methoxybenzonitrile (**5e**):* Yield 4.61g, 91%; a yellow oil; R_f = 0.40 (2:1 Hex/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.87 (quint, J = 6.5 Hz, 2H), 2.00 (br s, 1H), 2.58 (t, J = 7.0 Hz, 2H), 3.81 (s, 3H), 3.85 (t, J = 4.8 Hz, 2H),7.02 (dd, J = 9.0, 3.0 Hz, 1H), 7.07 (d, J = 2.5 Hz, 1H), 7.37 (d, J = 8.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.0, 31.0, 55.6, 61.2, 94.8, 116.1, 116.9, 117.7, 119.1, 120.1, 133.4, 158.6; MS (70 eV) m/z (%) 215 (90) [M^+], 197 (100), 182 (66); HRMS (EI-MS) calcd for $C_{13}H_{13}O_2N$ 215.0946, found 215.0949.

General Procedure for the Preparation of Compound 5f (5f−m). The solution of compound **12** (183 mg, 1.0 mmol) in THF (10 mL) under nitrogen was cooled to 0 °C. The Grignard reagent (1.2 mL, 1M) was then added dropwise to the solution for 0.5 h. The reaction mixture was warmed to room temperature and subsequently quenched with saturated $NH_4Cl_{(aq)}$ and extracted with CH_2Cl_2. The combined organic extracts were dried over anhydrous $MgSO_{4(s)}$. After filtration and removal of solvent, the residue was purified by column chromatography to give compounds **5f−m**.

*2-(5-Oxohex-1-ynyl)benzonitrile (**5f**):* Yield 179.13 mg, 90%; a yellow oil; R_f = 0.52 (2:1 Hex/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.22 (d, J = 6.5 Hz, 3H), 1.74 (q, J = 7.0 Hz, 2H), 2.41 (br s, 1H), 2.52−2.64 (m, 2H), 4.01−4.07 (m, 1H), 7.31 (td, J = 8.0, 1.0 Hz, 1H), 7.43−7.48 (m,2H) 7.56 (d, J = 7.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.0, 23.3, 37.1, 66.4, 77.3, 97.3, 115.0, 117.7, 127.6, 127.8, 132.0, 132.2, 132.3; MS (70 eV) m/z (%) 199 (45) [M^+], 180 (100), 154 (55); HRMS (EI-MS) calcd for $C_{13}H_{13}ON$ 199.0997, found 199.0997.

*2-(5-Oxoundec-1-ynyl)benzonitrile (**5g**):* Yield 231.34 mg, 86%; a yellow oil; R_f = 0.60 (2:1 Hex/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.86 (t, J = 7.0 Hz, 3H), 1.24−1.51 (m, 10H), 1.67−1.84 (m, 2H), 1.95 (br s, 1H), 2.57−2.68 (m, 2H), 3.83−3.88 (m, 1H), 7.33 (td, J = 7.5, 1.5 Hz, 1H), 7.45−7.50 (m, 2H), 7.58 (d, J = 7.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.0, 16.0, 22.5, 25.5, 29.3, 31.7, 35.5, 37.4, 70.4, 77.4, 97.5, 115.3, 117.8, 127.6, 127.9, 132.1, 132.2, 132.3; MS (70 eV) m/z (%) 269 (29) [M^+], 184 (100), 153 (73); HRMS (EI-MS) calcd for $C_{18}H_{23}ON$ 269.1780, found 269.1781.

*2-(5-Cyclohexyl-5-oxopent-1-ynyl)benzonitrile (**5h**):* Yield 240.3 mg, 90%; a yellow solid; R_f = 0.60 (2:1 Hex/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.99−1.27 (m, 5H), 1.31−1.38 (m, 1H), 1.63−1.86 (m, 7H), 1.93 (br s, 1H), 2.63 (t, J = 7.0 Hz, 2H), 3.59−3.63 (m, 1H), 7.33 (td, J = 7.5, 1.5 Hz, 1H), 7.45−7.50 (m, 2H), 7.59 (d, J = 7.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.3, 26.1, 26.2, 26.4, 27.8, 29.0, 32.4, 43.7, 77.3, 77.4, 97.6, 115.2, 117.8, 127.6, 127.9, 132.1, 132.2, 132.3; MS (70 eV) m/z (%) 267 (21) [M^+], 184 (100), 140 (58); HRMS (EI-MS) calcd for $C_{18}H_{21}ON$ 267.1623, found 267.1626.

*2-(6,6-Dimethyl-5-oxohept-1-ynyl)benzonitrile (**5i**):* Yield 183.27 mg, 76%; a colorless oil; R_f = 0.63 (2:1 Hex/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.94 (s, 9H), 1.56−1.64 (m, 1H), 1.79 (br s, 1H), 1.83−1.90 (m, 1H), 2.67 (t, J = 6.5 Hz, 2H), 3.52 (d, J = 10.5 Hz, 1H), 7.34 (td, J = 7.0, 2.0 Hz, 1H), 7.47−7.52 (m, 2H), 7.61 (d, J = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 17.0, 25.6, 29.9, 34.9, 77.6, 78.2, 97.7, 115.3, 117.9, 127.6, 128.0, 132.1, 132.3, 132.4; MS (70 eV) m/z (%) 241 (10) [M^+], 184 (100), 142 (43); HRMS (EI-MS) calcd for $C_{16}H_{19}ON$ 241.1467, found 241.1466.

*2-(5-Oxohept-6-en-1-ynyl)benzonitrile (**5j**):* Yield 122.38 mg, 58%; a brown oil; R_f = 0.62 (2:1 Hex/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.85 (q, J = 7.0 Hz, 2H), 2.35 (br s, 1H), 2.52−2.67 (m, 2H), 4.40 (q, J = 6.5 Hz, 1H), 5.14 (d, J = 10.5 Hz, 1H), 5.32 (d, J = 17.0 Hz, 1H), 5.85−5.92 (m, 1H), 7.33 (td, J = 7.5, 1.5 Hz, 1H), 7.45−7.50 (m, 2H), 7.58 (d, J = 7.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.7, 35.1, 71.4, 77.5, 97.0, 115.1, 115.1, 117.7, 127.6, 127.8, 132.1, 132.3, 132.3, 140.3; MS (70 eV) m/z (%) 211 (8) [M^+], 154 (100), 140 (73); HRMS (EI-MS) calcd for $C_{14}H_{13}ON$ 211.0997, found 211.0994.

*2-(5-Oxo-5-phenylpent-1-ynyl)benzonitrile (**5k**):* Yield 229.68 mg, 88%; a yellow oil; R_f = 0.58 (2:1 Hex/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.97−2.13 (m, 2H), 2.48−2.72 (m, 3H), 5.01 (t, J = 5.0 Hz, 1H), 7.27 (t, J = 7.5 Hz, 1H), 7.33−7.37 (m, 3H), 7.43−7.41 (m, 2H), 7.48−7.52 (m, 2H), 7.60 (d, J = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.2, 37.2, 72.6, 77.7, 97.0, 115.2, 117.8, 125.8, 125.8, 127.5, 127.6, 127.8, 128.4, 128.4, 132.1, 132.3, 132.4, 144.1; MS (70 eV) m/z (%) 261 (33) [M^+], 107 (100), 79 (90); HRMS (EI-MS) calcd for $C_{18}H_{15}ON$ 261.1154, found 261.1152.

*2-(5-Hydroxy-5-(naphthalen-1-yl)pent-1-yn-1-yl)benzonitrile (**5l**):* Yield 202.0 mg, 65%; a yellow oil; R_f = 0.25 (4:1 Hex/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (d, J = 8.0 Hz, 1H), 7.87 (d, J = 8.0 Hz, 1H), 7.78 (d, J = 8.0 Hz, 1H), 7.72 (d, J = 8.0 Hz, 1H), 7.63 (d, J = 8.0 Hz, 1H), 7.53−7.47 (m, 3H), 7.49 (d, J = 8.0 Hz, 1H), 7.48 (d, J = 8.0 Hz, 1H), 7.39−7.35 (m, 1H), 5.80 (dd, J = 9.0, 4.0 Hz, 1H), 2.90−2.80 (m, 1H), 2.68−2.62 (m, 1H), 2.46 (br s, 1H), 2.32−2.26 (m, 1H), 2.21−2.14 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.8, 133.8, 132.4, 132.3, 132.2, 130.2, 128.8, 128.0, 127.8, 127.7, 126.1, 125.5, 125.4, 123.2, 122.9, 117.9, 115.2, 97.1, 77.9, 69.7, 36.4, 16.5; MS (ESI) m/z (%) 334 (100) [M + Na]$^+$; HRMS (ESI-TOF) calcd for $C_{22}H_{17}NONa$ [M + Na]$^+$ 334.1208, found 334.1206.

*2-(5-Hydroxy-5-(4-methoxyphenyl)pent-1-yn-1-yl)benzonitrile (**5m**):* Yield 221.0 mg, 76%; a yellow oil; R_f = 0.15 (4:1 Hex/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (d, J = 8.0 Hz, 1H), 7.51 (d, J = 8.0 Hz, 1H), 7.50 (t, J = 8.0 Hz, 1H), 7.36 (t, J = 8.0 Hz, 1H), 7.35 (d, J = 8.0, 2H), 6.89 (d, J = 8.0 Hz, 2H), 4.97 (dd, J = 8.0, 5.5 Hz, 1H), 3.80 (s, 3H), 2.70−2.64 (m, 1H), 2.54−2.47 (m, 1H), 2.20 (br s, 1H), 2.14−2.07 (m, 1H), 2.04−1.95 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.1, 136.2, 132.4, 132.3, 132.2, 127.9, 127.7, 117.9, 115.3, 113.9, 97.0, 77.8, 72.4, 55.2, 37.2, 16.3; MS (ESI) m/z (%) 314 [M + Na]$^+$; HRMS (ESI-TOF) calcd for $C_{19}H_{17}NO_2Na$ [M + Na]$^+$ 314.1157, found 314.1156.

*6-(5-Hydroxypent-1-yn-1-yl)benzo[d][1,3]dioxole-5-carbonitrile (**5n**):* Yield 4.30 g, 85%; a yellow solid; R_f = 0.41 (2:1 Hex/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.77 (br s, 1H), 1.87 (quint, J = 6.5 Hz, 2H), 2.59 (t, J = 7.0 Hz, 2H), 3.84 (t, J = 6.0 Hz, 2H), 6.06 (s, 2H), 6.87 (s, 1H), 6.96 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.9, 30.8, 61.1, 77.5, 95.4, 102.5, 108.5, 111.2, 111.8, 118.0, 123.7, 147.3, 151.1; MS (70 eV) m/z (%) 229 (8) [M^+], 88 (100), 73 (63), 70 (96), 61 (98); HRMS (EI-MS) calcd for $C_{13}H_{11}O_3N$ 229.0739, found 229.0739.

General Procedure for the Preparation of 4-Amino-2,3-dihydronaphtho[2,3-*b*]furanes 6a−m. The solution of compounds **5a−m** (0.5 mmol) in DMSO (2.0 mL) containing NaOMe (0.75 mmol) was heated to 140 °C. The reaction mixture was stirred at that temperature for 0.5 h. The reaction mixture was cooled to room temperature, subsequently quenched with saturated $NH_4Cl_{(aq)}$, and extracted with EtOAc. The combined organic extracts were dried over anhydrous $MgSO_{4(s)}$. After filtration and removal of solvent, the residue was purified by silica gel column chromatography to give compounds **6a−m**. The physical and spectral data of **6a−m** are illustrated as follows.

*2,3-Dihydronaphtho[2,3-b]furan-4-amine (**6a**):* Yield 61.05 mg, 66%; a white solid; R_f = 0.60 (1:2:3 EA/DCM/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.16 (t, J = 8.0 Hz, 2H), 4.06 (br s, 2H), 4.66 (t, J = 8.5 Hz, 2H), 6.56 (s, 1H), 7.25 (t, J = 8.0 Hz, 1H), 7.35 (t, J = 7.0 Hz, 1H), 7.67−7.62 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.1, 71.3, 95.3, 110.1, 119.7, 120.2, 122.1, 125.8, 127.5, 135.6, 137.9, 159.1; mp 140−142 °C; MS (70 eV) m/z (%)185 (19) [M^+], 85 (86), 71 (100); HRMS (EI-MS) calcd for $C_{12}H_{11}ON$ 185.0841, found 185.0843.

*8-Methyl-2,3-dihydronaphtho[2,3-b]furan-4-amine (**6b**):* Yield 74.6 mg, 75%; a white solid; R_f = 0.54 (1:2:3 EA/DCM/Hex); ^{1}H

DOI: 10.1021/acs.joc.5b02514
J. Org. Chem. 2016, 81, 3882−3889

NMR (500 MHz, $CDCl_3$) δ 2.57 (s, 3H), 3.19 (t, J = 8.5 Hz, 2H), 4.09 (br s, 2H), 4.68 (t, J = 8.5 Hz, 2H), 6.79 (s, 1H), 7.17 (t, J = 8.5 Hz, 1H), 7.23 (d, J = 7.0 Hz, 1H), 7.56 (d, J = 8.0 Hz, 1H);^{13}C NMR (125 MHz, $CDCl_3$) δ 20.2, 27.1, 71.3, 92.1, 109.7, 118.4, 119.5, 121.6, 126.7, 133.6, 134.7, 138.4, 159.2; mp 202−204 °C; MS (70 eV) m/z (%) 199 (100) [M^+], 170 (20), 57 (16); HRMS (EI-MS) calcd for $C_{13}H_{13}ON$ 199.0997, found 199.0998.

7-Methyl-2,3-dihydronaphtho[2,3-b]furan-4-amine (**6c**): Yield 69.6 mg, 70%; a white solid; R_f = 0.55 (1:2:3 EA/DCM/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.44 (s, 3H), 3.14 (t, J = 8.0 Hz, 2H), 4.03 (br s, 2H), 4.64 (t, J = 8.5 Hz, 2H), 6.57 (s, 1H), 7.08 (dd, J = 8.5, 1.5 Hz, 1H), 7.40 (s, 1H), 7.55 (d, J = 8.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.4, 27.0, 71.2, 94.8, 109.2, 117.9, 120.0, 124.2, 126.7, 135.4, 135.9, 137.8, 159.2; mp 154−156 °C; MS (70 eV) m/z (%) 199 (100) [M^+], 170 (23), 156 (123); HRMS (EI-MS) calcd for $C_{13}H_{13}ON$ 199.0997, found 199.0994.

6-Methyl-2,3-dihydronaphtho[2,3-b]furan-4-amine (**6d**): Yield 76.6 mg, 77%; a white solid; R_f = 0.56 (1:2:3 EA/DCM/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.48 (s, 3H), 3.16 (t, J = 8.5 Hz, 2H), 4.04 (br s, 2H), 4.66 (t, J = 8.0 Hz, 2H), 6.63 (s, 1H), 7.20 (dd, J = 8.5, 1.5 Hz, 1H), 7.44 (s, 1H), 7.54 (d, J = 8.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.7, 27.1, 71.2, 95.1, 110.2, 119.5, 119.8, 127.4, 127.9, 131.5, 133.6, 137.3, 158.4; mp 112−114 °C; MS (70 eV) m/z (%) 199 (100) [M^+], 200 (39), 170 (52); HRMS (EI-MS) calcd for $C_{13}H_{13}ON$ 199.0997, found 199.0999.

6-Methoxy-2,3-dihydronaphtho[2,3-b]furan-4-amine (**6e**): Yield 77.4 mg, 72%; a white solid; R_f = 0.48 (1:2:3 EA/DCM/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.16 (t, J = 8.0 Hz, 2H), 3.91(s, 3H), 3.94 (br s, 2H), 4.65 (t, J = 8.5 Hz, 2H), 6.63 (s, 1H), 6.98 (d, J = 2.5 Hz, 1H), 7.07 (dd, J = 9.0, 2.5 Hz, 1H), 7.56 (d, J = 9.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.3, 55.4, 71.1, 95.4, 100.4, 111.1, 117.5, 120.3, 128.9, 130.6, 136.7, 155.4, 157.5; mp 156−158 °C; MS (70 eV) m/z (%) 215 (24) [M^+], 70 (66), 61 (100); HRMS (EI-MS) calcd for $C_{13}H_{13}O_2N$ 215.0946, found 215.0948.

2-Methyl-2,3-dihydronaphtho[2,3-b]furan-4-amine (**6f**): Yield 66.65 mg, 67%; a white solid; R_f = 0.54 (1:2:3 EA/DCM/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.52 (d, J = 6.5 Hz, 3H), 2.76 (dd, J = 8.0, 7.0 Hz, 1H), 3.27 (dd, J = 15.0, 8.5 Hz, 1H), 5.03 (br s, 2H), 5.04−5.02 (m, 1H), 6.64 (s, 1H), 7.27−7.26 (m, 1H), 7.36−7.34 (m, 1H), 7.67−7.63 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.0, 34.4, 79.7, 95.3, 110.4, 119.7, 120.2, 122.0, 125.7, 127.5, 135.6, 137.8, 158.7; MS (70 eV) m/z (%) 199 (100) [M^+], 184 (48), 156 (48); HRMS (EI-MS) calcd for $C_{13}H_{13}ON$ 199.0997, found 199.0996.

2-Hexyl-2,3-dihydronaphtho[2,3-b]furan-4-amine (**6g**): Yield 87.4 mg, 65%; a white solid; R_f = 0.56 (1:2:3 EA/DCM/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.91 (t, J = 7.0 Hz, 3H), 0.92−1.56 (m, 9H), 1.69−1.76 (m,1H), 1.85−1.92 (m, 1H), 2.80 (dd, J = 15.0, 7.0 Hz, 1H), 3.23 (dd, J = 15.0, 8.5 Hz, 1H), 4.87 (quint, J = 7.5 Hz, 1H), 6.63 (s, 1H), 7.25 (t, J = 8.5 Hz, 1H), 7.35 (t, J = 8.0 Hz, 1H), 7.65 (dd, J = 13.0, 8.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.1, 22.6, 25.4, 29.2, 31.8, 32.8, 36.3, 83.7, 95.2, 110.4, 119.6, 120.1, 121.9, 125.7, 127.5, 135.6, 137.7, 158.8; mp 56−58 °C; MS (70 eV) m/z (%) 269 (100) [M^+], 172 (55), 57 (59); HRMS (EI-MS) calcd for $C_{18}H_{23}ON$ 269.1780, found 269.1781.

2-Cyclohexyl-2,3-dihydronaphtho[2,3-b]furan-4-amine (**6h**): Yield 100.1 mg, 75%; a white solid; R_f = 0.58 (1:2:3 EA/DCM/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.08−1.34 (m,5H), 1.65−1.81 (m, 5H), 2.01 (d, J = 13.0 Hz, 1H), 2.89 (dd, J = 15.0, 7.5 Hz, 1H), 3.12 (dd, J = 15.0, 9.0 Hz, 1H), 4.02 (br s, 2H), 4.60 (q, J = 7.5 Hz, 1H), 6.63 (s, 1H), 7.24 (td, J = 7.0, 1.0 Hz, 1 H), 7.35 (td, J = 7.5, 0.5 Hz, 1H), 7.65 (t, J = 8.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 25.7, 25.9, 26.4, 28.3, 28.6, 30.3, 43.3, 87.7, 94.9, 110.5, 119.5, 120.1, 121.8, 125.6, 127.4, 135.6, 137.6, 159.0; mp 56−58 °C; MS (70 eV) m/z (%) 267 (49) [M^+], 172 (100), 57 (54); HRMS (EI-MS) calcd for $C_{18}H_{21}ON$ 267.1623, found 267.1622.

2-tert-Butyl-2,3-dihydronaphtho[2,3-b]furan-4-amine (**6i**): Yield 77.1 mg, 64%; a white solid; R_f = 0.58 (1:2:3 EA/DCM/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.02 (s, 9H), 2.95 (dd, J = 15.0, 8.0 Hz, 1H), 3.05 (dd, J = 15.0, 9.0 Hz, 1H), 4.04 (br s, 2H), 4.58 (t, J = 8.0 Hz, 1H), 6.65 (s, 1H), 7.24 (td, J = 8.0, 1.0 Hz, 1 H), 7.35 (t, J = 7.5 Hz, 1H), 7.65 (t, J = 10.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ25.1, 28.2, 34.6, 91.1, 94.7, 110.7, 119.5, 120.1, 121.8, 125.7, 127.5, 135.6, 137.5, 159.4; mp 114−116 °C; MS (70 eV) m/z (%) 241 (100) [M^+], 172 (92), 143 (39); HRMS (EI-MS) calcd for $C_{16}H_{19}ON$ 241.1467, found 241.1469.

2-Vinyl-2,3-dihydronaphtho[2,3-b]furan-4-amine (**6j**): Yield 50.6 mg, 48%; a white solid; R_f = 0.56 (1:2:3 EA/DCM/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.93(dd, J = 15.0, 7.0 Hz, 1H), 3.33 (dd, J = 15.0, 9.0 Hz, 1H), 4.04 (br s, 2H), 5.25−5.31(m, 2H), 5.43 (dt, J = 17.5, 1.0 Hz, 1H), 6.03−6.10 (m, 1H), 6.68 (s, 2H), 7.26 (td, J = 6.5, 1.0 Hz, 1H), 7.36 (td, J = 8.0, 1.0 Hz, 1H), 7.65 (t, J = 7.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 33.2, 83.6, 95.3, 109.7, 116.9, 119.7, 120.2, 122.1, 125.8, 127.6, 135.6, 137.3, 137.9, 158.5; mp 102−104 °C; MS (70 eV) m/z (%) 211 (100) [M^+], 196 (100), 165 (23); HRMS (EI-MS) calcd for $C_{14}H_{13}ON$ 211.0997, found 211.1000.

2-Phenyl-2,3-dihydronaphtho[2,3-b]furan-4-amine (**6k**): Yield 67.8 mg, 52%; a white solid; R_f = 0.50 (1:2:3 EA/DCM/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.13 (dd, J = 15.0, 7.0 Hz, 1H), 3.60 (dd, J = 15.0, 9.0 Hz, 1H), 4.05 (br s, 2H), 5.86 (t, J = 7.0 Hz, 1H), 6.77 (s, 1H), 7.27−7.44 (m, 7H), 7.69 (dd, J = 8.0, 5.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 35.8, 84.2, 95.3, 109.6, 119.8, 120.2, 122.1, 125.7, 125.9, 127.6, 128.1, 128.7, 135.7, 137.9, 142.1, 158.8; mp 116−118 °C; MS (70 eV) m/z (%) 261 (68) [M^+], 61 (90), 57 (100); HRMS (EI-MS) calcd for $C_{18}H_{15}ON$ 261.1154, found 261.1154.

2-(Naphthalen-1-yl)-2,3-dihydronaphtho[2,3-b]furan-4-amine (**6l**): Yield 70.0 mg, 45%; a brown solid; R_f = 0.60 (3:1 Hex/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, J = 8.0 Hz, 1H), 7.90 (d, J = 8.0 Hz, 1H), 7.80 (d, J = 8.0 Hz, 1H), 7.71 (d, J = 8.0 Hz, 1H), 7.67 (d, J = 8.0 Hz. 1H), 7.65 (d, J = 8.0 Hz, 1H), 7.55−7.50 (m, 2H), 7.43 (d, J = 8.0 Hz, 1H), 7.39 (d, J = 8.0 Hz, 1H), 7.27 (d, J = 8.0 Hz, 1H), 6.86 (s, 1H), 6.53 (dd, J = 9.5, 7.0 Hz, 1H), 4.03 (br s, 2H), 3.80 (dd, J = 15.0, 9.5 Hz, 1H), 3.18 (dd, J = 15.0, 7.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.9, 138.1, 137.5, 135.8, 133.9, 129.7, 129.1, 128.3, 127.6, 126.3, 125.9, 125.7, 125.5, 123.1, 122.7, 122.2, 120.2, 119.9, 109.5, 95.5, 82.1, 35.6; mp 161−162 °C; MS (ESI) m/z (%) 312 [M + H]$^+$; HRMS (ESI-TOF) calcd for $C_{22}H_{18}NO$ [M + H]$^+$ 312.1388, found 312.1386.

2-(4-Methoxyphenyl)-2,3-dihydronaphtho[2,3-b]furan-4-amine (**6m**): Yield 66.0 mg, 45%; a yellow oil; R_f = 0.50 (2:1 Hex/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (d, J = 7.5 Hz, 1H), 7.67 (d, J = 7.5 Hz, 1H), 7.38 (t, J = 7.5 Hz, 1H), 7.36 (d, J = 9.0 Hz, 2H), 7.28 (t, J = 7.5 Hz, 1H), 6.91 (d, J = 9.0 Hz, 2H), 6.73 (s, 1H), 5.81 (dd, J = 9.0, 7.5 Hz, 1H), 4.10 (br s, 2H), 3.81 (s, 3H), 3.56 (dd, J = 15.0, 9.0 Hz, 1H), 3.14 (dd, J = 15.0, 7.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.5, 158.8, 137.8, 135.7, 134.0, 127.6, 127.2, 125.9, 122.1, 120.2, 119.8, 114.0, 109.9, 95.3, 84.1, 55.3, 35.7; MS (ESI) m/z (%) 292 [M + H]$^+$; HRMS (ESI-TOF) calcd for $C_{19}H_{18}NO_2$ [M + H]$^+$ 292.1337, found 292.1338.

Furo[2′,3′:6,7]naphtho[2,3-d][1,3]dioxol-9-amine (**6n**): Yield 66.4 mg, 58%; a colorless solid; R_f = 0.48 (1:2:3 EA/DCM/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.15 (t, J = 8.0 Hz, 2H), 3.86 (br s, 2H), 4.64 (t, J = 8.0 Hz, 2H), 5.99 (s, 2H), 6.55 (s, 1H), 6.96 (s, 1H), 7.1 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.2, 71.3, 95.8, 97.6, 100.9, 104.1, 109.3, 115.1, 132.4, 137.3, 145.2, 147.5, 158.3; mp 214−216 °C; MS (70 eV) m/z (%) 229 (34) [M^+], 61 (100), 57 (53); HRMS (EI-MS) calcd for $C_{13}H_{11}O_3N$ 229.0739, found 229.0741.

(Z)-2-Benzylidenetetrahydrofuran (**7a**): Yield 70.0 mg, 64%; a colorless oil; R_f = 0.80 (2:1 Hex/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, J = 8.0 Hz, 1H), 7.54 (d, J = 8.0 Hz, 1H), 7.47 (t, J = 8.0 Hz, 1H), 7.10 (t, J = 8.0 Hz, 1H), 5.68 (s, 1H), 4.39 (t, J = 7.2 Hz, 2H), 2.82 (t, J = 7.2 Hz, 2H), 2.08 (quint, J = 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.9, 140.4, 132.5, 132.4, 127.6, 124.3, 118.9, 108.6, 93.1, 73.0, 31.6, 24.0; MS (ESI) m/z (%) 208 [M + Na]$^+$, 186 [M + H]$^+$; HRMS (ESI-TOF) calcd for $C_{12}H_{11}NONa$ [M + Na]$^+$ 208.0738, found 208.0736.

(E)-2-Benzylidenetetrahydrofuran (**8a**): Yield 13.0 mg, 51%; a colorless oil; R_f = 0.78 (2:1 Hex/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, J = 8.0 Hz, 1H), 7.47 (t, J = 8.0 Hz, 1H), 7.33 (d, J = 8.0 Hz, 1H), 7.14 (t, J = 8.0 Hz, 1H), 6.23 (s, 1H), 4.31 (t, J = 7.2 Hz, 2H), 2.82 (t, J = 7.2 Hz, 2H), 2.14 (quint, J = 7.2 Hz, 2H); ^{13}C

DOI: 10.1021/acs.joc.5b02514
J. Org. Chem. 2016, 81, 3882−3889

NMR (100 MHz, $CDCl_3$) δ 163.2, 141.6, 133.0, 132.2, 126.5, 124.6, 118.5, 110.6, 95.9, 70.2, 28.9, 25.0; MS (ESI) m/z (%) 208 $[M + Na]^+$, 186 $[M + H]^+$; HRMS (ESI-TOF) calcd for $C_{12}H_{11}NONa$ $[M + Na]^+$ 208.0738, found 208.0737.

*4-Amino-3-vinylnaphthalen-2-ol (**9a**):* Yield 41.0 mg, 43%; a yellow oil; R_f = 0.60 (2:1 Hex/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (s, 1H), 7.95 (d, J = 8.0 Hz, 1H), 7.49 (d, J = 8.0 Hz, 1H), 7.29 (t, J = 8.0 Hz, 1H), 7.17 (t, J = 8.0 Hz, 1H), 6.96 (dd, J = 18.4, 12.0 Hz, 1H), 6.63 (s, 1H), 5.76 (dd, J = 18.4, 2.0 Hz, 1H), 5.55 (dd, J = 12.0, 2.0 Hz, 1H), 5.30 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.7, 143.9, 136.3, 132.5, 127.7, 127.6, 123.6, 123.0, 120.6, 118.8, 110.3, 100.5; MS (ESI) m/z (%) 186 $[M + H]^+$; HRMS (ESI-TOF) calcd for $C_{12}H_{12}NO$ $[M + H]^+$ 186.0919, found 186.0917.

General Procedure for the Preparation of Dihydrofuranonaphthoquinones 10a−k and 10n. To the stirred solution of Fermy's salt (402 mg, 1.5 mmol) in H_2O (2 mL) containing KH_2PO_4 (204 mg, 1.5 mmol) was added a solution of compound **6a−k** or **6n** (0.5 mmol) in acetone (1 mL) at room temperature. The reaction mixture was stirred at room temperature for 2 h. Subsequently, the saturated $NaCl_{(aq)}$ was added, and the mixture was extracted with CH_2Cl_2. The combined organic extracts were dried over anhydrous $MgSO_{4(s)}$. After filtration and removal of solvent, the residue was purified by silica gel column chromatography to give compounds **10a−k** and **10n**. The physical and spectral data of **10a−k** and **10n** are illustrated as follows.

*2,3-Dihydronaphtho[2,3-b]furan-4,9-dione (**10a**):* Yield 88.0 mg, 88%; a yellow solid; R_f = 0.62 (1:2:3 EA/DCM/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.22 (t, J = 10.0 Hz, 2H), 4.80 (t, J = 10 Hz, 2H), 7.66−7.14 (m, 2H), 8.07 (dd, J = 7.5, 1.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.3, 73.2, 124.4, 126.0, 126.2, 131.4, 133.0, 133.0, 134.1, 160.7, 177.7, 182.1; mp 200−202 °C; MS (70 eV) m/z (%) 200 (100) $[M^+]$, 172 (39), 104 (47); HRMS (EI-MS) calcd for $C_{12}H_8O_3$ 200.0473, found 200.0475.

*8-Methyl-2,3-dihydronaphtho[2,3-b]furan-4,9-dione (**10b**):* Yield 49.22 mg, 46%; a yellow solid; R_f = 0.62 (1:2:3 EA/DCM/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.74 (s, 3H), 3.21 (t, J = 9.5 Hz, 2H), 4.78 (t, J = 9.5 Hz, 2H), 7.45 (dd, J = 7.5, 0.5 Hz, 1H), 7.56 (t, J = 7.5 Hz, 1H), 8.01 (dd, J = 8.0, 1.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.8, 27.2, 73.2, 122.6, 125.0, 128.9, 133.2, 134.7, 137.17, 141.8, 161.5, 179.6, 182.2; mp 168−170 °C; MS (70 eV) m/z (%) 214 (52) $[M^+]$, 61 (83), 57 (100); HRMS (EI-MS) calcd for $C_{13}H_{10}O_3$ 214.0630, found 214.0633.

*7-Methyl-2,3-dihydronaphtho[2,3-b]furan-4,9-dione (**10c**):* Yield 98.4 mg, 92%; a yellow solid; R_f = 0.64 (1:2:3 EA/DCM/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.47 (s, 3H), 3.20 (t, J = 10.0 Hz, 2H), 4.79 (t, J = 9.5 Hz, 2H), 7.45 (d, J = 8.0 Hz,1H), 7.85 (s, 1H), 7.94 (d, J = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.6, 27.3, 73.2, 124.3, 126.2, 126.8, 130.7, 131.4, 134.7, 144.0, 160.6, 178.0, 182.2; mp 196−198 °C; MS (70 eV) m/z (%) 214 (100) $[M^+]$, 186 (64), 118 (46); HRMS (EI-MS) calcd for $C_{13}H_{10}O_3$ 214.0630, found 214.0633.

*6-Methyl-2,3-dihydronaphtho[2,3-b]furan-4,9-dione (**10d**):* Yield 98.4 mg, 92%; a yellow solid; R_f = 0.60 (1:2:3 EA/DCM/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.48 (s, 3H), 3.20 (t, J = 10.0 Hz, 2H), 4.79 (t, J = 10.0 Hz, 2H), 7.46 (d, J = 8.0 Hz, 1H), 7.86 (s, 1H), 7.95 (d, J = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.9, 27.3, 73.3, 124.1, 126.5, 126.6, 129.2, 133.0, 133.5, 145.5, 160.9, 177.7, 182.5; mp 182−184 °C; MS (70 eV) m/z (%) 214 (100) $[M^+]$, 186 (65), 57 (70); HRMS (EI-MS) calcd for $C_{13}H_{10}O_3$ 214.0630, found 214.0633.

*6-Methoxy-2,3-dihydronaphtho[2,3-b]furan-4,9-dione (**10e**):* Yield 101.2 mg, 88%; a yellow solid; R_f = 0.55 (1:2:3 EA/DCM/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.20 (t, J = 10.0 Hz, 2H), 3.94 (s, 3H), 4.79 (t, J = 10.0 Hz, 2H), 7.10 (dd, J = 8.5, 3.5 Hz, 1H), 7.53 (d, J = 2.0 Hz, 1H), 8.01 (d, J = 8.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.3, 55.9, 73.4, 110.6, 118.4, 123.8, 124.8, 128.8, 135.6, 161.3, 164.6, 176.9, 182.0; mp 182−184 °C; MS (70 eV) m/z (%) 230 (15) $[M^+]$, 71 (71), 57 (100); HRMS (EI-MS) calcd for $C_{13}H_{10}O_4$ 230.0579, found 230.0578.

*2-Methyl-2,3-dihydronaphtho[2,3-b]furan-4,9-dione (**10f**):* Yield 98.42 mg, 92%; a yellow solid; R_f = 0.60 (1:2:3 EA/DCM/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.56 (d, J = 6.0 Hz, 3H), 2.80 (dd, J = 17.0, 9.0 Hz, 1H), 3.33 (dd, J = 17.0, 10.0 Hz, 1H), 5.15−5.22 (m, 1H), 7.65−7.72 (m, 2H), 8.06 (dd, J = 6.0, 4.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.9, 34.3, 83.1, 123.8, 126.0, 126.3, 131.5, 132.9, 133.1, 134.1, 159.8, 178.0, 182.4; MS(70 eV) m/z (%) 214 (100) $[M^+]$, 186 (56), 158 (42); HRMS (EI-MS) calcd for $C_{13}H_{10}O_3$ 214.0630, found 214.0632.

*2-Hexyl-2,3-dihydronaphtho[2,3-b]furan-4,9-dione (**10g**):* Yield 115.0 mg, 81%; a yellow solid; R_f = 0.60 (1:2:3 EA/DCM/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.87 (t, J = 6.5 Hz, 3H), 1.23−1.53 (m, 8H), 1.69−1.76 (m, 1H), 1.86−1.93 (m, 1H), 2.83 (dd, J = 17.0, 8.5 Hz, 1H), 3.26 (dd, J = 17.0, 10.0 Hz, 1H), 4.99−5.06 (m, 1H), 7.62−7.70 (m, 2H), 8.03 (td, J = 7.0, 1.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.0, 22.5, 24.7, 28.9, 31.6, 32.5, 35.9, 86.8, 123.9, 125.9, 126.2, 131.5, 132.8, 133.0, 134.0, 160.0, 177.9, 182.3; mp 84−86 °C; MS (70 eV) m/z (%) 284 (36) $[M^+]$, 71 (89), 57 (100); HRMS (EI-MS) calcd for $C_{18}H_{20}O_3$ 284.1412, found 284.1410.

*2-Cyclohexyl-2,3-dihydronaphtho[2,3-b]furan-4,9-dione (**10h**):* Yield 108.5 mg, 77%; a yellow solid; R_f = 0.60 (1:2:3 EA/DCM/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.07−1.31 (m, 5H), 1.70−1.81 (m, 5H), 1.96 (d, J = 13.0 Hz, 1H), 2.96 (dd, J = 17.0, 8.5 Hz, 1H), 3.17 (dd, J = 17.5, 10.5 Hz, 1H), 4.78−4.83 (m, 1H), 7.65−7.72 (m, 2H), 8.07 (td, J = 7.5, 1.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 25.5, 25.7, 26.2, 27.6, 28.0, 29.7, 30.0, 42.7, 90.7, 124.1, 125.9, 126.3, 131.6, 132.9, 133.1, 134.1, 160.3, 177.9, 182.3; mp 54−56 °C; MS (70 eV) m/z (%) 282 (32) $[M^+]$, 71 (86), 57 (100); HRMS (EI-MS) calcd for $C_{18}H_{18}O_3$ 282.1256, found 282.1256.

*2-(tert-Butyl)-2,3-dihydronaphtho[2,3-b]furan-4,9-dione (**10i**):* Yield 112.6 mg, 88%; a yellow solid; R_f = 0.62 (1:2:3 EA/DCM/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.01 (s, 3H), 2.99 (dd, J = 17.5, 9.0 Hz,1H), 3.10 (dd, J = 17.5, 11.0 Hz, 1H), 4.74 (t, J = 9.5 Hz, 1H), 7.65−7.72 (m, 2H), 8.07 (td, J = 7.5, 1.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.7, 28.3, 34.7, 94.2, 124.4, 125.9, 126.3, 131.6, 132.9, 133.0, 134.1, 160.4, 177.8, 182.4; mp 116−118 °C; MS (70 eV) m/z (%) 256 (40) $[M^+]$, 70 (100), 57 (100); HRMS (EI-MS) calcd for $C_{16}H_{16}O_3$ 256.1099, found 256.1098.

*2-Vinyl-2,3-dihydronaphtho[2,3-b]furan-4,9-dione (**10j**):* Yield 105.1 mg, 93%; a yellow solid; R_f = 0.61 (1:2:3 EA/DCM/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.00 (dd, J = 17.0, 8.0 Hz, 1H), 3.39 (dd, J = 17.5, 11.0 Hz, 1H), 5.33 (d, J = 10.5 Hz, 1H), 5.42−5.48 (m, 2H), 5.99−6.06 (m, 1H), 7.65−7.73 (m, 2H), 8.06 (td, J = 7.5, 1.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 33.0, 86.1, 118.4, 123.8, 126.0, 126.3, 131.5, 133.0, 134.1, 135.1, 159.7, 177.7, 182.2; mp 102−104 °C; MS (70 eV) m/z (%) 226 (58) $[M^+]$, 198 (100), 104 (99); HRMS (EI-MS) calcd for $C_{14}H_{10}O_3$ 226.0630, found 226.0632.

*2-Phenyl-2,3-dihydronaphtho[2,3-b]furan-4,9-dione (**10k**):* Yield 115.9 mg, 84%; a yellow solid; R_f = 0.58 (1:2:3 EA/DCM/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.27 (dd, J = 17.5, 8.5 Hz, 1H), 3.67 (dd, J = 17.0, 11.0 Hz, 1H), 5.02 (dd, J = 11.0, 7.5 Hz, 1H), 7.35−7.41 (m, 5H), 7.68−7.75 (m, 2H), 8.10 (td, J = 8.5, 1.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 35.3, 86.8, 123.8, 126.0, 126.1, 126.4, 128. 9, 131.6, 133.0, 134.2, 139.5, 159.8, 177.7, 182.2; mp 102−104 °C; MS (70 eV) m/z (%) 276 (6) $[M^+]$, 70 (100), 61 (100); HRMS (EI-MS) calcd for $C_{18}H_{12}O_3$ 276.0786, found 276.0789.

*7,8-Dihydrofuro[2′,3′:6,7]naphtho[2,3-d][1,3]dioxole-5,9-dione (**10n**):* Yield 91.5 mg, 75%; a yellow solid; R_f = 0.52 (1:2:3 EA/DCM/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.18 (t, J = 10.0 Hz, 2H), 4.77 (t, J = 10.0 Hz, 2H), 6.13 (s, 2H), 7.46 (d, J = 6.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.3, 73.4, 102.7, 106.0, 106.1, 123.4, 127.9, 130.4, 151.5, 152.5, 160.7, 176.7, 181.2; mp 220−222 °C; MS (70 eV) m/z (%) 244 (13) $[M^+]$, 71 (86), 57 (100); HRMS (EI-MS) calcd for $C_{13}H_8O_5$ 244.0372, found 244.0373.

General Procedure for the Preparation of Furanonaphthoquinones 11a−e, 4, 11g−i, 11k, and 11n. The solution of **10a−i**, **10k**, and **10n** (0.1 mmol) in diphenylether (2 mL) containing Pd/C (20.0 mg) was placed in the high-pressure reactor, and the reaction mixture was heated to 260 °C and stirred for 8 h. After being cooled to room temperature, the reaction mixture was directly purified by silica gel column chromatography to give compounds **11a−e**, **4**, **11g−i**, **11k**, and **11n**. The physical and spectral data of **11a−e**, **4**, **11g−i**, **11k**, and **11n** are illustrated as follows.

DOI: 10.1021/acs.joc.5b02514
J. Org. Chem. 2016, 81, 3882−3889

*Naphtho[2,3-b]furan-4,9-dione (**11a**):* Yield 14.8 mg, 75%; a yellow solid; R_f = 0.64 (1:2:3 EA/DCM/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.01 (d, J = 2.0 Hz, 1H), 7.75−7.78 (m, 3H), 8.19−8.24 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 108.6, 126.9, 127.1, 130.5, 132.5, 133.2, 133.9, 134.0, 148.6, 152.7, 173.6, 180.5; mp 198−200 °C; MS (70 eV) m/z (%) 198 (100) [M^+], 170 (42), 114 (40); HRMS (EI-MS) calcd for $C_{12}H_6O_3$ 198.0317, found 198.0317.

*8-Methylnaphtho[2,3-b]furan-4,9-dione (**11b**):* Yield 13.1 mg, 62%; a yellow solid; R_f = 0.60 (1:2:3 EA/DCM/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.84 (s, 3H), 6.95 (d, J = 1.5 Hz, 1H), 7.53 (d, J = 7.5 Hz, 1H), 7.59 (t, J = 7.5 Hz, 1H), 7.72 (d, J = 1.5 Hz, 1H), 8.14 (d, J = 7.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 23.0, 108.1, 126.1, 128.7, 129.6, 133.0, 134.9, 138.3, 142.5, 148.1, 153.5, 176.0, 180.6; mp 230−232 °C; MS (70 eV) m/z (%) 212 (100) [M^+], 61 (72), 57 (94); HRMS (EI-MS) calcd for $C_{13}H_8O_3$ 212.0473, found 212.0473.

*7-Methylnaphtho[2,3-b]furan-4,9-dione (**11c**):* Yield 16.3 mg, 77%; a yellow solid; R_f = 0.61 (1:2:3 EA/DCM/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.51 (s, 3H), 6.99 (d, J = 1.5 Hz, 1H), 7.53 (dd, J = 8.0, 1.0 Hz, 1H), 7.76 (d, J = 1.5 Hz, 1H), 8.02 (d, J = 0.5 Hz, 1H), 8.08 (d, J = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.8, 108.6, 127.3, 127.5, 130.5, 131.0, 132.4, 134.4, 145.2, 148.5, 152.7, 173.9, 180.5; mp 184−186 °C; MS (70 eV) m/z (%) 212 (43) [M^+], 85 (79), 57 (100); HRMS (EI-MS) calcd for $C_{13}H_8O_3$ 212.0473, found 212.0473.

*6-Methylnaphtho[2,3-b]furan-4,9-dione (**11d**):* Yield 15.2 mg, 72%; a yellow solid; R_f = 0.60 (1:2:3 EA/DCM/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.51 (s, 3H), 6.98 (d, J = 1.5 Hz, 1H), 7.55 (d, J = 8.0 Hz, 1H), 7.75 (d, J = 1.5 Hz, 1H), 7.98 (s, 1H), 8.10 (d, J = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.8, 108.6, 127.1, 127.6, 130.2, 130.3, 133.2, 134.5, 145.1, 148.4, 152.9, 173.6, 180.9; mp 174−176 °C; MS (70 eV) m/z (%) 212 (100) [M^+], 184 (26), 128 (35); HRMS (EI-MS) calcd for $C_{13}H_8O_3$ 212.0473, found 212.0470.

*6-Methoxynaphtho[2,3-b]furan-4,9-dione (**11e**):* Yield 16.4 mg, 68%; a yellow solid; R_f = 0.60 (1:2:3 EA/DCM/Hex);^{1}H NMR (500 MHz, $CDCl_3$) δ 6.16 (s, 2H), 6.95 (d, J = 2.0 Hz, 1H), 7.85 (s, 1H), 7.60 (s,1H), 7.72 (d, J = 2.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 29.7, 102.8, 106.6, 106.8, 108.6, 129.3, 123.0, 130.3, 148.2, 152.3, 152.6, 172.7, 179.5; mp 184−186 °C; MS (70 eV) m/z (%) 242 (25) [M^+], 70 (65), 61 (100); HRMS (EI-MS) calcd for $C_{13}H_6O_5$ 242.0215, found 242.0212.

*FNQ3 (**4**):* Yield 13.64 mg, 65%; a yellow solid; R_f = 0.65 (1:2:3 EA/DCM/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.52 (s, 3H), 6.61 (d, J = 0.5 Hz, 1H), 7.72−7.74 (m, 2H), 8.15−8.21 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.1, 29.7, 105.0, 126.8, 126.9, 131.9, 132.5, 133.1, 133.6, 133.8, 151.7, 160.5, 173.1, 180.9; MS (70 eV) m/z (%) 212 (100) [M^+], 184 (37), 183 (81); HRMS (EI-MS) calcd for $C_{13}H_8O_3$ 212.0473, found 212.0470.

*2-Hexylnaphtho[2,3-b]furan-4,9-dione (**11g**):* Yield 13.5 mg, 48%; a yellow solid; R_f = 0.65 (1:2:3 EA/DCM/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.88−0.91 (m, 3H), 1.25−1.33 (m, 8H), 1.58−1.77 (m, 2H), 2.80 (t, J = 7.5 Hz, 2H), 7.70−7.75 (m, 2H), 8.15−8.21 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.0, 22.5, 27.4, 28.3, 28.7, 29.7, 31.4, 104.2, 126.8, 126.8, 131.8, 132.6, 133.1, 133.5, 133.8, 151.5, 164.9, 173.1, 181.0; mp 86−88 °C; MS (70 eV) m/z (%) 282 (27) [M^+], 61 (100), 57 (85); HRMS (EI-MS) calcd for $C_{18}H_{18}O_3$ 282.1256, found 282.1258.

*2-Cyclohexylnaphtho[2,3-b]furan-4,9-dione (**11h**):* Yield 10.6 mg, 38%; a yellow solid; R_f = 0.66 (1:2:3 EA/DCM/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.24−1.54 (m, 6H), 1.72−1.86 (m, 2H), 2.80 (dd, J = 13.0, 3.0 Hz, 2H), 2.78−2.84 (m, 1H), 7.69−7.75 (m, 2H), 8.14−8.21 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 25.6, 25.7., 31.0, 37.5, 102.4, 126.8, 126.8, 131.7, 132.6, 133.1, 133.5, 133.8, 151.3, 168.9, 173.2, 181.1; mp 106−108 °C; MS (70 eV) m/z (%) 280 (80) [M^+], 71(87), 57 (100); HRMS (EI-MS) calcd for $C_{18}H_{16}O_3$ 280.1099, found 280.1099.

*2-(tert-Butyl)naphtho[2,3-b]furan-4,9-dione (**11i**):* Yield 21.8 mg, 86%; a yellow solid; R_f = 0.66 (1:2:3 EA/DCM/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ1.40 (s, 9H), 7.69−7.75 (m, 2H), 8.14−8.21 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.7, 29.7, 33.5, 101.6, 126.8, 131.6, 132.7, 133.1, 133.5, 133.8, 151.5, 172.2, 173.2, 181.1; mp 54−56 °C; MS (70 eV) m/z (%) 254 (18) [M^+], 240 (18), 239 (100); HRMS (EI-MS) calcd for $C_{16}H_{14}O_3$ 254.0943, found 254.0943.

*2-Phenylnaphtho[2,3-b]furan-4,9-dione (**11k**):* Yield 17.2 mg, 63%; a yellow solid; R_f = 0.62 (1:2:3 EA/DCM/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 (s, 1H), 7.43−7.51 (m, 3H), 7.73−7.79 (m, 2H), 7.90 (d, J = 7.5 Hz, 2H), 8.19−8.26 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 102.9, 125.5, 126.9, 126.9, 128.3, 129.1, 130.3, 132.4, 132.8, 133.7, 133.6, 134.0, 151.6, 160.3, 173.0, 180.8; mp 224−226 °C; MS (70 eV) m/z (%) 274 (7) [M^+], 71 (93), 57 (100); HRMS (EI-MS) calcd for $C_{18}H_{10}O_3$ 274.0630, found 274.0627.

*Furo[2′,3′:6,7]naphtho[2,3-d][1,3]dioxole-5,9-dione (**11n**):* Yield 12.5 mg, 52%; a yellow solid; R_f = 0.61 (1:2:3 EA/DCM/Hex); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.16 (s, 2H), 6.95 (d, J = 2.0 Hz, 1H), 7.85 (s, 1H), 7.60 (s, 1H), 7.72 (d, J = 2.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 29.7, 102.8, 106.6, 106.8, 108.6, 129.3, 123.0, 130.3, 148.2, 152.3, 152.6, 172.7, 179.5; mp 184−186 °C; MS (70 eV) m/z (%) 242 (25) [M^+], 70 (65), 61 (100); HRMS (EI-MS) calcd for $C_{13}H_6O_5$ 242.0215, found 242.0212.

*2-(5-Oxopent-1-yn-1-yl)benzonitrile (**12**).* To the solution of oxalyl dichloride (5.14 g, 40.53 mmol) in CH_2Cl_2 (50 mL) at −78 °C was added DMSO (3.16 g, 40.53 mmol) dropwise for 0.5 h. Subsequently, compound **5a** (5.0 g, 27.02 mmol) was added into the reaction mixture and stirred for another 1.5 h. Et_3N (20.46 g, 202.65 mmol) was then injected slowly to the reaction mixture. After being warmed to room temperature, the reaction mixture was poured into saturated $NH_4Cl_{(aq)}$ and extracted with EtOAc. The combined organic extracts were dried over anhydrous $MgSO_{4(s)}$. After filtration and removal of solvent, the residue was purified by column chromatography to give compound **12**: Yield 3.95 g, 80%; a yellow oil; R_f = 0.41 (3:1 Hex/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.71−2.86 (m, 4H), 7.34−7.37 (m, 1H), 7.46−7.52 (m, 2H), 7.60 (d, J = 7.5 Hz, 1H), 9.85 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.7, 15.2, 32.8, 77.9, 95.2, 115.3, 117.6, 127.3, 127.9, 132.1, 132.3, 132.3, 132.4, 132.4, 176.1, 199.9; MS (70 eV) m/z (%) 183 (11) [M^+], 154 (100), 127 (85), 57 (72); HRMS (EI-MS) calcd for $C_{12}H_9ON$ 183.0684, found 183.0684.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02514.

Scheme for the preparation of compounds **5a**−**5n**; ^{1}H NMR and ^{13}C NMR spectra of all compounds (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: mijuwu@faculty.nsysu.edu.tw.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank the Ministry of Science and Technology of the Republic of China for financial support.

■ REFERENCES

(1) (a) Inoue, K.; Inouye, H.; Chen, C. C. *Phytochemistry* **1981**, *20*, 2271. (b) Rao, M. M.; Kingston, D. G. *J. Nat. Prod.* **1982**, *45*, 600. (c) Heltzel, C. E.; Gunatilaka, A. A. L.; Glass, T. E.; Kingston, D. G. *J. Nat. Prod.* **1993**, *56*, 1500. (d) Takegami, T.; Simamura, E.; Hirai, K. I.; Koyama, J. *Antiviral Res.* **1998**, *37*, 37. (e) Nagata, K.; Hirai, K. I.; Koyama, J.; Wada, Y.; Tamura, T. *Antimicrob. Agents Chemother.* **1998**, *42*, 700. (f) Wu, C.; Johnson, R. K.; Mattern, M. R.; Wong, J. C.; Kingston, D. G. *J. Nat. Prod.* **1999**, *62*, 963. (g) Hayashi, K.-i.; Chang, F. R.; Nakanishi, Y.; Bastow, K. F.; Cragg, G.; McPhail, A. T.; Nozaki, H.; Lee, K. H. *J. Nat. Prod.* **2004**, *67*, 990. (h) Simamura, E.; Hirai, K. I.; Shimada, H.; Koyama, J.; Niwa, Y.; Shimizu, S. *Cancer Biol. Ther.*

DOI: 10.1021/acs.joc.5b02514
J. Org. Chem. 2016, 81, 3882−3889

2006, *5*, 1523. (i) Inagaki, R.; Ninomiya, M.; Tanaka, K.; Watanabe, K.; Koketsu, M. *Chem. Pharm. Bull.* **2013**, *61*, 670.
(2) (a) Kobayashi, K.; Shimizu, H.; Sasaki, A.; Suginome, H. *J. Org. Chem.* **1991**, *56*, 3204. (b) Kobayashi, K.; Shimizu, H.; Sasaki, A.; Suginome, H. *J. Org. Chem.* **1993**, *58*, 4614. (c) Suginome, H.; Konishi, A.; Sakurai, H.; Minakawa, H.; Takeda, T.; Senboku, H. *Tetrahedron* **1995**, *51*, 1377. (d) Kobayashi, K.; Uneda, T.; Kawakita, M.; Morikawa, O.; Konishi, H. *Tetrahedron Lett.* **1997**, *38*, 837. (e) Ohta, Y.; Doe, M.; Morimoto, Y.; Kinoshita, T. *J. Heterocycl. Chem.* **2000**, *37*, 731. (f) Knight, D. K.; Nott, A. P. *J. Chem. Soc., Perkin Trans. 1* **1981**, 1125. (g) Ohta, Y.; Onoshima, M.; Tamura, M.; Tanaka, R.; Morimoto, Y.; Yoshihara, K.; Kinoshita, T. *J. Heterocycl. Chem.* **1998**, *35*, 461. (h) Wu, Z.-Z.; Jang, Y.-J.; Lee, C.-J.; Lee, Y.-T.; Lin, W. *Org. Biomol. Chem.* **2013**, *11*, 828.
(3) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, *16*, 4467.
(4) Tsai, C. W.; Yang, S. C.; Liu, Y. M.; Wu, M. J. *Tetrahedron* **2009**, *65*, 8367.
(5) The detailed scheme for preparation of compounds **5a**−**5n** is available in the Supporting Information.
(6) (a) Kristensen, J. L.; Vedso, P.; Begtrup, M. *J. Org. Chem.* **2003**, *68*, 4091. (b) Petersen, I. N.; Crestey, F.; Kristensen, J. L. *Chem. Commun.* **2012**, *48*, 9092.
(7) (a) Fernàndez, I.; Cossio, F. P.; Sierra, M. A. *Organometallics* **2007**, *26*, 3010. (b) Li, S.; Luo, Y.; Wu, J. *Org. Lett.* **2011**, *13*, 3190. (c) Lu, P.; Wang, Y. *Chem. Soc. Rev.* **2012**, *41*, 5687.
(8) Zimmer, H.; Lankin, D. C.; Horgan, S. W. *Chem. Rev.* **1971**, *71*, 229.
(9) Horning, E. C.; Reisner, D. B. *J. Am. Chem. Soc.* **1950**, *72*, 1514.

DOI: 10.1021/acs.joc.5b02514
J. Org. Chem. 2016, 81, 3882−3889