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Silver-Catalyzed One-Pot Synthesis of Arylnaphthalene Lactones

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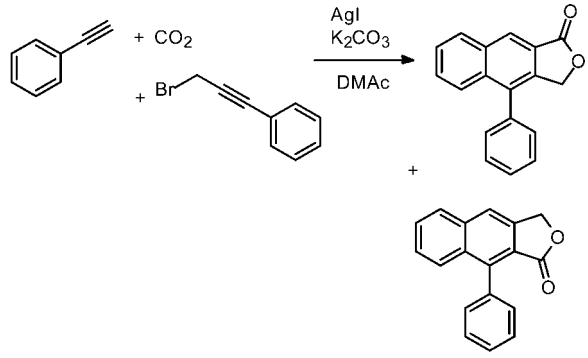
Received June 05, 2008



Arylnaphthalene lignan lactones are valuable natural products with promising anticancer and antiviral properties. In an effort to simplify their synthesis, we investigated a one-pot multicomponent coupling reaction between phenylacetylene, carbon dioxide, and 3-bromo-1-phenyl-1-propyne. After the corresponding 1,6-diyne was generated in situ, cyclization afforded the desired product. The level of regioselectivity was enhanced through the tuning of electronic properties. The use of cinnamyl bromide which led to the formation of a 1,6-enyne intermediate was also studied.

Arylnaphthalene lignan lactones are part of a large family of phytoestrogen natural products which has received widespread interest in the last decades due to their biological activities.[1] Specific examples include the known antiviral and antitumor agents daurinol and retrochinensin (Figure 1).[2,3] Several synthetic methodologies have been developed to access the naphthalene core; this includes cross-coupling reactions and cycloadditions of 1,6-diynes to generate the C-ring.[4] Most of those syntheses still, however, rely on a traditional multistep chemistry and are lacking in terms of atom economy and/or efficiency.[2,4] As an alternative approach, carbon dioxide has been recognized as a potential valuable C1 carbon source for the preparation of esters.[5] In an effort to utilize CO_2 and simplify the preparation of arylnaphthalene lignan lactones, we investigated a one-pot multicomponent coupling approach. Building on Inoue's work,[6] it was envisioned that the coupling between phenylacetylene, carbon dioxide, and 3-bromo-1-phenyl-1-propyne would generate the corresponding 1,6-diyne which could further cyclize to the naphthalene core through a [2 + 2 + 2] cycloaddition.[7]

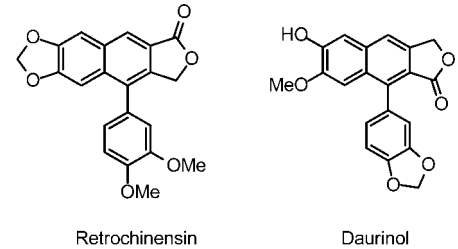


FIGURE 1. Structure of retrochinensin and daurinol.

Initially, CuI was chosen as the catalyst for the desired transformation, namely the coupling between phenylacetylene, carbon dioxide, and 3-bromo-1-phenyl-1-propyne. The major compound isolated from this reaction was, however, the coupling product between phenylacetylene and 3-bromo-1-phenyl-1-propyne. Carbon dioxide was not incorporated into the final product, even when the pressure was increased.[8]

Arylnaphthalene lactones were successfully prepared when the catalyst was switched to silver iodide. 4-phenylnaphtho[2,3-*c*]furan-1(3*H*)-one **2a** and 9-phenylnaphtho[2,3-*c*]furan-1(3*H*)-one **3a** were obtained in 41% and 25% yield, respectively (entries 3, Table 1). The ratio of regioisomers was slightly in favor of compound **2a**. The major byproduct of the reaction was identified as the corresponding symmetrical carbonate.[6] Silver complexes $AgSbF_6$ and AgOAc were also effective to catalyze this reaction (entries 7 and 8, Table 1). Unexpectedly gold(I) iodide and gold(I) chloride, which have demonstrated promising catalytic activities for the coupling of phenylacetylene, carbon dioxide, and alkyl halides,[9] failed to deliver the desired product.

Monitoring the silver-catalyzed reaction by ^{1}H NMR revealed that the coupling step was completed in less than 2 h while compound **1a** slowly cyclized over 6 h. To verify whether AgI had any effect on the cyclization, pure samples of the 1,6-diyne **1a** were heated in DMAc for 3 h. The results were the same in

(1) Westcott, N. D.; Muir, A. D. *Phytochem. Rev.* **2003**, *2*, 401. Suzuki, S.; Umezawa, *T. J. Wood Sci.* **2007**, *53*, 273. Clavel, T.; Dore, J.; Blaut, M. *Nutr. Res. Rev.* **2006**, *19*, 187.

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(3) Cow, C.; Leung, C.; Charlton, J. L *Chem. Can. J.* **2000**, *78*, 553. Gordaliza, M.; Garcia, P. A.; Miguel del Corral, J. M.; Castro, M. A.; Gomez-Zurita, M. A. *Toxicon* **2004**, *44*, 441.

(4) Klemm, L. H.; Gopinath, K. W.; HsuLee, D.; Kelly, F. W.; Trod, E.; McGuire, T. M. *Tetrahderon* **1966**, *22*, 1797. For recent reviews, see: Sellars, J. D.; Steel, P. G. *Eur. J. Org. Chem.* **2007**, 3815. Ward, R. S. *Tetrahedron* **1990**, *46*, 5029.

(5) Aresta, M.; Dibenedetto, A *Dalton Trans.* **2007**, 2975. Sakakura, T.; Choi, J.-C.; Yasuda, H. *Chem. Rev.* **2007**, *107*, 2365. Omae, I. *Catal. Today* **2006**, *115*, 33.

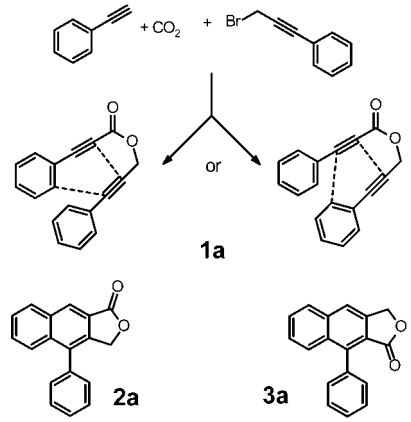
(6) Fukue, Y.; Oi, S.; Inoue, Y. *J. Chem. Soc., Chem. Commun.* **1994**, 2091.

(7) For reviews on [2 + 2 + 2] cycloaddition, see: Chopade, P. R.; Louie, J. *Adv. Synth. Catal.* **2006**, *348*, 2307. Kotha, S.; Brahmachary, E.; Lahiri, K. *Eur. J. Org. Chem.* **2005**, 4741. Clayden, J.; Moran, W. *J. Org. Biomol. Chem.* **2007**, *5*, 1028. For a recent review on dehydro-Diels−Alder reaction: Wessig, P.; Müller, G. *Chem. Rev.* **2008**, *108*, 2051.

(8) The coupling reaction (entry 1, Table 1) was also run in a pressure vessel under a higher carbon dioxide pressure (ca 10 atm); however, the results remain the same.

10.1021/jo801213m CCC: $40.75
Published on Web 08/06/2008

TABLE 1. Preparation of Arylnaphthalene Lactones 2a and 3a



				product[b]		
entry[a]	catalyst	time (h)	*T* (°C)	**1a**	**2a**	**3a**
1	CuI	8	100			
2	CuBr	8	100	<1	<1	<1
3	AgI	8	100		41.2	25.8
4	AgI	4	100	28.2	27.9	14.4
5	AgI	48	rt	10.2		
6	AgBr	8	100		23.8	20.5
7	AgOAc	8	100		33.2	19.8
8	$AgSbF_6$	8	100		21.4	18.2
9	AuI	8	100			
10	AuCl	8	100			

[a] Reaction conditions: The catalyst (5−10 mol %) was placed under 1 atm of CO_2 gas. DMAc (0.6 mL), K_2CO_3 (1.16 mmol), phenylacetylene (0.5 mmol), and 3-bromo-1-phenyl-1-propyne (0.5 mmol) were successively added. [b] The percentage given refers to the isolated yield.

the absence or presence of a catalyst (e.g., AgI, AuI). As expected, the cyclization is mainly a thermal process. Running the reaction at rt over 2 days resulted in the formation of a small amount of **1a**.

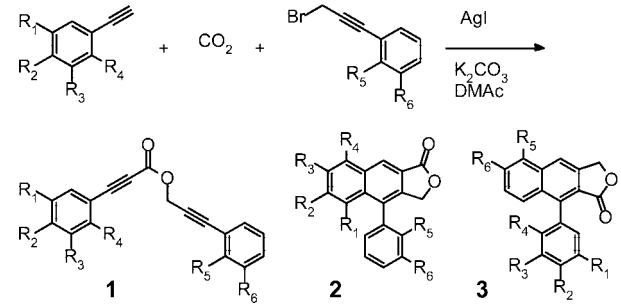
Although the regioisomers **2a** and **3a** could be separated by chromatography, further investigations were conducted to determine whether one of the products could be generated preferentially, if not exclusively.

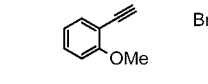
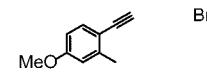
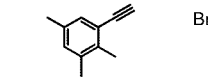
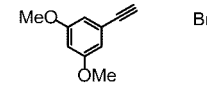
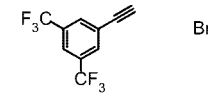
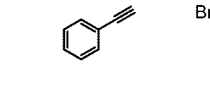
In an effort to expand the scope of the reaction and address the problem of regioselectivity, several substituted phenylacetylenes were tested under the previous conditions. Results are presented in Table 2.

As expected, electron-donating groups placed on the aromatic ring of the phenylacetylene tend to favor the formation of compounds **2** while electron-withdrawing groups favored the formation of isomers **3**. For instance, **3f** was isolated as major product (entry 5); only a trace of its isomer **2f** was observed by ^{1}HNMR (characteristic peaks include 5.16 ppm and 8.48 ppm). In the opposite situation, product **2e** was predominant over **3e** with a ratio close to 4:1.

Finally, the reactivity of the corresponding 1,6-enyne intermediate **4a** was studied. When 3-bromo-1-phenyl-1-propyne was replaced by the commercially available *trans*-cinnamyl bromide, a small quantity of 3a,4-dihydro-9-phenylnaphtho[2,3-*c*]furan-1(3*H*)-one **5a** was generated (Scheme 1). Although the reaction was successful, the major product remained the symmetrical carbonate resulting from the coupling of cinnamyl bromide and potassium carbonate. The product was obtained using AgOAc as catalyst. Again, copper salts were ineffective and no product could be isolated. Compound **5a** very slowly aromatized to **3a** upon exposure to air.

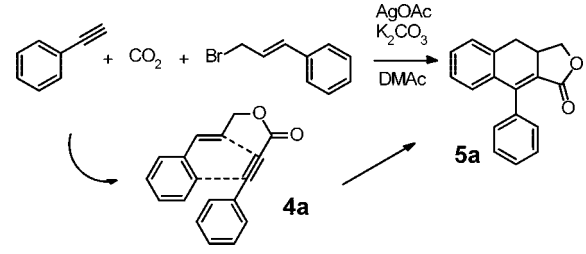
TABLE 2. Synthesis of Various Arylnaphthalene Lactones Using the Silver-Catalyzed One-Pot Multi-component Coupling Reaction



			Products[b]	
Entry[a]	Substrates	**1**	**2**	**3**
1		-	**2b** 27.6	**3b** 23.2
2		-	**2c** 20.1	**3c** 14.3
3		-	**2d** 33.4	**3d** 23.2
4		-	**2e** 40.6	**3e** 8.4
5		-	**2f** Trace	**3f** 38.8
6		-	**2g** 37.3	**3g** 21.9

[a] Reaction conditions: The catalyst (5−10 mol %) was placed under 1 atm of CO_2. DMAc (0.6 mL), K_2CO_3 (1.16 mmol), phenylacetylene (0.5 mmol), and 3-bromo-1-phenylpropyne (0.5 mmol) were successively added. The reaction mixture was heated at 100 °C for 8 h. [b] The percentage given below each compound refers to the isolated yield; carbonate byproduct, phenylacetylene dimer, and sometimes a significant amount of starting reagents were also isolated.

SCHEME 1. Preparation of Compound 5a



(9) When 1-bromo-2-pentyne was reacted with carbon dioxide and phenylacetylene in the presence of a catalytic amount of gold iodide, the corresponding coupling product **6a** was obtained in 43% yield. No other products were detected; in particular, no carbonate byproduct was generated. The remainder of the starting material was recovered at the end of the reaction. This constitutes a significant improvement in terms of reaction purity.

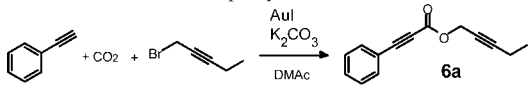


TABLE 3. Green Chemistry Metrics for the One-Pot Synthesis of Arylnaphthalene Lactone 2a

general and green chemistry metrics[11]	
% yield	41
no. of steps	1
no. of catalysts	1
no. of solvents	1
type of solvent	organic
E-factor	19.41
% atom economy	76.20
% effective mass yield	7.85
% carbon efficiency	23.06
% reaction mass efficiency	11.18

From a green chemistry perspective, the use of an alkyl halide constitutes the major shortcoming of the approach.[10] Switching to the corresponding alcohol (e.g., 3-phenyl-2-propyn-1-ol) is a more desirable alternative and is currently under investigation. The current strategy nevertheless remained an improvement as the *E*-factor is significantly reduced compared to the traditional multistep synthesis (Table 3).

In conclusion, we investigated the three-component coupling reaction between phenylacetylene, carbon dioxide, and 3-bromo-1-phenyl-1-propyne. Under the reaction conditions, the 1,6-diyne generated in situ undergoes a subsequent [2 + 2 + 2] cyclization affording the corresponding arylnaphthalene lactones. The regioselectivity was enhanced by tuning the electronic properties of the substrates.

Experimental Section

Representative Procedure for the Silver-Catalyzed One-Pot Synthesis of Arylnaphthalene Lactones 2a and 3a. In a round-bottom flask fitted with a condenser and a stir bar was introduced the catalyst AgI (23.4 mg, 0.1 mmol) under CO_2 atmosphere (1 atm). After addition of 1 mL of DMAc, potassium bicarbonate (160.1 mg, 1.16 mmol), phenylacetylene (0.11 mL, 1 mmol), and 3-bromo-2-phenyl-1-propyne (195 mg, 1 mmol), the mixture was placed in an oil bath at 100 °C. After 8 h, the reaction mixture was cooled and extracted with ethyl acetate to afford a 2:1 mixture of products **2a** and **3a**. The products were purified by column chromatography using 1:5 ethyl acetate/hexane.

3-Phenyl-2-propyn-1-ol phenylpropiolate (1a): ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.99 (s, 2H), 7.29 (m, 6H), 7.41 (m, 3H), 7.53 (d, 2H, J = 7.05 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 54.2, 80.0, 82.0, 87.3, 87.4, 119.3, 122.0, 127.5, 128.3, 128.6, 128.7, 128.9, 130.8, 132.0, 133.1, 153.3; HRMS calcd for $C_{18}H_{12}O_2$ $(M + H)^+$ 261.0910, found 261.09093.

4-Phenylnaphtho[2,3-*c*]furan-1(3*H*)-one (2a): ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.20 (s, 2H), 7.32 (d, 2H, J = 7.55 Hz), 7.49 (m, 5H), 7.74 (d, 1H, J = 7.55 Hz), 8.03 (d, 1H, J = 6.45 Hz), 8.46 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 69.5, 123.0, 125.9, 126.4, 126.7, 128.4, 129.0, 129.3, 130.1, 133.7, 134.1, 134.9, 135.8, 138.4, 171.2; HRMS calcd for $C_{18}H_{12}O_2$ $(M + H)^+$ 261.0910, found 261.09063.

9-Phenylnaphtho[2,3-*c*]furan-1(3*H*)-one (3a): ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.39 (s, 2H), 7.32 (m, 2H), 7.42 (t, 1H, J = 7.85, 8.35 Hz), 7.47 (m, 3H), 7.58 (t, 1H, J = 7.45 Hz), 7.74 (d, 1H, J = 8.80 Hz), 7.84 (s, 1H), 7.90 (d, 1H, J = 8.35 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 68.1, 120.2, 126.7, 128.0, 128.1, 128.3, 128.6, 130.0, 132.8, 134.4, 136.2, 140.1, 142.2; HRMS calcd for $C_{18}H_{12}O_2$ $(M + H)^+$ 261.0910, found 261.0907.

8-Methoxy-4-phenylnaphtho[2,3-*c*]furan-1(3*H*)-one (2b): ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.00 (s, 3H), 5.17 (s, 2H), 6.84 (d, 1H, J = 7.15 Hz), 7.28 (m, 3H), 7.44 (m, 4H), 8.90 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.8, 69.5, 104.5, 118.0, 121.4, 122.0, 126.4, 128.3, 128.9, 129.2, 129.3, 133.5, 135.9, 136.2, 139.3, 157.2, 171.5; HRMS calcd for $C_{19}H_{14}O_3$ $(M + H)^+$ 291.1016, found 291.1015.

9-(2-Methoxyphenyl)naphtho[2,3-*c*]furan-1(3*H*)-one (3b): ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.63 (s, 3H), 5.38 (s, 2H), 7.04 (m, 2H), 7.13 (d, 1H, J = 8.35 Hz), 7.42 (m, 4H), 7.55 (t, 1H, J = 7.3 Hz), 7.71 (d, 1H, J = 9.4 Hz), 7.82 (s, 1H), 7.88 (d, 1H, J = 8.35 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 56.2, 68.7, 111.5, 120.6, 120.8, 123.9, 127.0, 128.3, 128.5, 128.9, 130.5, 131.7, 132.1, 133.4, 136.8, 139.2, 140.6, 157.9, 169.9; HRMS calcd for $C_{19}H_{14}O_3$ $(M + H)^+$ 291.1016, found 291.1011.

6-Methoxy-8-methyl-4-phenylnaphtho[2,3-*c*]furan-1(3*H*)-one (2c): ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.81 (s, 3H), 3.76 (s, 3H), 5.24 (s, 2H), 6.93 (s, 1H), 7.14 (s, 1H), 7.41 (d, 2H, J = 7.8 Hz), 7.50 (m, 3H), 8.64 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.3, 55.5, 69.8, 102.7, 120.7, 120.8, 123.0, 128.7, 129.5, 129.7, 133.3, 137.0, 137.7, 139.0, 139.9, 160.1, 172.2; HRMS calcd for $C_{20}H_{16}O_3$ $(M + H)^+$ 305.1172, found 305.1171.

9-(4-Methoxy-2-methylphenyl)naphtho[2,3-*c*]furan-1(3*H*)-one (3c): ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.87 (s, 3H), 3.82 (s, 3H), 5.40 (s, 2H), 6.81 (d, 1H, J = 9.5 Hz), 6.86 (s, 1H), 7.00 (d, 2H, J = 8.45 Hz), 7.40 (t, 1H, J = 6.35, 8.45 Hz), 7.57 (t, 2H, J = 10.55, 9.5 Hz), 7.83 (s, 1H), 7.90 (d, 1H, J = 7.4 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.5, 55.6, 68.7, 111.5, 115.8, 120.4, 121.0, 127, 127.2, 128.3, 128.5, 129.0, 131.1, 133.5, 136.7, 138.4, 140.5, 142.1, 160.0, 170.0; HRMS calcd for $C_{20}H_{16}O_3$ $(M + H)^+$ 305.1172, found 305.1170.

5,7,8-Trimethyl-4-phenylnaphtho[2,3-*c*]furan-1(3*H*)-one (2d): ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.84 (s, 3H), 2.31 (s, 3H), 2.7 (s, 3H), 5.02 (s, 2H), 7.2 (m, 2H), 7.4 (m, 3H), 8.6 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.3, 20.5, 22.0, 70.5, 121.3, 123.6, 128.1, 129.1, 131.4, 131.7, 133.7, 134.4, 135.3, 139.3, 141.1, 141.4, 172.2; HRMS calcd for $C_{21}H_{18}O_2$ $(M + H)^+$ 303.1379, found 303.1378.

9-(2,3,5-Trimethylphenyl)naphtho[2,3-*c*]furan-1(3*H*)-one (3d): ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.82 (s, 3H), 2.19 (s, 3H), 2.27 (s, 3H), 5.38 (s, 1H), 6.84 (s, 1H), 7.08 (s, 1H), 7.39 (t, 1H, J = 6.7, 8.35 Hz), 7.57 (m, 2H), 7.82 (s, 1H), 7.89 (d, 1H, J = 8.35 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.6, 19.7, 20.0, 68.7, 120.3, 120.7, 127.0, 128.4, 128.5, 129.0, 131.2, 131.7, 132.0, 133.4, 133.9, 136.7, 137.0, 140.5, 142.6, 170.0; HRMS calcd for $C_{21}H_{18}O_2$ $(M + H)^+$ 303.1379, found 303.1379.

5,7-Dimethoxy-4-phenylnaphtho[2,3-*c*]furan-1(3*H*)-one (2e): ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.37 (s, 3H), 3.89 (s, 3H), 4.98 (s, 2H), 6.49 (d, 1H, J = 3.95 Hz), 6.87 (d, 1H, J = 2.5 Hz), 7.15 (d, 2H, J = 7.7 Hz), 7.30 (m, 3H), 8.24 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.7, 55.9, 70.3, 100.5, 102.3, 123.2, 124.0, 125.0, 127.2, 128.0, 133.8, 137.2, 138.5, 140.7, 158.4, 159.0, 171.8; HRMS calcd for $C_{20}H_{16}O_4$ $(M + H)^+$ 321.1121, found 321.1119.

6,8-Dimethoxy-9-phenylnaphtho[2,3-*c*]furan-1(3*H*)-one (3e): ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.75 (s, 6H), 5.38 (s, 2H), 6.45 (d, 2H, J = 2.05 Hz), 6.54 (t, 1H, J = 2.4 Hz), 7.43 (t, 1H, J = 7.75, 6.6 Hz), 7.57 (t, 1H, J = 7.75 Hz), 7.81 (d, 1H, J = 8.8 Hz), 7.84 (s, 1H), 7.89 (d, 1H, J = 8.85 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.8, 68.5, 100.8, 108.7, 120.3, 120.7, 127.2, 128.4, 128.6, 129.1, 133.1, 136.6, 136.8, 140.5, 142.4, 160.8, 169.7; HRMS calcd for $C_{20}H_{16}O_4$ $(M + H)^+$ 321.1121, found 321.1122.

4-(3,5-Bis(trifluoromethyl)phenyl)naphtho[2,3-*c*]furan-1(3*H*)-one (3f): ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.43 (s, 2H), 7.51 (t, 1H, J = 8.2 Hz), 7.58 (d, 1H, J = 8.15 Hz), 7.64 (t, 1H, J = 8.1, 7.45 Hz) 7.80 (s, 2H), 7.95 (s, 2H), 7.97 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 68.9, 121.0, 122.2, 127.2, 128.2, 129.0, 129.5, 131.0, 131.7, 132.0, 132.5, 136.8, 136.9, 138.4, 140.5, 169.6; HRMS calcd for $C_{20}H_{10}F_6O_2$ $(M + H)^+$ 397.0657, found 397.0642.

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4-(Naphthalen-1-yl)-naphtho[2,3-*c*]furan-1(3*H*)-one (2g): ^{1}H NMR (500 MHz, $CDCl_3$) δ ABq system 4.90 (d, 1H, J = 14.85 Hz), 5.09 (d, 1H, J = 14.85 Hz), 7.14 (d, 1H, J = 8.95 Hz), 7.27 (t, 1H, J = 8, 6.95 Hz), 7.45 (m, 6H), 7.92 (d, 1H, J = 9.95 Hz), 7.96 (d, 1H, J = 8 Hz), 8.08 (d, 1H, J = 7.95 Hz), 8.55 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 69.9, 123.5, 125.6, 126.0, 126.7, 126.8, 127.3, 128.0, 129.1, 129.5, 130.6, 132.0, 132.8, 133.6, 134.0, 134.3, 136.2, 140.1, 171.6; HRMS calcd for $C_{22}H_{14}O_2$ $(M + H)^+$ 311.1066, found 311.1067.

7-Phenylphenanthro[2,3-*c*]furan-8(10*H*)-one (3g): ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.47 (s, 2H), 7.34 (m, 2H), 7.49 (m, 3H), 7.65 (m, 4H), 7.85 (d, 1H, J = 8.1 Hz), 8.71 (d, 1H, J = 8.05 Hz), 8.73 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 67.4, 114.2, 119.7, 122.5, 123.9, 126.2, 126.8, 127.1, 127.3, 127.3, 127.8, 128.6, 129.1, 130.4, 131.7, 133.6, 133.8, 140.7, 141.1, 168.7; HRMS calcd for $C_{22}H_{14}O_2$ $(M + H)^+$ 311.1066, found 311.1067.

9-Phenyl-3a,4-dihydronaphtho[2,3-*c*]furan-1(3*H*)-one (5a). ^{1}HNMR (500 MHz, $CDCl_3$) δ 2.82 (t, 1H, J = 19.60, 14.75 Hz), 3.00 (m, 1H), 3.40 (m, 1H), 3.98 (t, 1H, J = 9.8 Hz), 4.67 (t, 1H, J = 12.25, 9.85 Hz), 6.89 (d, 1H, J = 8.8 Hz), 7.11 (t, 1H, J = 7.95, 7.2 Hz), 7.23 (m, 4H), 7.37 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 33.4, 36.0, 71.6, 122.5, 127.7, 128.2, 128.4, 128.9, 129.5, 130.2, 134.7, 135.8, 136.3, 147.7, 168.6; HRMS calcd for $C_{18}H_{14}O_2$ $(M + H)^+$ 263.1066, found 263.1066.

Acknowledgment. This research was supported by Yale University. The authors are grateful to Dr. Tukiet T. Lam for mass spectroscopy analysis.

Supporting Information Available: Additional experimental procedures, compound characterizations, and details for the green chemistry metrics. This material is available free of charge via the Internet at http://pubs. acs. org.

JO801213M