which might explain the observed dechlorination of HCB.

On the basis of the experimental data presented above, the following reaction scheme can be proposed to describe naphthalene-sensitized photodechlorination of HCB

$$^1N_0 + h\nu \rightarrow {}^1N^* \quad (4)$$

$$^1N^* \rightarrow {}^1N_0 + h\nu' \quad (5)$$

$$^1N^* \rightarrow {}^1N_0 \quad (6)$$

$$^1N^* \rightarrow {}^3N^* \quad (7)$$

$$^1N^* + {}^1HCB_0 \rightarrow ({}^1N^*\ HCB) \rightarrow N^{\bullet+} + HCB^{\bullet-} \quad (8)$$

$$HCB^{\bullet-} + RH \rightarrow PeCB + Cl^{\bullet}(Cl^-) + R^{\bullet} \quad (9)$$

where $^1N_0$, $^1N^*$, and $^3N^*$ represent the naphthalene molecule in the ground, excited singlet, and excited triplet states, respectively, $^1HCB_0$ is the molecule of HCB in ground state, ($^1N^*$ HCB) stands for naphthalene–HCB exciplex, $N^{\bullet+}$ is the naphthalene radical cation and $HCB^{\bullet-}$ is the HCB radical anion, and RH is the solvent molecule acting as the hydrogen donor.

The compounds formed as a result of dechlorination of HCB (i.e., pentachlorobiphenyl, tetrachlorobiphenyl, etc.) are also expected to form exciplexes with naphthalene and act as electron acceptors. This was experimentally shown for 2,2',3,3'-tetrachlorobiphenyl. It is therefore reasonable to postulate that the same reaction scheme proposed above is also valid for each chlorinated biphenyl formed in the system and can thus explain their stepwise dechlorination.

The above mechanism could be fully accepted if the radical intermediate could be detected and identified. The naphthalene radical cation has a distinct absorption spectrum that differs considerably from that of naphthalene.[32] An attempt to detect the presence of this intermediate by flash photolysis was undertaken but was unsuccessful, probably because of its short lifetime (<1 μs)[37] and limitations of the apparatus used.

It should be noted that while the mechanism proposed previously seems reasonable for the naphthalene-sensitized dechlorination of HCB, in the case of direct photolysis of HCB in an organic solvent as well as in an aqueous solution of PSSS-VN, the participation of the HCB excimer might also be of some importance. Due to steric factors, HCB cannot form a fully overlapped excimer. It can, however, form two types of partly overlapped excimers, characterized by two different geometries.[38] The creation of HCB excimer in the polymeric pseudophase is highly probable because of the high local concentration of the solubilized compound.

Conclusions

Irradiation of aqueous solutions of PSSS-VN containing solubilized HCB with solar-simulated radiation in an oxygen-free atmosphere results in dechlorination of HCB. On the basis of the model studies performed with use of a low molecular weight system, the mechanism of dechlorination of HCB involving a naphthalene–HCB exciplex intermediate followed by electron transfer has been proposed. Electron transfer generates the HCB radical anion, which then can easily expel a chlorine radical (or anion). This sequence can be repeated by chlorinated biphenyl compounds containing fewer chlorine atoms formed in the reaction. This could explain the step by step dechlorination of HCB that should ultimately result in the formation of a nonchlorinated biphenyl.

Acknowledgment. The financial support of the Natural Sciences and Engineering Research Council of Canada and the Ontario Centre for Materials Research is gratefully acknowledged.

Registry No. HCB, 38411-22-2; (SSS)(VN) (copolymer), 115468-37-6; naphthalene, 91-20-3.

(37) Asmus, K. D.; Graetzel, M. Report AED-CONF-73-187-001; *Chem. Abstr.* **1975**, *82*, 161783*r*.

(38) Nowakowska, M.; Tang, T-H.; Sustar, E.; Guillet, J. E.; Csizmadia, I. G. Manuscript in preparation.

Regiospecific Synthesis of Polysubstituted Naphthalenes and Iodoacylnaphthoquinones via Zirconocene Complexes of Naphthalynes

Stephen L. Buchwald*[1] and Susan M. King[2]

Contribution from the Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139. *Received July 16, 1990*

Abstract: Zirconocene complexes of substituted naphthalynes have been generated in situ and trapped with nitriles to form azametallacycles with excellent regiochemical control. These compounds can be converted into ketones, α-iodo ketones, and iodoacylnaphthoquinones with experimentally simple procedures.

Natural products that contain aromatic and/or quinoid structures are of great medicinal importance.[3] The requirement for efficient routes to these molecules has spurred an intensive effort to develop general methods for the regiospecific preparation of highly substituted aromatic systems.[4] Despite such efforts, a need for more efficient and flexible routes to many types of aromatic molecules still exists. In this paper, we describe a general route to highly substituted naphthalenes and iodoacylnaphthoquinones via intermediate zirconocene complexes of naphthalynes.

(1) Camille & Henry Dreyfus Teacher-Scholar Awardee, 1989–1994; American Cancer Society Junior Faculty Research Awardee, 1987–1989; Eli Lilly Grantee, 1988–1990; Alfred P. Sloan Research Fellow, 1988–1990; Union Carbide Innovation Recognition Program Awardee, 1989.

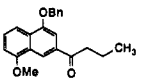
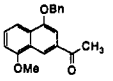
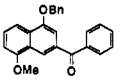
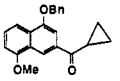
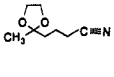
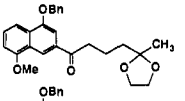
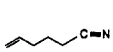
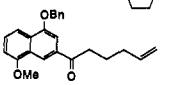
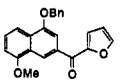
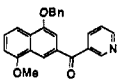
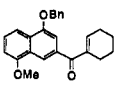
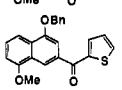
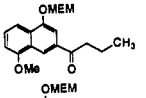
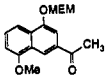
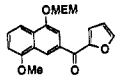
(2) NIH Trainee, 1987–1989 (NCI T32CA09112).

(3) (a) Moore, H. W. *Science (Washington, D.C.)* **1977**, *197*, 527 and references therein. (b) Driscoll, J. S.; Hazard, G. F.; Wood, H. B.; Goldin, A. *Cancer Chemother. Rep.* **1974**, *4*, 1. (c) Remers, W. A. *The Chemistry of Antitumor Antibiotics*; Wiley: New York, 1979. (d) Thomson, R. H. *Naturally Occurring Quinones III: Recent Advances*; Chapman and Hall: New York, 1987. (e) El Khaden, H. S., Ed. *Anthracycline Antibiotics*; Academic Press: New York, 1982. (f) Remers, W. A. *Antineoplastic Agents*; Wiley: New York, 1984.

(4) For recent efforts in this area, see: (a) Danheiser, R. L.; Gee, S. K. *J. Org. Chem.* **1984**, *49*, 1674 and references therein. (b) Moore, H. W.; Decker, O. H. W. *Chem. Rev.* **1986**, *86*, 821 and references therein. (c) Reed, M. W.; Moore, H. W. *J. Org. Chem.* **1988**, *53*, 4166 and references therein. (d) Wulff, W. D. In *Advances in Metal-Organic Chemistry*; Liebeskind, L. S., Ed.; JAI Press: Greenwich, CT, 1989; Vol. 1. (e) Wulff, W. D.; McCallum, J. S.; Kunng, F. A. *J. Am. Chem. Soc.* **1988**, *110*, 7419 and references therein. (f) Liebeskind, L. S.; Baysdon, S. L.; South, M. S.; Iyer, S.; Leeds, J. P. *Tetrahedron* **1985**, *41*, 5839. (g) Liebeskind, L. S.; South, M. S. *J. Am. Chem. Soc.* **1984**, *106*, 4181. (h) Semmelhack, M. F.; Bozell, J. J.; Keller, L.; Sato, T.; Spiess, E. J.; Wulff, W. D.; Zask, A. *Tetrahedron* **1985**, *41*, 5803. (i) Iwao, M.; Kuraishi, T. *Tetrahedron Lett.* **1985**, *26*, 6213 and references therein.

0002-7863/91/1513-258$02.50/0

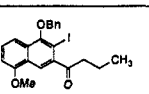
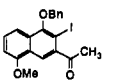
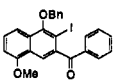
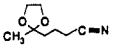
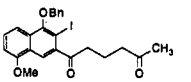
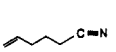
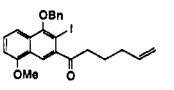
Table I

Entry	Starting Material	Nitrile	Product	Yield %
1				76
2				82
3				85
4				80
5				73
6				75
7				88
8				79
9				75
10				90
11				91
12				79
13				86

Over the past several years we have reported general methods for the preparation of zirconocene complexes of substituted benzynes and have shown that these can be used for the efficient construction of substituted aromatic and heterocyclic systems.[5] The importance of naphthalene derivatives and the lack of methods to prepare a number of highly desirable derivatives induced us to explore whether zirconocene complexes of naphthalynes could be employed in an analogous manner. Herein, we report our initial results in this area.

Our starting materials can be prepared on a multigram scale using the procedure of Rapoport[6] (Scheme I). Metal–halogen exchange, followed by addition of the aryllithium reagent at −78 °C to $Cp_2Zr(Me)Cl$,[7] produces intermediate **2**. Unlike the analogous benzyne cases,[5] **2** loses methane at room temperature, forming nascent complex **3**, which in the presence of a nitrile substrate produces metallacycle **4** in high yield. Treatment of **4** with aqueous HCl produces good to excellent yields of the substituted acylnaphthalenes, as shown in Table I. The yields reported are for the one-pot conversion of **1** to final organic product. These procedures require no isolation nor manipulation of any intermediate organometallic species. Note that only the single regioisomer is formed in all cases and that, overall, this is equivalent to the anti-Friedel–Crafts acylation of a 1,5-dialkoxynaphthalene. Of importance is that this method tolerates an extremely wide variety of functional groups. As can be seen, substrates that contain olefins, heteroaromatic groups, cyclopropanes, and protected ketones are accommodated in excellent yield.

Table II

Entry	Starting Material	Nitrile	Product	Yield %
1				91
2				62
3				90
4				67
5				76
6				84
7				79
8				81
9				79
10				84
11				82
12				65
13				79
14				70
15				51
16				64

If **3** is treated with I_2 prior to hydrolysis, iodoacylnaphthalenes **5** are produced in good to excellent yield as shown in Table II. These compounds, which contain one higher level of functionality, are also produced as a single regioisomer in a one-pot procedure. To our knowledge, molecules of general structure **5** are unknown (Table III).

Compounds **5b** can be readily transformed into the previously unknown iodoacylnaphthoquinones **6** upon treatment with Jones' reagent in acetone.[8,9] Presumably the MEM group is initially

(5) (a) Buchwald, S. L.; Watson, B. T.; Huffman, J. C. *J. Am. Chem. Soc.* **1986**, *108*, 7411. (b) Buchwald, S. L.; Sayers, A.; Watson, B. T.; Dewan, J. C. *Tetrahedron Lett.* **1987**, *28*, 3245. (c) Buchwald, S. L.; Lucas, E. A.; Dewan, J. C. *J. Am. Chem. Soc.* **1987**, *109*, 7137. (d) Buchwald, S. L.; Watson, B. T.; Lum, R. T.; Nugent, W. A. *J. Am. Chem. Soc.* **1987**, *109*, 7173. (e) Buchwald, S. L.; Fang, Q. *J. Org. Chem.* **1989**, *54*, 2793. (f) Buchwald, S. L.; Fang, Q. Manuscript in preparation.

(6) (a) Hannan, R. L.; Barber, R. B.; Rapoport, H. *J. Org. Chem.* **1979**, *44*, 2153. (b) Rutolo, D.; Lee, S.; Sheldon, R.; Moore, H. W. *J. Org. Chem.* **1978**, *43*, 2305. (c) Carter, A. H.; Race, E.; Row, F. M. *J. Chem. Soc.* **1942**, 236.

(7) Karle, I. L. *J. Chem. Phys.* **1952**, *20*, 65.

Scheme I

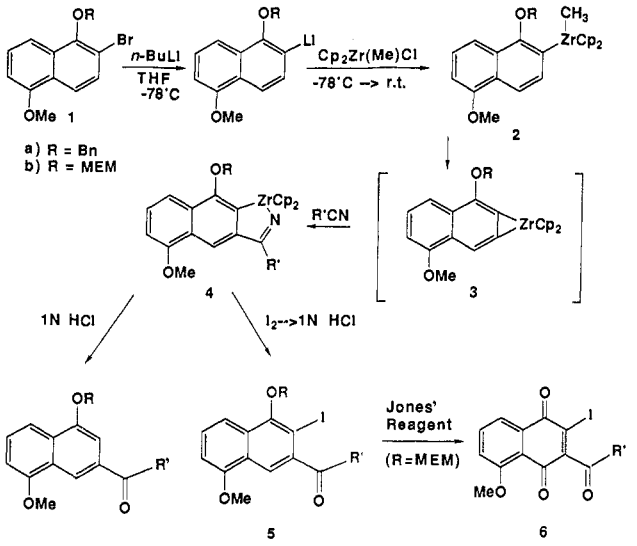
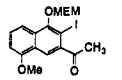
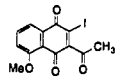
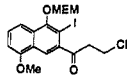
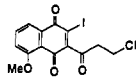
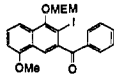
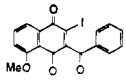
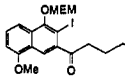
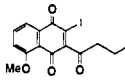
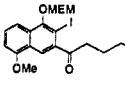
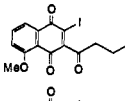
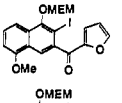
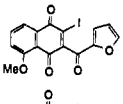
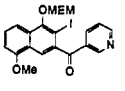
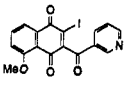
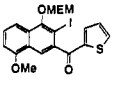
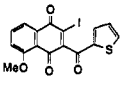


Table III

Entry	Starting Material	Product	Yield %
1			74
2			76
3			73
4			76
5			71
6			82
7			82
8			89

cleaved to provide the free naphthol, which is known to be readily transformed to naphthoquinones when exposed to oxidizing agents.[10]

In summary, we have developed a general, one-pot method for the regiospecific preparation of highly substituted naphthalenes including iodoacylnaphthalenes. These compounds can be simply transformed into iodoacylnaphthoquinones in high yield. The ease of preparation of these molecules and their high level of functionality should promote their wide use in the synthesis of aromatic molecules.

We are continuing work in our laboratory that utilizes this and related methodology for the synthesis of a number of naphthoquinone-based natural products.

Experimental Section

General Procedure. Unless otherwise indicated, all manipulations were conducted under a nitrogen or an argon atmosphere with standard Schlenk techniques. Transfers and storage of air- or moisture-sensitive reagents were performed in a Vacuum Atmospheres Co. drybox under an atmosphere of nitrogen. The sealable tubes used in the procedures were single-neck flasks fitted with Teflon O-ring screw valves. Nuclear magnetic resonance (NMR) spectra were recorded on Bruker WM-250, Bruker WM-270, Varian XL-300, Varian XL-400, or Varian VXR-500 Fourier-transform spectrometers. IR spectra were recorded on an IBM IR/30S Fourier-transform spectrometer or a Mattson Instruments Cygnus 100 Fourier-transform spectrometer. Melting points were recorded on a Fisher-Johns, Thomas Hoover, or Haake/Buchler melting point apparatus and are uncorrected. Gas chromatography analyses were performed on a Hewlett-Packard 5890 gas chromatograph with FID detector with a 25-m capillary column with cross-linked SE-30 as a stationary phase. Electron-impact mass spectra and high-resolution mass determinations (HRMS) were recorded on a Finnigan MAT System 8200 mass spectrometer. Combustion analyses were performed by Desert Analytics, Tucson, AZ.

Tetrahydrofuran and benzene were distilled or vacuum transferred from sodium/benzophenone ketyl. The nitriles were run through a short plug of alumina immediately prior to use. All other reagents were prepared according to published procedures, or they were available from commercial sources and used as received or purified with conventional procedures. Unless otherwise stated, preparative flash chromatography was performed on EM Science Kieselgel 60 (230–400 mesh). Chromatography was also performed on a Chromatotron, Model 7924T, Harrison Research, CA. The chromatography plates were prepared with E.M. Science silica gel/$CaSO_4$ No. $60PF_{254}$. Yields, unless otherwise indicated, refer to isolated material of ≥95% purity as determined by ^1H NMR, ^{13}C NMR, and GC (where applicable).

Preparation of 2-Bromo-1-(benzyloxy)-5-methoxynaphthalene (1a). To a slurry of NaH (1.2 g, 29.7 mmol, 60% dispersion in mineral oil, washed with hexane to remove mineral oil) in THF (20 mL) and DMF (10 mL) at 0 °C under a nitrogen atmosphere was added a solution of 2-bromo-5-methoxynaphthol[6] (5.0 g, 19.75 mmol) in THF (20 mL) dropwise over a period of 15 min, and the solution was allowed to stir at 0 °C for 30 min. A solution of benzyl bromide (2.6 mL, 21.7 mmol) in THF (20 mL) was added dropwise over a period of 15 min at 0 °C, and the reaction mixture was warmed to room temperature and allowed to stir for 17 h. Methanol (ca. 2 mL) was slowly added dropwise, and the mixture was poured into 100 mL of water and extracted with ether (3 × 100 mL). The organic layer was washed with brine (5 × 100 mL) and dried over $MgSO_4$, and the solvent was removed in vacuo to yield a yellow-brown solid. The solid was recrystallized from hexane to yield **1a** as pale yellow needles: 6.5 g, 95% yield; ^1H NMR (300 MHz, $CDCl_3$) δ 3.99 (s, 3 H), 5.11 (s, 2 H), 6.84 (d, J = 8.2 Hz, 1 H), 7.42 (m, 4 H), 7.61 (m, 3 H), 7.70 (d, J = 8.4 Hz, 1 H), 7.94 (d, J = 8.4 Hz, 1 H); $^{13}C\{^1H\}$ NMR (125.7 MHz, $CDCl_3$). δ 55.61, 75.55, 104.53, 114.21, 114.33, 119.84, 126.14, 127.07, 128.22, 128.26, 128.58, 129.26, 130.55, 136.98, 151.60, 155.79; IR (CCl_4 thin film) 3067, 3032, 2952, 2937, 2909, 2873, 1581, 1498, 1454, 1410, 1393, 1362, 1259, 1207, 1182, 1173, 1068, 1052, 972, 808, 791, 748, 696 cm^{-1}; mp 80.5–81.5 °C; high-resolution mass spectrum (EI) M^+ for $C_{18}H_{15}BrO_2$, calcd 342.0255, found 342.0255 (±0.0008).

Preparation of 2-Bromo-1-[(2-methoxyethoxy)methoxy]-5-methoxynaphthalene (1b). To a slurry of NaH (1.2 g, 29.7 mmol, 60% dispersion in mineral oil, washed with hexane to remove mineral oil) in THF (20 mL) and DMF (10 mL) at 0 °C under a nitrogen atmosphere was added a solution of 2-bromo-5-methoxynaphthol[6] (5.0 g, 19.75 mmol) in THF (20 mL) dropwise over a period of 15 min, and the solution was allowed to stir at 0 °C for 30 min. A solution of (2-methoxyethoxy)methyl chloride (3.8 mL, 33.6 mmol) in THF (20 mL) was added dropwise over a period of 15 min at 0 °C, and the reaction mixture was warmed to room temperature and allowed to stir for 17 h. Methanol (ca. 2 mL) was added slowly dropwise, and the mixture was poured into 100 mL of water and extracted with ether (3 × 100 mL). The organic layer was washed with brine (5 × 100 mL) and dried over $MgSO_4$, and the solvent was removed in vacuo to yield a yellow-brown oil. The oil was purified in two portions by spinning-plate chromatography with a Chromatotron (4-mm plate, hexane/ethyl acetate (98:2)) to yield **1b** as a colorless oil: 5.931 g, 88% isolated yield; ^1H NMR (300 MHz, $CDCl_3$) δ 3.40 (s, 3 H), 3.63 (m, 2 H), 3.99 (s, 3 H), 4.09 (m, 2 H), 5.35 (s, 2 H), 6.84 (d, J = 7.5 Hz, 1 H), 7.43 (t, J = 7.8 Hz, 1 H), 7.55 (d, J = 8.4 Hz, 1 H), 7.74 (d, J = 8.4 Hz, 1 H), 7.93 (d, J = 10.2 Hz, 1 H); $^{13}C\{^1H\}$ NMR (125.7 MHz, $CDCl_3$) δ 55.45, 58.96, 69.71, 71.59, 98.79, 104.41, 113.80, 114.41,

(8) Jones's reagent was prepared as described: Eisenbraun, E. J. *Org. Synth.* **1965**, *45*, 28.

(9) Greene, T. W. *Protective Groups in Organic Synthesis*; Wiley: New York, 1981.

(10) (a) Thomson, R. H. In *The Chemistry of Quinoid Compounds, Part 1*; Patai, S., Ed.; Wiley-Interscience: New York, 1974; pp 111–162. (b) Buehler, C. A.; Pearson, D. E. *Survey of Organic Syntheses*; Wiley-Interscience: New York, 1970, Vol. 1, Chapter 12, 1977, Vol. II, Chapter 12. (c) Parker, K. A.; Tallman, E. A. *Tetrahedron* **1984**, *40*, 4781.

119.88, 125.89, 126.94, 128.99, 130.68, 149.97, 155.45; IR (neat) 3073, 3054, 2935, 2839, 2819, 1582, 1498, 1463, 1445, 1408, 1383, 1373, 1260, 1205, 1167, 1154, 1131, 1109, 1045, 951, 808, 794 cm^{-1}; high-resolution mass spectrum (EI) M^+ for $C_{15}H_{17}BrO_4$, calcd 340.0310, found 340.0310 (±0.0012).

General Procedure for Preparation of Compounds in Table I. To a solution of 2-bromo-1-(benzyloxy)-5-methoxynaphthalene (**1a**) (1.0 mmol) in THF (8 mL) at −78 °C under an argon atmosphere was added *n*-butyllithium (0.66 mL of a 1.66 M solution in hexane, 1.1 mmol), and the solution was allowed to stir at −78 °C for 30 min. This solution was added dropwise to a solution of methylchlorodicyclopentadienylzirconium ($Cp_2Zr(Me)Cl$) (0.350 g, 1.29 mmol) in THF (10 mL) at −78 °C, and the reaction mixture was allowed to stir for an additional 15 min. The reaction mixture was warmed to room temperature, the nitrile (1.1 mmol) was added, and the reaction mixture was transferred via cannula to a sealable tube. The reaction mixture was allowed to stir at room temperature for 17 h, during which time a yellow solid precipitated. HCl (1.5 mL, 1 N) was added, and the mixture allowed to stir for 17 h. The reaction mixture was diluted with ether (200 mL), washed with water and brine, and dried over $MgSO_4$, and the solvent was removed (rotary evaporator) to yield an oil. The product was purified by spinning-plate chromatography with a Chromatotron.

1-(Benzyloxy)-5-methoxy-3-butyrylnaphthalene (Table I, Entry 1). The product was purified by spinning-plate chromatography with a Chromatotron (4-mm plate, hexane/ethyl acetate (98:2)) to yield maize crystals: 0.253 g, 76% isolated yield; ^1H NMR (400 MHz, $CDCl_3$) δ 1.05 (t, J = 7.2 Hz, 3 H), 1.83 (sextet, J = 7.2 Hz, 2 H), 3.11 (t, J = 7.2 Hz, 2 H), 4.04 (s, 3 H), 5.30 (s, 2 H), 6.91 (d, J = 7.2 Hz, 1 H), 7.45 (m, 8 H), 7.92 (d, J = 7.6 Hz, 1 H); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$, multiplicity of peaks from gated ^1H decoupling is given in parentheses) δ 13.96 (q), 18.13 (t), 40.19 (t), 55.62 (q), 70.20 (t), 102.88 (d), 105.32 (d), 114.51 (d), 117.22 (d), 125.53 (s), 127.50 (d), 127.98 (d), 128.18 (d), 128.56 (d), 129.18 (s), 133.97 (s), 136.83 (s), 154.64 (s), 156.24 (s), 200.53 (s); IR (KBr) 3078, 3028, 2963, 2949, 2934, 2894, 2873, 1680, 1595, 1508, 1459, 1405, 1373, 1270, 1166, 1086, 1071, 1028, 894, 803, 750, 734 cm^{-1}; mp 114.2–116.0 °C; high-resolution mass spectrum (EI) M^+ for $C_{22}H_{22}O_3$, calcd 334.1568, found 334.1567 (±0.0010).

1-(Benzyloxy)-5-methoxy-3-acetylnaphthalene (Table I, Entry 2). The product was purified by spinning-plate chromatography with a Chromatotron (4-mm plate, hexane/ethyl acetate (98:2–9:1 gradient)) to yield yellow crystals: 0.250 g, 82% isolated yield; ^1H NMR (300 MHz, $CDCl_3$) δ 2.74 (s, 3 H), 4.04 (s, 3 H), 5.30 (s, 2 H), 6.92 (d, J = 7.8 Hz, 1 H), 7.40 (m, 3 H), 7.54 (m, 4 H), 7.92 (d, J = 8.4 Hz, 1 H), 8.53 (s, 1 H); $^{13}C\{^1H\}$ NMR (75.4 MHz, $CDCl_3$) δ 26.27, 55.46, 70.09, 102.52, 105.30, 114.37, 117.94, 125.40, 127.36, 127.86, 128.21, 128.45, 129.16, 133.92, 136.76, 154.45, 156.15, 197.96; IR (KBr) 3083, 3040, 3013, 2958, 2933, 2904, 2865, 1666, 1595, 1505, 1462, 1424, 1408, 1372, 1279, 1255, 1208, 1077, 1061, 801 cm^{-1}; mp 130.0–131.2 °C; high-resolution mass spectrum (EI) M^+ for $C_{20}H_{18}O_3$, calcd 306.1256, found 306.1256 (±0.0003).

1-(Benzyloxy)-5-methoxy-3-benzoylnaphthalene (Table I, Entry 3). The product was purified by spinning-plate chromatography with a Chromatotron (4-mm plate, hexane/ethyl acetate (98:2–9:1 gradient)) to yield pale yellow crystals: 0.313 g, 85% isolated yield; ^1H NMR (300 MHz, $CDCl_3$) δ 3.94 (s, 3 H), 5.31 (s, 2 H), 6.90 (d, J = 7.9 Hz, 1 H), 7.48 (m, 10 H), 7.85 (m, 2 H), 7.95 (d, J = 8.8 Hz, 1 H), 8.27 (d, J = 1.8 Hz, 1 H); $^{13}C\{^1H\}$ NMR (75.4 MHz, $CDCl_3$) δ 55.27, 69.98, 104.72, 105.30, 114.19, 119.73, 125.06, 127.29, 127.78, 128.02, 128.39, 128.72, 129.84, 131.86, 133.77, 136.58, 137.97, 154.36, 156.09, 196.37; IR (KBr) 3082, 3063, 3038, 2997, 2934, 2909, 2831, 1642, 1625, 1594, 1505, 1460, 1445, 1422, 1407, 1377, 1282, 1261, 1069, 834, 755, 746, 732, 699 cm^{-1}; mp 123.6–125.0 °C; high-resolution mass spectrum (EI) M^+ for $C_{25}H_{20}O_3$, calcd 368.1412, found 368.1412 (±0.0007).

1-(Benzyloxy)-5-methoxy-3-(cyclopropylcarbonyl)naphthalene (Table I, Entry 4). The product was purified by spinning-plate chromatography with a Chromatotron (4-mm plate, hexane/ethyl acetate (95:5–9:1 gradient)) to yield white crystals: 0.261 g, 80% isolated yield; ^1H NMR (300 MHz, $CDCl_3$) δ 1.10 (m, 2 H), 1.29 (m, 2 H), 2.94 (m, 1 H), 4.05 (s, 3 H), 5.30 (s, 2 H), 6.93 (d, J = 6.7 Hz, 1 H), 7.40 (m, 3 H), 7.53 (m, 4 H), 7.93 (d, J = 8.3 Hz, 1 H), 8.69 (s, 1 H); $^{13}C\{^1H\}$ NMR (75.4 MHz, $CDCl_3$) δ 11.67, 16.90, 55.61, 70.26, 103.03, 105.38, 114.53, 117.32, 125.63, 127.50, 127.96, 128.12, 128.56, 129.15, 134.83, 136.88, 154.63, 156.31, 200.38; IR (KBr) 3080, 3019, 2930, 2899, 2851, 2830, 1651, 1595, 1505, 1467, 1450, 1429, 1409, 1375, 1277, 1196, 1165, 1089, 1074, 928, 751, 729 cm^{-1}; mp 118.5–120.0 °C; high-resolution mass spectrum (EI) M^+ for $C_{22}H_{20}O_3$, calcd 332.1412, found 332.1411 (±0.0008).

1-(Benzyloxy)-5-methoxy-3-[4-(2-methyl-1,3-dioxolan-2-yl)butyryl]naphthalene (Table I, Entry 5). The product was purified by spinning-plate chromatography with a Chromatotron (4-mm plate, hexane/ethyl acetate (95:5–85:15 gradient)) to yield white crystals: 0.305 g, 73% isolated yield; ^1H NMR (300 MHz, $CDCl_3$) δ 1.37 (s, 3 H), 1.80 (m, 2 H), 1.91 (m, 2 H), 3.17 (t, J = 7.1 Hz, 2 H), 3.96 (s, 4 H), 4.04 (s, 3 H), 5.30 (s, 2 H), 6.91 (d, J = 7.9 Hz, 1 H), 7.43 (m, 3 H), 7.53 (m, 4 H), 7.92 (d, J = 8.2 Hz, 1 H), 8.53 (s, 1 H); $^{13}C\{^1H\}$ NMR (75.4 MHz, $CDCl_3$) δ 19.13, 23.72, 38.06, 38.48, 55.50, 64.52, 70.21, 103.00, 105.31, 109.87, 114.45, 117.08, 125.57, 127.39, 127.86, 128.05, 128.45, 129.18, 133.97, 136.82, 154.60, 156.26, 199.93; IR (KBr) 3071, 2962, 2938, 2872, 1669, 1593, 1504, 1459, 1406, 1369, 1282, 1262, 1164, 1063, 1035, 809, 759, 751, 697 cm^{-1}; mp 131.6–133.4 °C; high-resolution mass spectrum (EI) M^+ for $C_{26}H_{28}O_5$, calcd 420.1937, found 420.1936 (±0.0015). Anal. Calcd for $C_{26}H_{28}O_5$: C, 74.26; H, 6.71. Found: C, 74.39; H, 6.74.

1-(Benzyloxy)-5-methoxy-3-(5-hexenoyl)naphthalene (Table I, Entry 6). The product was purified by spinning-plate chromatography with a Chromatotron (4-mm plate, hexane/ethyl acetate (98:2–7:3 gradient)) to yield off-white crystals: 0.270 g, 75% isolated yield; ^1H NMR (300 MHz, $CDCl_3$) δ 1.91 (quintet, J = 7.0 Hz, 2 H), 2.21 (m, 2 H), 3.15 (t, J = 7.3 Hz, 2 H), 4.05 (s, 3 H), 5.06 (m, 2 H), 5.31 (s, 2 H), 5.88 (m, 1 H), 6.92 (d, J = 7.8 Hz, 1 H), 7.43 (m, 4 H), 7.54 (m, 3 H), 7.92 (m, 1 H), 8.53 (d, J = 2.0 Hz, 1 H); $^{13}C\{^1H\}$ NMR (75.4 MHz, $CDCl_3$) δ 23.75, 33.24, 37.37, 55.55, 70.18, 102.86, 105.30, 114.47, 115.14, 117.15, 125.52, 127.44, 127.95, 128.16, 128.52, 129.16, 133.89, 136.79, 138.17, 154.57, 156.20, 200.22; IR (KBr) 3076, 3011, 2973, 2951, 2944, 2919, 2901, 2869, 2839, 1673, 1594, 1506, 1466, 1458, 1425, 1407, 1375, 1278, 1257, 1157, 1085, 1069, 905, 808, 751, 746 cm^{-1}; mp 101.0–101.7 °C; high-resolution mass spectrum (EI) M^+ for $C_{24}H_{24}O_3$, calcd 360.1725, found 360.1724 (±0.0005). Anal. Calcd for $C_{24}H_{24}O_3$: C, 79.97; H, 6.71. Found: C, 79.73; H, 6.61.

Preparation of 1-(Benzyloxy)-3-(2-furoyl)-5-methoxynaphthalene (Table I, Entry 7). The product was purified by spinning-plate chromatography with a Chromatotron (4-mm plate, hexane/ethyl acetate (95:5)) to yield maize crystals: 0.3135 g, 88% isolated yield; ^1H NMR (300 MHz, $CDCl_3$) δ 4.02 (s, 3 H), 5.32 (s, 2 H), 6.60 (m, 1 H), 6.92 (d, J = 7.8 Hz, 1 H), 7.24 (m, 1 H), 7.43 (m, 4 H), 7.54 (m, 3 H), 7.74 (m, 1 H), 7.95 (dd, J = 8.3, 1.1 Hz, 1 H), 8.60 (m, 1 H); $^{13}C\{^1H\}$ NMR (75.4 MHz, $CDCl_3$) δ 55.47, 70.11, 104.38, 105.33, 112.01, 114.24, 118.34, 120.44, 125.31, 127.32, 127.84, 128.09, 128.44, 128.87, 133.58, 136.62, 146.85, 152.18, 154.39, 156.20, 182.21; IR (KBr) 3136, 3119, 3009, 2945, 2918, 2891, 1641, 1624, 1594, 1566, 1502, 1467, 1406, 1390, 1360, 1298, 1266, 1127, 1081, 1069, 1031, 1021, 807, 770, 755, 738 cm^{-1}; mp 113.8–116.4 °C; high-resolution mass spectrum (EI) M^+ for $C_{23}H_{18}O_4$, calcd 358.1205, found 358.1205 (±0.0004).

1-(Benzyloxy)-5-methoxy-3-(pyrid-3-ylcarbonyl)naphthalene (Table I, Entry 8). The product was purified by spinning-plate chromatography with a Chromatotron (4-mm plate, hexane/ethyl acetate/triethylamine (90:5:5–80:15:5 gradient)) to yield yellow crystals: 0.292 g, 79% isolated yield; ^1H NMR (300 MHz, $CDCl_3$) δ 3.97 (s, 3 H), 5.34 (s, 2 H), 6.93 (d, J = 7.8 Hz, 1 H), 7.50 (m, 8 H), 7.97 (d, J = 9.5 Hz, 1 H), 8.17 (m, 1 H), 8.26 (d, J = 1.7 Hz, 1 H), 8.85 (dd, J = 4.9, 1.5 Hz, 1 H), 9.09 (d, J = 2.5 Hz, 1 H); $^{13}C\{^1H\}$ NMR (75.4 MHz, $CDCl_3$) δ 55.47, 70.26, 104.15, 105.61, 114.36, 120.38, 123.22, 125.15, 127.39, 127.96, 128.52, 128.64, 129.19, 133.12, 133.74, 136.52, 137.10, 150.72, 152.38, 154.83, 156.28, 194.62; IR (KBr) 3081, 3039, 3006, 2970, 2941, 2909, 1644, 1624, 1593, 1583, 1504, 1461, 1426, 1407, 1376, 1285, 1263, 1068, 837, 806, 761, 752, 705 cm^{-1}; mp 179–181 °C; high-resolution mass spectrum (EI) M^+ for $C_{24}H_{19}NO_3$, calcd 369.1365, found 369.1364 (±0.0004).

1-(Benzyloxy)-5-methoxy-3-(cyclohexenylcarbonyl)naphthalene (Table I, Entry 9). The product was purified by spinning-plate chromatography with a Chromatotron (4-mm plate, hexane/ethyl acetate (99:1–9:1 gradient)) to yield an off-white solid: 0.280 g, 75% isolated yield; ^1H NMR (300 MHz, $CDCl_3$) δ 1.74 (m, 4 H), 2.28 (m, 2 H), 2.47 (m, 2 H), 4.01 (s, 3 H), 5.28 (s, 2 H), 6.63 (m, 1 H), 6.89 (d, J = 7.6 Hz, 1 H), 7.25 (s, 1 H), 7.42 (m, 4 H), 7.52 (m, 2 H), 7.92 (d, J = 8.9 Hz, 1 H), 8.14 (d, J = 1.8 Hz, 1 H); $^{13}C\{^1H\}$ NMR (75.4 MHz, $CDCl_3$) δ 21.54, 21.92, 24.13, 25.90, 55.37, 70.01, 105.02, 105.15, 114.19, 117.54, 125.09, 127.26, 127.78, 128.25, 128.41, 134.84, 136.73, 138.54, 142.96, 154.23, 155.94, 197.96; IR (KBr) 3076, 3036, 2945, 2923, 2873, 2857, 2841, 1643, 1595, 1505, 1463, 1409, 1377, 1282, 1269, 1255, 1066, 802, 756, 749, 703 cm^{-1}; mp 107.2–109.5 °C; high-resolution mass spectrum (EI) M^+ for $C_{25}H_{24}O_3$, calcd 372.1725, found 372.1726 (±0.0006). Anal. Calcd for $C_{25}H_{24}O_3$: C, 80.62; H, 6.49. Found: C, 80.30; H, 6.40.

1-(Benzyloxy)-5-methoxy-3-(thien-2-ylcarbonyl)naphthalene (Table I, Entry 10). The product was purified by spinning-plate chromatography with a Chromatotron, (4-mm plate, hexane/ethyl acetate (95:5–8:2 gradient)) to yield yellow crystals: 0.337 g, 90% isolated yield: ^1H NMR (300 MHz, $CDCl_3$) δ 4.01 (s, 3 H), 5.33 (s, 2 H), 6.94 (d, J = 7.8 Hz, 1 H), 7.19 (dd, J = 5.4, 3.4 Hz, 1 H), 7.41 (m, 4 H), 7.55 (m, 3 H), 7.71 (dd, J = 4.0, 1.0 Hz, 1 H), 7.74 (dd, J = 4.9, 2.0 Hz, 1 H), 7.96 (m, 1 H), 8.47 (d, J = 1.7 Hz, 1 H); $^{13}C\{^1H\}$ NMR (75.4 MHz, $CDCl_3$) δ

55.53, 70.18, 104.73, 105.44, 114.33, 118.24, 125.31, 127.39, 127.92, 127.99, 128.53, 128.76, 133.67, 134.43, 134.64, 136.67, 143.75, 154.50, 156.26, 187.91; IR (KBr) 3097, 3070, 2975, 2938, 2912, 2858, 1627, 1595, 1505, 1464, 1425, 1412, 1407, 1375, 1288, 1252, 1082, 1067, 1053, 792, 753 cm^{-1}; mp 116.5–117.8 °C; high-resolution mass spectrum (EI) M^+ for $C_{23}H_{18}O_3S$, calcd 374.0977, found 374.0976 (±0.0007). Anal. Calcd for $C_{23}H_{18}O_3S$: C, 73.77; H, 4.85. Found: C, 73.59; H, 4.74.

Preparation of 1-[(2-Methoxyethoxy)methoxy]-5-methoxy-3-butyrylnaphthalene (Table I, Entry 11). The product was purified by spinning-plate chromatography with a Chromatotron (4-mm plate, hexane/ethyl acetate (95:5–8:2 gradient)) to yield a pale yellow solid: 0.302 g, 91% isolated yield; ^1H NMR (300 MHz, $CDCl_3$) δ 1.04 (t, J = 7.3 Hz, 3 H), 1.82 (sextet, J = 7.3 Hz, 2 H), 3.10 (t, J = 7.4 Hz, 2 H), 3.39 (s, 3 H), 3.59 (m, 2 H), 3.90 (m, 2 H), 4.04 (s, 3 H), 5.53 (s, 2 H), 6.91 (d, J = 7.9 Hz, 1 H), 7.51 (t, J = 7.9 Hz, 1 H), 7.67 (d, J = 1.5 Hz, 1 H), 7.84 (d, J = 8.3 Hz, 1 H), 8.56 (s, 1 H); $^{13}C\{^1H\}$ NMR (75.4 MHz, $CDCl_3$) δ 13.77, 17.89, 40.13, 55.43, 58.84, 68.06, 71.47, 93.69, 105.05, 105.65, 114.02, 117.58, 125.49, 128.07, 129.16, 133.89, 152.76, 156.18, 200.01; IR (neat) 3082, 2962, 2934, 2901, 2876, 2839, 1678, 1596, 1504, 1462, 1438, 1419, 1385, 1286, 1273, 1202, 1158, 1109, 1086, 1054, 989, 805 cm^{-1}; mp 52.4–53.3 °C; high-resolution mass spectrum (EI) M^+ for $C_{19}H_{24}O_5$, calcd 332.1624, found 332.1624 (±0.0006). Anal. Calcd for $C_{19}H_{24}O_5$: C, 68.66; H, 7.28. Found: C, 68.40; H, 7.24.

1-[(2-Methoxyethoxy)methoxy]-5-methoxy-3-acetylnaphthalene (Table I, Entry 12). The product was purified by spinning-plate chromatography with a Chromatotron (4-mm plate, hexane/ethyl acetate (9:1)) to yield pale yellow crystals: 0.211 g, 79% isolated yield; ^1H NMR (300 MHz, $CDCl_3$) δ 2.72 (s, 3 H), 3.38 (s, 3 H), 3.58 (m, 2 H), 3.89 (m, 2 H), 4.03 (s, 3 H), 5.52 (s, 2 H), 6.90 (dd, J = 7.7, 1.1 Hz, 1 H), 7.50 (dd, J = 8.4, 7.5 Hz, 1 H), 7.66 (d, J = 1.2 Hz, 1 H), 7.84 (m, 1 H), 8.55 (m, 1 H); $^{13}C\{^1H\}$ NMR (75.4 MHz, $CDCl_3$) δ 26.47, 55.55, 58.97, 68.17, 71.53, 93.77, 105.18, 105.53, 114.14, 118.49, 125.55, 128.30, 129.34, 134.06, 152.81, 156.29, 197.89; IR (KBr) 3102, 3082, 3024, 2991, 2970, 2933, 2902, 2885, 2840, 2820, 1662, 1502, 1460, 1395, 1384, 1282, 1252, 1164, 1108, 1092, 1046, 1031, 998, 868, 809 cm^{-1}; mp 77.0–77.4 °C; high-resolution mass spectrum (EI) M^+ for $C_{17}H_{20}O_5$, calcd 304.1311, found 304.1311 (±0.0007).

1-[(2-Methoxyethoxy)methoxy]-5-methoxy-3-(2-furoyl)naphthalene (Table I, Entry 13). The product was purified by spinning-plate chromatography with a Chromatotron (4-mm plate, hexane/ethyl acetate (85:15–1:1 gradient)) to yield a gold oil: 0.306 g, 86% isolated yield; ^1H NMR (300 MHz, $CDCl_3$) δ 3.38 (s, 3 H), 3.59 (m, 2 H), 3.92 (m, 2 H), 4.02 (s, 3 H), 5.55 (s, 2 H), 6.62 (m, 1 H), 6.92 (d, J = 7.8 Hz, 1 H), 7.30 (m, 1 H), 7.52 (t, J = 7.9 Hz, 1 H), 7.65 (d, J = 2.5 Hz, 1 H), 7.75 (d, J = 1.8 Hz, 1 H), 7.87 (d, J = 8.3 Hz, 1 H), 8.61 (d, J = 1.8 Hz, 1 H); $^{13}C\{^1H\}$ NMR (75.4 MHz, $CDCl_3$) δ 55.61, 58.99, 68.16, 71.55, 93.81, 105.25, 107.30, 112.09, 114.10, 118.95, 120.55, 125.54, 128.18, 129.08, 133.87, 146.97, 152.33, 152.76, 156.38, 182.32; IR (neat) 3131, 3084, 2934, 2890, 2887, 2840, 1650, 1647, 1642, 1639, 1504, 1467, 1463, 1391, 1386, 1292, 1265, 1106, 1103, 1084, 1063, 1059, 1052, 1050, 1045 cm^{-1}; high-resolution mass spectrum (EI) M^+ for $C_{20}H_{20}O_6$, calcd 356.1260, found 356.1260 (±0.0003).

General Procedure for Preparation of Compounds in Table II. To a solution of 2-bromo-1-(benzyloxy)-5-methoxynaphthalene (**1a**) (1.0 mmol) in THF (8 mL) at −78 °C under an argon atmosphere was added *n*-butyllithium (0.66 mL of a 1.64 M solution in hexane, 1.1 mmol), and the solution was allowed to stir at −78 °C for 30 min. This solution was added dropwise to a solution of $Cp_2Zr(Me)Cl$ (0.350 g, 1.29 mmol) in THF (10 mL) at −78 °C, and the reaction mixture was allowed to stir for an additional 15 min. The reaction mixture was warmed to room temperature, the nitrile (1.1 mmol) was added, and the reaction mixture was transferred via cannula to a sealable tube. The reaction mixture was allowed to stir at room temperature for 17 h during which time a yellow solid precipitated. A solution of iodine (0.635 g, 2.5 mmol) in benzene (20 mL) was added, and the reaction mixture was heated to 50 °C for 17 h. The reaction mixture was cooled to room temperature, 0.1 N HCl (10 mL) added, and the mixture allowed to hydrolyze for the specified period of time. The reaction mixture was diluted with ether (200 mL), washed with 15% Na_2SO_3 solution, water, and brine, and dried over $MgSO_4$, and the solvent was removed (rotary evaporator) to yield a yellow oil. The oil was purified by spinning-plate chromatography with a Chromatotron.

2-Iodo-1-(benzyloxy)-5-methoxy-3-butyrylnaphthalene (Table II, Entry 1). The reaction mixture was allowed to hydrolyze for 17 h. The product was purified by spinning-plate chromatography with a Chromatotron (4-mm plate, hexane/ethyl acetate (98:2–9:1 gradient)) to yield a maize solid: 0.419 g, 91% isolated yield; ^1H NMR (500 MHz, $CDCl_3$) δ 1.05 (t, J = 7.5 Hz, 3 H), 1.82 (sextet, J = 7.0 Hz, 2 H), 3.00 (t, J = 7.0 Hz, 2 H), 4.00 (s, 3 H), 5.08 (s, 2 H), 6.89 (d, J = 7.0 Hz, 1 H), 7.44 (m, 4 H), 7.68 (m, 2 H), 8.10 (s, 1 H); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$, multiplicity of peaks from gated ^1H decoupling is given in parentheses) δ 13.81 (q), 17.73 (t), 44.34 (t), 55.68 (q), 75.60 (t), 85.84 (s), 105.45 (d), 114.54 (d), 118.24 (d), 125.88 (s), 128.14 (d), 128.34 (d), 128.59 (d), 129.80 (s), 136.60 (s), 141.75 (s), 155.66 (s), 156.13 (s), 205.03 (s); IR (neat) 3033, 2962, 2935, 2874, 1696, 1571, 1456, 1431, 1394, 1385, 1354, 1263, 1243, 1069, 1051, 972, 791, 787, 697 cm^{-1}; mp 80.5–82.5 °C; high-resolution mass spectrum (EI) M^+ for $C_{22}H_{21}IO_3$, calcd 460.0535, found 460.0545 (±0.0014).

Preparation of 2-Iodo-1-(benzyloxy)-5-methoxy-3-acetylnaphthalene (Table II, Entry 2). The reaction mixture was allowed to hydrolyze for 17 h. The product was purified by spinning-plate chromatography with a Chromatotron (4-mm plate, hexane/ethyl acetate (95:5–8:2 gradient)) to yield tan needles: 0.2687 g, 62% isolated yield; ^1H NMR (500 MHz, $CDCl_3$) δ 2.69 (s, 3 H), 3.97 (s, 3 H), 5.04 (s, 2 H), 6.86 (d, J = 7.4 Hz, 1 H), 7.37 (m, 1 H), 7.43 (m, 3 H), 7.64 (m, 3 H), 8.18 (s, 1 H); $^{13}C\{^1H\}$ NMR (125.7 MHz, $CDCl_3$) δ 29.84, 55.67, 75.54, 85.59, 105.47, 114.57, 119.21, 125.77, 128.13, 128.31, 128.56, 128.88, 130.02, 136.56, 140.84, 155.80, 156.20, 201.78; IR (KBr) 3070, 2994, 2967, 2913, 2876, 1699, 1570, 1452, 1427, 1400, 1358, 1273, 1256, 1241, 1124, 1055, 1013, 977, 901, 798, 743 cm^{-1}; mp 118.5–119.5 °C; high-resolution mass spectrum (EI) M^+ for $C_{20}H_{17}IO_3$, calcd 432.0222, found 432.0222 (±0.0013). Anal. Calcd for $C_{20}H_{17}IO_3$: C, 55.57; H, 3.96. Found: C, 55.67; H, 3.86.

Preparation of 2-Iodo-1-(benzyloxy)-5-methoxy-3-benzoylnaphthalene (Table II, Entry 3). The reaction mixture was allowed to hydrolyze for 48 h with 1 N HCl. The product was purified by spinning-plate chromatography with a Chromatotron (4-mm plate, hexane/ethyl acetate (96:4–85:15 gradient)) to yield a maize solid: 0.424 g, 90% isolated yield; ^1H NMR (300 MHz, $CDCl_3$) δ 3.95 (s, 3 H), 5.13 (s, 2 H), 6.90 (d, J = 7.2 Hz, 1 H), 7.47 (m, 7 H), 7.61 (m, 1 H), 7.67 (m, 2 H), 7.74 (d, J = 8.2 Hz, 1 H), 7.87 (m, 2 H), 8.05 (s 1 H); $^{13}C\{^1H\}$ NMR (75.4 MHz, $CDCl_3$) δ 55.61, 75.66, 86.87, 105.50, 114.40, 119.12, 125.98, 128.09, 128.25, 128.38, 128.50, 129.70, 130.54, 133.46, 136.15, 136.55, 140.86, 155.45, 156.14, 196.81; IR (neat) 3064, 3032, 3006, 2959, 2937, 2871, 2839, 1670, 1667, 1571, 1455, 1450, 1431, 1392, 1354, 1316, 1277, 1260, 1210, 1059, 802, 737, 698 cm^{-1}; mp 141.1–142.2 °C; high-resolution mass spectrum (EI) M^+ for $C_{25}H_{19}IO_3$, calcd 494.0379, found 494.0379 (±0.0007).

2-Iodo-1-(benzyloxy)-5-methoxy-3-(5-oxohexanoyl)naphthalene (Table II, Entry 4). The reaction mixture was allowed to hydrolyze for 36 h. The product was purified by spinning-plate chromatography with a Chromatotron (4-mm plate, hexane/ethyl acetate (9:1–8:2 gradient)) to yield a maize solid: 0.334 g, 67% isolated yield; ^1H NMR (300 MHz, $CDCl_3$) δ 2.06 (quintet, J = 7.2 Hz, 2 H), 2.17 (s, 3 H), 2.64 (t, J = 7.1 Hz, 2 H), 3.06 (t, J = 6.6 Hz, 2 H), 4.00 (s, 3 H), 5.07 (s, 2 H), 6.89 (d, J = 7.8 Hz, 1 H), 7.46 (m, 4 H), 7.67 (m, 3 H), 8.11 (s, 1 H); $^{13}C\{^1H\}$ NMR (125.7 MHz, $CDCl_3$) δ 18.13, 29.93, 41.06, 42.44, 55.67, 75.57, 85.65, 105.49, 114.49, 118.43, 125.84, 128.11, 128.31, 128.56, 128.73, 129.86, 136.53, 141.11, 155.70, 156.13, 204.19, 208.34; IR (neat) 3033, 3006, 2958, 2903, 2880, 1717, 1700, 1571, 1456, 1431, 1399, 1353, 1308, 1265, 1249, 1098, 1063, 801, 787, 755, 698 cm^{-1}; mp 69.5–72.0 °C; high-resolution mass spectrum (EI) M^+ for $C_{24}H_{23}IO_4$, calcd 502.0641, found 502.0640 (±0.0015).

Preparation of 2-Iodo-1-(benzyloxy)-5-methoxy-3-(5-hexenoyl)naphthalene (Table II, Entry 5). The reaction mixture was allowed to hydrolyze for 36 h. The product was purified by spinning-plate chromatography with a Chromatotron (4-mm plate, hexane/ethyl acetate (95:5–85:15 gradient)) to yield a gold oil: 0.3712 g, 76% isolated yield; ^1H NMR (300 MHz, $CDCl_3$) δ 1.91 (quintet, J = 7.0 Hz, 2 H), 2.21 (m, 2 H), 3.03 (t, J = 7.3 Hz, 2 H), 4.02 (s, 3 H), 5.05 (m, 2 H), 5.08 (s, 2 H), 5.84 (m, 1 H), 6.90 (d, J = 7.8 Hz, 1 H), 7.44 (m, 5 H), 7.67 (m, 3 H), 8.10 (s, 1 H); $^{13}C\{^1H\}$ NMR (75.4 MHz, $CDCl_3$) δ 23.24, 32.99, 41.58, 55.66, 75.53, 85.75, 105.44, 114.47, 115.30, 118.21, 125.83, 128.09, 128.27, 128.50, 128.59, 129.74, 136.55, 137.88, 141.63, 155.60, 156.08, 204.71; IR (neat) 3068, 3033, 3004, 2937, 2872, 2840, 1698, 1572, 1456, 1431, 1394, 1354, 1308, 1265, 1080, 1056, 993, 972, 914, 800, 788, 754, 697 cm^{-1}; high-resolution mass spectrum (EI) M^+ for $C_{24}H_{23}IO_3$, calcd 486.0692, found 486.0692 (±0.0010).

Preparation of 2-Iodo-1-(benzyloxy)-5-methoxy-3-(2-furoyl)naphthalene (Table II, Entry 6). The reaction mixture was allowed to hydrolyze for 36 h with 1 N HCl. The product was purified by spinning-plate chromatography with a Chromatotron (4-mm plate, hexane/ethyl acetate (95:5–85:15 gradient)) to yield maize crystals: 0.4087 g, 84% isolated yield; ^1H NMR (300 MHz, $CDCl_3$) δ 3.93 (s, 3 H), 5.08 (s, 2 H), 6.54 (m, 1 H), 6.87 (d, J = 7.2 Hz, 1 H), 7.03 (m, 1 H), 7.44 (m, 4 H), 7.68 (m, 4 H), 8.17 (s, 1 H); $^{13}C\{^1H\}$ NMR (75.4 MHz, $CDCl_3$) δ 55.57, 75.56, 86.83, 105.50, 112.53, 114.28, 119.49, 121.96, 125.63, 128.04, 128.19, 128.45, 128.64, 129.87, 136.42, 139.25, 147.95, 151.46, 155.46, 156.09, 183.67; IR (CCl_4 thin film) 3066, 3033, 3008, 2962, 2939, 2873, 2839, 1661, 1652, 1572, 1464, 1432, 1391, 1354, 1262,

1080, 1062, 1013, 821, 788, 758 cm^{-1}; mp 114.9–115.6 °C; high-resolution mass spectrum (EI) M^+ for $C_{23}H_{17}IO_4$, calcd 484.0172, found 484.0171 (±0.0010). Anal. Calcd for $C_{23}H_{17}IO_4$: C, 57.04; H, 3.54. Found: C, 56.99; H, 3.52.

2-Iodo-1-(benzyloxy)-5-methoxy-3-(pyrid-3-ylcarbonyl)naphthalene (Table II, Entry 7). The reaction mixture was allowed to hydrolyze for 17 h. The product was purified by spinning-plate chromatography with a Chromatotron (4-mm plate, hexane/ethyl acetate/triethylamine (90:5:5–85:15:5 gradient)) to yield a maize solid: 0.392 g, 79% isolated yield; ^1H NMR (300 MHz, $CDCl_3$) δ 3.97 (s, 3 H), 5.14 (s, 2 H), 6.93 (d, J = 7.6 Hz, 1 H), 7.47 (m, 5 H), 7.67 (m, 2 H), 7.75 (d, J = 8.6 Hz, 1 H), 8.08 (d, J = 0.8 Hz, 1 H), 8.21 (dt, J = 8.1, 2.1 Hz, 1 H), 8.83 (dd, J = 4.9, 1.8 Hz, 1 H), 9.00 (d, J = 1.8 Hz, 1 H); $^{13}C\{^1H\}$ NMR (75.4 MHz, $CDCl_3$) δ 55.55, 75.66, 86.32, 105.64, 114.33, 119.72, 123.45, 125.81, 128.01, 128.24, 128.44, 128.82, 129.88, 131.62, 136.30, 137.22, 139.39, 151.72, 153.50, 155.65, 156.08, 195.35; IR (CCl_4 thin film) 3066, 3034, 2962, 2939, 2906, 2839, 1673, 1583, 1572, 1456, 1431, 1417, 1392, 1354, 1281, 1261, 1212, 1062, 963, 778, 768, 762, 700 cm^{-1}; mp 115.4–117.5 °C; high-resolution mass spectrum (EI) M^+ for $C_{24}H_{18}INO_3$, calcd 495.0331, found 495.0333 (±0.0010). Anal. Calcd for $C_{24}H_{18}INO_3$: C, 58.20; H, 3.66. Found: C, 57.96; H, 3.57.

2-Iodo-1-(benzyloxy)-5-methoxy-3-(thien-2-ylcarbonyl)naphthalene (Table II, Entry 8). The reaction mixture was allowed to hydrolyze for 36 h. The product was purified by spinning-plate chromatography with a Chromatotron (4-mm plate, hexane/ethyl acetate (95:5–85:15 gradient)) to yield maize crystals: 0.316 g, 81% isolated yield; ^1H NMR (300 MHz, $CDCl_3$) δ 3.97 (s, 3 H), 5.12 (s, 2 H), 6.91 (d, J = 7.9 Hz, 1 H), 7.13 (m, 1 H), 7.45 (m, 5 H), 7.68 (d, J = 7.3 Hz, 2 H), 7.73 (m, 1 H), 7.78 (dd, J = 4.9, 2.0, 1 H), 8.16 (s, 1 H); $^{13}C\{^1H\}$ NMR (75.4 MHz, $CDCl_3$) δ 55.66, 75.68, 86.84, 105.53, 114.45, 119.09, 125.81, 128.13, 128.32, 128.56, 129.84, 135.56, 136.22, 136.58, 140.46, 143.52, 155.63, 156.18, 189.01; IR (KBr) 3100, 3090, 3068, 3031, 3007, 2943, 2863, 2840, 1638, 1571, 1456, 1432, 1414, 1357, 1288, 1260, 1232, 1060, 1050, 806, 752, 746, 697 cm^{-1}; mp 125.9–127.8 °C; high-resolution mass spectrum (EI) M^+ for $C_{23}H_{17}IO_3S$, calcd 499.9943, found 499.9943 (±0.0007). Anal. Calcd for $C_{23}H_{17}IO_3S$: C, 55.21; H, 3.42. Found: C, 55.38; H, 3.28.

2-Iodo-1-[(2-methoxyethoxy)methoxy]-5-methoxy-3-butyrylnaphthalene (Table II, Entry 9). The reaction mixture was allowed to hydrolyze for 17 h. The product was purified by spinning-plate chromatography with a Chromatotron (4-mm plate, hexane/ethyl acetate (9:1–7:3 gradient)) to yield a gold oil: 0.362 g, 79% isolated yield; ^1H NMR (300 MHz, $CDCl_3$) δ 1.04 (t, J = 7.1 Hz, 3 H), 1.80 (sextet, J = 7.4 Hz, 2 H), 2.98 (t, J = 7.4 Hz, 2 H), 3.42 (s, 3 H), 3.66 (m, 2 H), 4.01 (s, 3 H), 4.13 (m, 2 H), 5.32 (s, 2 H), 6.90 (d, J = 6.9 Hz, 1 H), 7.49 (dd, J = 9.3, 6.9 Hz, 1 H), 7.76 (d, J = 8.4 Hz, 1 H), 8.08 (d, J = 2.4 Hz, 1 H); $^{13}C\{^1H\}$ NMR (125.7 MHz, $CDCl_3$) δ 13.78, 17.69, 44.30, 55.66, 59.10, 70.06, 71.64, 85.83, 99.31, 105.45, 114.87, 118.33, 125.75, 128.48, 130.23, 141.68, 154.51, 155.85, 204.98; IR (neat) 3072, 2962, 2934, 2875, 2839, 1698, 1572, 1456, 1431, 1381, 1359, 1264, 1241, 1211, 1169, 1150, 1117, 1077, 1044, 954, 890, 805 cm^{-1}; high-resolution mass spectrum (EI) M^+ for $C_{19}H_{23}IO_5$, calcd 458.0590, found 458.0590 (±0.0014).

2-Iodo-1-[(2-methoxyethoxy)methoxy]-5-methoxy-3-acetylnaphthalene (Table II, Entry 10). The reaction mixture was allowed to hydrolyze for 36 h. The product was purified by spinning-plate chromatography with a Chromatotron (4-mm plate, hexane/ethyl acetate (9:1–1:1 gradient)) to yield a pale yellow oil: 0.359 g, 84% isolated yield; ^1H NMR (500 MHz, $CDCl_3$) δ 2.71 (s, 3 H), 3.42 (s, 3 H), 3.66 (m, 2 H), 4.01 (s, 3 H), 4.12 (m, 2 H), 5.32 (s, 2 H), 6.90 (d, J = 7.4 Hz, 1 H), 7.50 (t, J = 8.1 Hz, 1 H), 7.77 (d, J = 8.5 Hz, 1 H), 8.20 (s, 1 H); $^{13}C\{^1H\}$ NMR (125.7 MHz, $CDCl_3$) δ 29.76, 55.63, 59.02, 70.01, 71.59, 85.52, 99.28, 105.50, 114.85, 119.25, 125.57, 128.77, 130.40, 140.72, 154.65, 155.86, 201.65; IR (neat) 3073, 2973, 2933, 2878, 2841, 1694, 1572, 1456, 1431, 1383, 1357, 1271, 1254, 1188, 1169, 1155, 1121, 1074, 1045, 949, 805 cm^{-1}; high-resolution mass spectrum (EI) M^+ for $C_{17}H_{19}IO_5$, calcd 430.0277, found 430.0276 (±0.0010).

2-Iodo-1-[(2-methoxyethoxy)methoxy]-5-methoxy-3-benzoylnaphthalene (Table II, Entry 11). The reaction mixture was allowed to hydrolyze for 24 h. The product was purified by spinning-plate chromatography with a Chromatotron (4-mm plate, hexane/ethyl acetate (9:1–7:3 gradient)) to yield a gold oil: 0.405 g, 82% isolated yield; ^1H NMR (300 MHz, $CDCl_3$) δ 3.42 (s, 3 H), 3.66 (m, 2 H), 3.94 (s, 3 H), 4.13 (m, 2 H), 5.36 (s, 2 H), 6.90 (d, J = 7.2 Hz, 1 H), 7.48 (m, 3 H), 7.61 (m, 1 H), 7.84 (m, 3 H), 8.03 (s, 1 H); $^{13}C\{^1H\}$ NMR (125.7 MHz, $CDCl_3$) δ 55.59, 59.05, 70.03, 71.63, 86.85, 99.36, 105.50, 114.75, 119.23, 125.83, 128.27, 128.51, 130.10, 130.55, 133.51, 136.05, 140.74, 154.30, 155.88, 196.88; IR (neat) 3063, 2969, 2934, 2881, 2838, 1669, 1596, 1576, 1570, 1457, 1448, 1358, 1273, 1267, 1261, 1209, 1168, 1109, 1046, 1018, 942, 933, 806, 736 cm^{-1}; high-resolution mass spectrum (EI) M^+ for $C_{22}H_{21}IO_5$, calcd 492.0434, found 492.0433 (±0.0012).

2-Iodo-1-[(2-methoxyethoxy)methoxy]-5-methoxy-3-(2-furoyl)naphthalene (Table II, Entry 12). The reaction mixture was allowed to hydrolyze for 48 h. The product was purified by spinning-plate chromatography with a Chromatotron (4-mm plate, hexane/ethyl acetate (95:5–8:2 gradient)) to yield a gold oil: 0.312 g, 65% isolated yield; ^1H NMR (300 MHz, $CDCl_3$) δ 3.42 (s, 3 H), 3.66 (m, 2 H), 3.98 (s, 3 H), 4.13 (m, 2 H), 5.35 (s, 2 H), 6.58 (m, 1 H), 6.92 (d, J = 7.9 Hz, 1 H), 7.04 (d, J = 2.7 Hz, 1 H), 7.52 (t, J = 8.4 Hz, 1 H), 7.73 (d, J = 1.8 Hz, 1 H), 7.80 (d, J = 8.9 Hz, 1 H), 8.16 (s, 1 H); $^{13}C\{^1H\}$ NMR (75.4 MHz, $CDCl_3$) δ 55.60, 58.97, 69.98, 71.53, 86.81, 99.28, 105.50, 112.52, 114.70, 119.61, 121.97, 125.55, 128.52, 130.34, 139.22, 147.97, 151.42, 154.40, 155.86, 183.65; IR (CCl_4 thin film) 3131, 2937, 2881, 2840, 2820, 1659, 1571, 1565, 1463, 1359, 1296, 1262, 1169, 1160, 1110, 1045, 1011, 948, 916, 820, 805, 787, 763 cm^{-1}; high-resolution mass spectrum (EI) M^+ for $C_{20}H_{19}O_6I$, calcd 482.0226, found 482.0225 (±0.0009).

2-Iodo-1-[(2-methoxyethoxy)methoxy]-5-methoxy-3-(pyrid-3-ylcarbonyl)naphthalene (Table II, Entry 13). The reaction mixture was allowed to hydrolyze for 17 h. The product was purified by spinning-plate chromatography with a Chromatotron (4-mm plate, hexane/ethyl acetate (8:2–4:6 gradient)) to yield a gold oil: 0.391 g, 79% isolated yield; ^1H NMR (300 MHz, $CDCl_3$) δ 3.43 (s, 3 H), 3.67 (m, 2 H), 3.97 (s, 3 H), 4.14 (m, 2 H), 5.37 (s, 2 H), 6.93 (d, J = 7.2 Hz, 1 H), 7.45 (m, 1 H), 7.54 (t, J = 8.0 Hz, 1 H), 7.81 (m, 1 H), 8.06 (s, 1 H), 8.19 (dt, J = 8.6, 2.0 Hz, 1 H), 8.83 (dd, J = 4.9, 1.3 Hz, 1 H), 8.99 (d, J = 2.3 Hz, 1 H); $^{13}C\{^1H\}$ NMR (75.4 MHz, $CDCl_3$) δ 55.60, 59.02, 70.05, 71.58, 86.29, 99.40, 105.68, 114.79, 119.92, 123.54, 125.75, 128.76, 130.39, 131.66, 137.33, 139.39, 151.75, 153.53, 154.65, 155.89, 195.38; IR (CCl_4 thin film) 3062, 3048, 2935, 2881, 2839, 2819, 1672, 1583, 1571, 1457, 1432, 1417, 1358, 1281, 1260, 1168, 1141, 1110, 1045, 1015, 941, 805, 790, 750 cm^{-1}; high-resolution mass spectrum (EI) M^+ for $C_{21}H_{20}INO_5$, calcd 493.0386, found 493.0387 (±0.0010).

2-Iodo-1-[(2-methoxyethoxy)methoxy]-5-methoxy-3-(thien-2-ylcarbonyl)naphthalene (Table II, Entry 14). The reaction mixture was allowed to hydrolyze for 48 h. The product was purified by spinning-plate chromatography with a Chromatotron (4-mm plate, hexane/ethyl acetate (99:1–96:4 gradient)) to yield maize crystals: 0.385 g, 70% isolated yield; ^1H NMR (300 MHz, $CDCl_3$) δ 3.42 (s, 3 H), 3.67 (m, 2 H), 3.97 (s, 3 H), 4.14 (m, 2 H), 5.36 (s, 2 H), 6.91 (d, J = 7.8 Hz, 1 H), 7.13 (dd, J = 4.8, 3.9 Hz, 1 H), 7.44 (dd, J = 4.2, 0.9 Hz, 1 H), 7.52 (t, J = 7.8 Hz, 1 H), 7.79 (m, 2 H), 8.14 (d, J = 2.4 Hz, 1 H); $^{13}C\{^1H\}$ NMR (75.4 MHz, $CDCl_3$) δ 55.58, 58.94, 69.95, 71.55, 86.72, 99.28, 105.50, 114.68, 119.09, 125.57, 128.22, 128.39, 130.13, 135.55, 136.16, 140.23, 143.32, 154.40, 155.79, 188.81; IR (CCl_4 thin film) 3080, 2936, 2880, 2839, 2819, 1656, 1649, 1644, 1457, 1431, 1412, 1359, 1286, 1261, 1168, 1135, 1111, 1046, 994, 931, 792, 779, 772, 766, 757 cm^{-1}; mp 87.9–89.5 °C; high-resolution mass spectrum (EI) M^+ for $C_{20}H_{19}IO_5S$, calcd 497.9998, found 497.9997 (±0.0007). Anal. Calcd for $C_{20}H_{19}IO_5S$: C, 48.21; H, 3.84. Found: C, 48.13; H, 3.83.

2-Iodo-1-[(2-methoxyethoxy)methoxy]-5-methoxy-3-(5-oxohexanoyl)naphthalene (Table II, Entry 15). The reaction mixture was allowed to hydrolyze for 48 h. The product was purified by spinning-plate chromatography with a Chromatotron (4-mm plate, hexane/ethyl acetate (8:2–1:1 gradient)) to yield a gold oil: 0.256 g, 51% isolated yield; ^1H NMR (300 MHz, $CDCl_3$) δ 2.05 (t, J = 7.1 Hz, 2 H), 2.17 (s, 3 H), 2.63 (t, J = 7.0 Hz, 2 H), 3.04 (t, J = 7.2 Hz, 2 H), 3.42 (s, 3 H), 3.66 (m, 2 H), 4.00 (s, 3 H), 4.12 (m, 2 H), 6.89 (d, J = 7.2 Hz, 1 H), 7.48 (dd, J = 9.0, 7.0 Hz, 1 H), 7.75 (d, J = 8.3 Hz, 1 H), 8.08 (s, 1 H); $^{13}C\{^1H\}$ NMR (75.4 MHz, $CDCl_3$) δ 18.25, 29.83, 41.18, 42.50, 55.69, 59.02, 70.12, 71.73, 85.51, 99.39, 105.61, 114.96, 118.41, 125.86, 128.55, 130.39, 141.41, 154.71, 155.95, 204.08, 208.08; IR (CCl_4 thin film) 3072, 2937, 2891, 2840, 1711, 1699, 1571, 1456, 1431, 1406, 1380, 1358, 1266, 1247, 1168, 1147, 1134, 1109, 1074, 1042, 950, 806 cm^{-1}; high-resolution mass spectrum (EI) M^+ for $C_{21}H_{25}IO_6$, calcd 500.0696, found 500.0696 (±0.0012).

2-Iodo-1-[(2-methoxyethoxy)methoxy]-5-methoxy-3-(5-hexenoyl)naphthalene (Table II, Entry 16). The reaction mixture was allowed to hydrolyze for 24 h. The product was purified by spinning-plate chromatography with a Chromatotron (4-mm plate, hexane/ethyl acetate (9:1–7:3 gradient)) to yield a pale yellow oil: 0.297 g, 64% isolated yield; ^1H NMR (300 MHz, $CDCl_3$) δ 1.89 (quintet, J = 7.4 Hz, 2 H), 2.20 (q, J = 7.0 Hz, 2 H), 3.00 (t, J = 7.4 Hz, 2 H), 3.42 (s, 3 H), 3.66 (m, 2 H), 4.01 (s, 3 H), 4.13 (m, 2 H), 5.04 (m, 2 H), 5.32 (s, 2 H), 5.84 (m, 1 H), 6.90 (d, J = 7.9 Hz, 1 H), 7.49 (t, J = 8.0 Hz, 1 H), 7.76 (d, J = 8.9 Hz, 1 H), 8.08 (s, 1 H); $^{13}C\{^1H\}$ NMR (75.4 MHz, $CDCl_3$) δ 22.98, 32.75, 41.32, 55.43, 58.77, 69.78, 71.41, 85.49, 99.08, 105.27, 114.54, 115.08, 118.04, 125.46, 128.30, 129.94, 137.65, 141.41, 154.31, 155.54, 204.32; IR (CCl_4 thin film) 3076, 2974, 2935, 2889, 2840, 2820, 1698, 1572, 1456, 1432, 1358, 1266, 1169, 1149, 1110, 1086, 1075, 1045, 953, 915, 805, 788, 763, 750 cm^{-1}; high-resolution mass spectrum (EI)

M^+ for $C_{21}H_{25}IO_5$, calcd 484.0747, found 484.0746 (±0.0007).

Preparation of Compounds in Table III. 3-Acetyl-2-iodo-5-methoxy-1,4-naphthoquinone (Table III, Entry 1). To a solution of 2-iodo-1-[(2-methoxyethoxy)methoxy]-5-methoxy-3-acetylnaphthalene (Table II, entry 10) (0.0925 g, 0.21 mmol) in acetone (20 mL) was added Jones' reagent[8] (3 mL), and the solution was allowed to stir at room temperature for 30 min, during which time blue-green Cr(III) salts precipitated. Isopropyl alcohol (ca. 3 mL) was added dropwise to destroy excess chromic acid followed by sodium bicarbonate (ca. 4 g), and the suspension was allowed to stir 5 min. The suspension was filtered and the filter cake washed with acetone (2 × 20 mL). The bright yellow filtrate was evaporated in vacuo (rotary evaporator), and the yellow residue was dissolved in ether (200 mL), washed with water, saturated $NaHCO_3$, and brine, and dried over $MgSO_4$. The solvent was removed (rotary evaporator) to yield a bright yellow oil. The oil was purified by spinning-plate chromatography with a Chromatotron (2-mm plate, hexane/ethyl acetate (8:2–6:4 gradient)) to yield a bright yellow solid: 0.055 g, 74% isolated yield; ^1H NMR (300 MHz, $CDCl_3$) δ 2.56 (s, 3 H), 4.02 (s, 3 H), 7.36 (dd, J = 8.3, 2.0 Hz, 1 H), 7.71 (t, J = 8.6 Hz, 1 H), 7.84 (dd, J = 8.0, 1.7 Hz, 1 H); $^{13}C\{^1H\}$ NMR (75.4 MHz, $CDCl_3$) δ 29.22, 56.61, 114.51, 118.50, 118.66, 121.22, 131.72, 135.61, 157.29, 160.31, 178.56, 178.89, 199.85; IR (KBr) 2991, 2961, 2922, 2853, 1714, 1663, 1644, 1601, 1581, 1477, 1458, 1440, 1268, 1246, 1142, 1109, 1033, 788, 735 cm^{-1}; mp 185–190 °C (decomposed); high-resolution mass spectrum (EI) M^+ for $C_{13}H_9IO_4$, calcd 355.9546, found 355.9545 (±0.0010).

2-Iodo-5-methoxy-3-butyryl-1,4-naphthoquinone (Table III, Entry 2). To a solution of 2-iodo-1-[(2-methoxyethoxy)methoxy]-5-methoxy-3-butyrylnaphthalene (Table II, entry 9) (0.088 g, 0.192 mmol) in acetone (20 mL) was added Jones's reagent[8] (3 mL), and the solution was allowed to stir at room temperature for 30 min, during which time blue-green Cr(III) salts precipitated. Isopropyl alcohol (ca. 3 mL) was added dropwise to destroy excess chromic acid followed by sodium bicarbonate (ca. 4 g), and the suspension was allowed to stir 5 min. The suspension was filtered and the filter cake washed with acetone (2 × 20 mL). The bright yellow filtrate was evaporated in vacuo (rotary evaporator), and the yellow residue was dissolved in ether (200 mL), washed with water, saturated $NaHCO_3$, and brine, and dried over $MgSO_4$. The solvent was removed (rotary evaporator) to yield a bright yellow oil. The oil was purified by spinning-plate chromatography with a Chromatotron (2-mm plate, hexane/ethyl acetate (9:1–1:1 gradient)) to yield a bright yellow solid: 0.056 g, 76% isolated yield; ^1H NMR (300 MHz, $CDCl_3$) δ 1.03 (t, J = 7.4 Hz, 3 H), 1.81 (sextet, J = 7.2 Hz, 2 H), 2.81 (t, J = 7.2 Hz, 2 H), 4.02 (s, 3 H), 7.36 (dd, J = 8.7, 0.9 Hz, 1 H), 7.70 (t, J = 8.0 Hz, 1 H), 7.83 (dd, J = 7.7, 1.1 Hz, 1 H); $^{13}C\{^1H\}$ NMR (125.7 MHz, $CDCl_3$) δ 13.62, 16.25, 43.71, 56.58, 114.94, 118.45, 118.59, 121.13, 131.67, 135.56, 157.31, 160.26, 178.55, 179.05, 202.15; IR (CCl_4 thin film) 3013, 2964, 2933, 2877, 2841, 1713, 1666, 1649, 1600, 1581, 1473, 1465, 1303, 1271, 1252, 1139, 1023, 737 cm^{-1}; mp 129.0–130.2 °C; high-resolution mass spectrum (EI) M^+ for $C_{15}H_{13}IO_4$, calcd 383.9859, found 383.9858 (±0.0011).

2-Iodo-5-methoxy-3-benzoyl-1,4-naphthoquinone (Table III, Entry 3). To a solution of 2-iodo-1-[(2-methoxyethoxy)methoxy]-5-methoxy-3-benzoylnaphthalene (Table II, entry 11) (0.052 g, 0.106 mmol) and Celite (0.300 g) in acetone (20 mL) was added Jones's reagent[8] (1.5 mL), and the solution was allowed to stir at room temperature for 30 min, during which time blue-green Cr(III) salts precipitated. Isopropyl alcohol (ca. 3 mL) was added dropwise to destroy excess chromic acid followed by sodium bicarbonate (ca. 4 g), and the suspension was allowed to stir 5 min. The suspension was filtered and the filter cake washed with acetone (2 × 20 mL). The bright yellow-orange filtrate was evaporated in vacuo (rotary evaporator), and the yellow-orange residue was dissolved in ether (200 mL), washed with water, saturated $NaHCO_3$, and brine, and dried over $MgSO_4$. The solvent was removed (rotary evaporator) to yield a bright yellow-orange oil. The oil was purified by spinning-plate chromatography with a Chromatotron (2-mm plate, hexane/ethyl acetate (8:2–6:4 gradient)) to yield a bright yellow-orange solid: 0.032 g, 73% isolated yield; ^1H NMR (500 MHz, $CDCl_3$) δ 3.98 (s, 3 H), 7.37 (d, J = 8.3 Hz, 1 H), 7.50 (m, 2 H), 7.62 (m, 1 H), 7.74 (t, J = 8.1 Hz, 1 H), 7.89 (d, J = 7.7 Hz, 1 H), 7.94 (m, 2 H); $^{13}C\{^1H\}$ NMR (125.7 MHz, $CDCl_3$) δ 56.51, 117.18, 118.56, 118.66, 121.14, 129.04, 129.47, 131.81, 133.43, 134.45, 135.58, 156.28, 160.38, 178.40, 178.98, 192.54; IR (KBr) 3081, 3073, 3067, 2970, 2967, 2932, 2839, 1682, 1665, 1646, 1606, 1598, 1578, 1472, 1449, 1308, 1276, 1263, 1236, 1152, 785, 736, 718 cm^{-1}; mp 185–190 °C (decomposed); high-resolution mass spectrum (EI) M^+ for $C_{18}H_{11}IO_4$, calcd 417.9702, found 417.9701 (±0.0008).

2-Iodo-5-methoxy-3-(5-oxohexanoyl)-1,4-naphthoquinone (Table III, Entry 4). To a solution of 2-iodo-1-[(2-methoxyethoxy)methoxy]-5-methoxy-3-(5-oxohexanoyl)naphthalene (Table II, entry 15) (0.0584 g, 0.117 mmol) in acetone (20 mL) was added Jones's reagent[8] (2 mL), and the solution was allowed to stir at room temperature for 30 min, during which time blue-green Cr(III) salts precipitated. Isopropyl alcohol (ca. 3 mL) was added dropwise to destroy excess chromic acid followed by sodium bicarbonate (ca. 4 g), and the suspension was allowed to stir 5 min. The suspension was filtered and the filter cake washed with acetone (2 × 20 mL). The bright yellow filtrate was evaporated in vacuo (rotary evaporator), and the yellow residue was dissolved in ether (200 mL), washed with water, saturated $NaHCO_3$, and brine, and dried over $MgSO_4$. The solvent was removed (rotary evaporator) to yield a bright yellow oil. The oil was purified by spinning-plate chromatography with a Chromatotron (2-mm plate, hexane/ethyl acetate (8:2–6:4 gradient)) to yield a bright yellow solid: 0.038 g, 76% isolated yield; ^1H NMR (300 MHz, $CDCl_3$) δ 2.04 (quintet, J = 6.6 Hz, 2 H), 2.18 (s, 3 H), 2.64 (t, J = 7.1 Hz, 2 H), 2.88 (t, J = 7.1 Hz, 2 H), 4.02 (s, 3 H), 7.36 (dd, J = 9.0, 1.7 Hz, 1 H), 7.70 (t, J = 8.1 Hz, 1 H), 7.82 (dd, J = 7.3, 1.5 Hz, 1 H); $^{13}C\{^1H\}$ NMR (75.4 MHz, $CDCl_3$) δ 16.78, 29.97, 40.55, 42.15, 56.63, 115.12, 118.37, 118.70, 121.15, 131.60, 135.67, 156.97, 160.27, 178.39, 178.99, 201.77, 208.08; IR (CCl_4 thin film) 2949, 2926, 2875, 2855, 1713, 1674, 1653, 1583, 1458, 1384, 1272, 1248, 1151, 1050, 1028, 985, 735 cm^{-1}; mp 145.0–146.6 °C; high-resolution mass spectrum (EI) M^+ for $C_{17}H_{15}IO_5$, calcd 425.9964, found 425.9965 (±0.0013).

2-Iodo-5-methoxy-3-(5-hexenoyl)-1,4-naphthoquinone (Table III, Entry 5). To a solution of 2-iodo-1-[(2-methoxyethoxy)methoxy]-5-methoxy-3-(5-hexenoyl)naphthalene (Table II, entry 16) (0.0714 g, 0.147 mmol) and Celite (0.300 g) in acetone (20 mL) was added Jones's reagent[8] (2 mL), and the solution was allowed to stir at room temperature for 40 min, during which time blue-green Cr(III) salts precipitated. Isopropyl alcohol (ca. 3 mL) was added dropwise to destroy excess chromic acid followed by sodium bicarbonate (ca. 4 g), and the suspension was allowed to stir 5 min. The suspension was filtered and the filter cake washed with acetone (2 × 20 mL). The bright yellow-orange filtrate was evaporated in vacuo (rotary evaporator), and the yellow-orange residue was dissolved in ether (200 mL), washed with water, saturated $NaHCO_3$, and brine, and dried over $MgSO_4$. The solvent was removed (rotary evaporator) to yield a bright yellow-orange oil. The oil was purified by spinning-plate chromatography with a Chromatotron (2-mm plate, hexane/ethyl acetate (8:2–6:4 gradient)) to yield a bright yellow solid: 0.043 g, 71% isolated yield; ^1H NMR (300 MHz, $CDCl_3$) δ 1.89 (quintet, J = 7.3 Hz, 2 H), 2.18 (q, J = 7.2 Hz, 2 H), 2.84 (t, J = 7.4 Hz, 2 H), 4.02 (s, 3 H), 5.03 (m, 2 H), 5.82 (m, 1 H), 7.36 (d, J = 8.1 Hz, 1 H), 7.70 (t, J = 7.9 Hz, 1 H), 7.83 (d, J = 7.9 Hz, 1 H); $^{13}C\{^1H\}$ NMR (75.4 MHz, $CDCl_3$) δ 21.83, 32.79, 41.06, 56.58, 114.94, 115.39, 118.40, 118.58, 121.08, 131.63, 135.56, 137.68, 157.24, 160.22, 178.45, 178.97, 202.03; IR (KBr) 3079, 2972, 2958, 2944, 2937, 2924, 2917, 2901, 2851, 1711, 1698, 1670, 1659, 1645, 1599, 1582, 1574, 1474, 1466, 1431, 1388, 1299, 1267, 1253, 1135, 1024, 827, 781, 733 cm^{-1}; mp 116.6–118.9 °C; high-resolution mass spectrum (EI) M^+ for $C_{17}H_{15}IO_4$, calcd 410.0015, found 410.0014 (±0.0004).

2-Iodo-5-methoxy-3-(2-furoyl)-1,4-naphthoquinone (Table III, Entry 6). To a solution of 2-iodo-1-[(2-methoxyethoxy)methoxy)-5-methoxy-3-(2-furoyl)naphthalene (Table II, entry 12) (0.0644 g, 0.13 mmol) and Celite (0.300 g) in acetone (20 mL) was added Jones's reagent[8] (2 mL), and the solution was allowed to stir at room temperature for 40 min, during which time blue-green Cr(III) salts precipitated. Isopropyl alcohol (ca. 3 mL) was added dropwise to destroy excess chromic acid followed by sodium bicarbonate (ca. 4 g), and the suspension was allowed to stir 5 min. The suspension was filtered and the filter cake washed with acetone (2 × 20 mL). The bright yellow-orange filtrate was evaporated in vacuo (rotary evaporator), and the yellow-orange residue was dissolved in methylene chloride (300 mL), washed with water, saturated $NaHCO_3$, and brine, and dried over $MgSO_4$. The solvent was removed (rotary evaporator) to yield a bright orange-yellow solid. The solid was washed with ether (5 mL) and dried in vacuo to yield a bright orange-yellow solid (recrystallized from acetone to yield orange crystals): 0.044 g, 82% isolated yield; ^1H NMR (300 MHz, $CDCl_3$) δ 4.00 (s, 3 H), 6.62 (dd, J = 3.5, 2.0 Hz, 1 H), 7.36 (m, 2 H), 7.64 (d, J = 1.8 Hz, 1 H), 7.73 (t, J = 8.6 Hz, 1 H), 7.88 (d, J = 7.8 Hz, 1 H); $^{13}C\{^1H\}$ NMR (125.7 MHz, $CDCl_3$) δ 56.56, 113.09, 117.84, 118.63, 118.67, 120.36, 121.22, 131.83, 135.53, 148.07, 150.00, 154.92, 160.41, 178.63, 178.56, 183.05; IR (KBr) 3149, 3131, 3102, 2981, 2841, 1670, 1667, 1663, 1642, 1570, 1562, 1460, 1446, 1285, 1269, 1251, 1227, 1146, 1446, 1438, 1285, 1269, 1251, 1227, 1147, 1018, 795, 778, 737 cm^{-1}; mp 236–240 °C (decomposed); high-resolution mass spectrum (EI) M^+ for $C_{16}H_9IO_5$, calcd 407.9495, found 407.9494 (±0.0008).

2-Iodo-5-methoxy-3-(pyrid-3-ylcarbonyl)-1,4-naphthoquinone (Table III, Entry 7). To a solution of 2-iodo-1-[(2-methoxyethoxy)methoxy]-5-methoxy-3-(pyrid-3-ylcarbonyl)naphthalene (Table II, entry 13) (0.0644 g, 0.13 mmol) and Celite (0.300 g) in acetone (20 mL) was added Jones's reagent[8] (2 mL), and the solution was allowed to stir at room temperature for 35 min, during which time blue-green Cr(III) salts precipitated. Isopropyl alcohol (ca. 3 mL) was added dropwise to destroy

excess chromic acid followed by sodium bicarbonate (ca. 4 g), and the suspension was allowed to stir 5 min. The suspension was filtered and the filter cake washed with acetone (2 × 20 mL). The bright yellow-orange filtrate was evaporated in vacuo (rotary evaporator), and the yellow-orange residue was dissolved in methylene chloride (200 mL), washed with water, saturated $NaHCO_3$, and brine, and dried over $MgSO_4$. The solvent was removed (rotary evaporator) to yield a bright yellow-orange solid. The solid was washed with ether (5 mL) and dried in vacuo to yield a bright yellow-orange solid: 0.045 g, 82% isolated yield; ^1H NMR (300 MHz, $CDCl_3$) δ 3.99 (s, 3 H), 7.39 (dd, J = 8.3, 1.9 Hz, 1 H), 7.48 (m, 1 H), 7.75 (t, J = 8.0 Hz, 1 H), 7.90 (dd, J = 8.4, 1.4 Hz, 1 H), 8.26 (dt, J = 8.7, 1.9 Hz, 1 H), 8.84 (dd, J = 4.9, 2.2 Hz, 1 H), 9.10 (d, J = 1.4 Hz, 1 H); $^{13}C\{^1H\}$ NMR (75.4 MHz, $CDCl_3$) δ 56.55, 117.83, 118.44, 118.75, 121.28, 123.99, 129.15, 131.71, 135.78, 136.28, 150.90, 154.46, 155.13, 160.44, 178.11, 178.92, 191.55; IR (KBr) 2999, 2950, 2930, 2842, 1676, 1668, 1654, 1644, 1602, 1583, 1577, 1474, 1274, 1242, 1194, 1154, 1052, 1038, 988, 795, 787, 761, 736, 700 cm^{-1}; mp 180-185 °C (decomposed); high-resolution mass spectrum (EI) M^+ for $C_{17}H_{10}INO_4$, calcd 418.9655, found 418.9654 (±0.0006).

2-Iodo-5-methoxy-3-(thien-2-ylcarbonyl)-1,4-naphthoquinone (Table III, Entry 8). To a solution of 2-iodo-1-[(2-methoxyethoxy)methoxy)-5-methoxy-3-(thien-2-ylcarbonyl)naphthalene (Table II, entry 14) (0.1004 g, 0.2 mmol) in acetone (20 mL) was added Jones's reagent[8] (3 mL), and the solution was allowed to stir at room temperature for 40 min, during which time blue-green Cr(III) salts precipitated. Isopropyl alcohol (ca. 3 mL) was added dropwise to destroy excess chromic acid followed by sodium bicarbonate (ca. 4 g), and the suspension was allowed to stir 5 min. The suspension was filtered and the filter cake washed with acetone (2 × 20 mL). The bright yellow-orange filtrate was evaporated in vacuo (rotary evaporator), and the yellow-orange residue was dissolved in methylene chloride (200 mL), washed with water, saturated $NaHCO_3$, and brine, and dried over $MgSO_4$. The solvent was removed (rotary evaporator) to yield a bright yellow solid. The solid was washed with diethyl ether (5 mL) and dried in vacuo to yield a bright yellow-orange solid (recrystallized from ether to yield bright orange crystals): 0.075 g, 89% isolated yield; ^1H NMR (300 MHz, $CDCl_3$) δ 3.99 (s, 3 H), 7.15 (dd, J = 5.4, 3.5 Hz, 1 H), 7.37 (m, 1 H), 7.64 (dd, J = 4.0, 0.8 Hz, 1 H), 7.73 (t, J = 8.1 Hz, 1 H), 7.80 (dd, J = 5.4, 1.2 Hz, 1 H), 7.89 (dd, J = 8.4, 1.4 Hz, 1 H); $^{13}C\{^1H\}$ NMR (75.4 MHz, $CDCl_3$) δ 56.56, 117.72, 118.58, 118.73, 121.18, 128.62, 131.80, 135.15, 135.58, 136.10, 140.40, 155.68, 160.41, 178.45, 178.59, 184.47; IR (KBr) 3111, 3090, 2975, 2839, 1664, 1643, 1617, 1599, 1578, 1473, 1432, 1411, 1358, 1306, 1267, 1236, 1189, 1152, 1043, 829, 775, 737, 726 cm^{-1}; mp 237.5-238.6 °C. Anal. Calcd for $C_{16}H_9IO_4S$: C, 45.30; H, 2.14. Found: C, 45.32; H, 1.97.

Acknowledgment. We thank the National Institutes of Health (Grant GM 34917), the National Cancer Institute (Training Grant NCI T32CA09112), Eli Lilly, and the American Cancer Society for support.

Cyclic Vanadium(V) Alkoxide: An Analogue of the Ribonuclease Inhibitors

Debbie C. Crans,* Robert A. Felty, and Mary M. Miller

Contribution from the Department of Chemistry, Colorado State University, Fort Collins, Colorado 80523. *Received February 15, 1990*

Abstract: This article reports the preparation and structural characterization of the first cyclic vanadium alkoxide. This pinacol-vanadium(V) complex was formed from $VOCl_3$ and pinacol in methylene chloride and recrystallized from chloroform in 83% yield. The vanadium atoms in the complex were pentacoordinate in a distorted trigonal-bipyrimid geometry achieved by dimerization through bridging of one of the oxygen atoms of each of the pinacol moieties. The vanadium(V)-pinacol crystals are prismatic and possess the following crystalline properties: $P2_1/c$, Z = 2, a = 6.642 (3) Å, b = 9.834 (2) Å, c = 13.972 (7) Å, β = 99.06 (9)°, 153 K, R = 0.026. This compound is the first example of the trigonal-bipyramidal geometry of an alkyl vanadium derivative that is presumed to be a good transition-state analogue for enzymes catalyzing hydrolytic organic phosphate reactions. ^1H, ^{13}C, and ^{51}V VT-NMR studies suggest the solution structure is also dimeric in vanadium. The structural properties of the vanadium-pinacol complex are compared to the corresponding organic phosphates and the vanadate-uridine ribonuclease complex. The major structural differences between organic phosphate compounds and the vanadium-pinacol complex are the nuclearity and asymmetry in the vanadium(V)-pinacol complex. The vanadium-oxygen bond lengths to the pinacol differ by 0.19 Å, whereas the phosphate compound is symmetric. The observed asymmetry is also observed in the ribonuclease-uridine-vanadate complex and may be important for the tight binding of the vanadate-uridine complex by ribonuclease.

Introduction

Vanadium is a dietary trace element with no known function.[1] Vanadium at low concentrations is beneficial, whereas at high concentrations it is toxic. Its beneficial effects include reduction in cardiovascular degeneration; it is a known insulin mimetic agent and an epidermal growth factor.[1] Vanadium affects cAMP levels, protein kinase activity, and protein phosphatase activity.[1] Very little is currently understood about the mechanisms of action of vanadium in mammals and plants. It is very likely that the chemical and structural properties of the vanadium will dictate the biological activities of vanadium derivatives.[1-4] Vanadium(V) in the form of monomeric vanadate is a potent inhibitor for a series of enzymes including ATPases, phosphatases, and nucleases.[1,2,5] It has been suggested that vanadate coordinates so tightly to the enzyme (1000-fold tighter than subtrate) because it can easily adopt a trigonal-bipyramidal geometry and this geometry simulates a hydrolytic transition state (or a high-energy intermediate) in the enzyme reaction.[5] The initial suggestion by Linquist et al. in 1973[5] was presented without any structural precedence for such

(1) For reviews, see: (a) Nechay, B. R.; Nanninga, L. B.; Nechay, P. S. E.; Post, R. L.; Grantham, J. J.; Macara, I. G.; Kubena, L. F.; Phillips, T. D.; Nielsen, F. H. *Fed. Proc., Fed. Am. Soc. Exp. Biol.* **1986**, *45*, 123-32. (b) Chasteen, N. D. *Struct. Bonding (Berlin)* **1983**, *53*, 105-38. (c) Boyd, D. W.; Kustin, K. *Adv. Inorg. Biochem.* **1984**, *6*, 311-65.

(2) Crans, D. C.; Bunch, R. L.; Theisen, L. T. *J. Am. Chem. Soc.* **1989**, *111*, 7597-607.

(3) (a) Crans, D. C.; Willging, E. M.; Butler, S. R. *J. Am. Chem. Soc.* **1990**, *112*, 427-32. (b) Crans, D. C.; Simone, C. M.; Saha, A. K.; Glew, R. H. *Biochem. Biophys. Res. Commun.* **1989**, *165*, 246-50. (c) Crans, D. C.; Schelble, S. M. *Biochemistry* **1990**, *29*, 6698-706.

(4) (a) Crans, D. C.; Tawara, J.; Wong, C. H.; Drueckhammer, D. G. *Abstracts of Papers*, 194th National Meeting of the American Chemical Society, New Orleans, LA, 1987; INOR 345 (manuscript submitted to *J. Am. Chem. Soc.*). (b) Drueckhammer, D. G.; Durrwachter, J. R.; Pederson, R. L.; Crans, D. C.; Daniels, L.; Wong, C. H. *J. Org. Chem.* **1989**, *54*, 70-7.

(5) Linquist, R. N.; Lynn, J. L., Jr.; Lienhard, G. E. *J. Am. Chem. Soc.* **1973**, *95*, 8762-8.

0002-7863/91/1513-265$02.50/0