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Novel Reactivity of SeO_2 with 1,3-Dienes: Selenophene Formation

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Abstract: A novel and efficient method for the synthesis of selenophenes is disclosed. Selenophenes were synthesized in high yields in a single operation from 1,3-dienes containing a carbonyl group at the C-1 position and selenium dioxide. The bidirectional synthesis of selenophenes can also be demonstrated using this method. The selenophene is believed to form via a [4 + 2] cycloaddition between diene and selenium dioxide.

Five-membered ring heteroaromatic compounds, such as furan, thiophene, oxazole, imidazole, and thiazole, continue to attract significant synthetic efforts due to their important performance in a variety of disciplines.[1] Recently, the synthesis of oligomers and polymers of these heterocycles has drawn much attention because of their promising optical and electronic properties.[2] Compared to other congeners, however, selenophenes and their derivatives have drawn less attention.[3] In this report we wish to disclose a novel synthesis of selenophenes from the reaction of conjugated 1,3-dienes with selenium dioxide (SeO_2).

The reaction between SeO_2 and 1,3-dienes is known to form selenino lactone via a [4 + 2] cycloaddition, but little is known about the subsequent chemistry of this adduct. Mock has shown that the reaction of SeO_2 with 2,3-dimethylbutadiene produces a selenino lactone at room temperature, the structure of which was confirmed by the reduction of the Se—O bond followed by the formation of the corresponding benzyl selenide.[4] Recently we have shown that selenino lactone **2** derived from the reaction of 1,3-diene **1** with SeO_2 spontaneously transformed to cyclic selenites **3** and **4** (Scheme 1).[5] As opposed to these examples, the 1,3-dienes with an electron-withdrawing group at the C-1 position have been shown to react with SeO_2 to form furans and selenophenes. Takeda and co-workers disclosed that the reaction of 2,4-alkadienoic esters with SeO_2 at elevated temperatures produced a mixture of furan (major) and selenophene (minor).[6] Wender and co-workers reported that selenophenes could be generated from reaction of SeO_2 with β,γ-unsaturated ketones.[7] In the latter case the β,γ-unsaturated carbonyl compounds were oxidized by SeO_2 to the corresponding 1,3-diene, which reacted further with SeO_2. On the basis of these observations, we anticipated that 1,3-dienes with a carbonyl substituent at the C-1 position should be general substrates for the SeO_2-mediated selenophene synthesis.

Our investigation into this novel selenophene forming reaction began with an efficient preparation of 1,3-diene dienes **5** from (1*S*)-verbenone **10** and a variety of aromatic aldehydes under thermodynamic aldol condensation conditions (KOH, MeOH, 60 °C) (Table 1).[8] With these dienes on hand, we started to study the selenophene formation with the simplest diene **5a** (Scheme 2). When the reaction was performed in dioxane at 60 °C, three main products were obtained: selenophene **6a**, furan **7**, and the intensely red-colored diselenide **8**. Compounds **6a**, **7**, and **8** were fully characterized by ^1H, ^{13}C, ^{77}Se (**6a** and **8** only) NMR, and X-ray crystallography, respectively. Although not directly observed, the selenino lactone **9** seems to be a common intermediate to **6a**, **7**, and **8**. Reaction of a variety of verbenone-derived dienes (**5b**—**k**) under similar conditions consistently gave the corresponding selenophene, furan, and diselenide derivatives.

Optimization experiments have identified that the addition of pyridine (1,4-dioxane/pyridine, 5:1) to the reaction minimizes or, in most cases, suppresses the formation of the furan and diselenide. Under these conditions, selenophene **6a** was obtained in 86% yield. Other amine bases, such as diisopropylamine, triethylamine, and diisopropylethylamine, are not as effective as pyridine. Alkoxide base, such as potassium *tert*-butoxide, prevents the formation of selenophene.

Typically, the reactions of dienes **5** with SeO_2 (20 equiv) in 1,4-dioxane/pyridine (5:1) at 80 °C lead to high yields of selenophenes **6** (Table 1).[8] This protocol appears to be general for dienes we examined. Both the dienes with electron-withdrawing and electron-donating substituents on the aromatic ring give selenophenes in high yields. Longer reaction times are required for dienes with more

(1) (a) Belen'kii, L. I.; Kruchkovskaya, N. D.; Gramenitskaya, V. N. *Adv. Heterocycl. Chem*. **1999**, *73*, 296—395. (b) For a comprehensive listing of reviews of five-membered ring heterocycles from 1982 to 1995, see *J. Heterocycl. Chem*. **1999**, *36*, 559—561. (c) *Progress in Heterocyclic Chemistry*; Gribble, G. W.; Gilchrist, T. L., Eds; Elsevier: Amsterdam, 1999; Vol. 11.

(2) (a) Tovar, J.; Swager, T. M. *Adv. Mater*. **2001**, *13*, 1775—1780. (b) Zhu, S. S.; Kingsborough, R. P.; Swager, T. M. *J. Mater. Chem*. **1999**, *9*, 2123-2131. (c) Ng, S. C.; Chan, H. S. O.; Ong, T. T.; Kumura, K.; Mazaki, Y.; Kobayashi, K. *Macromolecules* **1998**, *31*, 1221—1228 and references therein. (d) Mahatsekake, C.; Catel, J. M.; Andrieu, C. G.; Ebel, M.; Mollier, Y.; Tourillon, G. *Phosphorus, Sulfur, Silicon* **1990**, *47*, 35—41. (e) Vogel, E.; Frode, C.; Breihan, A.; Schmickler, H.; Lex, J. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2609—2612.

(3) (a) Gronowitz, S. *Phosphorus, Sulfur Silicon Relat. Elem*. **1998**, *136*, *137*, *138*, 59—90 and references therein. (b) Aqad, E.; Lakshmikantham, M. V.; Cava, M. P. *Org. Lett*. **2001**, *3*, 4283—4285. (c) Welch, M.; Phillips, R. S. *Bioorg. Med. Chem. Lett*. **1999**, *9*, 637—640. (d) Shilkina, T. A.; Papernaya, L. K.; Deryagina, E. N. *Russ. J. Gen. Chem*. **1998**, *68*, 831. (e) Koketsu, M.; Miyajima, Y.; Ishihara, H. *Chem. Lett*. **1998**, 645—646. (f) Sashida, H.; Sadamori, K.; Tshuchiya, T. *Synth. Commun*. **1998**, *28*, 713—727. (g) Deryagina, E. N.; Kochervin, N. A. *Russ. J. Gen. Chem*. **1997**, *67*, 1582. (h) Lyons, J. E.; Schiesser, C. H.; Sutej, K. *J. Org. Chem*. **1993**, *58*, 5632—5638. (i) Nakayama, J.; Murai, F.; Hoshino, M.; Ishii, A. *Tetrahedron Lett*. **1988**, *29*, 1399—1400. (j) Fagan, P. J.; Nugent, W. A. *J. Am. Chem. Soc*. **1988**, *110*, 2310—2312. (k) Kulik, W.; Verkruijsse, H. D.; de Jong, R. L. P.; Hommes, H.; Brandsma, L. *Tetrahedron Lett*. **1983**, *24*, 2203—2204. (l) See also *The Chemistry of Organic Selenium and Tellurium Compounds*; Patai, S.; Rappoport, Z., Eds.; Wiley: New York, 1986.

(4) Mock, W. L.; McCausland, J. H. *Tetrahedron Lett*. **1968**, *3*, 91—392.

(5) Nguyen, T. M.; Lee, D. *Org. Lett*. **2001**, *3*, 3161—3163.

(6) Tsuboi, S.; Mimura, S.; Ono, S.; Watanabe, K.; Takeda, A. *Bull. Chem. Soc. Jpn*. **1987**, *60*, 1807—1812.

(7) Wender, P. A.; Lee, D.; Lal, T. K.; Horwitz, S. B.; Rao, S. *Bioorg. Med. Chem. Lett*. **1997**, *7*, 1941—1944. An intriguing selenophene synthesis from carvone, an γ,δ-unsaturated ketone, was reported. See Schmitt, J.; Seilert, J. *Ann. Chem*. **1949**, *562*, 15—23.

(8) Please see Experimental Section for details. We chose these dienes on the basis of their prompt and efficient synthesis. Another reason for choosing these dienes is that they do not have any oxidizable allylic protons or enolizable protons.

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SCHEME 1

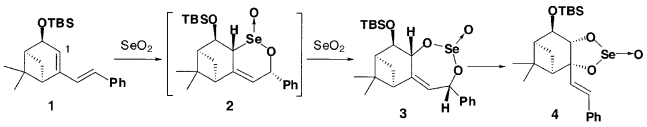
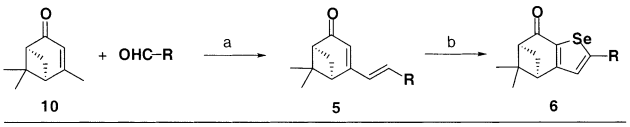


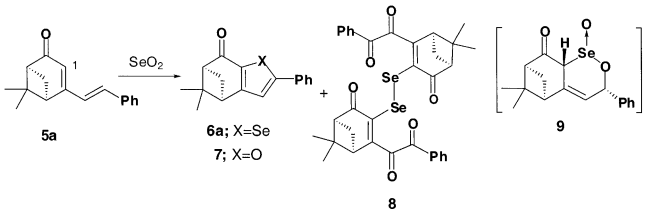
TABLE 1. Formation of Selenophenes 6



entry	aldehyde (**R**)	time (h)	yield for **5** (%)	time (h)	yield for **6** (%)
a		6	92	15	86
b		0.25	95	84	67
c		1	95	72	79
d		2	77	18	45
e		6	98	12	63
f		6	94	10	55
g		6	91	10	65
h		6	94	10	90
i		10	48	3	48
j		6	86	18	48
k		10	71	1	5[c]

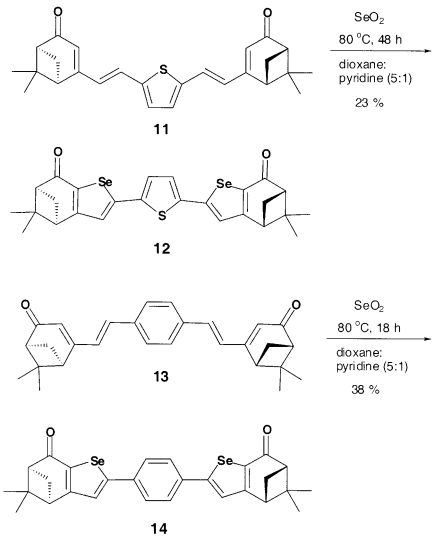
[a] RCHO, KOH, MeOH, 60 °C. [b] SeO_2, dioxane:pyridine (5:1), 80 °C. [c] The corresponding furan derivative was obtained in 41% yield.

SCHEME 2



electron-withdrawing aromatic substituents. This observation is consistent with our hypothesis of the initial [4 + 2] cycloaddition between diene and SeO_2. Electron-donating substituents on the aromatic ring should increase the reactivity of the diene, whereas electron-withdrawing substituents should decrease it. Triene **5j**, derived from cinnamaldehyde, produces selenophene **6j** in moderate yield (48%), without any signs of the other selenophene regioisomer. The pivaldehyde-derived diene

SCHEME 3



5k yielded only 5% of selenophene **6k**, with the corresponding furan as the major product (41%) within very short reaction time. This reversal of the trend, so as to generate more furan is not currently understood.

Our protocol would be flexible in that various aromatic and heteroaromatic spacers could potentially be used in the synthesis of oligoselenophenes. To demonstrate the effectiveness of this approach, the bis-aldol products **11** and **13** were prepared from 2,5-thiophenedicarboxaldehyde and terephthaldicarboxaldehyde with verbenone, respectively. Treatment of these tetraenes with SeO_2 produced the bis-selenophenes **12** and **14** in 23% and 38% yield, respectively (Scheme 3). In these reactions, the monoselenophenes were initially observed, which in turn were eventually converted to the bis-selenophenes.

To the best of our knowledge, this is the first efficient synthesis of selenophenes from dienes with SeO_2 under mild neutral or slightly basic reaction conditions. Without much precedent, it is not possible to propose a detailed mechanism for the formation of selenophenes **6**, furan **7**, and diselenide **8.** Our working hypothesis is that **6**, **7**, and **8** are formed from the common selenino lactone intermediate **9**, the [4 + 2] cycloaddition product of SeO_2 with diene **5a** (Scheme 2). In contrast to the Mock precedent in which the Diels−Alder type reaction occurred at room temperature,[4] the reaction of dienes **5** with SeO_2 occurs only at higher temperature (>50 °C), probably due to the deactivating nature of the carbonyl substituent at the C-1 position. The intermediate **9** then undergoes a series of transformations via yet unknown mechanisms leading to selenophenes **6**, furan **7**, and diselenide **8**, respectively. The formation of diselenide **8** strongly suggests the intermediacy of the selenino lactone **9** together with the involvement of complicated redox processes, involving a disproportionation mechanism of selenium species of different oxidation states. It is also intriguing how pyridine is involved in the reaction to promote the formation of selenophene and suppress the formation of furan and diselenide.

Interestingly, the carbonyl group at the C-1 position, although detrimental for the initial [4 + 2] cycloaddition reaction, is absolutely essential for the formation of selenophenes and furans. It is assumed that the in-

creased acidity of the α-proton to the carbonyl group is crucial to initiate the decomposition of the selenino lactone intermediate to the final products. This rationale is supported by the experiments in Scheme 1 where the reaction of TBS-ether **1** with SeO_2 at room temperature under otherwise identical reaction conditions afforded only cyclic selenites **3** and **4** without yielding any of the corresponding selenophene, furan, or diselenide.[5] This result clearly indicates that the reduction of the C-1 carbonyl group led to the increased reactivity of diene **1** for the initial [4 + 2] reaction with SeO_2, but the corresponding selenino lactone **2**, without the carbonyl group, took a different reaction pathway.

In summary, we have demonstrated that an efficient one-step synthesis of selenophenes can be realized from the reaction of SeO_2 with 1,3-dienes containing a carbonyl group at the C-1 position. The generality and mechanistic study of these reactions will be explored in due course.

Experimental Section

Materials and Methods. All reactions were monitored by thin-layer chromatography (TLC) using 0.25 mm E. Merck precoated silica gel 60 (particle size 0.040−0.063 mm). Yields refer to chromatographically and spectroscopically pure compounds, except as noted. Proton and carbon-13 NMR spectra were recorded on Bruker AC-300 and Varian Unity-500 spectrometers. Proton and carbon-13 chemical shifts are reported in δ values relative to the internal standard, tetramethylsilane (TMS). High-resolution mass spectra were obtained with JEOL AX-505 and JEOL SX-102 spectrometers.

A Typical Procedure for the Synthesis of Diene 5. To a stirred solution of (1S)-(−)-verbenone **10** (3.52 g, 23.4 mmol) and 2,4,6-trimethoxybenzaldehyde (5.52 g, 28.1 mmol) in 50 mL of MeOH was added KOH (pellet, 2.6 g, 46.0 mmol). The mixture was stirred at 60 °C for 6 h and then cooled to room temperature. A few drops of H_2O were added, and the mixture was allowed to stand at room temperature for 24 h. Yellow solid **5h** was obtained by filtration and drying under vacuum (6.8 g, 94%).

Diene 5a (92%, oil): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.51−7.49 (m, 2H), 7.39−7.32 (m, 3H), 6.97 (d, *J* = 16.2 Hz, 1H), 6.92 (d, *J* = 16.2 Hz, 1H), 5.93 (s, 1H), 3.12 (t, *J* = 5.8 Hz, 1H), 2.92 (dt, *J* = 9.3, 5.6 Hz, 1H), 2.73 (td, *J* = 5.6, 1.6 Hz, 1H), 2.12 (d, *J* = 9.4 Hz, 1H), 1.58 (s, 3H), 1.02 (s, 3H); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 203.9, 164.1, 135.8, 134.9, 129.0, 128.7, 127.2, 122.5, 58.0, 52.7, 43.6, 39.9, 26.6, 22.0; HRMS (EI) calcd for $C_{17}H_{18}O$ (M^+) 238.1358, found 238.1353.

Diene 5b (95%, solid, mp 72−74 °C): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.37−7.34 (m, 2H), 7.18−7.12 (m, 1H), 7.04 (d, *J* = 16.5 Hz, 1H), 6.95 (d, *J* = 16.5 Hz, 1H), 5.95 (s, 1H), 3.13 (td, *J* = 5.7, 1.0 Hz, 1H), 2.96 (dt, *J* = 9.3, 5.7 Hz, 1H), 2.76 (td, *J* = 5.6, 1.7 Hz, 1H), 2.18 (d, *J* = 9.3 Hz, 1H), 1.60 (s, 3H), 1.05 (s, 3H); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 204.0, 163.5, 135.6, 134.5, 133.3, 129.0, 128.7, 128.5, 123.9, 58.2, 53.1, 43.3, 39.9, 26.7, 22.0; HRMS (EI) calcd for $C_{17}H_{16}OCl_2$ (M^+) 306.0578, found 306.0588.

Diene 5c (95%, solid, mp 100−102 °C): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.61 (d, *J* = 8.4 Hz, 1H), 7.42 (d, *J* = 2.0 Hz, 1H), 7.28−7.24 (m, 1H), 7.25 (d, *J* = 15.7 Hz, 1H), 6.92 (d, *J* = 16.2 Hz, 1H), 5.98 (s, 1H), 3.13 (td, *J* = 5.7, 1.1 Hz, 1H), 2.95 (dt, *J* = 9.3, 5.6 Hz, 1H), 2.76 (td, *J* = 5.5, 1.1 Hz, 1H), 2.14 (d, *J* = 9.5 Hz, 1H), 1.60 (s, 3H), 1.03 (s, 3H); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 203.9, 163.6, 130.1, 129.8, 129.3, 127.6, 127.5, 123.9, 58.2, 52.9, 43.7, 40.0, 26.7, 22.1; HRMS (EI) calcd for $C_{17}H_{16}OCl_2$ (M^+) 306.0578, found 306.0564.

Diene 5d (77%, oil): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.46−7.41 (m, 2H), 7.36−7.32 (m, 2H), 6.94 (d, *J* = 16.2 Hz, 1H), 6.86 (d, *J* = 16.2 Hz, 1H), 5.94 (s, 1H), 3.10 (td, *J* = 5.7, 1.3 Hz, 1H), 2.93 (dt, *J* = 9.6, 5.7 Hz, 1H), 2.74 (td, *J* = 5.7, 1.7 Hz, 1H), 2.12 (d, *J* = 9.4 Hz, 1H), 1.59 (s, 3H), 1.02 (s, 3H); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 204.0, 163.8, 134.8, 134.5, 129.1, 128.5, 127.9, 123.0, 58.2, 52.9, 43.6, 40.0, 26.7, 22.1; HRMS (EI) calcd for $C_{17}H_{17}OCl$ (M^+) 272.0968, found 272.0956.

Diene 5e (98%, solid, mp 104−106 °C): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.48−7.43 (m, 2H), 6.92−6.89 (m, 2H), 6.90 (d, *J* = 16.2 Hz, 1H), 6.83 (d, *J* = 16.2 Hz, 1H), 5.89 (t, *J* = 1.7 Hz, 1H), 3.84 (s, 3H), 3.12 (td, *J* = 5.9, 1.3 Hz, 1H), 2.91 (dt, *J* = 9.2, 5.7 Hz, 1H), 2.72 (td, *J* = 5.7, 1.7 Hz, 1H), 2.12 (d, *J* = 9.2 Hz, 1H), 1.58 (s, 3H), 1.02 (s, 3H); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 204.2, 164.7, 142.6, 134.6, 130.0, 128.8, 125.1, 121.7, 114.3, 58.0, 55.3, 52.7, 43.6, 39.9, 26.7, 22.1; HRMS (EI) calcd for $C_{18}H_{20}O_2$ (M^+) 268.1463, found 268.1470.

Diene 5f (94%, oil): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.51 (d, *J* = 8.7 Hz, 1H), 7.25 (d, *J* = 16.4 Hz, 1H), 6.89 (d, *J* = 16.4 Hz, 1H), 6.51 (dd, *J* = 8.6, 2.4 Hz, 1H), 6.45 (d, *J* = 2.4 Hz, 1H), 5.87 (s, 1H), 3.87 (s, 3H), 3.84 (s, 3H), 3.16 (td, *J* = 5.7, 1.0 Hz, 1H), 2.90 (dt, *J* = 9.2, 5.7 Hz, 1H), 2.71 (td, *J* = 5.7, 1.7 Hz, 1H), 2.10 (d, *J* = 9.2 Hz, 1H), 1.57 (s, 3H), 1.02 (s, 3H); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 204.3, 165.5, 161.8, 158.7, 129.6, 128.1, 125.1, 121.1, 117.9, 105.3, 98.2, 58.0, 55.4, 55.3, 52.6, 43.5, 39.9, 26.7, 22.0; HRMS (EI) calcd for $C_{19}H_{22}O_3$ (M^+) 298.1569, found 298.1561.

Diene 5g (91%, solid, mp 124−126 °C): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.29 (d, *J* = 16.3 Hz, 1H), 7.09 (s, 1H), 6.84 (d, *J* = 16.3 Hz, 1H), 6.51 (s, 1H), 5.90 (s, 1H), 3.93 (s, 3H), 3.91 (s, 3H), 3.89 (s, 3H), 3.18 (t, *J* = 5.3 Hz, 1H), 2.91 (dt, *J* = 9.2, 5.5 Hz, 1H), 2.72 (t, *J* = 4.9 Hz, 1H), 2.11 (d, *J* = 9.2 Hz, 1H), 1.59 (s, 3H), 1.03 (s, 3H); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 204.4, 165.8, 151.2, 143.4, 129.3, 125.0, 121.2, 116.5, 109.3, 96.8, 58.1, 56.5, 56.3, 56.0, 52.7, 43.6, 40.0, 26.7, 22.1; HRMS (EI) calcd for $C_{20}H_{24}O_4$ (M^+) 328.1675, found 328.1684.

Diene 5h (94%, solid, mp 107−110 °C): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.38 (d, *J* = 16.6 Hz, 1H), 7.30 (d, *J* = 16.6 Hz, 1H), 6.14_(s, 2H), 5.85 (t, *J* = 1.5 Hz, 1H), 3.89 (s, 6H), 3.85 (s, 3H), 3.18 (td, *J* = 5.9, 1.1 Hz, 1H), 2.90 (dt, *J* = 9.2, 5.7 Hz, 1H), 2.70 (td, *J* = 5.9, 1.7 Hz, 1H), 2.11 (d, *J* = 9.2 Hz, 1H), 1.58 (s, 3H), 1.03 (s, 3H); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 204.6, 167.3, 161.7, 160.3, 127.7, 126.5, 120.4, 106.9, 90.5, 58.1, 55.7, 55.2, 52.5, 43.1, 40.0, 26.7, 22.1; HRMS (EI) calcd for $C_{20}H_{24}O_4$ (M^+) 328.1675, found 328.1681.

Diene 5i (48%, solid, mp 125−128 °C): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.43−7.38 (m, 2H), 6.88 (d, *J* = 16.0 Hz, 1H), 6.77 (d, *J* = 16.0 Hz, 1H), 6.70−6.65 (m, 2H), 5.84 (s, 1H), 3.13 (td, *J* = 5.9, 1.1 Hz, 1H), 2.89 (dt, *J* = 9.4, 5.5 Hz, 1H), 2.70 (td, *J* = 5.9, 1.7 Hz, 1H), 2.11 (d, *J* = 9.2 Hz, 1H), 1.57 (s, 3H), 1.02 (s, 3H); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 204.4, 165.4, 151.0, 135.6, 128.9, 124.0, 122.6, 120.3, 112.0, 58.1, 52.6, 43.8, 40.2, 40.0, 26.8, 22.2; HRMS (EI) calcd for $C_{19}H_{23}ON$ (M^+) 281.1780, found 281.1768.

Diene 5j (86%, oil): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.47 (d, *J* = 7.3 Hz, 2H), 7.38 (t, *J* = 7.3 Hz, 2H), 7.32−7.29 (m, 1H), 6.96 (dd, *J* = 16.1, 11.2 Hz, 1H), 6.83−6.78 (m, 2H), 6.55 (d, *J* = 15.6 Hz, 1H), 5.89 (s, 1H), 3.06 (td, *J* = 5.8, 1.0 Hz, 1H), 2.92 (dt, *J* = 9.3, 5.9 Hz, 1H), 2.74 (td, *J* = 5.9, 1.9 Hz, 1H), 2.12 (d, *J* = 9.3 Hz, 1H), 1.60 (s, 3H), 1.03 (s, 3H); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 203.8, 164.0, 136.9, 136.4, 135.5, 131.2, 12.6, 128.3, 128.1, 126.7, 121.9, 57.9, 52.5, 43.6, 39.7, 26.6, 22.0; HRMS (EI) calcd for $C_{19}H_{20}O$ (M^+) 264.1514, found 264.1512.

Diene 5k (71%, solid, mp 60−62 °C): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.19 (d, *J* = 16.0 Hz, 1H), 6.13 (d, *J* = 16.0 Hz, 1H), 5.75 (s, *J* = 1.7 Hz, 1H), 2.96 (td, *J* = 5.7, 1.3 Hz, 1H), 2.87 (dt, *J* = 9.0, 5.7 Hz, 1H), 2.68 (td, *J* = 5.7, 1.8 Hz, 1H), 2.06 (d, *J* = 9.2 Hz, 1H), 1.55 (s, 3H), 1.09 (s, 9H), 0.98 (s, 3H); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 204.2, 165.1, 149.0, 124.4, 120.8, 57.9, 52.6, 43.6, 40.0, 33.8, 29.3, 29.1, 26.6, 21.9; HRMS (EI) calcd for $C_{15}H_{22}O$ (M^+) 218.1671, found 218.1665.

Tetraene 11 (75%): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.08 (s, 2H), 7.02 (d, *J* = 15.8 Hz, 2H), 6.77 (d, *J* = 15.8 Hz, 2H), 5.92 (s, 2H), 3.06 (t, *J* = 5.7 Hz, 2H), 2.92 (dt, *J* = 9.4, 5.7 Hz, 2H), 2.72 (td, *J* = 5.9, 1.7 Hz, 2H), 2.10 (d, *J* = 9.4 Hz, 2H), 1.58 (s, 6H), 1.01 (s, 6H); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 203.5, 163.2, 142.8, 129.8, 127.8, 127.7, 122.5, 57.9, 52.5, 43.4, 39.7, 26.5, 21.9; HRMS (ESI) calcd for $C_{26}H_{28}O_2S + Na^+$ ($M^+ + Na^+$) 427.1708, found 427.1710.

Tetraene 13 (90%): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.53 (s, 4H), 7.02 (d, *J* = 16.2 Hz, 2H), 6.93 (d, *J* = 16.0 Hz, 2H), 5.96 (s,

2H), 3.14 (t, J = 5.0 Hz, 2H), 2.94 (dt, J = 9.4, 5.5 Hz, 2H), 2.74 (td, J = 5.7, 1.7 Hz, 2H), 2.12 (d, J = 9.4 Hz, 2H), 1.59 (s, 6H), 1.02 (s, 6H); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 203.8, 163.8, 136.5, 134.0, 127.8, 127.7, 122.8, 58.0, 52.6, 43.4, 39.8, 26.6, 22.0; HRMS (ESI) calcd for $C_{28}H_{30}O_2 + Na^+$ ($M^+ + Na^+$) 421.2144, found 421.2155.

A Typical Procedure for the Synthesis of Selenophene 6. To a stirred solution (open to air) of diene **5h** (100 mg, 0.32 mmol) in 6 mL of 1,4-dioxane/pyridine (5:1) was added selenium dioxide (390 mg, 3.5 mmol). The mixture was vigorously stirred at 80 °C for 10 h and then cooled to room temperature. The reaction was quenched with water, washed with aqueous $CuSO_4$, extracted (4×) with ether, and dried over $MgSO_4$. Evaporation of solvent, followed by flash column chromatography (hexanes−ether, 4:1), provided selenophene **6h** (130 mg, 90%).

Selenophene 6a (86%, solid, mp 102−104 °C): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.59 (dd, J = 6.5, 1.2 Hz, 1H), 7.40−7.33 (m, 4H), 3.13 (t, J = 5.6 Hz, 1H), 3.04 (dt, J = 9.5, 5.7 Hz, 1H), 2.81 (t, J = 5.8 Hz, 1H), 2.33 (d, J = 9.5 Hz, 1H), 1.57 (s, 3H), 0.88 (s, 3H); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 196.3, 163.8, 158.8, 135.5, 134.9, 129.0, 128.9, 126.4, 124.9, 57.9, 57.1, 46.7, 42.5, 26.7, 22.9; ^{77}Se NMR ($CDCl_3$, external Me_2Se) δ 569.4; HRMS (EI) calcd for $C_{17}H_{16}OSe$ (M^+) 316.0366, found 316.0351.

Selenophene 6b (67%, solid, mp 127−130 °C): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.43−7.40 (m, 2H), 7.30−7.24 (m, 1H), 7.07 (s, 1H), 3.17 (t, J = 5.6 Hz, 1H), 3.09 (dt, J = 9.5, 5.6 Hz, 1H), 2.85 (t, J = 5.7 Hz, 1H), 2.45 (d, J = 9.5 Hz, 1H), 1.61 (s, 3H), 0.92 (s, 3H); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 197.4, 163.3, 151.5, 139.1, 136.0, 134.9, 131.7, 131.0, 128.9, 58.7, 58.6, 47.4, 43.5, 27.5, 23.6; ^{77}Se NMR ($CDCl_3$, external Me_2Se) δ 618.5; HRMS (EI) calcd for $C_{17}H_{14}OCl_2Se$ (M^+) 383.9583, found 383.9601.

Selenophene 6c (79%, solid, mp 100−102 °C): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.51 (d, J = 2.8 Hz, 1H), 7.50 (d, J = 7.5 Hz, 1H), 7.42 (s, 1H), 7.29 (dd, J = 8.5, 2.2 Hz, 1H), 3.17 (t, J = 5.7 Hz, 1H), 3.08 (dt, J = 9.4, 5.7 Hz, 1H), 2.84 (t, J = 5.7 Hz, 1H), 2.38 (d, J = 9.4 Hz, 1H), 1.60 (s, 3H), 0.90 (s, 3H); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 197.2, 163.0, 153.0, 138.4, 135.5, 133.8, 133.3, 132.4, 131.2, 130.5, 128.1, 58.8, 58.1, 47.4, 43.5, 27.5, 23.7; ^{77}Se NMR ($CDCl_3$, external Me_2Se) δ 615.0; HRMS (EI) calcd for $C_{17}H_{14}OCl_2Se$ (M^+) 383.9583, found 383.9576.

Selenophene 6d (45%, solid, mp 124−127 °C): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.55−7.50 (m, 2H), 7.38−7.33 (m, 3H), 3.14 (t, J = 5.8 Hz, 1H), 3.06 (dt, J = 9.5, 5.5 Hz, 1H), 2.83 (t, J = 5.8 Hz, 1H), 2.35 (d, J = 9.5 Hz, 1H), 1.59 (s, 3H), 0.89 (s, 3H); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 196.3, 163.8, 157.2, 135.6, 134.9, 134.2, 129.3, 127.6, 125.4, 57.9, 57.2, 46.8, 42.6, 26.8, 23.0; ^{77}Se NMR ($CDCl_3$, external Me_2Se) δ 572.4; HRMS (EI) calcd for $C_{17}H_{15}OClSe$ (M^+) 349.9977, found 349.9988.

Selenophene 6e (63%, solid, mp 136−139 °C): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.56−7.51 (m, 2H), 7.27 (s, 1H), 6.94−6.87 (m, 2H), 3.84 (s, 3H), 3.12 (t, J = 5.9 Hz, 1H), 3.04 (dt, J = 9.2, 5.9 Hz, 1H), 2.80 (t, J = 5.5 Hz, 1H), 2.34 (d, J = 9.2 Hz, 1H), 1.58 (s, 3H), 0.89 (s, 3H); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 196.3, 164.1, 160.4, 159.0, 133.7, 128.4, 127.8, 123.8, 114.4, 57.9, 57.2, 55.3, 46.8, 42.5, 26.7, 22.9; ^{77}Se NMR ($CDCl_3$, external Me_2Se) δ 563.7; HRMS (EI) calcd for $C_{18}H_{18}O_2Se$ (M^+) 346.0472, found 346.0461.

Selenophene 6f (55%, solid, mp 127−129 °C): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.69 (d, J = 8.5 Hz, 1H), 7.49 (s, 1H), 7.27 (s, 1H), 6.61−6.52 (m, 2H), 3.97 (s, 3H), 3.86 (s, 3H), 3.14 (t, J = 5.5 Hz, 1H), 3.05 (dt, J = 9.6, 5.5 Hz, 1H), 2.79 (t, J = 5.9 Hz, 1H), 2.34 (d, J = 9.2 Hz, 1H), 1.58 (s, 3H), 0.86 (s, 3H); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 197.3, 162.3, 161.2, 156.9, 151.9, 135.0, 128.0, 123.7, 117.5, 105.7, 98.7, 58.0, 57.3, 55.5, 55.4, 46.8, 42.7, 26.9, 23.0; ^{77}Se NMR ($CDCl_3$, external Me_2Se) δ 610.8; HRMS (EI) calcd for $C_{19}H_{20}O_3Se$ (M^+) 376.0578, found 376.0589.

Selenophene 6g (65%, solid, mp 113−115 °C): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.48 (s, 1H), 7.26 (s, 1H), 6.60 (s, 1H), 3.99 (s, 3H), 3.95 (s, 3H), 3.92 (s, 3H), 3.15 (t, J = 5.5 Hz, 1H), 3.06 (dt, J = 9.6, 5.5 Hz, 1H), 2.79 (t, J = 5.9 Hz, 1H), 2.35 (d, J = 9.6 Hz, 1H), 1.59 (s, 3H), 0.87 (s, 3H); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 198.0, 162.8, 152.1, 151.6, 144.2, 135.2, 124.2, 116.8, 110.7, 98.2, 58.7, 58.0, 57.4, 57.0, 56.8, 47.5, 43.4, 27.6, 23.7; ^{77}Se NMR ($CDCl_3$, external Me_2Se) δ 615.16; HRMS (EI) calcd for $C_{20}H_{22}O_4Se$ (M^+) 406.0683, found 406.0686.

Selenophene 6h (90%, solid, mp 167−170 °C): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.91 (s, 1H), 6.23 (s, 2H), 3.92 (s, 6H), 3.87 (s, 3H), 3.15 (t, J = 5.8 Hz, 1H), 3.04 (dt, J = 9.2, 5.8 Hz, 1H), 2.78 (t, J = 5.8 Hz, 1H), 2.37 (d, J = 9.5 Hz, 1H), 1.58 (s, 3H), 0.87 (s, 3H); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 198.3, 162.9, 161.6, 158.9, 148.7, 134.0, 129.4, 108.0, 91.8, 58.8, 58.1, 56.4, 56.1, 47.6, 43.6, 27.6, 23.7; ^{77}Se NMR ($CDCl_3$, external Me_2Se) δ 632.7; HRMS (EI) calcd for $C_{20}H_{22}O_4Se$ (M^+) 406.0683, found 406.0667.

Selenophene 6i (48%, solid, mp >180 °C): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.52−7.47 (m, 2H), 7.22 (s, 1H), 6.71−6.67 (m, 2H), 3.11 (t, J = 5.5 Hz, 1H), 3.03 (dt, J = 9.2, 5.5 Hz, 1H), 3.02 (s, 6H), 2.79 (t, J = 5.5 Hz, 1H), 2.35 (d, J = 9.2 Hz, 1H), 1.57 (s, 3H), 0.89 (s, 3H); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 197.0, 165.2, 161.3, 151.7, 132.7, 128.3, 124.4, 122.9, 112.9, 58.7, 57.9, 47.6, 43.2, 40.9, 27.5, 23.7; ^{77}Se NMR ($CDCl_3$, external Me_2Se) δ 554.5; HRMS (EI) calcd for $C_{19}H_{21}ONSe$ (M^+) 359.0788, found 359.0780.

Selenophene 6j (48%, solid, mp 145−147 °C): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.48 (d, J = 7.1 Hz, 2H), 7.39−7.27 (m, 3H), 7.20 (d, J = 15.8 Hz, 1H), 7.11 (s, 1H), 7.00 (d, J = 15.8 Hz, 1H), 3.08 (t, J = 5.5 Hz, 1H), 3.01 (dt, J = 9.3, 5.7 Hz, 1H), 2.80 (t, J = 5.8 Hz, 1H), 2.30 (d, J = 9.3 Hz, 1H), 1.56 (s, 3H), 0.87 (s, 3H); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 196.2, 163.3, 156.5, 136.1, 133.6, 132.6, 128.7, 128.4, 128.0, 126.7, 123.7, 57.9, 57.0, 46.5, 42.3, 26.7, 22.8; ^{77}Se NMR ($CDCl_3$, external Me_2Se) δ 555.2; HRMS (EI) calcd for $C_{19}H_{18}OSe$ (M^+) 342.0523, found 342.0511.

Selenophene 6k (5%, oil): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.93 (s, 1H), 3.08−2.97 (m, 2H), 2.76 (t, J = 5.8 Hz, 1H), 2.32 (d, J = 9.0 Hz, 1H), 1.56 (s, 3H), 1.41 (s, 9H), 0.83 (s, 3H); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 197.3, 176.5, 164.0, 133.7, 124.8, 58.7, 58.3, 47.6, 43.6, 38.0, 33.6, 27.6, 23.6; ^{77}Se NMR ($CDCl_3$, external Me_2Se) δ 568.2; HRMS (EI) calcd for $C_{15}H_{20}OSe$ (M^+) 296.0679, found 296.0671.

Furan 7: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.79 (dd, J = 8.4, 1.6 Hz, 2H), 7.43−7.30 (m, 3H), 6.72_(s, 1H), 3.07 (dt, J = 9.6, 5.5 Hz, 1H), 2.99 (t, J = 5.5 Hz, 1H), 2.76 (t, J = 5.8 Hz, 1H), 2.33 (d, J = 9.5 Hz, 1H), 1.58 (s, 3H), 0.88 (s, 3H); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 188.9, 157.9, 149.9, 145.9, 129.3, 129.2, 128.9, 125.1, 105.5, 59.4, 58.0, 44.2, 42.5, 27.2, 22.4; HRMS (EI) calcd for $C_{17}H_{16}O_2$ (M^+) 252.1150, found 252.1160.

Diselenide 8: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.93 (d, J = 8.2 Hz, 2H), 7.65 (t, J = 7.6 Hz, 1H), 7.50 (t, J = 7.6 Hz, 2H), 3.01 (t, J = 6.1 Hz, 1H), 2.91 (q, J = 5.8 Hz, 1H), 2.28 (t, J = 7.3 Hz, 1H), 2.28 (d, J = 9.5 Hz, 1H), 1.51 (s, 3H), 1.01 (s, 3H); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 198.0, 192.4, 191.5, 157.6, 141.1, 134.8, 132.6, 130.1, 128.9, 58.2, 55.0, 46.6, 39.7, 26.3, 22.3; ^{77}Se NMR ($CDCl_3$, external Me_2Se) δ 487.6; LRMS (EI) calcd for $(C_{17}H_{15}O_2Se)_2$ (M^+) 694.0, found 694.0.

Bis-selenophene 12 (27%): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.27 (s, 2H), δ 7.20 (s, 2H), 3.13 (t, J = 5.5 Hz, 2H), 3.06 (dt, J = 9.6, 5.5 Hz, 2H), 2.83 (t, J = 5.9 Hz, 2H), 2.34 (d, J = 9.6 Hz, 2H), 1.59 (s, 6H), 0.90 (s, 6H); ^{13}C NMR ($CDCl_3$, 125.7 MHz) 196.8, 164.2, 149.7, 140.5, 135.8, 127.7, 126.2, 58.7, 57.8, 47.5, 43.1, 27.5, 23.7; ^{77}Se NMR ($CDCl_3$, external Me_2Se) δ 583.6; HRMS (FAB) calcd for $C_{26}H_{24}O_2SSe_2 + Na^+$ 582.9729, found 582.9720.

Bis-selenophene 14 (16%): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.637 (s, 4H), δ 7.45 (s, 2H), 3.17 (t, J = 5.5 Hz, 2H), 3.08 (dt, J = 9.6, 5.5 Hz, 2H), 2.84 (t, J = 5.7 Hz, 2H), 2.36 (d, J = 9.6 Hz, 2H), 1.60 (s, 6H), 0.91 (s, 6H); ^{13}C NMR ($CDCl_3$, 125.7 MHz) 197.1, 164.6, 158.2, 136.9, 136.4, 127.8, 126.1, 58.7, 57.9, 47.5, 43.3, 27.5, 23.7; ^{77}Se NMR ($CDCl_3$, external Me_2Se) δ 571.5; LRMS (EI) calcd for ($C_{28}H_{26}O_2Se_2$) (M^+) 554.0, found 554.0.

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Supporting Information Available: Spectral data for **5a**−**k**, **6a**−**k**, **7**, **8**, and **11**−**14**. X-ray structure for **6a**, **6j**, **7**, and **8**. This material is available free of charge via the Internet at http://pubs.acs.org.

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