

Notes

2,7-Bis-*N,N*-dimethylaminochalcogenoxanthen-9-ones via Electrophilic Cyclization with Phosphorus Oxychloride

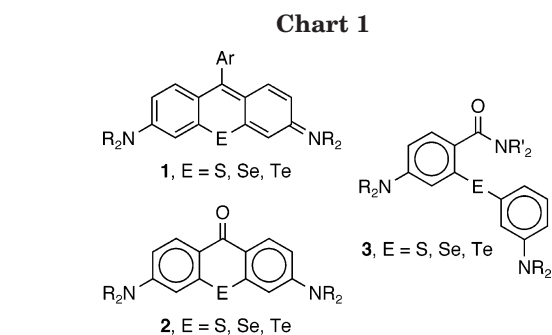
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Summary: The electrophilic cyclization of *N,N*-diethyl 4-*N,N*-(dimethylamino)-2-(3-*N,N*-dimethyldimethylaminophenylchalcogeno)benzamides **7** with POCl₃ and triethylamine in CH₂Cl₂ or with POCl₃ in acetonitrile gave excellent yields (77–97% in CH₂Cl₂, 73–77% in acetonitrile) of the corresponding 2,7-bis-*N,N*-dimethylaminochalcogenoxanthen-9-ones **6**. 3-Methoxyphenylchalcogeno-substituted benzamide derivatives were much less reactive toward POCl₃ and phenylchalcogeno-substituted benzamide derivatives gave no reaction with POCl₃ after 48 h.

The rhodamines and related molecules have found utility as fluorescent stains for various subcellular organelles,¹ as tumor-selective dyes that accumulate in the mitochondria of cancer cells relative to normal cells,² as chemotherapeutic agents against certain tumor lines,³ and as transport substrates for the multidrug-resistance efflux protein P-glycoprotein.⁴ We have recently described the preparation of thioxanthylum and selenoxanthylum analogues of the rhodamines,⁵ which have markedly different photophysical properties than the xanthylum analogues.⁶ The heavy chalcogen analogues have higher triplet yields and, consequently, higher quantum yields for the generation of singlet oxygen. The heavy chalcogen analogues of the rhodamines have been examined as photosensitizers for use in photodynamic therapy (PDT) in both chemosensitive⁵ and multidrug-resistant cancer cells.⁷ Tellurium-containing analogues of the rhodamines have yet to be described, and one would expect these molecules to have



higher triplet yields and longer wavelengths of absorption of light than sulfur- or selenium-containing analogues.

The preparation of heavy chalcogen analogues of the rhodamine dyes **1** has been limited by the paucity of synthetic routes to 2,7-diamino-substituted chalcogenoxanthen-9-ones **2**. The addition of an aryllithium or aryl Grignard reagent to the carbonyl of chalcogenoxanthen-9-ones **2** leads directly to the heavy chalcogen analogues of the rhodamines (Chart 1).⁵ However, the only successful synthesis of 2,7-diamino-substituted chalcogenoxanthen-9-ones **2** is via metalation and cyclization of 2-arylchalcogenobenzamide derivatives **3**.⁸ Unfortunately, the cyclization of compounds **3** gives relatively low yields (13–24%) of the corresponding chalcogenoxanthen-9-one, although the regiochemistry of cyclization gives only the desired 2,7-disubstituted chalcogenoxanthen-9-one. Our attempts to prepare telluroxanthenes via this approach have been unsuccessful.

A general, high-yield approach to 2,7-diamino-substituted chalcogenoxanthenes would allow the chemistry of the corresponding rhodamine derivatives to be more easily developed. Because of the Brønsted and Lewis basicity of the 2,7-diamino substituents, traditional Friedel–Crafts approaches to xanthenes have failed. For example, attempted electrophilic cyclizations of carboxylic acid **4** with methanesulfonic acid or acid chloride **5** with aluminum chloride to give chalcogenoxanthen-9-ones **6** were unsuccessful (Scheme 1). However, we have found that 2-arylchalcogenobenzamides **7** can be cyclized to the corresponding chalcogenoxanthen-9-ones

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(1) Haugland, R. P. *Handbook of fluorescent probes and research chemicals*, 6th ed.; Molecular Probes, Inc., 1996.

(2) (a) Summerhayes, I. C.; Lampidis, T. J.; Bernal, S. D.; Nadakavukaren, K. K.; Shepard, E. L.; Chen, L. B. *Proc. Natl. Acad. Sci. U.S.A.* **1982**, *79*, 5292–5296. (b) Davis, S.; Weiss, M. J.; Wong, J. R.; Lampidis, T. J.; Chen, L. B. *J. Biol. Chem.* **1985**, *260*, 13844–13850. (c) Lampidis, T. J.; Bernal, S. D.; Summerhayes, I. C.; Chen, L. B. *Ann. N. Y. Acad. Sci.* **1982**, *395*, 299–303.

(3) Bernal, S. D.; Lampidis, T. J.; McIsaac, R. M.; Chen, L. B. *Science* **1986**, *222*, 169–172.

(4) Eytan, G. D.; Regec, R.; Oren, G.; Hurwitz, C. D.; Assaraf, Y. G. *Eur. J. Biochem.* **1997**, *248*, 104–112.

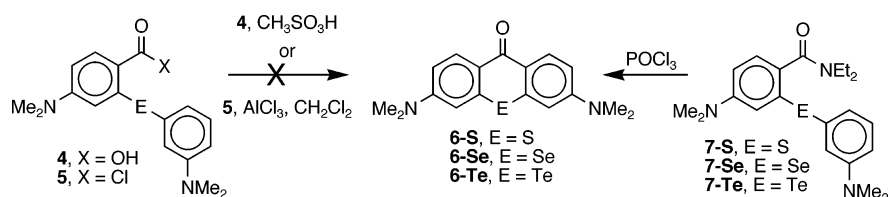
(5) Detty, M. R.; Prasad, P. N.; Donnelly, D. J.; Ohulchanskyy, T.; Gibson, S. L.; Hilf, R. *Bioorg. Med. Chem.* **2004**, *12*, 2537–2544.

(6) Ohulchanskyy, T.; Donnelly, D. J.; Detty, M. R.; Prasad, P. N. *J. Phys. Chem. B* **2004**, *108*, 8668–8672.

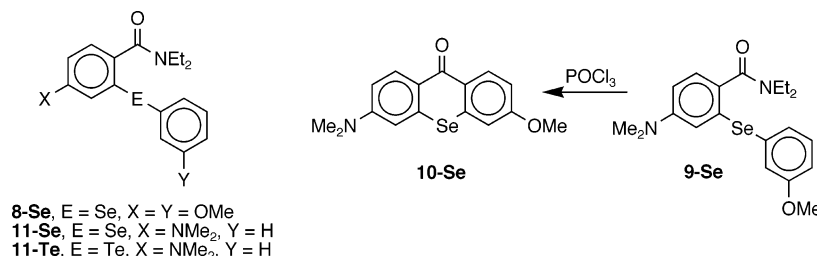
(7) Gibson, S. L.; Hilf, R.; Donnelly, D. J.; Dety, M. R. *Bioorg. Med. Chem.* **2004**, *12*, 4625–4631.

(8) Brennan, N. K.; Donnelly, D. J.; Detty, M. R. *J. Org. Chem.* **2003**, *68*, 3344–3347.

Scheme 1



Scheme 2



6 including telluroxanthen-9-one **6-Te** in high yields under electrophilic conditions using POCl₃.

Results and Discussion

Telluroxanthen-9-one **6-Te** was prepared by the addition of 12 equiv of POCl₃ to a solution of 2-aryltellurobenzamide **7-Te** and 12 equiv of triethylamine in CH₂Cl₂ at 0 °C followed by stirring the resulting mixture at ambient temperature for 48 h. Unreacted POCl₃ was hydrolyzed with aqueous NaOH, and **6-Te** was isolated with an extractive workup. Recrystallization from CH₂Cl₂/hexanes gave **6-Te** in 77% isolated yield.

The 2,7-bis-*N,N*-dimethylamino regioisomer **6-Te** was formed as the major if not exclusive regioisomer in this reaction. We could detect none of the 2,5-isomer in the crude reaction mixture prior to recrystallization. The ¹³C NMR spectrum of **6-Te** displayed the expected eight signals for a symmetrical xanthenone, and the ¹H NMR spectrum gave splitting patterns consistent with 1,2,4-trisubstituted phenyl rings.

Cyclization of 2-arylthiobenzamide **7-S** under the same conditions gave thioxanthenone **6-S** in 97% isolated yield, while cyclization of 2-arylselenobenzamide **7-Se** under the same conditions gave selenoxanthenone **6-Se** in 91% isolated yield. These yields are much higher than the 13% and 24% isolated yields for the preparation of **6-S** and **6-Se**, respectively, via metalation–cyclization reported previously.^{5,8} Again, none of the corresponding 2,5-regioisomers were detected in the reaction mixtures.

The cyclization of benzamides **7** with POCl₃ was much faster using acetonitrile as solvent. Ten equivalents of POCl₃ were added dropwise to benzamide **7** in acetonitrile at ambient temperature, and the resulting solution was then heated at reflux for 1.5 h. Unreacted POCl₃ was hydrolyzed with aqueous NaOH at 0 °C, and the chalcogenoxanthenones were isolated with an extractive workup. Isolated yields of chalcogenoxanthenones **6** were 73–77% following recrystallization from CH₂Cl₂/hexanes. Triethylamine was not necessary under these reaction conditions, and the addition of triethylamine had no impact on isolated yields. While yields with this procedure are not as high as the yields obtained with CH₂Cl₂ and triethylamine, the shorter reaction times may offer advantages.

Unfortunately, the POCl₃ cyclization does not appear to be a general reaction for the preparation of chalcogenoxanthenones. Replacing the dimethylamino substituents with methoxy substituents as in 2-arylselenobenzamide **8-Se** gave a substrate that did not react with POCl₃ after 48 h. In our earlier studies,⁸ the reaction of **8-Se** with lithium diisopropyl amide (LDA) gave the 2,5-dimethoxyselenoxanthenone as the only regioisomer in 90% isolated yield. Replacing only one dimethylamino substituent with a methoxy substituent as in 2-arylselenobenzamide **9-Se** gave a substrate that cyclized to selenoxanthenone **10-Se**, but in only 8% yield after 48 h of reaction.

Further deactivation of the arylchalcogeno ring to electrophilic attack gave substrates that did not react with POCl₃. Neither phenylselenobenzamide **11-Se**⁸ nor phenyltellurobenzamide **11-Te** gave chalcogenoxanthenone products after 48 h of reaction with POCl₃ in acetonitrile at reflux.

Summary and Conclusions

We have found a novel synthetic entry to 2,7-diamino-substituted and 2-amino-7-alkoxy-substituted chalcogenoxanthen-9-ones from the corresponding *N,N*-diethyl 4-amino-2-(3-aminophenylchalcogeno)benzamides and *N,N*-diethyl 4-amino-2-(3-methoxyphenylchalcogeno)benzamides using excess POCl₃. The mild, electrophilic cyclization has provided the first example of a 2,7-diamino-substituted telluroxanthen-9-one. The chalcogenoxanthenones can be prepared in gram quantities via this procedure.

Experimental Section

N,N-Diethyl 4-*N,N*-(dimethylamino)-2-[3-(*N,N*-dimethylamino)phenylthio]benzamide (**7-S**) was prepared according to ref 5. *N,N*-Diethyl 4-*N,N*-(dimethylamino)-2-[3-(*N,N*-dimethylamino)phenylseleno]benzamide (**7-Se**), *N,N*-diethyl 4-methoxy-2-(3-methoxyphenylseleno)benzamide (**8**), and *N,N*-diethyl 4-*N,N*-(dimethylamino)-2-phenylselenobenzamide (**11-Se**) were prepared according to ref 8. Di-3-methoxyphenyl diselenide was prepared according to ref 9. Di-3-(*N,N*-dimethylamino)phenyl diselenide was prepared according to ref 10.

Preparation of the Di-3-*N,N*-dimethylaminophenyl Ditelluride. 3-Bromo-*N,N*-dimethylaniline (10.0 g, 50.0 mmol)

was added to a stirred solution of ground magnesium turnings (24.3 g, 54.0 mmol) in 50 mL of anhydrous THF. The resulting mixture was heated at reflux for 2 h and was then cooled to ambient temperature. Ground tellurium shot (6.38 g, 50.0 mmol) was added, and the reaction mixture was heated at 40 °C for 2 h. The reaction mixture was then cooled to ambient temperature and poured over 30 g of ice. Hydrochloric acid (13 mL of a 20% solution) was then added, and the reaction mixture was filtered through Celite to remove unreacted magnesium turnings. Air was bubbled through the reaction mixture for 1 h. The reaction mixture was extracted with ether (3 × 100 mL), and the combined organic extracts were washed with brine, dried over MgSO_4 , and concentrated. The crude product was recrystallized from methanol to give 13.4 g (54%) of an orange crystalline solid, mp 76–78 °C: ^1H NMR [500 MHz, CDCl_3] δ 7.17 (m, 4 H), 7.01 (t, 2 H, $J = 7.7$), 6.57 (d, 2 H, $J = 2.0$, 7.7 Hz), 2.90 (s, 12 H); ^{13}C NMR [500 MHz, CDCl_3] δ 150.7, 129.4, 125.2, 121.5, 112.2, 109.0, 40.3; HRMS (ESI) m/z 499.9753 (calcd for $\text{C}_{16}\text{H}_{20}\text{N}_2\text{Te}$: 499.9751). Anal. Calcd for $\text{C}_{16}\text{H}_{20}\text{N}_2\text{Te}$: C, 38.78; H, 4.07; N, 5.65. Found: C, 38.49; H, 4.42; N, 5.33.

Preparation of *N,N*-Diethyl 4-*N,N*-Dimethylamino-2-[3-(*N,N*-dimethylamino)phenyltelluro]benzamide (7-Te). *sec*-Butyllithium (1.3 M in cyclohexane, 7.1 mL, 9.3 mmol) was added dropwise to a stirred solution of TMEDA (1.1 g, 9.3 mmol) and *N,N*-diethyl 4-*N,N*-dimethylaminobenzamide (1.9 g, 8.4 mmol) in 130 mL of THF at –78 °C. The resulting solution was stirred at –78 °C for 0.5 h. A solution of di-3-(*N,N*-dimethylamino)phenyl ditelluride (4.6 g, 9.3 mmol) in 30 mL of THF was then added dropwise. The resulting mixture was stirred at –78 °C for 1.0 h and was then warmed to ambient temperature for 14 h. The reaction mixture was poured into 200 mL of saturated NaCl, and the products were extracted with CH_2Cl_2 (3 × 100 mL). The combined organic extracts were washed with brine, dried over Na_2SO_4 , and concentrated. The resulting orange oil was purified via column chromatography on SiO_2 eluted with 20% diethyl ether in CH_2Cl_2 ($R_f = 0.6$) to give 2.2 g (51%) of **7-Te** as an orange oil, which was used without further purification: ^1H NMR [500 MHz, CDCl_3] δ 7.46 (d, 1 H, $J = 1.5$, 2 Hz), 7.40 (br d, 1 H, $J = 8$ Hz), 7.29 (d, 1 H, $J = 8.5$ Hz), 7.26 (t, 1 H, $J = 8$ Hz), 6.84 (d, 1 H, $J = 2.5$, 8.5 Hz), 6.81 (d, 1 H, $J = 2.5$ Hz), 6.57 (d, 1 H, $J = 2.5$, 8.5 Hz), 3.60 (q, 4 H, $J = 7.0$ Hz), 3.04 (s, 6 H), 2.87 (s, 6 H), 1.37 (t, 6 H, $J = 7.0$ Hz); ^{13}C NMR [300 MHz, CDCl_3] δ 172.2, 151.2, 150.9, 129.7, 128.9, 127.6, 126.2, 124.9, 122.1, 118.4, 117.5, 112.6, 109.0, 43.0 (br), 40.6, 39.9, 13.7 (br); IR (NaCl) 1622, 1595. cm^{-1} ; HRMS (ESI) m/z 470.1423 (calcd for $\text{C}_{21}\text{H}_{28}\text{N}_3\text{O}^{130}\text{Te} + \text{H}$: 470.1451).

Preparation of 2,7-Bis(*N,N*-dimethylamino)telluroxanthone-9-one (6-Te). Phosphorus oxychloride (2.3 mL, 23.9 mmol) was added dropwise to a solution of *N,N*-diethyl 4-*N,N*-(dimethylamino)-2-[3-(*N,N*-dimethylaminophenyltelluro)benzamide (**7-Te**, 0.93 g, 2.0 mmol) in anhydrous triethylamine (3.3 mL, 24 mmol) and anhydrous CH_2Cl_2 (40 mL) at 0 °C. After addition was complete, the reaction mixture was stirred at ambient temperature for 48 h. A solution of 3 M NaOH (40 mL) was added, and the resulting mixture was stirred for 1 h at ambient temperature. The products were extracted with CH_2Cl_2 (3 × 50 mL). The combined organic extracts were washed with brine, dried over Na_2SO_4 , and concentrated. The resulting yellow solid was recrystallized from acetonitrile/ether to give 0.615 g (77%) of **6-Te** as a yellow powder, mp 271–274 °C: ^1H NMR (400 MHz, CDCl_3) δ 8.53 (d, 2 H, $J = 9.2$ Hz), 6.76 (d, 2 H, $J = 2.4$ Hz), 6.70 (d, 2 H, $J = 9.2$, 2.4 Hz), 3.03 (s, 12 H); ^{13}C NMR [75 MHz, CDCl_3] δ 171.1, 151.5, 133.9, 123.5, 121.5, 113.9, 112.0, 39.9; IR (NaCl) 1588

cm^{-1} ; λ_{max} (EtOH) 388 nm; HRMS (ES) m/z 397.0585 (calcd for $\text{C}_{17}\text{H}_{18}\text{ON}_2^{130}\text{Te} + \text{H}$: 397.0560). Anal. Calcd for $\text{C}_{17}\text{H}_{18}\text{ON}_2\text{Te}$: C, 51.83; H, 4.61; N, 7.11. Found: C, 51.67; H, 4.66; N, 6.93.

Preparation of 2,7-Bis(*N,N*-dimethylamino)thioxanthone-9-one (6-S).⁵ Phosphorus oxychloride (9.0 mL, 96.0 mmol) was added dropwise to a solution of *N,N*-diethyl 4-*N,N*-(dimethylamino)-2-[3-(*N,N*-dimethylamino)phenylthio]benzamide (**7-S**, 3.4 g, 8.1 mmol) in anhydrous triethylamine (15.5 mL, 96 mmol) and anhydrous CH_2Cl_2 (150 mL) at 0 °C. This crude reaction mixture was then stirred continuously for 48 h at ambient temperature. The reaction was diluted with 3 M NaOH (200 mL), and the products were extracted with CH_2Cl_2 (3 × 100 mL). The combined organic extracts were washed with brine, dried over Na_2SO_4 , and concentrated. The resulting yellow solid was purified via column chromatography on SiO_2 eluted with 10% diethyl ether in CH_2Cl_2 ($R_f = 0.62$) to give 2.64 g (97%) of **6-S** as a yellow-green, crystalline powder, mp 260–261 °C (lit.⁵ mp: 260–261 °C): ^1H NMR (500 MHz, CD_2Cl_2) δ 8.42 (d, 2 H, $J = 9.2$ Hz), 6.81 (d, 2 H, $J = 2.4$, 9.2 Hz), 6.74 (d, 2 H, $J = 2.4$ Hz), 3.11 (s, 12 H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 177.2, 151.7, 138.6, 130.3, 118.5, 110.9, 104.8, 39.6; IR (KBr) 1589 cm^{-1} ; λ_{max} (EtOH) 377 nm.

Preparation of 2,7-Bis(*N,N*-dimethylamino)selenoxanthone-9-one (6-Se).⁸ Phosphorus oxychloride (2.7 mL, 28.7 mmol) was added dropwise to a solution of *N,N*-diethyl 4-*N,N*-(dimethylamino)-2-[3-(*N,N*-dimethylamino)phenylseleno]benzamide (**7-Se**, 1.0 g, 2.4 mmol) in anhydrous triethylamine (4.6 mL, 28.7 mmol) and anhydrous CH_2Cl_2 (50 mL) at 0 °C. After addition was complete, the reaction mixture was stirred at ambient temperature for an additional 48 h. The reaction mixture was diluted with 3 M NaOH (100 mL) and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic extracts were washed with brine, dried over Na_2SO_4 , and concentrated. The crude yellow solid was recrystallized from acetonitrile/ether to give 0.750 g (91%) of **6-Se** as a yellow powder, mp 225–226 °C (lit.⁸ mp: 224–225 °C): ^1H NMR (500 MHz, CD_2Cl_2) δ 8.38 (d, 2 H, $J = 8.9$ Hz), 6.80 (d, 2 H, $J = 8.9$, 1.2 Hz), 6.75 (d, 2 H, $J = 1.2$ Hz), 3.11 (s, 12 H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 179.1, 151.6, 136.1, 131.6, 119.9, 111.0, 107.5, 39.5; IR (KBr) 1592 cm^{-1} ; λ_{max} (EtOH) 388 nm.

General Procedure for Preparation of Chalcogenoxanthones with POCl_3 in Acetonitrile. **Preparation of Telluroxanthone 6-Te.** Phosphorus oxychloride (1.9 mL, 20 mmol) was added dropwise to a solution of benzamide **7-Te** (0.910 g, 1.95 mmol) in 50 mL of acetonitrile. The resulting solution was heated at reflux for 1.5 h and was then poured into a mixture of 60 mL of 1 M NaOH and 60 g of ice. The resulting mixture was stirred for 1 h, and the products were extracted with CH_2Cl_2 (3 × 50 mL). The combined organic extracts were washed with brine, dried over MgSO_4 , and concentrated. The crude product was purified via recrystallization from CH_2Cl_2 /hexanes to give 0.605 g (77%) of **6-Te** as a yellow crystalline solid, mp 271–274 °C.

Preparation of Thioxanthone 6-S⁵ in Acetonitrile. Phosphorus oxychloride (2.7 mL, 29 mmol) and arylthiobenzamide **7-S** (1.08 g, 2.9 mmol) were heated at reflux in 50 mL of acetonitrile for 1.5 h. Workup as described gave 0.65 g (75%) of **6-S**, mp 261–262 °C (lit.⁵ mp: 260–261 °C).

Preparation of Selenoxanthone 6-Se⁸ in Acetonitrile. Phosphorus oxychloride (2.4 mL, 26 mmol) and arylselenobenzamide **7-Se** (1.09 g, 2.6 mmol) were heated at reflux in 30 mL of acetonitrile for 1.5 h. Workup as described gave 0.66 g (73%) of **6-Se**, mp 224–225 °C (lit.⁸ mp: 224–225 °C).

Preparation of *N,N*-Diethyl 4-Dimethylamino-2-[3-methoxyphenylseleno]benzamide (9-Se). *sec*-Butyllithium (1.2 M in cyclohexane, 5.1 mL, 6.1 mmol) was added dropwise to a stirred solution of TMEDA (0.70 g, 6.1 mmol) and *N,N*-diethyl 4-*N,N*-dimethylaminobenzamide (1.21 g, 5.5 mmol) in 130 mL of THF at –78 °C. The resulting solution was stirred at –78 °C for 0.5 h. A solution of di-3-methoxyphenyl diselen-

(9) Evers, M.; Christiaens, L. *Tetrahedron Lett.* **1983**, 24, 377–380.

(10) Waschulzik, G.; Schuldes, H.; Oelschlaeger, H. *Ger. Offen.* DE 3125296 A1 19839113, 1983; *Chem. Abstr.* **1983**, 98, 215600.

(11) Detty, M. R.; Murray, B. J. *J. Am. Chem. Soc.* **1983**, 105, 883–892.

nide⁹ (2.27 g, 6.1 mmol) in 30 mL of THF was then added dropwise. The resulting mixture was stirred at -78°C for 1.0 h and then warmed to ambient temperature for 14 h. The reaction mixture was poured into 200 mL of saturated NaCl, and the products were extracted with CH_2Cl_2 (3×100 mL). The combined organic extracts were washed with brine, dried over Na_2SO_4 , and concentrated. The resulting oil was purified via column chromatography on SiO_2 eluted with 20% diethyl ether in CH_2Cl_2 ($R_f = 0.6$) to give 1.57 g (70%) of **9-Se** as a yellow oil, which was used without further purification: ^1H NMR (500 MHz, CDCl_3) δ 7.18 (d, 1 H, $J = 1.5$, 8.0 Hz), 7.06–7.12 (m, 3 H), 6.79 (d, 1 H, $J = 1$, 2.5, 8 Hz), 6.61 (d, 1 H, $J = 2.5$ Hz), 6.84 (d, 1 H, $J = 2.5$, 8 Hz), 6.57 (d, 1 H, $J = 2.4$, 8.5 Hz), 3.74 (s, 3 H), 3.37 (br s, 4 H), 2.81 (s, 6 H), 1.13 (br s, 6 H); IR (NaCl) 1622, 1595 cm^{-1} ; HRMS (ESI) m/z 407.1235 (calcd for $\text{C}_{20}\text{H}_{26}\text{N}_2\text{O}_2^{80}\text{Se} + \text{H}$: 407.1232).

Preparation of 2-*N,N*-Dimethylamino-7-methoxysele-noxanthene-9-one (10-Se) in Acetonitrile. Phosphorus oxychloride (1.9 mL, 20 mmol) was added dropwise to a solution of *N,N*-diethyl 4-*N,N*-(dimethylamino)-2-[3-methoxyphenylse-lenol]benzamide (0.81 g, 2.0 mmol) in 30 mL of acetonitrile. The resulting solution was heated at reflux for 1.5 h and was then poured into a mixture of 30 mL of 1 M NaOH and 30 g of ice. The resulting mixture was stirred for 1 h, and the products were extracted with CH_2Cl_2 (3×30 mL). The combined organic extracts were washed with brine, dried over MgSO_4 , and concentrated. The crude product was purified via chromatography on SiO_2 eluted with 5% EtOAc/ CH_2Cl_2 to give 0.054 g (8%) of selenoxanthone **10-Se**, mp $158\text{--}160^{\circ}\text{C}$: ^1H NMR (500 MHz, CDCl_3) δ 8.54 (d, 1 H, $J = 9$ Hz), 8.46 (d, 1 H, $J = 9$ Hz), 6.96 (d, 1 H, $J = 2.5$ Hz), 6.93 (d, 1 H, $J = 2.5$, 9 Hz), 6.73 (d, 1 H, $J = 2.5$, 9 Hz), 6.62 (d, 1 H, $J = 2.5$ Hz), 3.90 (s, 3 H), 3.08 (s, 6 H); ^{13}C NMR (75 MHz, CDCl_3) δ 179.9, 161.7, 151.9, 136.8, 136.4, 132.8, 132.5, 125.0, 119.9, 114.1, 111.6, 110.8, 107.6, 55.5, 39.9; HRMS (ESI) m/z 334.0335 (calcd for $\text{C}_{16}\text{H}_{15}\text{NO}_2^{80}\text{Se} + \text{H}$: 334.0341). Anal. Calcd for $\text{C}_{16}\text{H}_{15}\text{NO}_2\text{Se}$: C, 57.84; H, 4.55; N, 4.22. Found: C, 58.01; H, 4.35; N, 3.98.

Preparation of *N,N*-Diethyl 4-*N,N*-Dimethylamino-2-phenyltellurobenzamide (11-Te). *tert*-Butyllithium (1.7 M

in pentane, 1.6 mL of 2.7 mmol) was added dropwise to a solution of 4-*N,N*-(dimethylamino)-*N,N*-diethylbenzamide (0.50 g, 2.7 mmol) and 0.45 mL (2.7 mmol) of *N,N,N,N*-tetramethylethylenediamine in 25 mL of THF at -78°C . The resulting solution was stirred at -78°C for 0.5 h, and a solution of diphenyl ditelluride (1.10 g, 2.7 mmol) in 5 mL of THF was added dropwise via syringe. The resulting mixture was stirred at -78°C for 0.5 h and was then warmed to ambient temperature. The reaction mixture was poured into saturated ammonium chloride (100 mL), and the products were extracted with CH_2Cl_2 (3×50 mL). The combined organic extracts were washed with brine, dried over Na_2SO_4 , and concentrated. The resulting yellow oil was purified via chromatography on SiO_2 eluted with 5% diethyl ether in dichloromethane ($R_f = 0.65$) to give 0.40 g (41%) of **11-Te** as a clear, colorless oil, which was used without further purification: ^1H NMR [500 MHz, CD_2Cl_2] δ 7.93 (d, 2 H, $J = 7$ Hz), 7.39 (t, 1 H, $J = 7$ Hz), 7.30 (t, 2 H, $J = 7$ Hz), 7.20 (d, 1 H, $J = 8.5$ Hz), 6.53 (d, 1 H, $J = 2$ Hz), 6.48 (d, 1 H, $J = 2$, 8.5 Hz), 3.44 (br, 4 H), 2.75 (s, 6 H), 1.22 (br, 6 H); ^{13}C NMR [300 MHz, CD_2Cl_2] δ 172.4, 151.5, 141.2, 129.7, 128.7, 128.2, 126.5, 122.6, 118.6, 117.9, 109.5, 42.3 (broad), 39.9, 13.9 (broad); IR (NaCl) 1591 cm^{-1} ; HRMS (ESI) m/z 427.1020 (calcd for $\text{C}_{19}\text{H}_{24}\text{N}_2\text{O}^{130}\text{Te} + \text{H}$: 427.1024).

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Supporting Information Available: ^1H NMR and ^{13}C NMR spectra for *N,N*-diethyl 2-arylchalcogenobenzamide derivatives **7-Te**, **9-Se**, and **11-Te**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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