Synthetic Routes to 4*H*-7-Hydroxybenzo[*b*]tellurin-4-ones

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Intramolecular acylation of *Z*-3-(3-hydroxyphenyltelluro)propenoic acids **9** with P_2O_5/CH_3SO_3H gave 4*H*-7-hydroxybenzo[*b*]tellurin-4-ones **10a**−**c** in 42%, 25%, and 20% isolated yields, respectively. 4*H*-7-Hydroxybenzo[*b*]tellurin-4-ones **10a**−**d** were also prepared by demethylation of 4*H*-7-methoxybenzo[*b*]tellurin-4-ones **11** with BBr_3 in CH_2Cl_2 in 88%, 70%, 66%, and 78% isolated yields.

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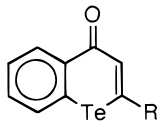
The 4*H*-benzo[*b*]tellurin-4-ones (**1**) and related compounds are useful intermediates for the preparation of benzotelluropyrylium dyes[1−5] and various benzotelluropyranyl compounds,[1b,6,7] both of which have found utility in a number of applications.[1−7] The development of materials derived from **1** has been limited by the paucity of synthetic routes to these and related molecules.[1b] Compound **1a** ("telluroflavone") remains an unknown molecule although both **1b** and **1c** ("tellurochromones) have been described.[8] Numerous attempts to prepare these molecules have been thwarted by the unexpected reactivity of the Te−C bond relative to Se−C and S−C bonds.[1b]

The most common approach to compounds **1** is the cyclization of linear precursors to **1**. These reactions have been complicated by the reactivity of the Te−C bonds of the precursors and, perhaps, by the reactivity of the Te−C bonds of benzotellurin-4-ones themselves.[1b] This point is illustrated in Scheme 1 where cyclization of 3-(phenylthio)- or 3-(phenylseleno)propenoyl chloride derivatives under Friedel−Crafts conditions gives *ortho*-acylation with formation of the corresponding 4*H*-benzo[*b*]thiopyran-4-ones or 4*H*-benzo[*b*]selenopyran-4-ones, respectively.[9] In contrast, 3-(phenyltelluro)propenoyl chlorides under Friedel−Crafts conditions give *ipso*-acylation and formation of rearrangement products **2**.[9] This dichotomy in reactivity is related in part to the electronegativities of Te and C where Te−C bonds are polarized $Te^{\delta+}-C^{\delta-}$ relative to the $E^{\delta-}-C^{\delta+}$ polarization observed for the lighter chalcogen−carbon bonds.[10]



1a, R = Ph
1b, R = Me
1c, R = H

The polarization of the Te−C bond also contributes to the regiochemical differences observed in the cleavage of "telluroethers" relative to ethers and thioethers. Cleavage of the Te−C bonds of organotellurides with acidic compounds has given Te−C bond cleavage with nucleophilic attack at Te—not at C.[11]

More highly substituted derivatives of **1**, including derivatives of **1a**, have been prepared by a second route as shown in Scheme 2.[12] The *ortho*-acylation of propenoic acids **3** to give **4** can be made competitive with *ipso*-acylation to give **5** by placing substituents in the 3- and/or 5-positions of the aryltelluro group that are both *ortho*−*para*-directing and *meta*-deactivating. Prior to the submission of this paper, only fluoro and methoxy substituents in compounds **4** had given products of *ortho*-acylation.

In this paper, we describe the preparation of the previously unknown 4*H*-7-hydroxybenzo[*b*]tellurin-4-

(1) For reviews, see: (a) *Infrared Absorbing Dyes*; Matsuoka, M., Ed.; Plenum Press: New York, 1990. (b) Detty, M. R.; O'Regan, M. B. Tellurium-Containing Heterocycles. *The Chemistry of Heterocyclic Compounds*; Taylor, E. C., Ed.; Wiley-Interscience: New York, 1994; Vol. 53.

(2) For use as electron acceptors in electrophotographic processes, see: (a) Detty, M. R.; Murray, B. J.; Perlstein, J. H. Benzotelluropyrylium Electron-Accepting Dye Sensitizers for Electron-Donating Photoconductive Compositions. U.S. Patent 4,365,017, 1982. (b) Detty, M. R.; Murray, B. J.; Perlstein, J. H. Benzotelluropyrylium Diketonate Electron-Accepting Dye Sensitizers for Electron-Donating Photoconductive Compositions. U.S. Patent 4,365,016, 1982. (c) Detty, M. R.; Murray, B. J.; Perlstein, J. H. Substituted Benzotelluropyrones. U.S. Patent 4,434,098, 1984.

(3) For use as heat-generating elements compatible with gallium−arsenide diode lasers for optical recording, see: Detty, M. R.; Thomas, H. T. Recording and Information Record Elements Comprising Telluropyrylium Dyes. US Patent 4,584,258, 1986.

(4) For use as heat-generating elements compatible with gallium−arsenide diode lasers for thermal imaging, see: Burberry, M. S.; Tutt, L. W.; Detty, M. R. IR Absorber for Laser-Induced Thermal Dye Transfer. U.S. Patent 5,256,620, 1993.

(5) For use as the information element from leuco forms in optical recording media, see: (a) Fleming, J. C.; Detty, M. R. Recordable Optical Element Having a Leuco Dye. U.S. Patent 5,356,685, 1994. (b) Fleming, J. C.; Detty, M. R.; Saeva, F. D. Recordable Optical Element Having a Leuco Dye. U.S. Patent 5,362,536, 1994. (c) Detty, M. R.; Fleming, J. C. Optical Retrieval Apparatus Using a Tellurium-(IV) Leuco Dye. U.S. Patent 5,326,677, 1994.

(6) For use as electron-accepting, charge-transport materials in electrophotographic applications, see: (a) Detty, M. R.; Murray, B. J.; Scozzafava, M. 4-*H* Tellurin Tellurane Compositions of Matter as Sensitizers for Electrophotography. U.S. Patent 4,634,553, 1987. (b) Detty, M. R.; Murray, B. J. *J. Org. Chem.* **1987**, *52*, 2123.

(7) For use as electron-donating compounds in dark-conducting, organic complexes, see: Detty, M. R.; Murray, B. J. *J. Org. Chem.* **1982**, *47*, 1146. (b) Detty, M. R.; Murray, B. J.; Perlstein, J. H. *Tetrahedron Lett.* **1983**, 539.

(8) Dereu, N.; Renson, M. *J. Organomet. Chem.* **1981**, *208*, 11.

(9) Detty, M. R.; Murray, B. J.; Smith, D. L.; Zumbulyadis, N. *J. Am. Chem. Soc.* **1983**, *105*, 875.

(10) Pauling, L. *The Nature of the Chemical Bond*, 3rd ed.; Cornell University Press: Ithaca, NY, 1960.

(11) Piette, J.-L.; Renson, M. *Bull. Soc. Chim. Belg.* **1971**, *80*, 669.

(12) (a) Detty, M. R.; Murray, B. J. *J. Am. Chem. Soc.* **1983**, *105*, 883. (b) Detty, M. R. *Organometallics* **1988**, *7*, 2188.

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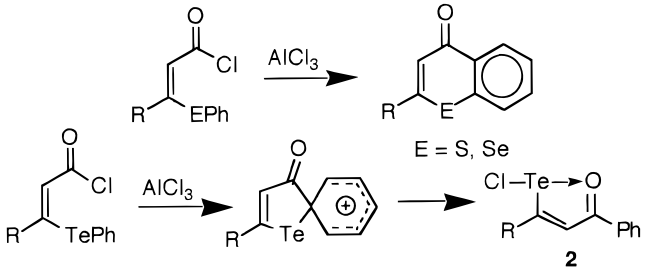
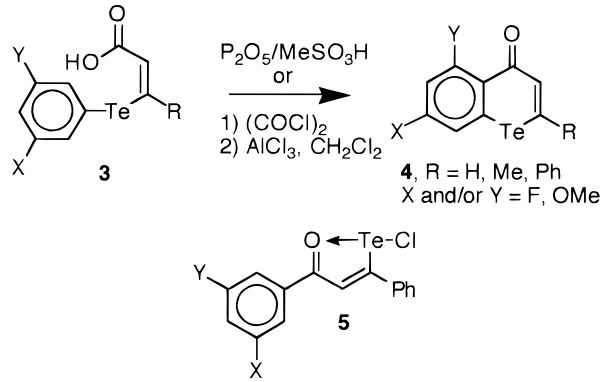
Scheme 1



Scheme 2



ones via two different routes—cyclization of compounds **3** where X is OH and Y is H or demethylation of 7-methoxybenzo[*b*]tellurin-4-ones with BBr_3. Reductive removal of the 7-hydroxy substituent provided an alternative synthesis of 4*H*-benzo[*b*]tellurin-4-ones **1b** and **1c**, although in low yield. Attempts to prepare 4*H*-2-phenylbenzo[*b*]tellurin-4-one (**1a**) by reductive removal of a 7-hydroxy substituent failed due to competitive reduction of Te—C bonds.

Results and Discussion

Cyclization of *Z*-3-(3-Hydroxyphenyltelluro)propenoic Acids. In electrophilic reactions of aromatic molecules, OH as a substituent is strongly *ortho*—*para*-activating ($\sigma_p^+ = -0.92$) and weakly *meta*-deactivating ($\sigma_m^+ = 0.12$).[13] Consequently, one might expect intramolecular cyclization from *ortho*-acylation of substrates such as **3** where X and/or Y is OH. Such substrates were prepared as shown in Scheme 3. *m*-Bromophenol was protected as its *tert*-butyldimethylsilyl (TBS) ether **6** in 96% yield with *tert*-butyldimethylsilyl chloride and imidazole in dimethylformamide (DMF).[14] Ether **6** was converted to the ditelluride **7** (71% yield) by initial formation of the corresponding Grignard reagent, insertion of Te metal, and air-oxidation of the resulting magnesium aryltelluride.[12] The Te—Te bond of the ditelluride was reduced with $NaBH_4$ in EtOH, and the resulting sodium aryltelluride was added to ethyl phenylpropiolate, ethyl 2-butynoate, and ethyl propiolate to give esters **8a**—**c**, respectively, in 66—69% isolated yields. Saponification of the esters with KOH in aqueous ethanol also removed the TBS protecting groups to give phenolic carboxylic acids **9a**—**c** in 55%, 76%, and 74% isolated yields, respectively.

The carboxylic acids **9** cyclized in P_2O_5/CH_3SO_3H[15] to give 4*H*-7-hydroxybenzotellurin-4-ones **10**. 4*H*-7-Hydroxy-2-phenylbenzo[*b*]tellurin-4-one (**10a**) was isolated in 42% yield, while 4*H*-7-hydroxy-2-methylbenzo[*b*]-tellurin-4-one (**10b**) and 4*H*-7-hydroxybenzo[*b*]tellurin-4-one (**10c**) were isolated in 25% and 20% yields, respectively. The structure of compounds **10** followed from their ^1H and ^{13}C NMR spectra, which were quite similar to those of the known 4*H*-7-methoxybenzo[*b*]-tellurin-4-ones **11**.[12a]

Demethylation of 4*H*-7-Methoxybenzo[*b*]tellurin-4-ones 11 with BBr_3. The demethylation of 4*H*-5-methoxybenzo[*b*]tellurin-4-ones (**4**, Y = OMe) with BF_3-etherate has been described.[12b] The demethylation forms a difluoroboron diketonate intermediate, which is then hydrolyzed with aqueous base to give the corresponding 5-hydroxy compounds. The Te—C bonds in the benzo[*b*]tellurin-4-ones are not reactive with BF_3-etherate. For compounds **4** where both X and Y are OMe, the 7-methoxy substituent is unreactive in the presence of BF_3-etherate. Similarly, the 4*H*-7-methoxybenzo[*b*]tellurin-4-ones **11** are unreactive toward BF_3-etherate. Demethylation of these substrates requires a stronger Lewis acid.

The 7-hydroxybenzo[*b*]tellurin-4-ones **10** were successfully prepared by demethylation of 7-methoxy derivatives **11** with BBr_3 in anhydrous CH_2Cl_2 (Scheme 4). Compounds **10a**—**d** were isolated in 88%, 70%, 66%, and 78% isolated yields, respectively. The demethylation of compounds **11** with BBr_3 gave **10** and small quantities (<5%) of unreacted **11** as the only products of reaction.

Reductive Removal of the 7-Hydroxy Substituent as a Synthetic Entry to 4*H*-Benzo[*b*]tellurin-4-ones. The 7-hydroxy derivatives **10** are readily prepared via the two routes described above. Reductive removal of the 7-hydroxy group without cleavage of the Te—C bonds would provide another route to benzo[*b*]-tellurin-4-ones **1** and other derivatives. Especially important would be the reductive removal of the HO group from 4*H*-7-hydroxy-2-phenylbenzo[*b*]tellurin-4-one (**10a**) to give the parent 4*H*-2-phenylbenzo[*b*]tellurin-4-one (**1a**), which remains an unknown compound. Unfortunately, attempts to remove the 7-hydroxy group reductively via the phosphonate ester[16] gave competing reduction of the Te—C bonds with the formation of trace amounts, if any, of the corresponding benzo[*b*]tellurin-4-ones **1**.

Summary and Conclusions

3-(3-Hydroxyphenyltelluro)propenoic acids cyclize to give benzo[*b*]tellurin-4-one products from *ortho*-acylation of the aromatic ring. The hydroxy substituent minimizes competing *ipso*-acylation at the Te—C bond leading to rearrangement products. The 4*H*-7-hydroxybenzo[*b*]tellurin-4-ones **10** were also prepared by demethylation of 7-methoxy derivatives **11** with BBr_3 without competing cleavage of Te—C bonds.

Experimental Section

General Methods. Solvents (HPLC-grade $CHCl_3$, CH_2Cl_2, hexanes, EtOAc, Et_2O, CH_3CN, anhydrous THF, anhydrous

(13) Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165—195.
(14) Corey, E. J.; Venkateswarlu, A. *J. Am. Chem. Soc.* **1972**, *94*, 6190—6191.
(15) Eaton, P. E.; Carlson, G. R.; Lee, J. T. *J. Org. Chem.* **1973**, *38*, 4071—4073.
(16) Rossi, R. A.; Bunnett, J. F. *J. Org. Chem.* **1973**, *38*, 2314—2318.

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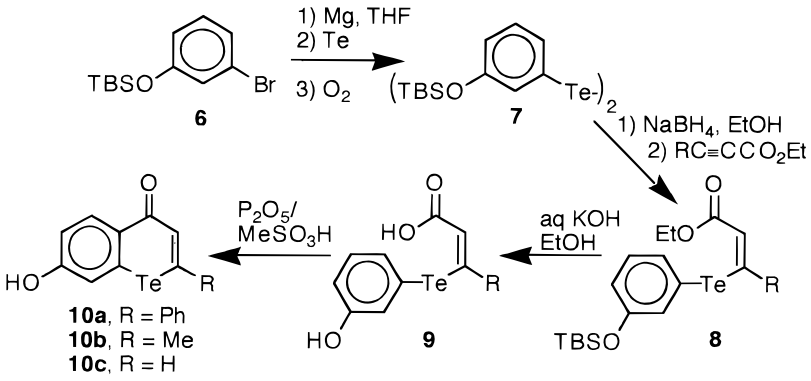
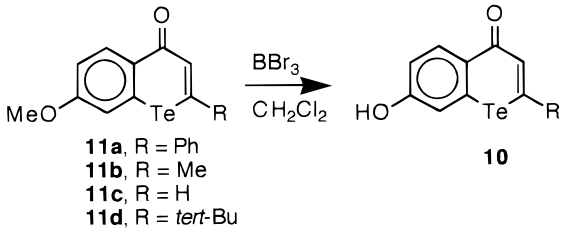
Scheme 3



Scheme 4



DMF, acetone, CH_3SO_3H) were used as received from Aldrich Chemical Co. Imidazole was purchased from Kodak Laboratory Chemicals. 3-Bromophenol, *tert*-butyldimethylsilyl chloride, magnesium turnings, tellurium granules, ethyl phenylpropiolate, ethyl propiolate, ethyl 2-butynoate, boron tribromide, and diethyl chloro phosphate were used as received from Aldrich Chemical Co. Preparative reactions were stirred magnetically. Concentration in vacuo was performed on a Büchi rotary evaporator. Nuclear magnetic resonance (NMR) spectra were recorded at 30.0 °C on a Varian Gemini-300 instrument with residual solvent signal as the internal standard: $CDCl_3$ (δ 7.26 for proton, δ 77.0 for carbon). Infrared spectra of samples were determined as KBr pellets or as chloroform solutions on a Mattson Polaris TM Fourier transmission infrared spectrophotometer. Elemental analyses were performed by Atlantic Microlab, Inc. (Atlanta, GA). Melting points were determined on a Thomas-Hoover Mel-Temp apparatus and are uncorrected. 4*H*-Benzo[*b*]tellurin-4-ones **11a**−**c** were prepared according to ref 12a.

3-Bromophenol *tert*-Butyldimethylsilyl Ether (6). To a solution of 3-bromophenol (10.0 g, 0.0577 mol) in 50 mL of anhydrous DMF were added *tert*-butyldimethylsilyl chloride (9.14 g, 0.606 mol) and imidazole (4.56 g, 0.0684 mol). The reaction mixture was stirred for 15 h under an Ar atmosphere at ambient temperature. The reaction mixture was poured into water (200 mL), and the products were extracted with hexanes (3 × 100 mL). The combined organic extracts were washed with cold 3% HCl (3 × 50 mL) and saturated $NaHCO_3$ solution (2 × 50 mL), dried over $MgSO_4$, and concentrated. The crude product was purified via distillation to give 16.0 g (96%) of **6** as a colorless oil, bp 52−60 °C (5 Torr): ^{1}H NMR ($CDCl_3$) δ 7.05 (overlapping d × d × d, 2 H, J = 1, 8 Hz for major coupling), 7.05 (d × d, 1 H, J = 1, 8 Hz), 6.99 (d × d × d, 1 H, J = 0.7, 1.1, 1.3 Hz), 6.74 (t, 1 H, J = 8 Hz), 0.93 (s, 9 H), 0.20 (s, 6 H); CI MS m/z 286 (M^+, $C_{12}H_{20}{}^{79}BrOSi$). Anal. Calcd for $C_{12}H_{19}BrOSi$: C, 50.17; H, 6.67. Found: C, 50.12; H, 6.59.

Di-3-*tert*-butyldimethylsilyloxyphenyl Ditelluride (7). A solution of 3-bromophenol *tert*-butyldimethylsilyl ether (**6**, 15.0 g, 0.0622 mol) in 60 mL of anhydrous THF was added slowly to Mg turnings (1.7 g, 0.084 mg-at) under an Ar atmosphere. After addition of ~5 mL of solution, a small crystal of iodine was added to initiate reaction. The remainder of the solution was added dropwise at a rate sufficient to maintain reflux. After addition was complete, reflux was maintained for an additional 0.5 h. The reaction mixture was cooled to ambient temperature, and finely ground Te granules (7.66 g, 0.0600 mg-at) were added. The resulting mixture was heated under an Ar atmosphere for 40 min and was then cooled to 0 °C. To this mixture was added 60 mL of saturated NH_4Cl solution. The resulting mixture was filtered through a pad of Celite. The filter cake was washed with saturated NH_4Cl solution (100 mL) and ether (3 × 50 mL). The combined filtrates were extracted with additional ether (3 × 50 mL). The combined ether extracts were washed with brine (2 × 100 mL), dried over Na_2SO_4, and concentrated. The crude ditelluride was purified by chromatography on SiO_2 eluted with hexanes to give 15.0 g (72%) of **7** as a dark red oil: ^{1}H NMR ($CDCl_3$) δ 7.35 (d × d × d, 2 H, J = 1.1, 1.3, 8 Hz), 7.28 (d × d, 2 H, J = 1.3, 2.3 Hz), 6.99 (t, 2 H, J = 1 Hz), 6.66 (d × d × d, 2 H, J = 1.1, 2.3, 8 Hz), 0.91 (s, 18 H), 0.13 (s, 12 H); EI MS m/z 674.0459 (Calcd for $C_{24}H_{38}O_2Si_2{}^{130}Te_2$: 674.0522).

A second product was present as approximately 8% of the product mixture based on singlets at δ 0.90 and 0.17. This product was assumed to be the monotelluride and was observed in the EI MS: m/z 544 (M^+, $C_{24}H_{38}O_2Si_2{}^{130}Te$). This impurity was not separated from the desired ditelluride **7** before subsequent use.

General Procedure for Preparation of Esters 8. Addition of Sodium 3-*tert*-Butyldimethylsilyloxyphenyl Telluride to Acetylenic Esters. Diaryl ditelluride **7** was dissolved in 1/1 THF/EtOH (1 mmol/10 mL) under an Ar atmosphere. Sodium borohydride was added in 0.1 g portions every 5 min until the characteristic dark red color of the ditelluride faded. At this point, the appropriate acetylenic ester (ethyl phenylpropiolate, ethyl propiolate, or ethyl 2-butynoate) in ethanol (2 mmol/mL) was added in one portion and the resulting solution was stirred for 0.5 h at ambient temperature. The excess $NaBH_4$ was quenched by the addition of acetic acid, and the reaction mixture was concentrated in vacuo. The residue was partitioned between CH_2Cl_2 and water. The organic phase was dried over Na_2SO_4 and concentrated. The esters **8** were purified via chromatography on SiO_2 eluted with 30% CH_2Cl_2−hexanes prior to saponification. Analytical samples were prepared by microdistillation at 150 °C and 0.05 Torr.

For ethyl *Z*-3-(3-*tert*-butyldimethylsilyloxyphenyltelluro)-3-phenylpropenoate (**8a**): oil, 67%; ^{1}H NMR ($CDCl_3$) δ 7.57 (d × d, 2 H, J = 1.2, 7.7 Hz), 7.35 (d × d, 1 H, J = 1.2, 7.7 Hz), 7.00 (m, 5 H), 6.77 (t, 1 H, J = 7.7 Hz), 6.68 (s, 1 H), 4.28 (q, 2 H, J = 7 Hz), 1.32 (t, 3 H, J = 7 Hz), 0.91 (s, 9 H), 0.18 (s, 6 H); $\nu_{C=O}$ (KBr) 1678.6 cm^{-1}; FAB(+) MS, m/z 513 ($M-H^+$, $C_{23}H_{31}O_3Si{}^{130}Te$). Anal. Calcd for $C_{23}H_{30}O_3SiTe$: C, 54.14; H, 5.93. Found: C, 54.03; H, 5.92.

For ethyl *Z*-3-(3-*tert*-butyldimethylsilyloxyphenyltelluro)-2-butenoate (**8b**): oil, 70%; ^{1}H NMR ($CDCl_3$) δ 7.49 (d × d × d, 1 H, J = 1.1, 1.3, 7.7 Hz), 7.42 (d × d, 1 H, J = 1.1, 1.3 Hz), 7.14 (t, 1 H, J = 8 Hz), 6.89 (d, 1 H, J = 8 Hz), 6.60 (q, 1 H,

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J = 1.2 Hz), 4.23 (q, 2 H, J = 7 Hz), 2.07 (d, 3 H, J = 1.2 Hz), 1.30 (t, 3 H, J = 7 Hz), 0.97 (s, 9 H), 0.18 (s, 6 H); $n_{C=O}$ (KBr) 1678.4 cm^{-1}; FAB(+) MS, m/z 451 (M−H$^+$, $C_{18}H_{29}O_3Si^{130}Te$). Anal. Calcd for $C_{18}H_{28}O_3SiTe$: C, 48.24; H, 6.30. Found: C, 48.51; H, 6.02.

For ethyl *Z*-3-(3-*tert*-butyldimethylsilyloxyphenyltelluro)-propenoate (**8c**): oil, 66%; ^{1}H NMR ($CDCl_3$) δ 8.48 (d, 1 H, J = 9.4 Hz), 7.36 (d × d × d, 1 H, J = 1.1, 2.3, 8 Hz), 7.29 (d × d, 1 H, J = 1.1, 2.4 Hz), 7.12 (t, 1 H, J = 8 Hz), 6.96 (d, 1 H, J = 9.4 Hz), 6.80 (d × d × d, 1 H, J = 1.3, 2.4, 8 Hz), 4.26 (q, 2 H, J = 7 Hz), 1.31 (t, 3 H, J = 7 Hz), 0.97 (s, 9 H), 0.19 (s, 6 H); FT IR ($CHCl_3$) 1568.9 cm^{-1}; FD MS m/z 436 (M$^+$, $C_{17}H_{26}O_3Si^{130}Te$). Anal. Calcd for $C_{17}H_{26}O_3SiTe$: C, 47.04; H, 6.03. Found: C, 47.13; H, 5.92.

General Procedure for Preparation of Carboxylic Acids 9. Saponification of Esters 8. A solution of ester **8** in EtOH (1 g/20 mL) was warmed to 50 °C. An aqueous 30% KOH solution (2 mL/g of **8**) was added dropwise, and the resulting mixture was stirred for 2 h at 50 °C. The reaction mixture was diluted with cold water (50 mL/g of **8**). The resulting aqueous solution was extracted with ether to remove unreacted starting materials. The aqueous phase was acidified with 10% HCl. The products were extracted with CH_2Cl_2. The CH_2Cl_2 extracts were dried over Na_2SO_4 and concentrated. The crude acids were recrystallized from CH_3CN to give carboxylic acids **9** as crystalline solids.

For *Z*-(3-hydroxyphenyltelluro)-3-phenylpropenoic acid (**9a**): mp 169−171 °C, 55%; ^{1}H NMR ($CDCl_3$) δ 12.82 (br s, 1 H), 9.15 (br s, 1 H), 7.04 (m, 3 H), 6.95 (m, 2 H), 6.81 (d × d, 1 H, J = 1.3, 2.4 Hz), 6.74 (m, 2 H), 6.62 (s, 1 H), 6.46 (d × t, 1 H, J = 2.4, 8 Hz); $n_{C=O}$ (KBr) 1654.8 cm^{-1}; FD MS m/z 370 (M$^+$, $C_{15}H_{12}O_3{}^{130}Te$). Anal. Calcd for $C_{15}H_{12}O_3Te$: C, 48.94; H, 3.26. Found: C, 49.26; H, 3.26.

For *Z*-(3-hydroxyphenyltelluro)-2-butenoic acid (**9b**): mp 167−169 °C, 76%; ^{1}H NMR ($CDCl_3$) δ 12.45 (br s, 1 H), 9.52 (s, 1 H), 7.25 (overlapping signals, 2 H), 7.11 (t, 1 H, J = 8 Hz), 7.23 (d × t, 1 H, J = 2.3, 8 Hz), 6.62 (q, 1 H, J = 1.2 Hz), 2.00 (d, 3 H, J = 1.2 Hz); $n_{C=O}$ (KBr) 1653.9 cm^{-1}; FD MS m/z 294 (M$^+$, $C_9H_8O_3{}^{130}Te$). Anal. Calcd for $C_9H_8O_3Te$: C, 37.05; H, 2.74. Found: C, 37.15; H, 2.77.

For *Z*-(3-hydroxyphenyltelluro)propenoic acid (**9c**): mp 165−167 °C, 74%; ^{1}H NMR ($CDCl_3$) δ 12.05 (br s, 1 H), 9.5 (br s, 1 H), 8.51 (d, 1 H, J = 9.2 Hz), 7.15 (overlapping signals, 2 H), 7.09 (t, 1 H, J = 8 Hz), 6.99 (d, 1 H, J = 9.2 Hz), 6.71 (d × d × d, 1 H, J = 1.1, 1.3, 8 Hz); $n_{C=O}$ (KBr) 1655.8 cm^{-1}; FD MS m/z 308 (M$^+$, $C_{10}H_{10}O_3{}^{130}Te$). Anal. Calcd for $C_{10}H_{10}O_3Te$: C, 39.28; H, 3.27. Found: C, 39.26; H, 3.32.

General Procedure for Cyclization of Carboxylic Acids 9. Preparation of 4*H*-7-Hydroxy-2-phenylbenzo[*b*]tellurin-4-one (10a). Carboxylic acid **9a** (1.45 g, 3.92 mmol) was added to a solution of 1 g of P_2O_5 in 10 mL of CH_3SO_3H. The resulting solution was stirred for 4 h at ambient temperature. The reaction mixture was added dropwise to 250 mL of saturated $NaHCO_3$ solution. The products were extracted with CH_2Cl_2 (3 × 50 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated. For **10a**, the crude product was recrystallized from acetone to give 0.66 g (48%) of fine yellow needles of product. For **10b** and **10c**, the crude reaction mixture was purified by chromatography on SiO_2 eluted with 10% EtOAc−CH_2Cl_2 to give the benzo[*b*]-tellurin-4-ones, which were then recrystallized from acetone to give **10b** and **10c** in 15% and 10% isolated yields, respectively.

For 4*H*-7-hydroxy-2-phenylbenzo[*b*]tellurin-4-one (**10a**): mp 240−241 °C, 48%; ^{1}H NMR (DMSO-d_6) δ 10.55 (s, 1 H), 8.39 (d, 1 H, J = 8.9 Hz), 7.58 (m, 2 H), 7.50 (m, 3 H), 7.48 (d, 1 H J = 2.4 Hz), 7.39 (s, 1 H), 6.94 (d × d, 1 H, J = 2.4, 8.9 Hz); ^{13}C NMR (DMSO-d_6) δ 184.4, 160.2, 144.4, 140.8, 132.7, 130.2, 130.0, 129.4, 126.6, 126.3, 125.6, 119.0, 117.2; $n_{C=O}$ (KBr) 1577.7 cm^{-1}; EI MS m/z 351.9737 (Calcd for $C_{15}H_{10}O_2{}^{130}Te$: 351.9743). Anal. Calcd for $C_{15}H_{10}O_2Te$: C, 51.50; H, 2.85. Found: C, 51.52; H, 2.82.

For 4*H*-7-hydroxy-2-methylbenzo[*b*]tellurin-4-one (**10b**): mp 196−197 °C, 25%; ^{1}H NMR (DMSO-d_6) δ 10.41 (s, 1 H), 8.33 (d, 1 H, J = 8.9 Hz), 7.37 (d, 1 H, J = 2.4 Hz), 6.96 (q, 1 H, J = 1.3 Hz), 6.88 (d × d, 1 H, J = 2.4, 8.9 Hz), 2.50 (d, 3 H, J = 1.3 Hz); ^{13}C NMR (DMSO-d_6) δ 184.1, 159.7, 142.8, 132.4, 131.1, 126.2, 125.8, 118.9, 116.6, 28.1; $n_{C=O}$ (KBr) 1585.0 cm^{-1}; EI MS m/z 289.9597 (Calcd for $C_{10}H_8O_2{}^{130}Te$: 285.9586). Anal. Calcd for $C_{15}H_{10}O_2Te$: C, 51.50; H, 2.85. Found: C, 51.52; H, 2.82.

For 4*H*-7-hydroxybenzo[*b*]tellurin-4-one (**10c**): mp 210−211 °C, 20%; ^{1}H NMR (DMSO-d_6) δ 10.41 (s, 1 H), 8.81 (d, 1 H, J = 12 Hz), 8.38 (d, 1 H, J = 8.9 Hz), 7.38 (d, 1 H, J = 2.4 Hz), 7.28 (d, 1 H, J = 12 Hz), 6.89 (d × d, 1 H, J = 2.4, 8.9 Hz); ^{13}C NMR (DMSO-d_6) δ 183.8, 159.3, 133.1, 132.4, 131.3, 127.3, 119.1, 116.9; $n_{C=O}$ (KBr) 1587.0 cm^{-1}; EI MS m/z 275.9425 (Calcd for $C_9H_6O_2{}^{130}Te$: 275.9430). Anal. Calcd for $C_{15}H_{10}O_2$-Te: C, 39.49; H, 2.19. Found: C, 39.54; H, 2.26.

General Procedure for Demethylation of 7-Methoxybenzo[*b*]tellurin-4-ones 11. Preparation of 7-Hydroxybenzo[*b*]tellurin-4-ones 10. A 1 M solution of BBr_3 in CH_2Cl_2 was added dropwise to a 0.1 M solution of **11** in anhydrous CH_2Cl_2 (1.5 mmol of BBr_3/mmol of **11**) cooled to 0 °C under an Ar atmosphere. The resulting solution was stirred 0.5 h at 0 °C and was then warmed to ambient temperature, where stirring was continued for 15 h. The reaction mixture was slowly added to ice water to quench excess BBr_3, and the aqueous phase was made basic with a 4 N NaOH solution. The organic phase was separated. The aqueous phase was acidified with 4 N HCl and the products were extracted into CH_2Cl_2. The product extracts were dried over $MgSO_4$ and concentrated. The residue was recrystallized from acetone to give **10a** in 88% isolated yield, **10b** in 70% yield, **10c** in 66% yield, and **10d** in 78% yield.

For 4*H*-7-hydroxy-2-*tert*-butylbenzo[*b*]tellurin-4-one (**10d**): mp 191−192 °C; ^{1}H NMR (DMSO-d_6) δ 10.42 (s, 1 H), 8.30 (d, 1 H, J = 8.9 Hz), 7.38 (d, 1 H, J = 2.4 Hz), 7.04 (s, 1 H), 6.89 (d × d, 1 H, J = 2.4, 8.9 Hz), 1.28 (s, 9 H); $n_{C=O}$ (KBr) 1585.0 cm^{-1}; EI MS m/z 332.0087 (Calcd for $C_{13}H_{14}O_2{}^{130}Te$: 332.0057). Anal. Calcd for $C_{13}H_{14}O_2Te$: C, 47.33; H, 4.28. Found: C, 47.52; H, 4.16.

Preparation of 4*H*-7-Methoxy-2-*tert*-butylbenzo[*b*]tellurin-4-one (11d). A. Preparation of Di-3-methoxyphenyl Ditelluride. Di-3-methoxyphenyl ditelluride was prepared according to ref 12a. Careful chromatography on SiO_2 eluted with 5% EtOAc−hexanes gave the ditelluride in 85% yield as a purple crystalline solid, mp 56−60 °C: ^{1}H NMR ($CDCl_3$) δ 7.34 (overlapping signals, 4 H), 7.06 (t, 2 H, J = 8 Hz), 6.74 (d × d × d, 2 H, J = 1, 2.3, 8 Hz), 3.74 (s, 6 H). Anal. Calcd for $C_{14}H_{14}O_2Te_2$: C, 35.81; H, 3.01. Found: C, 36.03; H, 3.34.

B. Preparation of Ethyl *Z*-3-(3-Methoxyphenyltelluro)-4,4-dimethylpentenoate. The general procedure for the preparation of esters **8** was followed except that di-3-methoxyphenyl ditelluride was substituted for ditelluride **7**. The product was isolated in 85% yield as a pale yellow crystalline solid, mp 40−43 °C: ^{1}H NMR ($CDCl_3$) δ 7.55 (overlapping signals, 2 H), 7.12 (t, 1 H, J = 8 Hz), 6.84 (d × d × d, 2 H, J = 1, 2.3, 8 Hz), 6.45 (s, 1 H), 4.13 (q, 2 H, J = 7 Hz), 3.77 (s, 3 H), 1.25 (t, 3 H, J = 7 Hz), 1.17 (s, 9 H); $n_{C=O}$ (KBr) 1679 cm^{-1}; FAB(+) MS, m/z 393 (M−H$^+$, $C_{16}H_{23}O_3{}^{130}$-Te). Anal. Calcd for $C_{16}H_{22}O_3Te$: C, 49.28; H, 5.69. Found: C, 49.51; H, 6.02.

C. Preparation of *Z*-3-(3-Methoxyphenyltelluro)-4,4-dimethylpentenoic Acid. The general procedure for the preparation of acids **9** was followed. The product was isolated in 93% yield as a yellow crystalline solid following recrystallization from CH_3CN, mp 170−173 °C: ^{1}H NMR ($CDCl_3$) δ 10.5 (br s, 1 H), 7.53 (overlapping signals, 2 H), 7.13 (t, 1 H, J = 8 Hz), 6.84 (d × d × d, 2 H, J = 1, 2.3, 8 Hz), 6.49 (s, 1 H), 3.78

(s, 3 H), 1.19 (s, 9 H); $n_{C=O}$ (KBr) 1654 cm^{-1}; FAB(+) MS, *m*/*z* 365 ($M-H^+$, $C_{14}H_{19}O_3{}^{130}Te$). Anal. Calcd for $C_{14}H_{18}O_3Te$: C, 46.47; H, 5.01. Found: C, 46.51; H, 5.12.

D. Preparation of 4*H*-7-Methoxy-2-*tert*-butylbenzo[*b*]-tellurin-4-one (11d). *Z*-3-(3-Methoxyphenyltelluro)-4,4-dimethylpentenoic acid (1.45 g, 4.00 mmol) was added to a solution of 1 g of P_2O_5 in 10 mL of CH_3SO_3H. The resulting solution was stirred for 4 h at ambient temperature. The reaction mixture was added dropwise to 250 mL of saturated $NaHCO_3$ solution. The products were extracted with CH_2Cl_2 (3 × 50 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated. The crude reaction mixture was purified by chromatography on SiO_2 eluted with 10% EtOAc−CH_2Cl_2 to give 7-methoxybenzo[*b*]tellurin-4-one **11d** in 82% yield following recrystallization from CH_3CN: mp 143−146 °C; ^1H NMR ($CDCl_3$) δ 8.57 (d, 1 H, J = 8.9 Hz), 7.21 (s, 1 H), 7.16 (d, 1 H, J = 2.4 Hz), 6.96 (d × d, 1 H, J = 2.4, 8.9 Hz), 3.86 (s, 3 H), 1.33 (s, 9 H); $n_{C=O}$ (KBr) 1585.0 cm^{-1}; FAB(+) MS, *m*/*z* 347 ($M-H^+$, $C_{14}H_{17}O_2{}^{130}Te$). Anal. Calcd for $C_{14}H_{16}O_2Te$: C, 48.90; H, 4.69. Found: C, 48.91; H, 4.87.

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