Toward Novel Antioxidants: Preparation of Dihydrotellurophenes and Selenophenes by Alkyltelluride-Mediated Tandem $S_{RN}1/S_Hi$ Reactions[1]

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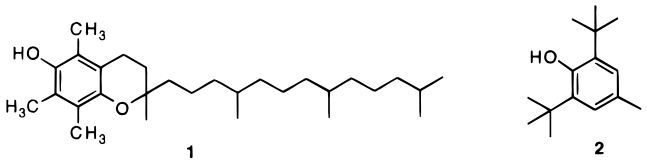
Reaction of 1-(2-iodophenyl)-1-methyloxirane (**12**) with 2 equiv of sodium *n*-butyltellurolate (*n*-BuTeNa), generated by the sodium borohydride reduction of di-*n*-butyl ditelluride, in THF, affords 2,3-dihydro-3-hydroxy-3-methylbenzo[*b*]tellurophene (**13**) in 62% yield, together with a small quantity of 1-(*n*-butyltelluro)-2-phenyl-2-propanol (**27**). This transformation presumably involves a tandem $S_{RN}1/S_Hi$ sequence. Similar reactions of 1-(benzylseleno)-2-phenyl-2-propanol (**5a**, R = Me) and 1-allyloxy-2-iodobenzene (**15**) afforded 2,3-dihydro-3-hydroxy-3-methylbenzo[*b*]selenophene (**17**, 74%), and 3-(*n*-butyltelluro)methyl-2,3-dihydrobenzo[*b*]furan (**18**, 50%), respectively. Lithium alkyltellurolates, generated by direct tellurium insertion into the required alkyllithium, or *sec*-butyl or *tert*-butyl substitution on tellurium provide product distributions similar to those observed for reactions involving *n*-BuTeNa. Lithium or sodium phenyltellurolate returned only starting materials from these reaction mixtures. The 2-[2-(*n*-butyltelluro)-1-hydroxy-1-methyl]ethylphenyl radical (**14**) is estimated to cyclize with $k_c = 5 \times 10^8\ s^{-1}$ at 25 °C. The tandem $S_{RN}1/S_Hi$ sequence has been applied to the preparation of the antioxidant analogues, 5-hydroxy-2,3-dihydrobenzo[*b*]-tellurophene and selenophene (**31**, **32**).

Introduction

α-Tocopherol (**1**) is a lipid-soluble antioxidant present in human blood and the major component of vitamin E.[4] The activity of **1** is most likely due to its ability to quench active peroxyl radicals in vivo through the rapid transfer of the phenolic hydrogen in **1**.[5] 2,6-Di-*tert*-butyl-4-methylphenol (BHT) (**2**) is a further example of a common antioxidant that finds application in the food industry.[6] Benzofuran (**3**) displays enhanced antioxidant activity when compared with **1**; this enhanced activity has been explained in terms of the better overlap between the nonphenolic 2p-type lone pair and the aromatic π-system in **3** as compared to **1**.[7]



We have been engaged in the development of novel antioxidants carrying sulfur, selenium, and tellurium.[8] Divalent organochalcogen compounds react readily with many types of oxidants (peroxides, peroxyl radicals, peroxynitrite, singlet oxygen, ozone), and the resulting tetravalent organochalcogens are reduced by many mild reducing agents. Therefore, compounds of this sort have the potential to act as catalytic antioxidants in the presence of suitable stoichiometric reductants. Some of us have been developing methods for the preparation of chalcogen-modified analogues (**4a**−**c**).[9] Others of us have developed useful methodology based on intramolecular

(1) Part of this work has been published in preliminary form: Laws, M. J.; Schiesser, C. H. *Tetrahedron Lett.* **1997**, *38*, 8429.
(2) Uppsala University.
(3) The University of Melbourne.
(4) Burton, G. W.; Ingold, K. U. *Acc. Chem. Res.* **1986**, *19*, 194.
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(6) Forrester, AS. R.; Hay, J. M.; Thomson, R. H. *Organic Chemistry of Stable Free Radicals*; Academic Press: London, 1968; Chapter 7, p 281.
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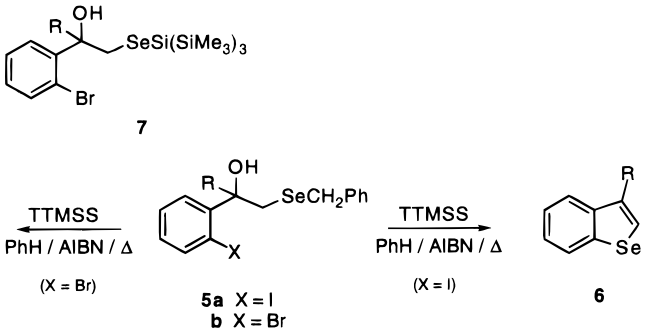
free-radical homolytic substitution at selenium for the preparation of a wide cross-section of selenium-containing ring systems including dihydrobenzo[*b*]selenophenes.[10,11] It seemed reasonable, therefore, to explore the use of this chemistry for the preparation of selenium- and tellurium-containing analogues of **4a**.

The choice of radical precursor and leaving radical on selenium is crucial to the success of homolytic substitution chemistry at selenium.[10,12] We reported that the combination of iodide precursor and benzyl leaving group are ideal for ring-closure using standard radical techniques.[10.11] For example, iodide (**5a**) provides an excellent yield of benzo[*b*]selenophene (**6**) upon treatment with tris(trimethylsilyl)silane (TTMSS) under standard radical conditions, whereas bromide (**5b**) reacted to afford predominantly the selenosilane (**7**) under identical conditions.[10]

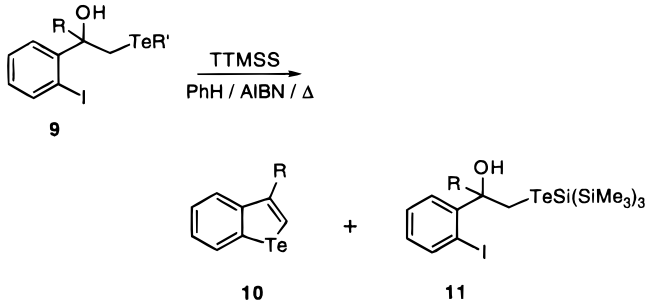


Rate studies, as well as ab initio computational data, suggest that the rate of homolytic substitution at the halogen and chalcogen in a given row are very similar.[12] For example, rate constants at 50 °C of 7×10^4, 2.6×10^7, 1×10^5, and 2.3×10^7 M^{-1} s^{-1} have been determined, respectively, for the attack of primary alkyl radical at the halogen or chalcogen center in the series of substituted ethyl acetates (**8a**−**d**).[13]

YCH_2CO_2Et

8a	Y = Br	(7.0×10^4 $M^{-1}s^{-1}$ at 50°)
b	Y = I	(2.6×10^7)
c	Y = SePh	(1.0×10^5)
d	Y = TePh	(2.3×10^7)

What precursor then are we to choose for the preparation of tellurium-containing rings through the use of analogous intramolecular homolytic chemistry? Both rate constant and computational data suggest that iodide precursors of type **9** may only be expected to afford a 50% yield of the required cyclized product (**10**) together with about the same quantity of the undesired tellurosilane (**11**) under the conditions employed for the construction of **6**.[14,15]



Without recourse to a satisfactory solution, we chose to nevertheless explore chemistry analogous to that described for the construction of **6**. In this paper, we report the serendipitous discovery that sodium alkyltellurolates are excellent reagents for the generation of aryl radicals from the corresponding iodides in the dark. This chemistry can be used to effect ring closure by intramolecular homolytic substitution at selenium and tellurium, as well as intramolecular addition to alkenes and alkynes.

Results and Discussion

Serendipity in Action. In a fashion analogous to that reported for the preparation of benzo[*b*]selenophenes (**6**), our initial experiments were directed toward the preparation of iodides of type **9**.[10] Accordingly, 1-(2-iodophenyl)-1-methyloxirane (**12**)[10] was reacted with 2 equiv of sodium *n*-butyltellurolate,[16] generated by the reduction of di-*n*-butyl ditelluride[17] with sodium borohydride in THF followed by the addition of a small quantity of methanol.[18] ^1H NMR spectroscopy of the crude reaction mixture after workup revealed the absence of starting material (**12**), while ^{125}Te NMR spectroscopy indicated the presence of di-*n*-butyl ditelluride (δ 110.5),[19] di-*n*-butyl telluride (δ 225.9),[19] and a third signal at δ 418.0 that presumably corresponds to the major product (TLC). To our surprise, none of the expected telluride (**9**, R = Me, R′ = Bu) was isolated from the reaction mixture by flash chromatography; rather, the major product was determined to be 2,3-dihydro-3-hydroxy-3-methylbenzo[*b*]tellurophene (**13**), which was isolated in 62% yield (Scheme 1). Compound **13** was readily converted into

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(14) Schiesser, C. H.; Smart, B. A.; Tran, T.-A. *Tetrahedron* **1995**, *51*, 3327. Schiesser, C. H.; Smart, B. A. *Tetrahedron* **1995**, *51*, 6051. See correction in: Schiesser, C. H.; Smart, B. A.; Tran, T.-A. *Tetrahedron* **1995**, *51*, 10651.

(15) The use of radioactive astatine as the halogen precursor was not attractive to us.

(16) Reactions involving sodium alkyl- or aryltellurolates are sensitive to small quantities of oxygen. As organic tellurides are easily removed by chromatography, we commonly add excess reagent in order provide maximum yield.

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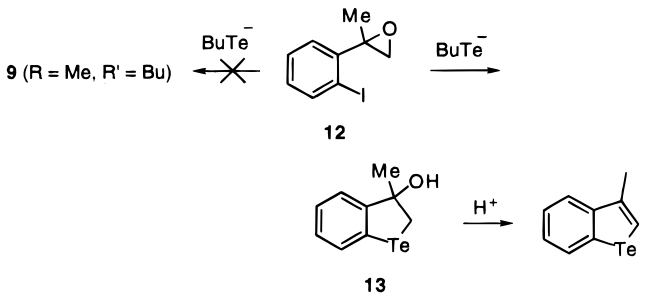
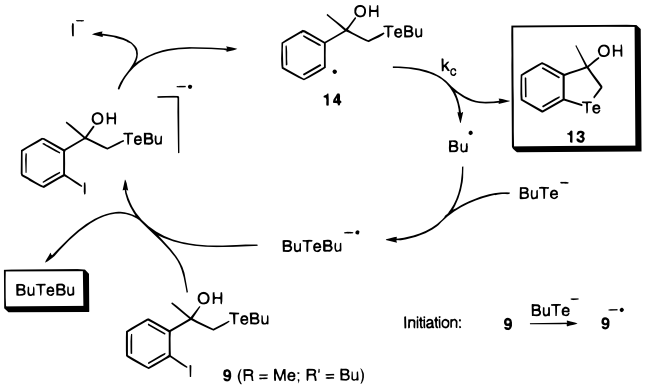
(18) Lucas, M. A.; Schiesser, C. H. *J. Org. Chem.* **1996**, *61*, 5754.

(19) Luthra, N. P.; Odom, J. D. In *The Chemistry of Organic Selenium and Tellurium Compounds*; Patai, S., Rappoport, Z., Eds.; Wiley: New York, 1986; Vol. 1, Chapter 6, p 189. ^1H NMR spectroscopy revealed that di-*n*-butyl telluride (δ 2.65, 4H, t) and **9** (R = Me, R′ = Bu) were produced in approximately equal proportions.

Scheme 1



Scheme 2

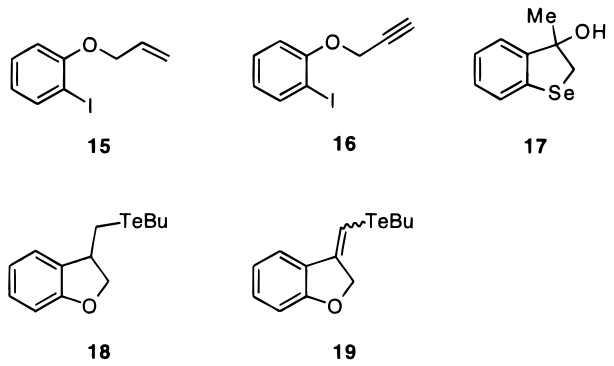


3-methylbenzo[*b*]tellurophene by treatment with a catalytic amount of *p*-toluenesulfonic acid in benzene under reflux.[19,20]

The conversion of **12** to **13** is a three-step reaction. Presumably, dihydrotellurophene **13** arises via intramolecular homolytic substitution at the tellurium atom in radical **14** with expulsion of *n*-butyl radical. The aryl radical **14** is presumably generated as part of a butyltelluride-mediated $S_{RN}1$ mechanism[21] (Scheme 2), which relies on the rapid in situ generation of telluride (**9**, R = Me, R′ = Bu) from $BuTe^-$ and epoxide (**12**). This chain reaction is most likely initiated by an electron transfer from *n*-butyltellurolate to aryl iodide (**9**, R = Me, R′ = Bu). To the best of our knowledge, the transformation depicted in Scheme 2 represents the first example of intramolecular homolytic substitution at tellurium.

It is interesting to note that the use of 1 equiv of sodium *n*-butyltellurolate results in a diminished yield of **13**, while more than 2 equiv results in no measurable improvement in reaction outcome. These observations are consistent with the mechanism proposed in Scheme 2, as 2 equiv of *n*-butyltellurolate is required to generate 1 equiv of **13** together with 1 equiv of di-*n*-butyl telluride.

To establish the intermediacy of aryl radicals in these reactions, we next examined the reaction of benzyl selenide (**5a**, R = Me)[10] as well as 1-allyloxy-2-iodobenzene (**15**)[22] and 1-propargyloxy-2-iodobenzene (**16**)[22] with 1 or 2 equiv of sodium *n*-butyltellurolate in THF under the previously described conditions. To our delight, after 24 h, **5a** (R = Me) had been completely consumed. Apart from small amounts of unidentifiable material, ^{1}H NMR spectroscopy revealed that **5a** had been transformed predominantly into 2,3-dihydro-3-hydroxy-3-methylbenzo[*b*]selenophene (**17**), which was isolated in 74% yield after flash chromatography.



In contrast, the reaction involving **15** proceeded much more slowly under the conditions described and was only 50% complete after 24 h. ^{1}H NMR spectroscopy of the crude reaction mixture indicated the presence of starting material (**15**, 50%) and ring-closed material (**18**, 50%). Telluride **18** appeared to be unstable and could only be isolated in 17% yield as a yellow oil after flash chromatography. Crich and co-workers recently reported similar stability problems with structurally related tellurides.[23] It is interesting to note that Beckwith and Palacios reported similar intramolecular homolytic addition chemistry involving $S_{RN}1$ sequences involving PhS^- and Ph_2P^-.[24]

Similar chemistry involving the alkyne **16** resulted in a complex mixture of products as determined by TLC. ^{1}H NMR spectroscopy of the crude reaction mixture indicated the absence of starting iodide **16**; the appearance of signals at δ 4.8−5.5 are consistent with the formation of the expected product **19**; however, if it is being formed, its extreme lability precludes its isolation and characterization by standard techniques.

The formation of ring-closed products **17** and **18** from precursors **5a** (R = Me) and **15** leaves no doubt about the involvement of aryl radicals. The formation of the organotellurium compound can be rationalized by assuming 5-exo cyclization, reaction of the resulting radical with *n*-butyltellurolate, and electron transfer to the aryl iodide. Rate data presented below provide further evidence for a radical pathway for this chemistry.

Role of Alkyl Substituent on Tellurium. Having established that sodium *n*-butyltellurolate in THF can be used for the preparation of dihydrobenzotellurophenes and that this chemistry most likely involves intramolecular homolytic substitution at tellurium, we were curious to explore the effect of other tellurolates in these reactions. The alkyl group present on the tellurium center might be expected to affect the electron-transfer properties of the tellurolate and the ease with which the aryl

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radical generated might undergo homolytic substitution at tellurium. We therefore chose to examine reactions analogous to those described above using oxirane (**12**) together with *sec*-butyltellurolate (*s*-BuTe$^-$) and *tert*-butyltellurolate (*t*-BuTe$^-$). In addition, as the borohydride used for the preparation of the tellurolates in this study may play a role in the chemistry described, we also generated lithium *n*-butyltellurolate and lithium *tert*-butyltellurolate in situ by insertion of tellurium metal into the carbon−lithium bond of the appropriate (commercially available) alkyllithium.

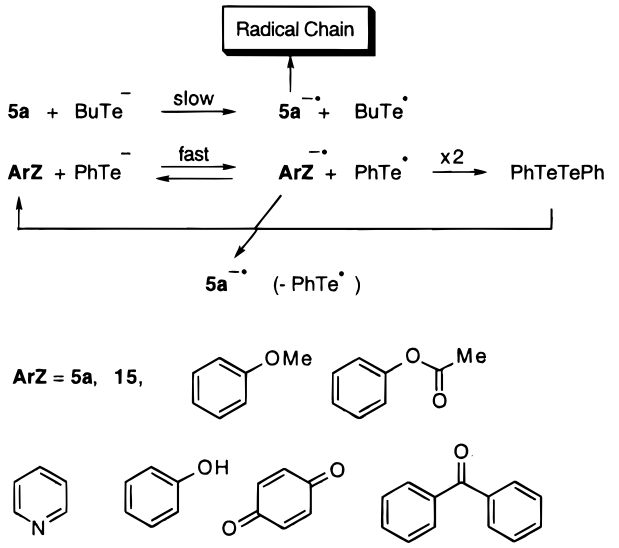
Interestingly, reactions involving *s*-BuTe$^-$ and *t*-BuTe$^-$ appear to proceed less cleanly than the reaction involving the original reagent (*n*-BuTe$^-$). Our studies reveal that alkyl substitution at tellurium appears to affect the reaction outcome slightly, with the *sec*-butyl and *tert*-butyl reagents providing yields of **13** of 38 and 43%, respectively. In addition, the method of generation of reagent appears not to be a major factor, with lithium *n*-butyltellurolate, prepared in the absence of borohydride, providing a yield of 50% compared with the 62% yield of **13** obtained under the original reaction conditions. Once again, the reaction involving the in situ generation of the lithium reagent proved to be less clean than that performed under the original reaction conditions.

We conclude from these experiments that borohydride probably does not play an important role in the $S_{RN}1$ chemistry depicted in Scheme 2 and that alkyl substitution has no significant effect on either the electron-transfer properties of the tellurolate or the intramolecular homolytic substitution chemistry at tellurium.

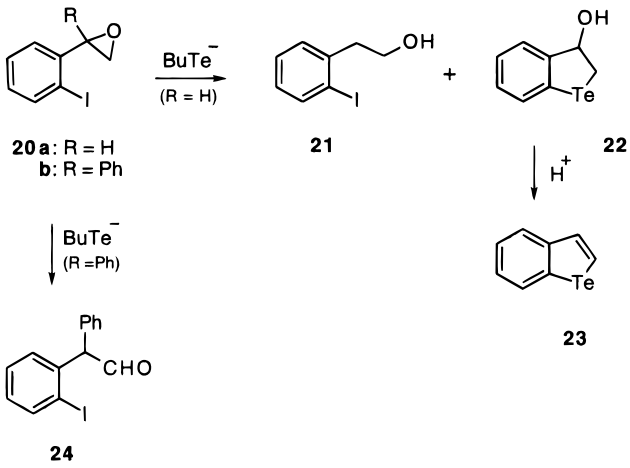
Reactions Involving Diphenyl Ditelluride. Reactions involving **5a** and **15** might be expected to be carried out using readily available diphenyl ditelluride. We therefore subjected these compounds to the previously described reaction conditions using diphenyl ditelluride instead of di-*n*-butyl ditelluride. Surprisingly, addition of either **5a** or **15** to a colorless solution of sodium phenyltellurolate in THF resulted in immediate red coloration of the solution. Workup and isolation by chromatography afforded only starting materials (**5a** or **15**) and diphenyl ditelluride. We conclude that the substrate (**5a** or **15**) undergoes rapid electron transfer from PhTe$^-$, and the resulting phenyltellanyl radical then undergoes rapid recombination to afford diphenyl ditelluride. Indeed, many classes of aromatic substrate were found to behave similarly (Scheme 3). Similar chemistry is observed with lithium phenyltellurolate in THF, prepared by the insertion of elemental tellurium into the carbon−lithium bond of commercially available phenyllithium.

We are unable to provide a completely satisfactory explanation for these observations. We speculate that a radical chain reaction similar to that depicted in Scheme 2 is unable to be sustained in reactions involving phenyltellurolate. This might arise because of unfavorable equilibria established during "attempted" chain-initiation processes (Scheme 3); the red coloration may well represent a static concentration of the highly colored diphenyl ditelluride. This mechanism would also help to explain why seemingly innocuous aromatic substrates also react to give red solutions. We are currently further exploring the mechanistic implications of these observations.

Scheme 3



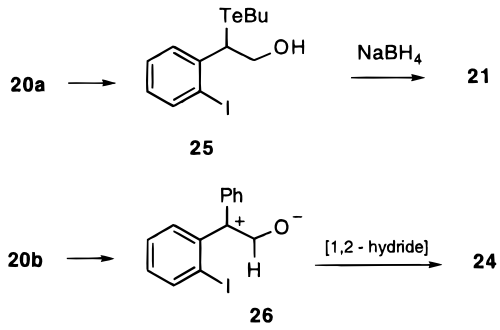
Scheme 4



Other Tellurophenes. We were interested in determining whether the substituent on the oxirane plays any significant role in the chemistry described above. Accordingly, (2-iodophenyl)oxirane (**20a**) and 1-(2-iodophenyl)-1-phenyloxirane (**20b**) were prepared as described previously.[10] Interestingly, when **20a** was treated with *n*-BuTeNa [$(n\text{-BuTe})_2/NaBH_4$], ^{1}H NMR spectroscopy of the crude reaction mixture revealed an approximately equal mixture of what we assigned to be 3-hydroxy-2,3-dihydrobenzo[*b*]tellurophene (**22**) and 2-(2-iodophenyl)-ethanol (**21**). Unfortunately, we were unable to separate **21** from **22** by flash chromatography. Instead, the mixture was treated with a catalytic amount of *p*-toluenesulfonic acid in benzene under reflux to obtain benzo[*b*]-tellurophene[20] (**23**) free from **21** after chromatography (Scheme 4).

The origin of **22** is clear; however, **21** is less obvious. We suggest that, as was observed in the analogous selenium chemistry,[10] **20a** is attacked by *n*-BuTe$^-$ at each end of the oxirane moiety approximately equally. Attack at the less substituted (primary) end leads ultimately to dihydrotellurophene (**22**), while attack at the benzylic position would be expected to give the telluride (**25**),

which we speculate is rapidly reduced to **21**.



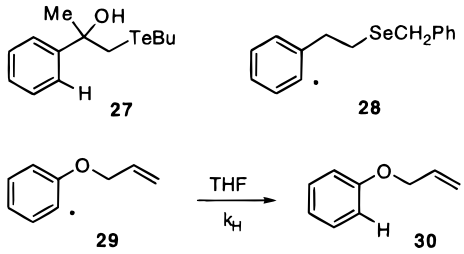
When **20b** was treated with *n*-BuTeNa as described previously, none of the expected dihydrotellurophene was isolated. Instead, the major product proved to be (2-iodophenyl)phenylacetaldehyde (**24**, 45%) as well as significant quantities of unrecognizable material. We attribute this observation to the inherent instability of oxirane (**20b**), which was observed to quantitatively rearrange to **24** upon prolonged standing at room temperature.

Kinetics. Close examination of the products obtained during the reaction of **12** with *n*-BuTe$^-$ revealed the presence of small quantities of directly reduced telluride (**27**). The observed distribution of **13** and **27** allows, for the first time, an estimate for the rate constant for intramolecular homolytic substitution at tellurium. Application of the appropriate integrated rate expression[10] (eq 1), which integrates to eq 2 under pseudo-first-order conditions in THF, and given that [THF] = 12 M,[25] that [**13**]/[**27**] = 8.14 by ^{1}H NMR integration, and that the rate constant for abstraction of hydrogen atom by aryl radical from THF (k_H) is 5.1×10^6 M^{-1} s^{-1} at 25 °C,[26] the rate constant for ring closure of **14** (k_c) can be determined to be approximately 5×10^8 s^{-1} at 25 °C. This value is to be compared with the estimated rate constant for the similar ring closure at selenium atom in selenide (**28**) with expulsion of benzyl radical, which is estimated to be approximately 3×10^7 s^{-1} at 80 °C.[10] The increase in the rate constant for the ring closure of **14** over **28** is expected on the basis of well-established trends in the rate constants for intermolecular homolytic substitution at selenium and tellurium and relative leaving-group abilities.[12]

$$\mathrm{d}[\mathbf{13}]/\mathrm{d}[\mathbf{27}] = k_c/(k_H[\mathrm{THF}]) \quad (1)$$

$$[\mathbf{13}]/[\mathbf{27}] = k_c/(k_H[\mathrm{THF}]) \quad (2)$$

To assess the validity of the above approach, we applied the same procedure to the ring closure of the aryl radical derived from the iodide **15**. Recognizing the cleanness of this reaction and assuming that ^{1}H NMR spectroscopy has a 1% detection limit (i.e., [**18**]/[**30**] > 99), the rate constant (k_c) for the cyclization of radical (**29**) can be estimated to be greater than approximately 6×10^9 s^{-1} at 25 °C, consistent with the well-established value of 6.3×10^9 s^{-1} (30 °C).[26]



Application. We have demonstrated that sodium *n*-butyltellurolate is an effective reagent for the generation of aryl radicals from aryl iodides and that these radicals can undergo further synthetically useful transformations. It seemed reasonable, therefore, to apply the chemistry developed to the preparation of phenolic dihydrotellurophenes and selenophenes (**31**, **32**). Clearly, the chemistry used in their preparation would be expected to be useful in the construction of more advanced α-tocopherol analogues such as selenium- and tellurium-containing compounds **4b** and **4c**.

A convenient synthesis should start with ethyl 3-hydroxyphenylacetate (**33**). Accordingly, ethyl 3-hydroxyphenylacetate (**33**) was TBDMS-protected and reduced following standard procedures to afford alcohol (**34**) in 96% yield (Scheme 5). Further treatment with iodine and silver trifluoroacetate followed by methanesulfonation using standard methodology and further reaction with sodium iodide in acetone afforded diiodide (**35**) in 85% overall yield. Reaction of **35** with sodium benzylselenolate afforded selenide (**36**) in 84% yield.

To our delight, when the diiodide (**35**) was reacted with 2 equiv of sodium *n*-butyltellurolate as described previously, the dihydrobenzo[*b*]tellurophene (**37**) was isolated in 47% yield after chromatography, while the analogous reaction involving **36** and 1 equiv of NaTeBu resulted in the required dihydrobenzo[*b*]selenophene (**38**) being isolated in 65% yield after chromatography. Simple TBAF deprotection afforded the model antioxidants (**31**, **32**) in good to excellent yields.

Experimental Section

Di-*n*-butyl ditelluride,[17] bis(*sec*-butyl) ditelluride,[17] bis(*tert*-butyl) ditelluride,[17] diphenyl ditelluride,[27] 1-(benzylseleno)-2-(2-iodophenyl)propan-2-ol[10] (**5a**, R = Me), 1-(2-iodophenyl)-1-methyloxirane[10] (**12**), 1-allyloxy-2-iodobenzene (**15**),[22] 1-iodo-2-propargyloxybenzene (**16**),[22] (2-iodophenyl)oxirane[10] (**20a**), 1-(2-iodophenyl)-1-phenyloxirane[10] (**20b**), ethyl 3-hydroxyphenylacetate (**33**),[28] and dibenzyl diselenide[29] were prepared according to previously published procedures. All melting points and boiling points are uncorrected. NMR spectra were recorded in $CDCl_3$ unless otherwise stated. ^{77}Se and ^{125}Te NMR chemical shifts (δ) are given in ppm relative to externally referenced diphenyl diselenide (δ 464) and diphenyl ditelluride (δ 420), respectively. Elemental analyses were carried out by Chemical and Micro Analytical Services Pty. Ltd, Geelong, Victoria, Australia, or by Analytical Laboratories, Lindlar, Germany.

Standard Protocol (A) for the Reaction of Aryl Iodides with Sodium *n*-Butyltellurolate. 2,3-Dihydro-3-hydroxy-3-methylbenzo[*b*]tellurophene (13). Sodium borohydride (47 mg, 1.24 mmol) was added with stirring to a solution of di-*n*-butyl ditelluride (216 mg, 0.59 mmol) in THF (2 mL). The

(25) The concentration of THF is approximately 12 M based on a density of 0.886 (25 °C).

(26) *Landolt-Börnstein, Numerical Data and Functional Relationships in Science and Technology*; Fischer, H., Ed.; Springer-Verlag: Berlin, 1994; Vol. II/18.

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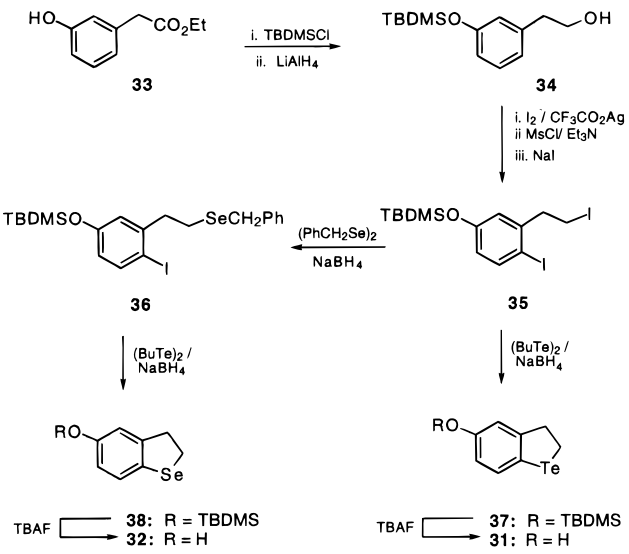
(29) Reich, H. J.; Jasperse, C. P.; Renga, J. M. *J. Org. Chem.* **1986**, *51*, 2981.

Scheme 5



reaction vessel was purged with nitrogen, and methanol (ca. 1 mL) was added dropwise, with caution, until a persistent pale yellow solution was obtained. 1-(2-Iodophenyl)-1-methyloxirane (**12**) (118 mg, 0.45 mmol) in THF (1 mL) was added rapidly and the resultant mixture stirred overnight while shielded from background light. Water (5 mL) was added, the product was extracted into ether (3 × 10 mL), the combined extracts were dried ($MgSO_4$), and the solvent was removed in vacuo. The residue was purified by flash chromatography (85:15 petroleum ether/ether to give **13** as a yellow solid (74 mg, 62%): mp = 71−73 °C; ^{1}H NMR δ 1.71 (3H, s), 2.43 (1H, s(br)), 3.74 (1H, d, J = 10.5 Hz), 3.79 (1H, d, J = 10.5 Hz), 7.17−7.24 (3H, m), 7.39−7.42 (1H, m); ^{13}C NMR δ 23.8, 26.9, 86.4, 116.6, 125.7, 126.7, 129.1, 132.9, 151.7; ^{125}Te NMR δ 418. Anal. Calcd for $C_9H_{10}OTe$: C, 41.3; H, 3.9. Found: C, 41.7; H, 4.1.

3-Methylbenzo[*b*]tellurophene.[19,20] A solution of **13** (17 mg, 65 μmol) and *p*-toluenesulfonic acid (ca. 10 mg) in benzene (2 mL) was heated under reflux for 30 min. The solution was cooled and the solvent removed in vacuo. Dichloromethane (5 mL) was added, the solution washed with water (2 × 5 mL) and dried ($MgSO_4$), and the solvent removed in vacuo to afford the title compound (16 mg, 94%) as a yellow oil exhibiting spectral data identical to those reported previously:[19,20] ^{1}H NMR δ 2.40 (3H, d, J = 0.6 Hz), 7.22 (1H, t, J = 7.8 Hz), 7.42 (1H, t, J = 7.8 Hz), 7.69 (1H, d, J = 8.1 Hz), 7.96 (1H, d, J = 7.7 Hz), 8.22 (1H, s); ^{13}C NMR δ 19.8, 114.6, 124.5, 124.9, 126.2, 132.4, 143.0, 147.3; ^{125}Te NMR δ 652.

2,3-Dihydro-3-hydroxy-3-methylbenzo[*b*]selenophene (17) was prepared according to the standard protocol (A) using 1-benzylseleno-2-(2-iodophenyl)propan-2-ol (**5a**, R = Me) (106 mg, 0.25 mmol), di-*n*-butyl ditelluride (85 mg, 0.23 mmol), and sodium borohydride (35 mg, 0.93 mmol). Flash chromatography (70:30 petroleum ether/ether) afforded **17** as a pale yellow solid (39 mg, 74%): mp = 69−70 °C; ^{1}H NMR δ 1.63 (3H, s), 2.37 (1H, s(br)), 3.37 (1H, d, J = 10.8 Hz), 3.43 (1H, d, J = 10.8 Hz), 7.11−7.20 (3H, m), 7.25−7.28 (1H, m); ^{13}C NMR δ 25.9, 41.0, 83.8, 124.3, 125.6, 126.5, 129.3, 134.8, 146.4; ^{77}Se NMR δ 259. Anal. Calcd for $C_9H_{10}OSe$: C, 50.7; H, 4.7. Found: C, 50.6; H, 4.8.

3-(*n*-Butyltelluro)methyl-2,3-dihydrobenzo[*b*]furan (18) was prepared according to the standard protocol (A) using 1-allyloxy-2-iodobenzene (**15**) (105 mg, 0.41 mmol), di-*n*-butyl ditelluride (72 mg, 0.21 mmol), and sodium borohydride (21 mg, 0.56 mmol). Flash chromatography (95:5 petroleum ether/ether) afforded **18** as an unstable yellow oil (22 mg, 17%): ^{1}H NMR δ 0.91 (3H, t, J = 7.5 Hz), 1.31−1.43 (2H, m), 1.66−1.76 (2H, m), 2.64 (2H, t, J = 7.5 Hz), 2.79 (1H, dd, J = 6.1, 9.3 Hz), 3.07 (1H, dd, J = 4.5, 12.0 Hz), 3.71−3.80 (1H, m), 4.29 (1H, dd, J = 6.1, 9.3 Hz), 4.68 (1H, t, J = 8.7 Hz), 6.79 (1H, d, J = 7.8 Hz), 6.87 (1H, t, J = 7.5 Hz), 7.15 (1H, t, J = 7.8 Hz), 7.23 (1H, d, J = 7.5 Hz); ^{13}C NMR δ 3.5, 7.5, 13.4, 25.1, 29.7, 34.3, 43.4, 109.9, 120.5, 124.1, 128.7, 131.0, 160.0; ^{125}Te NMR δ 202; HRMS calcd for $C_{13}H_{18}O^{130}Te$ 320.0420, found 320.0425.

Reaction of 20a with Sodium *n*-Butyltellurolate: Preparation of Benzo[*b*]tellurophene[19,20] (23) and 2-(2-Iodophenyl)ethanol[30] (21). Oxirane (**20a**) (49 mg, 0.21 mmol) was reacted according to the standard protocol (A) with di-*n*-butyl ditelluride (145 mg, 0.33 mmol) and sodium borohydride (27 mg, 0.72 mmol). Flash chromatography (90:10 petroleum ether/ether) afforded a 1:1 mixture of compounds consistent with **21** and **22**. The crude mixture was dissolved in benzene (1.5 mL), *p*-toluenesulfonic acid (ca. 5 mg) added, and the mixture heated at reflux for 30 min. Workup and vacuum chromatography afforded 2-(2-iodophenyl)ethanol (**21**) and benzo[*b*]tellurophene (**23**) exhibiting NMR spectral data identical to those previously reported.[19,20,28]

2-(2-Iodophenyl)ethanol (**21**): ^{1}H NMR δ 3.03 (2H, t, J = 6.6 Hz), 3.87 (2H, t, J = 6.6 Hz), 6.89−6.95 (2H, m), 7.23−7.26 (2H, m), 7.84 (1H, d, J = 8.4 Hz).

Benzo[*b*]tellurophene (**23**): ^{1}H NMR δ 7.15 (1H, t, J = 7.2 Hz), 7.38 (1H, t, J = 7.8 Hz), 7.85 (1H, d, J = 6.9 Hz), 7.97 (2H, d, J = 7.2 Hz), 8.71 (1H, d, J = 6.8 Hz); ^{125}Te NMR δ 727.

Reaction of 20b with Sodium *n*-Butyltellurolate: 2-(2-Iodophenyl)-2-phenylacetaldehyde (24). Oxirane (**20b**) (56 mg, 0.174 mmol) was reacted according to the standard protocol (A) with di-*n*-butyl ditelluride (119 mg, 0.269 mmol) and sodium borohydride (22 mg, 0.587 mmol). Flash chromatography (90:10 petroleum ether/ether) afforded **24** as a pale oil (25 mg, 45%): ^{1}H NMR δ 5.40 (1H, s), 6.99 (1H, t, J = 7.8 Hz), 7.18−7.32 (5H, m), 7.62 (1H, t, J = 7.2 Hz), 7.82 (2H, d, J = 7.8 Hz), 9.98 (1H, s); HRMS calcd for $C_{13}H_{10}IO$ 308.9776, found 308.9780.

Ethyl 3-(*tert*-Butyldimethylsilyloxy)phenylacetate. To a solution of *tert*-butylchlorodimethylsilane (2.70 g, 17.8 mmol) in DMF (8 mL) at ambient temperature were added imidazole (3.03 g, 44.5 mmol) and ethyl 3-hydroxyphenylacetate (3.20 g, 17.8 mmol) under an atmosphere of dry nitrogen. The resulting mixture was then stirred at ambient temperature for 72 h. Standard workup (addition of water, extraction with diethyl ether (3×), washing with water, brine, drying ($MgSO_4$), and concentration in vacuo) afforded the title compound (5.14 g, 98%), which was isolated as a pale yellow oil and was used in the next step without further purification: ^{1}H NMR δ 0.20 (6H, s), 0.98 (9H, s), 1.25 (3H, t, J = 7.1 Hz), 3.55 (2H, s), 4.14 (2H, q, J = 7.1 Hz), 6.75 (1H, m), 6.78 (1H, m), 6.87 (1H, m), 7.17 (1H, t, J = 7.8 Hz); ^{13}C NMR δ −4.4, 14.2, 18.2, 25.7, 41.4, 60.8, 118.7, 121.0, 122.2, 129.4, 135.5, 155.7, 171.4. MS *m*/*z* (relative intensity) 294 (M^+, 66.4). Anal. Calcd for $C_{16}H_{26}O_3Si$: C, 65.26; H, 8.90. Found: C, 65.08; H, 8.88.

***tert*-Butyldimethylsilyl 3-(2-Hydroxyethyl)phenyl Ether (34).** To a solution of ethyl 3-(*tert*-butyldimethylsilyloxy)phenylacetate (2.50 g, 8.49 mmol) in dry diethyl ether (80 mL) was added $LiAlH_4$ (0.400 g, 10.2 mmol) in one portion at −20 °C under an atmosphere of dry nitrogen. After 70 min of stirring at 0 °C, the reaction was quenched by addition of aqueous HCl (1 M) and the organic layer separated. Standard workup afforded the title compound (2.07 g, 96%) as a pale yellow oil, which was used in the next step without further purification: ^{1}H NMR δ 0.20 (6H, s), 0.98 (9H, s), 1.43 (1H, s(br)) 2.82 (2H, t, J = 6.6 Hz), 3.84 (2H, m), 6.69−6.73 (2H, m), 6.82 (1H, m), 7.17 (1H, dd, J = 8.8, 7.5 Hz); ^{13}C NMR δ −4.4, 18.2, 25.7, 39.1, 63.6, 118.1, 120.8, 121.9, 129.5, 139.9, 155.8. MS *m*/*z* (relative intensity) 252 (M^+, 37.5). Anal. Calcd for $C_{14}H_{24}O_2Si$: C, 66.61; H, 9.58. Found: C, 66.34; H, 9.70.

***tert*-Butyldimethylsilyl 3-(2-Hydroxyethyl)-4-iodophenyl Ether.** A solution of iodine (1.82 g, 7.17 mmol) in chloroform (30 mL) was added dropwise to a magnetically stirred solution of compound **34** (1.81 g, 7.17 mmol) and silver trifluoroacetate (1.59 g, 7.17 mmol) in chloroform (40 mL) under an atmosphere of dry nitrogen. The reaction was then stirred at ambient temperature for 2.5 h. After filtration from

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silver salt, water was added and the organic layer separated. The aqueous phase was then extracted with dichloromethane (3×). The combined organic phases were washed with sodium thiosulfate, water, and brine. The organic phase was then dried ($MgSO_4$), filtered, and concentrated under reduced pressure to give the title compound (2.60 g, 96%) as a yellow oil. The crude product was used in the next step without further purification: ^{1}H NMR δ 0.18 (6H, s), 0.97 (9H, s), 1.42 (1H, s(br)) 2.94 (2H, t, J = 6.8 Hz), 3.83 (2H, t, J = 6.8 Hz), 6.47 (1H, dd, J = 8.6, 2.9 Hz), 6.78 (1H, d, J = 2.9 Hz), 7.63 (1H, d, J = 8.6 Hz); ^{13}C NMR δ −4.5, 18.2, 25.6, 43.7, 62.3, 90.1, 120.5, 122.5, 140.0, 142.1; MS *m*/*z* (relative intensity) 378 (M^+, 44.6). Anal. Calcd for $C_{14}H_{23}IO_2Si$: C, 44.45; H, 6.13. Found: C, 44.70; H, 5.95.

***tert*-Butyldimethylsilyl 4-Iodo-3-(2-iodoethyl)phenyl Ether (35).** To a solution of *tert*-butyldimethylsilyl 3-(2-hydroxyethyl)-4-iodophenyl ether (2.47 g, 6.53 mmol) in dichloromethane (75 mL) at 0 °C were added triethylamine (1.20 mL, 8.20 mmol) and methansulfonyl chloride (610 μL, 7.84 mmol) under an atmosphere of dry nitrogen. The resulting mixture was then stirred at 0 °C for 1 h. Standard workup afforded *tert*-butyldimethylsilyl 4-iodo-3-(2-mesyloxyethyl)-phenyl ether as a pale yellow oil: ^{1}H NMR δ 0.19 (6H, s), 0.97 (9H, s), 2.91 (3H, s), 3.12 (2H, t, J = 7.0 Hz), 4.39 (2H, t, J = 7.0 Hz), 6.50 (2H, dd, J = 8.6, 2.8 Hz), 6.79 (1H, d, J = 2.9 Hz), 7.64 (1H, d, J = 8.5 Hz); ^{13}C NMR δ −4.5, 18.2, 25.6, 37.3, 40.2, 68.5, 89.6, 121.2, 122.8, 139.9, 140.2, 156.3. The crude material (2.97 g, 6.49 mmol) was dissolved in acetone (70 mL), and sodium iodide (2.05 g, 13.6 mmol) was added. The resulting mixture was then refluxed for 17 h. Water was added, and the layers were separated. Standard workup gave the title compound (3.04 g; 88%) as a pale yellow oil, which was used in the next step without further purification. An analytical sample obtained after additional purification melted at 31−32 °C: ^{1}H NMR δ 0.20 (6H, s), 0.98 (9H, s), 3.20 (2H, m), 3.31 (2H, m), 6.50 (1H, dd, J = 8.6, 2.9 Hz), 6.75 (1H, d, J = 2.7 Hz), 7.62 (1H, d, J = 8.6 Hz); ^{13}C NMR δ −4.4, 3.4, 18.2, 25.6, 44.8, 89.2, 120.9, 122.0, 140.1, 144.2, 156.2. Anal. Calcd for $C_{14}H_{22}I_2OSi$: C, 34.44; H, 4.54. Found: C, 34.49; H, 4.46.

Benzyl 2-[5-(*tert*-Butyldimethylsilyl)-2-iodophenyl]-ethyl Selenide (36). Sodium borohydride was added, in portions under nitrogen, to a suspension of dibenzyl diselenide (419 mg, 1.23 mmol) in absolute ethanol (25 mL) until the characteristic yellow color of the diselenide had disappeared. Compound **35** (1.00 g, 2.05 mmol) dissolved in absolute ethanol (10 mL) was added and the reaction stirred at ambient temperature for 17 h. Water was added, and the phases were separated. Standard workup followed by flash chromatography (EtOAc/pentane 1:99) provided 0.917 g (84%) of the title compound as a pale yellow oil: ^{1}H NMR δ 0.18 (6H, s), 0.98 (9H, s), 2.69 (2H, m), 2.94 (2H, m), 3.81 (2H, s), 6.44 (1H, dd, J = 8.5, 2.9 Hz,), 6.67 (1H, d, J = 2.9 Hz) 7.18−7.23 (1H, m), 7.27−7.32 (4H, m), 7.59 (1H, d, J = 8.5 Hz); ^{13}C NMR δ −4.4, 18.2, 23.2, 25.6, 27.4, 41.9, 89.6, 120.4,121.8, 126.7, 128.5, 128.9, 139.3, 139.9, 144.7, 156.1; ^{77}Se NMR δ 267. Anal. Calcd for $C_{21}H_{29}IOSeSi$: C, 47.46; H 5.50. Found: C, 47.51; H, 5.49.

5-(*tert*-Butyldimethylsilyloxy)-2,3-dihydrobenzo[*b*]selenophene (38). Sodium borohydride (22 mg, 0.582 mmol) was added with stirring to a solution of di-*n*-butyl ditelluride (72 mg, 0.195 mmol) in dry THF (20 mL) under an atmosphere of dry nitrogen. The reaction vessel was purged with nitrogen, and methanol (∼500 μL) was added dropwise until the red solution turned colorless. When the evolution of hydrogen had ceased, **36** (200 mg, 0.377 mmol), dissolved in dry THF (5 mL), was added by syringe, and the resulting mixture was stirred for a further 24 h. Standard workup followed by flash chromatography (EtOAc/pentane 1:99) afforded 77 mg (65%) of the title compound as a light yellow oil: ^{1}H NMR δ 0.18 (6H, s), 0.98 (9H, s), 3.30 (2H, m), 3.40 (2H, m), 6.60 (1H, m), 6.70 (1H, m), 7.12 (1H, d, J = 8.3 Hz); ^{13}C NMR δ −4.4, 18.2, 25.7, 27.0, 38.9, 117.2, 119.1, 125.9, 127.5, 144.7, 153.6; ^{77}Se NMR δ 309. Anal. Calcd for $C_{14}H_{22}OSeSi$: C, 53.66; H, 7.08. Found: C, 53.83; H, 7.05.

5-(*tert*-Butyldimethylsilyloxy)-2,3-dihydrobenzo[*b*]tellurophene (37). Sodium borohydride (24 mg, 0.639 mmol) was added with stirring to a solution of di-*n*-butyl ditelluride (159 mg, 0.430 mmol) in dry THF (20 mL) under an atmosphere of dry nitrogen. The reaction vessel was purged with nitrogen, and methanol (∼500 μL) was added dropwise until the red solution turned colorless. When the evolution of hydrogen had ceased, **35** (200 mg, 0.410 mmol), dissolved in dry THF (5 mL), was added by syringe, and the resulting mixture was stirred for a further 24 h. Water and dichloromethane were added and the layers separated. The aqueous phase was extracted with dichloromethane (3×), and the combined organic phases were washed with water and brine and then dried over $MgSO_4$. The solvent was removed in vacuo, and the residue was purified by flash chromatography (EtOAc/pentane 1:99) to afford 70 mg (47%) of the title compound as a yellow oil: ^{1}H NMR δ 0.18 (6H, s), 0.98 (9H, s), 3.40 (2H, m), 3.63 (2H, m), 6.58 (1H, m), 6.70 (1H, m), 7.17 (1H, d, J = 8.2 Hz); ^{13}C NMR δ − 4.4, 7.9, 18.2, 25.7, 42.8, 11.1, 117.4, 119.1, 132.7, 151.0, 154.7. Due to the lability of this material, it was subjected to deprotection without further characterization.

Typical Procedure for Deprotection of the TBDMS Group (5-Hydroxy-2,3-dihydrobenzo[*b*]selenophene (32)). To a solution of compound **38** (70 mg, 0.223 mmol) in dry THF (10 mL) was added tetra-*n*-butylammonium fluoride (1.0 M in THF) (235 μL, 0.235 mmol) under an atmosphere of dry nitrogen. The reaction mixture was then stirred at ambient temperature for 1 h. Standard workup followed by flash chromatography (EtOAc/pentane 10:90) afforded the title compound (42 mg, 95%) as white crystals: mp 88−89 °C; ^{1}H NMR δ 3.30 (2H, m), 3.40 (2H, m), 4.87 (1H, s), 6.60 (1H, m), 6.71 (1H, m), 7.13 (1H, m); ^{13}C NMR δ 26.9, 38.8, 112.6, 114.5, 126.1, 126.8, 145.0, 153.6; ^{77}Se NMR δ 310. Anal. Calcd for C_8H_8OSe: C, 48.26; H, 4.05. Found: C, 48.19; H, 3.99.

5-Hydroxy-2,3-dihydrobenzo[*b*]tellurophene (31) was isolated as yellow crystals in 65% yield from the crude material by column chromatography (EtOAc/pentane 10:90): mp 79−81°C dec; ^{1}H NMR δ 3.42 (2H, m), 3.62 (2H, m), 4.73 (1H, s), 6.59 (1H, m), 6.72 (1H, m), 7.19 (1H, d, J = 8.1 Hz); ^{13}C NMR δ 7.8, 42.8, 109.2, 112.8, 114.5, 132.9, 151.3, 154.6; ^{125}Te NMR δ 503. Anal. Calcd for C_8H_8OTe: C, 38.78; H, 3.25. Found: C, 38.54; H, 3.16.

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