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Regenerable Radical-Trapping Tellurobistocopherol Antioxidants

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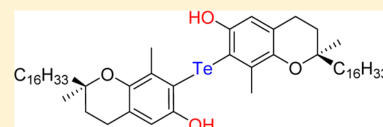
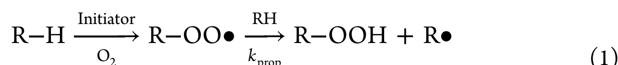
Supporting Information

ABSTRACT: Tellurobistocopherols **9−11** were prepared by lithiation of the corresponding bromotocopherols, reaction with tellurium tetrachloride and reductive workup. Compounds **9−11** quenched linoleic-acid-derived peroxyl radicals much more efficiently than *α*-tocopherol in a chlorobenzene/water two-phase system. *N*-Acetylcysteine or tris(2-carboxylethyl)phosphine as co-antioxidants in the aqueous phase could regenerate the tellurobistocopherols and increase their inhibition times. Antioxidant **11** inhibited peroxidation for 7-fold longer than that recorded with *α*-tocopherol. Thiol consumption in the aqueous phase was monitored and found to be inversely related to the inhibition time.



Oxidative stress is characterized by an imbalance between the production of reactive oxygen species (ROS) and the antioxidant defense systems in favor of the former.[1] ROS is known to target lipids in biological systems, and this is generally known as lipid peroxidation, an undesired free radical process whereby organic substances, RH, are oxidized to the corresponding hydroperoxides, ROOH (eq 1).

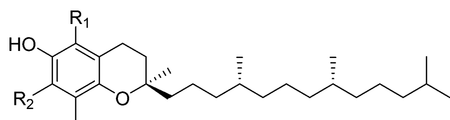
Vitamin E, the most important lipid-soluble antioxidant in humans, offers protection against lipid peroxidation. Briefly, vitamin E (AH) competes with the propagation event and scavenges peroxyl radicals, ROO•, by hydrogen-atom transfer with a rate $k_{inh} \gg k_{prop}$ (eq 2). The resulting resonance-stabilized radical A• is unable to propagate the reaction.



$$\mathrm{R{-}H} \xrightarrow[\mathrm{O_2}]{\text{Initiator}} \mathrm{R{-}OO\bullet} \xrightarrow[k_{prop}]{\mathrm{RH}} \mathrm{R{-}OOH + R\bullet} \quad (1)$$

$$\mathrm{R{-}OO\bullet + A{-}H} \xrightarrow{k_{inh}} \mathrm{ROOH + A\bullet} \quad (2)$$

Vitamin E was first reported by Evans and Bishop in 1922,[2] but its antioxidant properties were revealed by Emerson and co-workers when they showed that it could slow down the autoxidation of fats.[3] Vitamin E is a collective name for a family of compounds including four tocopherols **1−4** and four tocotrienols. Structurally, they are all 6-chromanols. They differ in the number and position of methyl groups in the phenolic part and in the side chain which is saturated in tocopherols and triply unsaturated in the corresponding tocotrienols. In the tocopherol family, *α*-tocopherol (**1**) is the most reactive compound (k_{inh} = 3.2 × 10^6 M^{-1} s^{-1}).[4]



1 α-Tocopherol $R_1 = R_2$ = Me
2 β-Tocopherol R_1 = Me; R_2 = H
3 γ-Tocopherol R_1 = H; R_2 = Me
4 δ-Tocopherol $R_1 = R_2$ = H

Considerable efforts have been invested in order to improve the reactivity of **1**. Ingold and co-workers found that compound **5** was a slightly more reactive antioxidant (k_{inh} = 4.7 × 10^6 M^{-1} s^{-1})[5] due to better overlap between the chromane oxygen lone pair and the aromatic ring, resulting in a lower bond dissociation energy, BDE_{O-H}, of the phenol. More recently, Pratt and co-workers introduced nitrogen into the aromatic ring of *α*-tocopherol. Thus, strongly electron-donating groups such as amines could be installed to lower the BDE_{O-H}, while the ionization potential of the compound did not drop below the critical point where electron transfer to dioxygen becomes a problem. Naphthyridinols **6**, representing compounds of this type, were recently found to efficiently quench peroxyl radicals in lipid bilayers.[6] Suitably positioned chalcogens (Se, S) have also been found to increase the radical-trapping activity of phenolic compounds.[7]

Recently, our group showed that alkyltelluro-substituted *β*-, *γ*-, and *δ*-tocopherols **7a−7d** were at least 10-fold more reactive as radical-trapping agents than their respective parents.[8]

Computational studies on alkyltellurophenols suggested that oxygen-atom transfer from the peroxyl radical to tellurium is a key step in the antioxidant mechanism. The resulting alkoxyl radical in the solvent cage can then abstract a hydrogen atom from the phenolic O−H.[9] Regeneration of the antioxidant from the phenoxyl radical/telluroxide formed was brought about by thiols (Figure 1). Indeed, the inhibition time for compound **7** was 6.5-fold longer than that recorded with *α*-tocopherol in a two-phase lipid peroxidation system.

It occurred to us that it may be possible to benefit even more from the unusual reactivity of the heteroatom. The idea that emerged was to link two molecules of a tocopherol to tellurium. Surprisingly, only very few compounds of this kind are reported in the literature. They include the methano and ethano dimers **8**.[10] To the best of our knowledge, dimers linked together by a chalcogen are as yet unknown.

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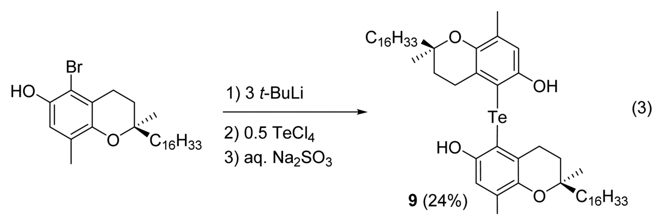
7a X = Me; Y = Te-Octyl
7b X = Te-Octyl; Y = Me
7c X = Te-Octyl; Y = H
7d X = H; Y = Te-Octyl

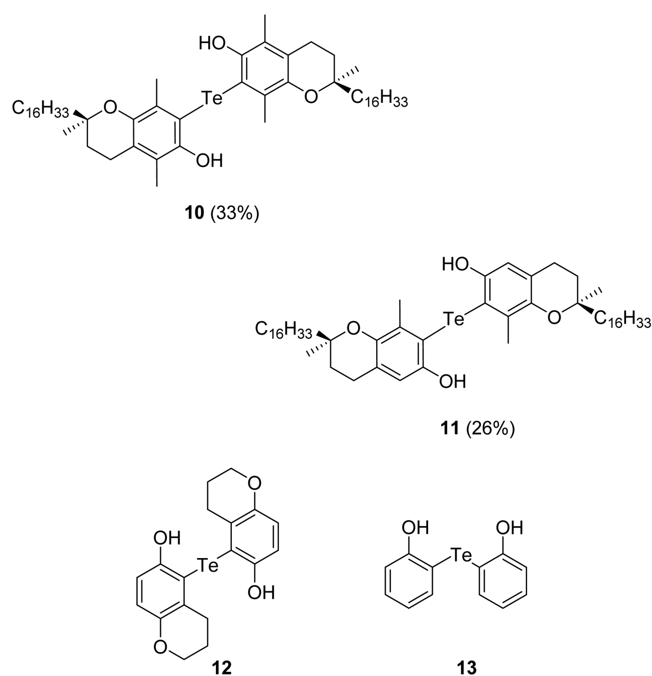
8 X = CH_2 or CH_2CH_2

Figure 1. Proposed catalytic mechanism for quenching of peroxyl radicals by 2-(alkyltelluro)phenols in the presence of thiols.

Synthesis. Symmetrical diorganyl tellurides can be obtained in high yields by copper-induced detelluration of the corresponding diorganyl ditellurides.[11] This procedure was tried for the preparation of tellurobistocopherol **9**. Although the ditelluride required was conveniently obtained from 5-bromo-δ-tocopherol by dilithiation, Te insertion into the C−Li bond and air oxidation, extrusion of tellurium was unsuccessful. Instead, we were pleased to find that a similar strategy, using $TeCl_4$ in place of elemental tellurium, provided compound **9** in low yield after reductive workup (eq 3). In a similar fashion, 7-bromo-β-



tocopherol and 7-bromo-δ-tocopherol provided the corresponding tellurobistocopherols **10** and **11** in 33 and 26% yield, respectively. Curious to study the effects of the phytyl chain, the methyl groups, and the benzannulated cyclic ether on antioxidant capacity, we prepared compounds **12** and **13** using a similar procedure.



Evaluation. To determine the radical-trapping capacity and regenerability, all tellurobisphenolic antioxidants were evaluated in a two-phase lipid peroxidation system reminiscent of a biological membrane.[12] Briefly, azobis(2,4-dimethylvaleronitrile) (AMVN) was added as an initiator to chlorobenzene at 42 °C containing the antioxidant and linoleic acid as the oxidizable substrate. The aqueous phase contained *N*-acetylcysteine (NAC) or tris(2-carboxylethyl)phosphine (TCEP), which could serve as co-antioxidants and continuously regenerate the antioxidants in the lipid phase. The chlorobenzene phase was assayed by HPLC every 20 min, and the concentration of conjugated diene, formed by peroxidation of linoleic acid, was determined by HPLC with UV detection at 234 nm. Initially, lipid peroxidation is efficiently inhibited by the antioxidant, and the rate of conjugated diene formation, R_{inh}, is low. After some time, when the antioxidant is all consumed, the R value increases considerably to a value corresponding to uninhibited peroxidation. This point is referred to as the inhibition time, T_{inh}, of the antioxidant. Our reference compound, α-tocopherol, at 40 μM could inhibit peroxidation efficiently (R_{inh} = 25 μM/h) for ≈100 min in the presence of aqueous-phase NAC or TCEP (Table 1 and Figure 2). The similar T_{inh} and R_{inh} values recorded in the absence of the co-antioxidant show that α-tocopherol is not regenerable under the conditions of the two-phase model.

In the absence of NAC/TCEP, all organotellurium antioxidants tested quenched peroxyl radicals at least (R_{inh} = 7−25 μM/h) as efficiently as **1**. For compounds **9**−**11**, the T_{inh} values (165−214 min) were significantly longer than that recorded for α-tocopherol.

When NAC (1 mM) was present in the aqueous phase, the R_{inh} values were significantly lower for all compounds (R_{inh} = 1−4 μM/h), and the T_{inh} values were longer (Table 1). 7,7′-Tellurobis-δ-tocopherol (**11**) inhibited peroxidation for 742 min or 7.6-fold longer than recorded for **11** (Figure 2). This is the longest inhibition time we have ever recorded in the two-phase model. Removal of the phytyl chain and the 2,2′,8,8′-methyls caused a drop in the inhibition time (compound **12**;

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Table 1. Inhibited Rates of Conjugated Diene Formation (R_{inh}) and Inhibition Times (T_{inh}) in the Presence and Absence of NAC (1.0 mM) or TCEP (0.5 mM) in the Two-Phase Model

	with NAC		with TCEP		without NAC/TCEP	
antioxidants (40 μM)	R_{inh}[a] (μM/h)	T_{inh}[b] (min)	R_{inh}[a] (μM/h)	T_{inh}[b] (min)	R_{inh}[a] (μM/h)	T_{inh}[b] (min)
9	1 ± 1	634 ± 9	2 ± 0	451 ± 9	8	170
10	2 ± 0	653 ± 12	2 ± 1	510 ± 5	7	165
11	4 ± 1	742 ± 13	2 ± 0	507 ± 8	21	214
12	1 ± 1	544 ± 4	2 ± 1	208 ± 10	25	92
13	2 ± 1	365 ± 6	3 ± 1	125 ± 13	11	49
α-tocopherol	25 ± 1	97 ± 15	21 ± 2	123 ± 7	28	109

[a]Rate of peroxidation during the inhibited phase (uninhibited rate ≈ 479 μM/h). Errors correspond to ± SD for triplicates. [b]Inhibited phase of peroxidation. Reactions were monitored for 880 min. Errors correspond to ± SD for triplicates.

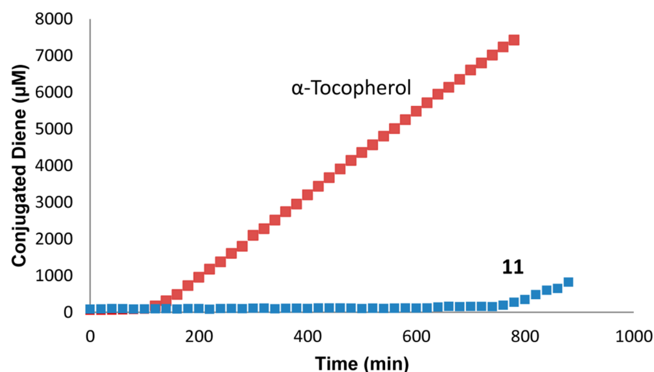


Figure 2. Peroxidation traces (conjugated diene concentration vs time) recorded using compound **11** and α-tocopherol as antioxidants in chlorobenzene and NAC (1 mM) in the aqueous phase.

Table 2. NAC Consumption in the Aqueous Phase during Peroxidation Inhibited by Telluriobisphenol Antioxidants

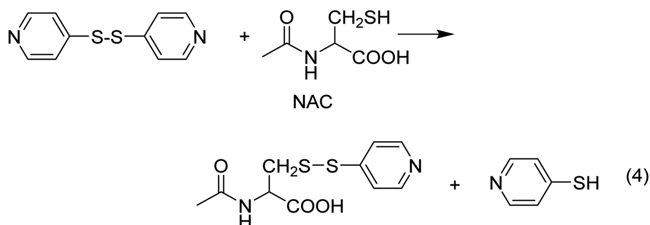
antioxidant (40 μM)	rate of NAC consumption (μM/h)[a]
9	131 ± 4
10	125 ± 10
11	119 ± 13
12	150 ± 10
13	164 ± 4
α-tocopherol	33 ± 4
b	37 ± 8
c	27 ± 5

[a]Errors correspond to ± SD for triplicates. [b]Linoleic acid and AMVN in the chlorobenzene and NAC in the aqueous phase. [c]Nothing in the chlorobenzene and NAC in the aqueous phase.

T_{inh} = 544 min), which continued upon further simplification of the structure (compound **13**; T_{inh} = 365 min). We speculate that this is a lipophilicity effect or the result of an increasing BDE_{O-H} (vide infra).

When TCEP (0.5 mM) was used as a co-antioxidant, similarly low R_{inh} values were recorded as with NAC (Table 1). Whereas the inhibition times were generally shorter, the similar trend was seen when the compounds were arranged according to falling T_{inh}.

We were also curious to see how quickly NAC was consumed during a normal peroxidation experiment. Following a recently described procedure,[13] the aqueous phase was sampled every 30 min and the thiol was allowed to react with bis-4-pyridyl disulfide. The concentration of pyridine-4-thiol formed (eq 4), as determined by UV spectroscopy at 324 nm,



was used for monitoring the disappearance of NAC with time. For α-tocopherol, the rate of NAC consumption (33 μM/h) was low and essentially the same as that recorded in control experiments (nothing but NAC in the two-phase system or NAC + linoleic acid + AMVN; Table 2). When a telluride antioxidant was present, the NAC was consumed more quickly. In the presence of tellurobistocopherols **9**−**11**, 119−131 μM/h of the thiol was consumed. The rate increased to 150 and 164 μM/h, respectively, with compounds **12** and **13**.

Thus, the rate of thiol consumption is inversely related to the T_{inh} recorded in the two-phase model. Extrapolation in the NAC concentration versus time plots to find the time where the aqueous phase was depleted of NAC showed that this always fell short of the corresponding T_{inh}. It therefore seems that the availability of aqueous-phase NAC is a limiting factor for the inhibition time.

In an attempt to see if the turnover number of catalyst **11** could be increased, the concentration was lowered from the standard 40 μM to 30, 20, 10, and 5 μM. As shown in Figure 3, this was not the case. When the concentration was lowered, the T_{inh} was accordingly reduced. A similar trend was seen with TCEP.

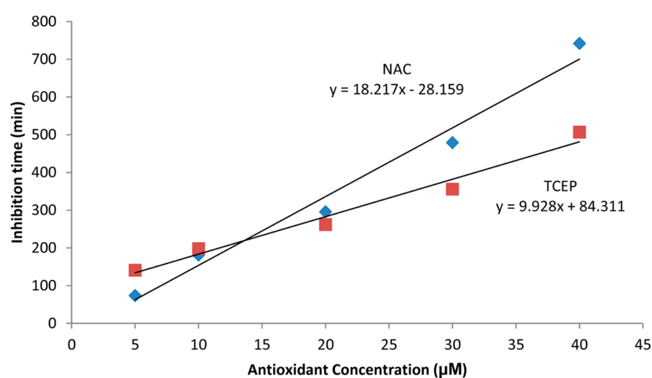


Figure 3. Inhibition times recorded for **11** at different concentrations in the presence of NAC (1.0 mM) or TCEP (0.5 mM).

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Concluding Remarks. As observed previously with the "monomeric" tocopherol derivatives **7**, the "dimeric" tellurobistocopherols **9−11** showed considerable antioxidant capacity also in the absence of a co-antioxidant. This may be because the heteroatom is sterically protected. Otherwise, residual amounts of linoleic acid hydroperoxide tend to oxidize the telluride antioxidant to the corresponding telluroxide, which is considerably less reactive toward peroxyl radicals.

In the presence of NAC as a co-antioxidant, T_{inh} values for the "dimers" **9−11** were always longer but never close to twice as long as those recorded for the corresponding "monomers" **7a−7d**.[8b] The largest improvement, +38%, was seen with δ-tocopherol derivative **9** (634 min instead of 458 min for the corresponding monomer **7c**). For compounds **10** (653 min instead of 591 min for **7a**) and **11** (742 min instead of 630 min for **7d**), the increase in T_{inh} was only modest. On the other hand, diaryl tellurides are chemically more robust than alkyl aryl tellurides. Some time ago, we probed the stabilizing capacity of a series of electron-rich diaryl tellurides in polymeric materials.[14] As determined by thermogravimetric analysis, many of the compounds were stable at least up to 210 °C. Diaryl tellurides as well as alkyl aryl tellurides are easily oxidized to the corresponding telluroxides. In case the system is depleted in reducing agents, there is a risk that the alkyl aryl telluroxide (but not the diaryl telluroxide) may decompose via a telluroxide elimination reaction.[15]

The reactivity of the tellurobistocopherols did not change much upon removal of the phytyl chain, the 2,2′,8,8′-methyls, and the benzannulated cyclic ether. However, a noteworthy drop in the T_{inh} was recorded for compounds **12** and **13**. This could be a lipophilicity effect. Highly lipophilic antioxidants would distribute almost exclusively into the lipid phase and give a maximal antioxidant protection there. Removal of the benzannulated cyclic ether and any methyl groups flanking the aromatic OH would also be expected to cause an increase in the BDE_{O-H} (electron-donating substituents here are known to weaken the O−H bond). This would increase leakage of chain-propagating alkoxyl radicals from the solvent cage into the bulk of the solution (Figure 1). Whenever this happens, 2 equiv of thiol is wasted in order to regenerate the catalyst. In fact, such an increase in the rate of thiol consumption was observed for compounds **12** and **13**.

■ EXPERIMENTAL SECTION

^{1}H and ^{13}C NMR spectra were recorded on 400 MHz (^{1}H, 399.97 MHz; ^{13}C, 100.58 MHz) and 500 MHz (^{1}H, 499.93 MHz; ^{13}C, 125.70 MHz) spectrometers, using the residual solvent peaks of $CDCl_3$ (^{1}H, δ 7.26; ^{13}C, δ 77.0) as an indirect reference to TMS. ^{125}Te NMR spectra were recorded on a 400 MHz spectrometer (^{125}Te, 126.19 MHz) using Ph_2Te_2 (423 ppm) as external standard. The melting points are uncorrected. Flash column chromatography was performed using silica gel (0.04−0.06 mm). Tetrahydrofuran was dried in a solvent purification system by passing it through an activated alumina column. 5-Bromo-δ-tocopherol,[8b] 7-bromo-δ-tocopherol,[8b] 7-bromo-β-tocopherol,[8b] and 6-bromochromane[16] were prepared according to literature procedures.

General Procedure: Synthesis of Tellurobisphenols. To a solution of the appropriate 2-bromophenol derivate (1.0 equiv) in anhydrous THF (10 mL) at −78 °C under nitrogen, *tert*-butyl lithium (1.7 M in pentane, 3.0 equiv) was added. After being stirred for 2 h at −78 °C, tellurium tetrachloride (0.5 equiv) was added and the solution was allowed to stir overnight at ambient temperature. After addition of Na_2SO_3 (aq, 20 mL) and extraction with diethyl ether (25 mL × 3), the organic layer was dried over magnesium sulfate, filtered, and evaporated under reduced pressure. The residue was purified by column chromatography (pentane/ethyl acetate = 90:10) to give the title compound.

5,5′-Tellurobis-δ-tocopherol (9). 5-Bromo-δ-tocopherol (964 mg, 2.0 mmol), *tert*-butyl lithium (1.7 M in pentane, 3.5 mL, 6.0 mmol), and tellurium tetrachloride (269 mg, 1.0 mmol) were reacted according to the general procedure to give the title compound as a yellow oil (225 mg, 24%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.71 (s, 2H), 6.33 (s, 2H), 2.82 (m, 4H), 2.14 (s, 6H), 1.78 (m, 4H), 1.08−1.58 (several peaks, 48H), 0.87−0.91 (several peaks, 24H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.9, 146.3, 130.4, 125.5, 114.5, 102.0, 75.2, 39.7, 39.4, 37.5, 37.4, 37.3, 32.8, 32.7, 32.2, 28.7, 28.0, 24.8, 24.4, 23.7, 22.7, 22.6, 21.0, 19.8, 19.6, 16.3; ^{125}Te NMR (126 MHz, $CDCl_3$) δ −3; HRMS (TOF MS EI$^+$) *m*/*z* calcd for $C_{54}H_{90}O_4Te$ $[M]^+$ 932.5901, found 932.5928.

7,7′-Tellurobis-β-tocopherol (10). 7-Bromo-β-tocopherol (496 mg, 1.0 mmol), *tert*-butyl lithium (1.7 M in pentane, 1.8 mL, 3.0 mmol), and tellurium tetrachloride (134 mg, 0.5 mmol) were reacted according to the general procedure to give the title compound as a yellow oil (158 mg, 33%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.73 (s, 2H), 2.62 (t, *J* = 6.4 Hz, 4H), 2.42 (s, 6H), 2.12 (s, 6H), 1.77 (m, 4H), 1.01−1.56 (several peaks, 48H), 0.83−0.88 (several peaks, 24H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.6, 145.5, 129.1, 123.1, 119.1, 105.3, 75.0, 39.8, 39.4, 37.4, 37.3, 32.8, 32.7, 31.4, 28.0, 24.8, 24.4, 23.7, 22.7, 22.6, 21.2, 21.1, 20.9, 19.8, 19.6, 12.6; ^{125}Te NMR (126 MHz, $CDCl_3$) δ 33; HRMS (MALDI) *m*/*z* calcd for $C_{56}H_{94}O_4Te$ $[M]^+$ 960.6214, found 960.6217.

7,7′-Tellurobis-δ-tocopherol (11). 7-Bromo-δ-tocopherol (964 mg, 2.0 mmol), *tert*-butyl lithium (1.7 M in pentane, 3.5 mL, 6.0 mmol), and tellurium tetrachloride (269 mg, 1.0 mmol) were reacted according to the general procedure to give the title compound as a yellow oil (238 mg, 26%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.65 (s, 2H), 6.61 (s, 2H), 2.68 (m, 4H), 2.52 (s, 6H), 1.75 (m, 4H), 1.06−1.60 (several peaks, 48H), 0.88−0.92 (several peaks, 24H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.5, 145.4, 132.5, 124.0, 111.5, 105.9, 76.0, 40.1, 39.4, 37.4, 37.3, 32.8, 32.7, 31.2, 28.0, 24.8, 24.4, 24.0, 22.7, 22.6, 22.5, 22.4, 21.0, 19.7, 19.6; ^{125}Te NMR (126 MHz, $CDCl_3$) δ 49; HRMS (TOF MS ESI) *m*/*z* calcd for $C_{54}H_{90}O_4Te$ $[M + Na]^+$ 955.5794, found 955.5801.

6-Chromanol. To a mixture of magnesium turnings (248 mg, 10.2 mmol) and iodine (90 mg, 0.35 mmol) in THF (4 mL) under nitrogen was added a solution of 6-bromochromane (378 mg, 1.8 mmol) in anhydrous THF (2 mL). After being heated at 60 °C for 20 min, a solution of 6-bromochromane (1.14 g, 5.3 mmol) in anhydrous THF (6 mL) was added dropwise over a period of 50 min at 30 °C. The Grignard reagent was transferred to a solution of trimethyl borate (0.79 mL, 7.1 mmol) in anhydrous THF (4 mL) at −10 °C over a period of 1 h. The reaction mixture was allowed to stir for 30 min prior to hydrolysis with HCl (2 M, 12 mL) and extraction with diethyl ether (10 mL). The organic phase was washed with water (10 mL × 2) and then transferred to a two-neck round-bottomed flask. To the solution was added peracetic acid (1.2 mL, 39% in acetic acid) dropwise at 0 °C under nitrogen. After being stirred at ambient temperature for 3 h, the reaction mixture was quenched with $NaHSO_3$ (10% aq, 30 mL) and extracted with diethyl ether (30 mL × 3). The organic layer was dried over magnesium sulfate, filtered, and evaporated under reduced pressure. The residue was purified by column chromatography (pentane/ethyl acetate = 95:5) to give the title compound as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.67 (d, *J* = 8.8 Hz, 1H), 6.57 (dd, *J* = 2.8, 8.8 Hz, 1H), 6.53 (d, *J* = 2.8 Hz, 1H), 4.40 (s, 1H), 4.13 (t, *J* = 4.8 Hz, 2H), 2.74 (d, *J* = 6.4 Hz, 2H), 1.98 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.9, 148.8, 123.0, 117.3, 115.8, 114.3, 66.3, 25.0, 22.4. ^{1}H and ^{13}C spectra were in accord with the literature.[17]

5-Bromo-6-chromanol. To a solution of 6-chromanol (651 mg, 4.3 mmol) in dichloromethane (50 mL) was added dropwise a solution of tetrabutylammonium tribromide (2.1 g, 4.3 mmol) in dichloromethane (50 mL). After being stirred for 1 h, the solution was evaporated and the residue was purified by column chromatography (pentane/ethyl acetate = 95:5) to give the title compound as a white solid (685 mg, 70%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.82 (d, *J* = 6.8

Hz, 1H), 6.73 (d, J = 6.8 Hz, 1H), 5.16 (s, 1H), 4.08 (m, 2H), 2.73 (t, J = 5.6 Hz, 2H), 2.02 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.5, 146.1, 1221, 116.8, 113.9, 112.6, 65.8, 26.3, 22.3. ^{1}H and ^{13}C spectra were in accord with the literature.[17]

5,5′-Tellurobis-6-chromanol (12). 5-Bromo-6-chromanol (458 mg, 2.0 mmol), *tert*-butyl lithium (1.7 M in pentane, 3.5 mL, 6.0 mmol), and tellurium tetrachloride (269 mg, 1.0 mmol) were reacted according to the general procedure to give the title compound as a red solid (135 mg, 32%): mp = 158−160 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.79 (d, J = 9.0 Hz, 2H), 6.73 (d, J = 9.0 Hz, 2H), 6.23 (s, 2H), 4.03 (t, J = 5.0 Hz, 4H), 2.80 (t, J = 7.0 Hz, 4 H), 1.98 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.9, 149.1, 127.5, 120.0, 113.0, 106.4, 65.7, 31.2, 23.2; ^{125}Te NMR (126 MHz, $CDCl_3$) δ 216; HRMS (TOF MS EI$^+$) m/z calcd for $C_{18}H_{18}O_4Te$ $[M]^+$ 428.0267, found 428.0272.

2,2′-Tellurobisphenol (13). 2-Bromophenol (692 mg, 4.0 mmol), *tert*-butyl lithium (1.7 M in pentane, 7.0 mL, 12.0 mmol), and tellurium tetrachloride (538 mg, 2.0 mmol) were reacted according to the general procedure to give the title compound as a pale yellow solid (270 mg, 44%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 (dd, J = 2.0, 8.0 Hz, 2H), 7.26 (m, 2H), 6.96 (dd, J = 1.5, 8.5 Hz, 2H), 6.78 (m, 2H), 5.92 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.9, 139.5, 131.3, 122.2, 114.2, 102.2; ^{125}Te NMR (126 MHz, $CDCl_3$) δ 285. The ^{1}H spectrum was in accord with the literature.[18]

HPLC Peroxidation Assay. The experimental setup for the two-phase lipid peroxidation model for determination of R_{inh} and T_{inh} has been previously described.[12] The values for R_{inh} and T_{inh} in the presence of NAC and TCEP are reported as means ± SD based on triplicates. The initial concentration of linoleic acid hydroperoxide was ≈175 μM at the beginning of each experiment.

NAC Consumption Assay. The experimental setup for determination of the rate of NAC consumption in the two-phase lipid peroxidation model was recently described.[13] The values reported are means ± SD based on triplicates.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02450.

^{1}H, ^{13}C, and ^{125}Te NMR data for all new compounds prepared (PDF)

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Notes

The authors declare no competing financial interest.

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