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In Search of Catalytic Antioxidants—(Alkyltelluro)phenols, (Alkyltelluro)resorcinols, and Bis(alkyltelluro)phenols

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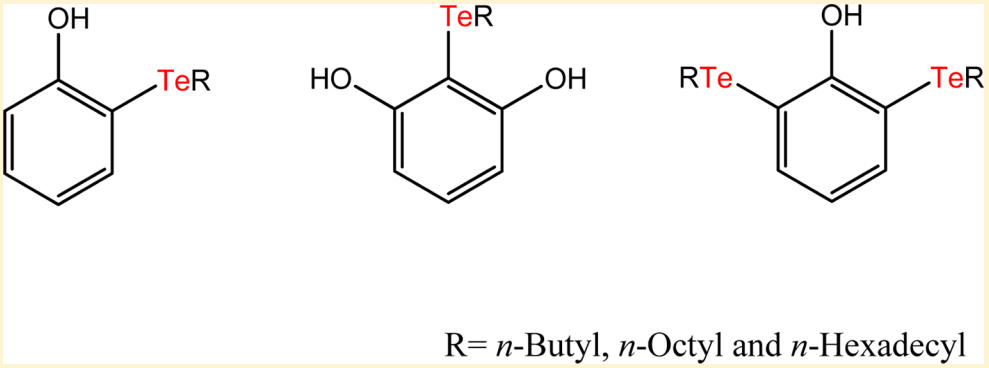
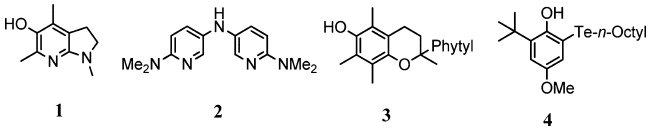
Supporting Information



ABSTRACT: The quenching of peroxyl radicals by *ortho*-(alkyltelluro)phenols occurs by a more complex mechanism than formal H-atom transfer. In an effort to improve on this concept, we have prepared (alkyltelluro)resorcinols and bis(alkyltelluro)phenols and evaluated their catalytic chain-breaking and preventive antioxidative properties. The in situ formed trianion produced from 2-bromophenol and 3 equiv of *tert*-butyllithium was allowed to react with dialkyl ditellurides to provide *ortho*-(alkyltelluro)phenols in low yields. 2-Bromoresorcinols after treatment with 4 equiv of *tert*-butyllithium similarly afforded 2-(alkyltelluro)resorcinols. Bis(alkyltelluro)phenols were accessed by allowing the trianion produced from the reaction of 2,6-dibromophenol with 5 equiv of *tert*-butyllithium to react with dialkyl ditellurides. The novel phenolic compounds were found to inhibit azo-initiated peroxidation of linoleic acid much more efficiently than α-tocopherol in a two-phase peroxidation system containing excess *N*-acetylcysteine as a stoichiometric thiol reducing agent in the aqueous phase. Whereas most of the (alkyltelluro)phenols and resorcinols could inhibit peroxidation for only 89−228 min, some of the bis(alkyltelluro)phenols were more regenerable and offered protection for >410 min. The novel (alkyltelluro)phenols were also evaluated for their capacity to catalyze reduction of hydrogen peroxide in the presence of thiophenol (glutathione peroxidase-like activity). (Alkyltelluro)-resorcinols **7a−c** were the most efficient catalysts with activities circa 65 times higher than those recorded for diphenyl diselenide.

INTRODUCTION

Phenols and aromatic amines are often vital parts of the structures of antioxidants found in biological systems or added to man-made materials. Their antioxidant capacity is due to the quenching (by formal H-atom transfer) of chain-carrying peroxyl radicals accompanied by the formation of less reactive phenoxyl and aminyl radicals that cannot propagate autoxidation. Electron-donating substituents in the aromatic moiety are known to weaken the bond dissociation enthalpy in the H−O and H−N bonds, and the antioxidant capacity can be improved in a predictable manner[1] until the oxidation potentials become so low that electron transfer to dioxygen becomes the predominating reaction of the antioxidant. The past decade has seen significant progress in the development of new phenolic and aromatic amine antioxidants. The most notable advance is the finding by Pratt and co-workers that the substitution of carbon for nitrogen in the aromatic core not only increases the oxidation potentials but also improves the reactivity toward peroxyl radicals.[2] Thus, pyridinol (compound **1**; $k_{inh} = 28.0 \times 10^7$ M^{-1} s^{-1})[3] and diarylamine (compound **2**; $k_{inh} = 3.4 \times 10^7$ M^{-1} s^{-1})[4] react significantly faster with peroxyl radicals than α-tocopherol (α-TOC, compound **3**; $k_{inh} = 3.2 \times 10^6$ M^{-1} s^{-1}). During the past decade, we have studied the antioxidative properties of organotellurium compounds. When an alkyltelluro group was introduced into butylated hydroxyanisole (BHA, compound **4**), reactivity toward peroxyl radicals was notably improved ($k_{inh} = 1 \times 10^7$ M^{-1} s^{-1}). Also, in a



1 2 3 4

model two-phase lipid peroxidation system, the antioxidant could be continuously regenerated by the *N*-acetylcysteine (NAC) contained in the aqueous phase.[5] The observed high

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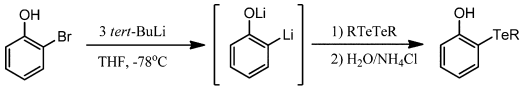
reactivity toward peroxyl radicals was surprising, but it was not until we started to examine simple phenols that we realized that a less conventional antioxidant mechanism than formal H-atom transfer could be operative. For example, alkyltellurophenols **5a–c** (Table 1) were found to quench peroxyl radicals some 10 times more efficiently than α-TOC (vide infra). Considering the fact that phenol itself is reported to react with peroxyl radicals with a rate constant of $k_{inh} = 2.9 \times 10^3$ M^{-1} s^{-1} at 65 °C,[6] the *ortho*-alkyltelluro group causes a circa 4 order of magnitude increase in reactivity. This cannot be accounted for by the substituent effect of an alkyltelluro group.[7] Rather, it suggests that a mechanism involving the chalcogen could be operative. We have proposed that the rate-limiting step could be O transfer from peroxyl to tellurium, followed by intramolecular H transfer to the resulting alkoxyl radical from the nearby HO group.[8] Spurred by these results, we were curious to see if we could take this concept one step further. We asked the following questions: How would the antioxidant capacity and regenerability be affected if two aromatic hydroxyls are flanking an alkyltelluro group? Conversely, what would the antioxidant characteristics be of a phenol carrying alkyltelluro groups in both *ortho*-positions? To the best of our knowledge, such compounds have not been previously described. In the following sections, we report the synthesis of (alkyltelluro)-phenols, (alkyltelluro)resorcinols, and bis(alkyltelluro)phenols. The new compounds were evaluated both for regenerability and for their capacity to quench peroxyl radicals in a two-phase system for the peroxidation of linoleic acid containing NAC as a stoichiometric reducing agent in the aqueous phase. Also, the catalytic hydroperoxide-decomposing (glutathione peroxidase-like) activity of the organotelluriums was assessed.

RESULTS AND DISCUSSION

Synthesis. Our approach to the title compounds is based on the lithium–halogen exchange and the reaction with electrophilic tellurium in the form of dialkyl ditellurides.[5] Lithiation of commercially available 2-bromophenol with 3 equiv of *tert*-butyllithium in THF followed by addition of di-*n*-butyl ditelluride, di-*n*-octyl ditelluride, and di-*n*-hexadecyl ditelluride to the resulting dianion afforded the *ortho*-(alkyltelluro)phenols **5a–c** of increasing lipophilicity in low yields (eq 1). Because

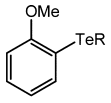


(1)

5a R= Butyl (31%)
5b R= Octyl (21%)
5c R= Hexadecyl (23%)

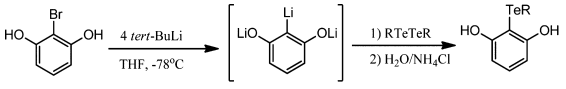
compounds **6a–c**, the O-methylated compounds corresponding to (alkyltelluro)phenols **5a–c**, respectively, were required for reference purposes, 2-bromoanisole was subjected to similar reaction conditions (using 2 equiv of *tert*-butyllithium). The isolated yields of (alkyltelluro)anisoles **6a–c** were significantly better than those obtained for the corresponding phenols. Our initial plan for the preparation of (alkyltelluro)resorcinols **7a–c** therefore involved *ortho*-lithiation of 1,3-dimethoxybenzene followed by reaction with a dialkyl ditelluride and a final demethylation induced by BBr_3 or dodecanemercaptan. However, both of these agents caused decomposition of the organotellurium compound accompanied by dialkyl ditelluride re-formation.

We therefore returned to the procedure shown in eq 1 and modified it slightly. The required starting material, 2-



6a R= Butyl (77%)
6b R= Octyl (36%)
6c R= Hexadecyl (43%)

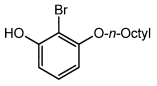
bromoresorcinol, was prepared by tribromination of resorcinol followed by the selective debromination in positions 4 and 6 brought about by Na_2SO_3.[9] Treatment of this material with 4 equiv of *tert*-butyllithium, followed by the addition of the appropriate dialkyl ditelluride to the in situ-formed trianion, afforded compounds **7a–c** in low yields (eq 2). Concerned



(2)

7a R= Butyl (24%)
7b R= Octyl (10%)
7c R= Hexadecyl (10%)

about the high water solubility of some of compounds **7a–c**, we decided to alkylate one of the phenolic groups in 2-bromoresorcinol with octyl bromide before dilithiation and introduction of the alkyltelluro moiety. Because of competing dialkylation, compound **8** was obtained at best in 28% yield. It is worth noting that the isolated yields of compounds **9a–c** were substantially higher than those obtained for compounds **5a–c**.



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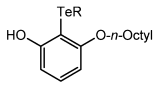
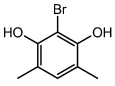
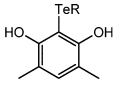


9a R= Butyl (65%)
9b R= Octyl (53%)
9c R= Hexadecyl (53%)



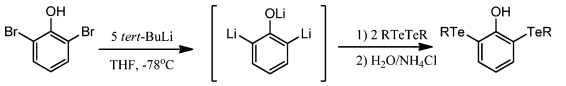
10 (77%)



11a R= Butyl (15%)
11b R= Octyl (15%)
11c R= Hexadecyl (5%)

In an effort to increase the lipophilicity of compounds **7a–c** while leaving the two phenolic groups untouched, two extra methyl groups were introduced into positions 4 and 6 of resorcinol[10] before bromination (77% yield by using tetrabutylammonium tribromide). Following the procedure in eq 2, bromoresorcinol **10** produced the desired alkyltelluro-resorcinols **11a–c**, again in low yields.

To obtain 2,6-bis(alkyltelluro)phenols **12a–c** via a lithiation protocol, 2,6-dibromophenol[11] was treated with 5 equiv of *tert*-butylithium, and the resulting trianion was allowed to react with dialkyl ditellurides for some time at ambient temperature (eq 3). Not surprisingly, the isolated yields were again unimpressive.



(3)

12a R= Butyl (24%)
12b R= Octyl (10%)
12c R= Hexadecyl (10%)

Inhibition Studies in a Two-Phase Lipid Peroxidation System. Homogeneous-phase, azo-initiated peroxidation of linoleic acid or the derivatives thereof has been employed for evaluation of the chain-breaking capacity of both synthetic and natural antioxidants.[12] Some time ago, we modified the system by introducing an aqueous phase containing a water-soluble thiol (*N*-acetylcysteine) that could continuously regenerate the active antioxidant in the lipid layer.[13] Thus, the antioxidant could act in a catalytic fashion where the duration of inhibition

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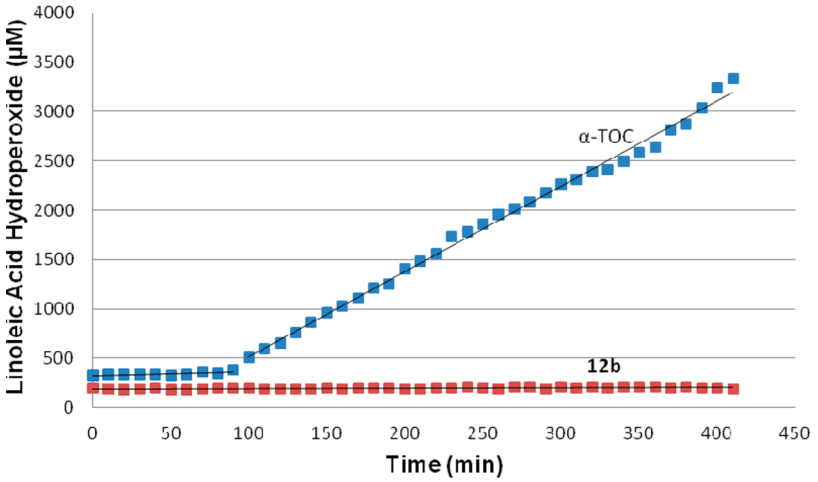

Figure 1. Peroxidation traces (linoleic acid hydroperoxide concentration vs time) recorded using compound **12b** and α-TOC as antioxidants in the chlorobenzene layer in the presence of NAC in the aqueous phase.

is restricted only by the availability of the co-antioxidant contained in the aqueous phase. In the experimental setup,[14] linoleic acid and a catalytic amount (40 μM) of the antioxidant in chlorobenzene were stirred at 42 °C in the presence of NAC (1 mM) in the aqueous phase. The peroxidation of linoleic acid was initiated by the addition of 2,2′-azobis(2,4-dimethylvaleronitrile) (AMVN), and the formation of conjugated diene hydroperoxide in the chlorobenzene was monitored by HPLC at 234 nm. By plotting the concentration of linoleic acid hydroperoxide versus time, we can determine the inhibited rate of peroxidation, R_{inh}, as the slope of the line during the inhibited phase, and the inhibition time, T_{inh}, from the crossing point of the inhibited and uninhibited lines (Figure 1). A small value of R_{inh} and a long inhibition time are characteristics of an efficient and highly regenerable antioxidant. In the presence of a poor antioxidant, no inhibited phase of peroxidation can be distinguished, and the inhibited rate of peroxidation is close to the value recorded in the absence of any antioxidant (circa 650 μM h^{-1}). α-Tocopherol is used as a benchmark. It is known to quench two peroxyl radicals before it is converted into nonradical products. Whether or not NAC is present in the aqueous phase, the antioxidant capacity of α-tocopherol is essentially the same (R_{inh} = 24−25 μM h^{-1} and T_{inh} = 80−87 min; Table 1). Thus, NAC cannot regenerate α-tocopherol across the aqueous−lipid interphase under the conditions of our assay.

In the absence of NAC, relatively high inhibited rates of peroxidation were observed for all (alkyltelluro)phenol derivatives (R_{inh} = 85−508 μM h^{-1}; Table 1). This is probably because the organotellurium catalyst had been oxidized to the corresponding telluroxide by the residual amount of linoleic acid hydroperoxide that is always present in commercial samples of linoleic acid. The short inhibited phases of peroxidation and inefficient quenching of peroxyl radicals that were observed for the (alkyltelluro)resorcinols **7a−c** and **11a−c** in the absence of NAC are in accord with what we have seen before with BHA-analogue **4** (R_{inh} = 252 μM h^{-1} and T_{inh} = 80 min[5]).

In the presence of NAC, all (alkyltelluro)phenol derivatives studied clearly outperformed both α-tocopherol and the BHA-analogue **4** (R_{inh} = 14 μM h^{-1}) when it came to chain-breaking capacity (R_{inh} = 1.6−5.4 μM h^{-1}). Considering the fact that compound **4** in chlorobenzene reacted with styrene-derived peroxyl radicals with a rate constant k_{inh} as high as 1.0 × 10^7 M^{-1} s^{-1}, the prediction is that all compounds in **5**, **7**, **9**, **11**, and **12** would be even more reactive. Anisoles **6a−c**, lacking a hydrogen donating group next to the alkyltelluro moiety, turned out to be significantly poorer quenchers (R_{inh} = 53−66 μM h^{-1}) of peroxyl radicals than all the other compounds studied. The only conceivable antioxidant mechanism here is electron transfer from the chalcogen. Obviously, it does not occur as efficiently as the formal hydrogen atom transfer which seems to be operative with the other antioxidants.

Large variations in regenerability were observed among the various organotellurium antioxidants prepared. (Alkyltelluro)-resorcinols **7a−c** and **11a−c** inhibited peroxidation for only 90−99 min, and the inhibition time was not affected very much by increasing the size of the alkyl group (butyl, octyl, hexadecyl) in the alkyltelluro substituent. It may be that the 1,3-dihydroxybenzene part of the molecule is buried in the aqueous phase and does not offer more than temporary antioxidant protection in the chlorobenzene layer. The more lipophilic alkyltelluro phenols **5a−c** and mono-*O*-alkylated resorcinols **9a−c** offered longer protection against autoxidation (T_{inh} = 220−242 min). The bis(alkyltelluro)phenols **12a−c** were the most regenerable antioxidants in the series, with inhibition times (T_{inh} > 410 min) exceeding those recorded previously for compound **4**. We hypothesize that this compound is lipophilic enough to remain in the lipid phase and yet is able to "communicate" with the thiol contained in the aqueous layer to bring about the reduction of telluroxide to telluride and the regeneration of phenol from the corresponding phenoxyl radical. The peroxidation plots shown in Figure 1 are recorded with α-tocopherol and the most regenerable organotellurium antioxidant, **12b**.

Glutathione Peroxidase-like Antioxidant Activity. Divalent organotelluriums are easily oxidized by hydroperoxides and other mild oxidizing agents, and the resulting organotellurium(IV) species are readily reduced by thiols to reform organotellurium(II) compounds. Thus, they can act as catalysts for hydroperoxide reduction just like the glutathione peroxidase (GPx) enzymes do when using glutathione (GSH) as the stoichiometric reducing agent (eq 4).[15]

$$H_2O_2 + 2GSH \xrightarrow{GPx} GSSG + H_2O \quad (4)$$

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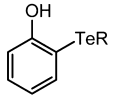
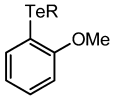
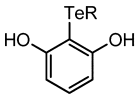
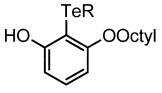
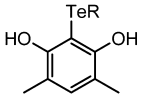
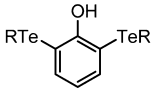
Table 1. Inhibited Rates of Linoleic Acid Peroxidation (R_{inh}) and Inhibition Times (T_{inh}) in the Presence and Absence of NAC (1 mM) in the Two-Phase System and GPx Activities As Determined by the Thiol Peroxidase Assay

		With NAC		Without NAC		GPx activities
Antioxidant (40 mM)		R_{inh}[a] ($\mu M\ h^{-1}$)	T_{inh}[b] (min)	R_{inh}[a] ($\mu M\ h^{-1}$)	T_{inh}[b] (min)	v_0[c] ($\mu M\ min^{-1}$)
	**5a** R = Butyl	5.4 ± 1.2	228 ± 3	508	0	28.0 ± 2.2
	5b R = Octyl	2.0 ± 0.8	220 ± 10	444	0	24.9 ± 2.4
	5c R = Hexadecyl	2.3 ± 0.9	223 ± 5	441	0	24.0 ± 1.0
	**6a** R = Butyl	66 ± 4	87 ± 7	446	0	9.4 ± 2.6
	6b R = Octyl	64 ± 5	94 ± 6	461	0	9.7 ± 0.5
	6c R = Hexadecyl	53 ± 5	99 ± 5	466	0	9.5 ± 2.2
	**7a** R = Butyl	3.0 ± 0.2	92 ± 8	155	50	80.7 ± 1.2
	7b R = Octyl	2.1 ± 1.2	90 ± 3	166	50	80.2 ± 2.9
	7c R = Hexadecyl	2.5 ± 0.8	90 ± 1	128	50	79.8 ± 0.4
	**9a** R = Butyl	1.9 ± 0.8	198 ± 1	449	0	28.8 ± 2.0
	9b R = Octyl	2.4 ± 1.1	242 ± 6	442	0	31.0 ± 0.9
	9c R = Hexadecyl	1.7 ± 0.5	235 ± 7	437	0	31.9 ± 1.0
	**11a** R = Butyl	4.7 ± 0.6	89 ± 5	85	90	70.1 ± 2.7
	11b R = Octyl	3.0 ± 1.1	98 ± 2	100	130	44.3 ± 1.3
	11c R = Hexadecyl	3.0 ± 0.5	99 ± 3	97	140	44.4 ± 1.1
	**12a** R = Butyl	2.5 ± 0.5	396 ± 12	396	0	58.4 ± 2.0
	12b R = Octyl	1.6 ± 0.7	> 410	422	0	63.5 ± 1.5
	12c R = Hexadecyl	3.6 ± 1.2	> 410	411	0	31.7 ± 3.0
α-tocopherol		25 ± 1	87 ± 6	24	80	
Ph_2Se_2						1.2 ± 0.5

[a]Rate of peroxidation during the inhibited phase (uninhibited rate circa 650 $\mu M\ h^{-1}$). Errors correspond to ± SD for triplicates. [b]Inhibited phase of peroxidation. Reactions were monitored for 410 min. Errors correspond to ± SD for triplicates. [c]Values corrected for the uncatalyzed oxidation of PhSH in the presence of H_2O_2. Errors correspond to ± SD for triplicates.

Although catalysis does not occur nearly as efficiently as in nature, the organotellurium mimics react with a variety of mild oxidizing agents, and the reducing agents required for a catalytic performance include not only thiols but also other mild reducing agents such as ascorbate. Two assays are commonly used for assessing glutathione peroxidase-like activity. The oldest and most complex one is the coupled reductase method developed by Wendel.[16] In this assay, hydrogen peroxide, glutathione, NADPH, catalyst, and an enzyme, GSSG reductase, are mixed in water, and NADPH consumption (ν_o) is recorded by UV spectroscopy for the first 10 s of reaction (eq 5).

$$NADPH + H_2O_2 + H^{\oplus} \xrightarrow{\text{GSSG reductase}} NADP^{\oplus} + 2H_2O \quad (5)$$

Telluroxide formed by the hydrogen peroxide oxidation of the organotellurium catalyst is rapidly reduced by glutathione, and the resulting disulfide, GSSG, is then enzymatically reduced with consumption of NADPH. Initial rates of ν_o have to be corrected both for the spontaneous oxidation of GSH induced by hydrogen peroxide and for any reduction of telluroxide to

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telluride brought about by GSSG reductase under the conditions of the assay. Ebselen is commonly used as a reference compound. The other assay, introduced by Tomoda,[17] measures thiol peroxidase activity. It is more straightforward and involves monitoring the formation of diphenyl disulfide by UV spectroscopy at 304 nm for the first 10 s of reaction (ν_o) in a system containing thiophenol, hydrogen peroxide, and catalyst in methanol (eq 6).

$$2\mathrm{PhSH} + \mathrm{H_2O_2} \xrightarrow[\mathrm{CH_3OH}]{\text{catalyst}} \mathrm{PhSSPh} + \mathrm{H_2O} \qquad (6)$$

Initial rates of diphenyl disulfide formation in this system have to be corrected for the spontaneous oxidation of thiophenol induced by hydrogen peroxide, and diphenyl diselenide is commonly used as a reference compound. All new catalysts prepared were tested using both the coupled reductase method and the thiol peroxidase assay. However, less than half of the compounds showed any activity in the enzymatic assay (Supporting Information). This is probably due to poor water solubility of the catalysts. Methanol turned out to be a better solvent for the compounds. (Alkyltelluro)resorcinols **7a−c** and **11a** were the most active catalysts according to the thiol peroxidase assay. They catalyzed reduction of hydrogen peroxide circa 65 times more efficiently than diphenyl diselenide. Increasing the length of the alkyl chain in the alkyltelluro group in these and other catalysts had only a marginal effect on activity. Because the oxidation of telluride to telluroxide is expected to be rate determining in catalysis,[18] steric hindrance due to the alkyl group does not seem to be very important. Rather, catalytic efficiency reflects the electron density at tellurium in the nucleophilic attack on hydrogen peroxide. Compounds **7a−c** and **11a−c**, with two OH groups *ortho* to tellurium, are likely to be the most nucleophilic species in the series studied. Also, the capacity of the OH groups to preorganize the reacting partners by hydrogen bonding to hydrogen peroxide may improve catalysis. Next, among compounds with only one OH group flanking the chalcogen, were compounds **12a−c**. The presence of two *ortho*-alkyltelluro groups in the molecule (instead of one) may be the rationale for their better catalytic performance compared to that of compounds **5a−c**. Despite an additional *ortho*-octyloxy group, compounds **9a−c** perform essentially the same as compounds **5a−c**. One may argue here that the substituent causes a steric hindrance. Anisoles **6a−c**, incapable of serving as hydrogen bond donors, were by far the poorest catalysts among the compounds investigated.

CONCLUSIONS

Simple (alkyltelluro)phenols, (alkyltelluro)resorcinols, and bis(alkyltelluro)phenols were all found to be much more reactive toward peroxyl radicals than α-tocopherol. This is probably because quenching occurs via an unconventional mechanism involving an O transfer to tellurium followed by an H-atom transfer to alkoxyl radical rather than a direct H transfer from the OH group.[8] The novel organotellurium compounds were also found to be better quenchers of peroxyl radicals than BHA-analogue **4**. Presumably, this is because one or several steps in the proposed mechanism are slowed by the bulky alkyl substituent. Although the various (alkyltelluro)-resorcinols showed the highest thiol peroxidase activity of all of the compounds studied, they did not inhibit lipid peroxidation for long (89−99 min) when tested in a lipid peroxidation biphasic system containing excess *N*-acetylcysteine in the aqueous phase. They were easily outperformed by the simple (alkyltelluro)phenols **5a−c** (T_{inh} = 220−228 min) in this respect, and thus, it does not seem that the added aromatic OH group confers regenerability. We can only speculate that the resorcinol part of the molecule is so soluble in the aqueous layer that the effective concentration of the antioxidant in the lipid layer becomes too low. On the other hand, the incorporation of an additional alkyltelluro group into compounds **5a−c** caused a 2-fold increase in the inhibition time (T_{inh} > 410 min for compounds **12b** and **12c**). The rationale for the improved regenerability could be the high solubility in the organic phase. Out of the various (alkyltelluro)-phenol catalysts studied, compounds **12b** and **12c** are probably the most lipophilic. One may also argue that the long inhibition times could be the result of a statistical effect. If the regeneration of a catalyst across the aqueous−lipid interphase does not occur efficiently enough, various decomposition pathways causing cleavage of the labile carbon−tellurium bonds may come into play. With two alkyltelluro moieties in the molecule, the accidental loss of one of them would still leave a functioning catalyst that could offer protection for some time more.

EXPERIMENTAL SECTION

^{1}H and ^{13}C NMR spectra were recorded on 300 (^{1}H: 300 MHz; ^{13}C: 75 MHz) and 400 (^{1}H: 399.97 MHz; ^{13}C: 100.58 MHz) 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. Flash column chromatography was performed using silica gel (0.04−0.06 mm). Melting points are uncorrected. Tetrahydrofuran was dried in a solvent purification system by passing it through an activated alumina column. Di-*n*-butyl ditelluride,[19] di-*n*-octyl ditelluride,[20] di-*n*-hexadecyl ditelluride,[21] 2-bromoresorcinol,[9] 4,6-dimethylresorcinol,[10] and 2,6-dibromophenol[11] were prepared according to literature methods.

General Procedure A for the Preparation of (Alkyltelluro)-phenols, (Alkyltelluro)anisoles, and (Alkyltelluro)resorcinols. *tert*-BuLi (2−4 equiv) was added to a solution of *ortho*-brominated phenol/anisole/resorcinol (1 equiv) in anhydrous THF under nitrogen at −78 °C. The solution was stirred for 2 h at −78 °C before addition of the dialkyl ditelluride (1.0−1.5 equiv). After being stirred at ambient temperature overnight, the solution was quenched with a saturated ammonium chloride solution (40 mL) and extracted with ether (50 mL × 3). The organic layer was dried over magnesium sulfate, filtered, and evaporated under reduced pressure. The residue was purified by flash chromatography using pentane/ethyl acetate as an eluent.

*2-(Butyltelluro)phenol (**5a**).* 2-Bromophenol (0.35 mL, 3 mmol), *tert*-BuLi (1.7 M in pentane, 5.3 mL, 9 mmol), and dibutyl ditelluride (1.7 g, 4.5 mmol) were reacted in THF (20 mL) according to general procedure A. The mixture was purified by flash chromatography (pentane/ethyl acetate = 95:5) to give the title compound as a yellow oil (0.162 g, 31%). ^{1}H NMR ($CDCl_3$): δ 7.77 (dd, J = 1.6, 7.6 Hz, 1H), 7.29 (m, 1H), 7.06 (dd, J = 1.2, 8.4 Hz, 1H), 6.75 (m, 1H), 6.25 (s, 1H), 2.70 (t, J = 7.6 Hz, 2H), 1.69 (m, 2H), 1.35 (m, 2H), 0.88 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 157.9, 142.2, 131.9, 121.2, 113.1, 101.3, 33.7, 24.8, 13.3, 9.5. HRMS (ESI-TOF) m/z: $[M]^+$ calcd for $C_{10}H_{14}OTe$ 280.0107; found 280.0119.

*2-(Octyltelluro)phenol (**5b**).* 2-Bromophenol (0.35 mL, 3 mmol), *tert*-BuLi (1.7 M in pentane, 5.3 mL, 9 mmol), and dioctyl ditelluride (2.1 g, 4.5 mmol) were reacted in THF (20 mL) according to general procedure A. The mixture was purified by flash chromatography (pentane/ethyl acetate = 95:5) to give the title compound as a yellow oil (0.209 g, 21%). ^{1}H NMR ($CDCl_3$): δ 7.77 (dd, J = 1.6, 7.6 Hz, 1H), 7.28 (dd, J = 1.6, 8.8 Hz, 1H), 7.05 (dd, J = 1.2, 8.4 Hz, 1H), 6.75 (m, 1H), 6.25 (s, 1H), 2.70 (t, J = 7.6 Hz, 2H), 1.68 (m, 2H), 1.24−1.32 (several peaks, 10H), 0.88 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 157.9, 142.2, 131.9, 121.2, 113.1, 101.3, 31.7 (2C), 31.6,

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29.1, 28.8, 22.6, 14.1, 9.8. HRMS (ESI-TOF) m/z: $[M]^+$ calcd for $C_{14}H_{22}OTe$ 336.0733; found 336.0708.

*2-(Hexadecyltelluro)phenol (**5c**).* 2-Bromophenol (0.35 mL, 3 mmol), *tert*-BuLi (1.7 M in pentane, 5.3 mL, 9 mmol), and dihexadecyl ditelluride (2.1 g, 3 mmol) were reacted in THF (20 mL) according to general procedure A. The mixture was purified by flash chromatography (pentane/ethyl acetate = 95:5) to give the title compound as a pale yellow solid (0.308 g, 23%). Mp: 40−41 °C. ^{1}H NMR ($CDCl_3$): δ 7.78 (dd, J = 1.6, 7.2 Hz, 1H), 7.29 (m, 1H), 7.06 (dd, J = 1.2, 8.4 Hz, 1H), 6.75 (m, 1H), 6.27 (s, 1H), 2.71 (t, J = 7.6 Hz, 2H), 1.70 (m, 2H), 1.18−1.32 (several peaks, 26H), 0.90 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 157.9, 142.1, 131.9, 121.2, 113.2, 101.3, 31.9, 31.7, 31.6, 29.7, 29.6 (2C), 29.5, 29.4 (2C), 28.8, 22.7, 14.1, 9.8. HRMS (ESI-TOF) m/z: $[M]^+$ calcd for $C_{22}H_{38}OTe$ 448.1985; found 448.1964.

*2-(Butyltelluro)anisole (**6a**).* 2-Bromoanisole (0.561 g, 3 mmol), *tert*-BuLi (1.7 M in pentane, 3.5 mL, 6 mmol), and dibutyl ditelluride (1.1 g, 3 mmol) were reacted in THF (20 mL) according to general procedure A. The mixture was purified by flash chromatography (pentane/ethyl acetate = 98:2) to give the title compound as a yellow oil (0.675 g, 77%). ^{1}H NMR ($CDCl_3$): δ 7.41 (dd, J = 1.2, 7.6 Hz, 1H), 7.22 (td, J = 1.2, 7.6, 8.4 Hz, 1H), 6.87 (t, J = 7.6 Hz, 1H), 6.79 (d, J = 8.4 Hz, 1H), 3.86 (s, 3H), 2.88 (t, J = 7.6 Hz, 2H), 1.83 (m, 2H), 1.33 (m, 2H), 0.94 (t, J = 7.6 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 159.3, 134.3, 128.0, 122.0, 109.7, 103.9, 55.8, 33.5, 25.3, 13.4, 5.2. HRMS (ESI-TOF) m/z: $[M]^+$ calcd for $C_{11}H_{16}OTe$ 294.0263; found 294.0233.

*2-(Octyltelluro)anisole (**6b**).* 2-Bromoanisole (0.374 g, 2 mmol), *tert*-BuLi (1.7 M in pentane, 2.4 mL, 4 mmol), and dioctyl ditelluride (0.963 g, 2 mmol) were reacted in THF (15 mL) according to general procedure A. The mixture was purified by flash chromatography (pentane/ethyl acetate = 98:2) to give the title compound as a yellow oil (0.250 g, 36%). ^{1}H NMR ($CDCl_3$): δ 7.40 (dd, J = 1.2, 6.4 Hz, 1H), 7.21 (m, 1H), 6.87 (td, J = 0.9, 7.2 Hz, 1H), 6.79 (d, J = 8.1 Hz, 1H), 3.86 (s, 3H), 2.86 (t, J = 7.6 Hz, 2H), 1.81 (m, 2H), 1.27−1.43 (several peaks, 10H), 0.88 (t, J = 6.9 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 159.3, 134.4, 128.0, 122.0, 109.7, 103.9, 55.9, 32.2, 31.8, 31.5, 29.2, 29.0, 22.7, 14.1, 5.6. HRMS (ESI-TOF) m/z: $[M]^+$ calcd for $C_{15}H_{24}OTe$ 350.0889; found 350.0875.

*2-(Hexadecyltelluro)anisole (**6c**).* 2-Bromoanisole (0.374 g, 2 mmol), *tert*-BuLi (1.7 M in pentane, 2.4 mL, 4 mmol), and dihexadecyl ditelluride (1.4 g, 2 mmol) were reacted in THF (15 mL) according to general procedure A. The mixture was purified by flash chromatography (pentane/ethyl acetate = 98:2) to give the title compound as a pale yellow solid (0.397 g, 43%). Mp: 43−46 °C. ^{1}H NMR ($CDCl_3$): δ 7.41 (dd, J = 1.6, 7.6 Hz, 1H), 7.20 (m, 1H), 6.89 (td, J = 0.8, 7.6 Hz, 1H), 6.79 (d, J = 8.0 Hz, 1H), 3.86 (s, 3H), 2.87 (t, J = 7.6 Hz, 2H), 1.83 (m, 2H), 1.27−1.43 (several peaks, 26H), 0.89 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 159.3, 134.3, 128.0, 122.0, 109.7, 103.9, 55.8, 32.2, 31.9, 31.4, 29.7 (3C), 29.6, 29.5, 29.4, 29.0, 22.7, 14.1, 5.6. HRMS (ESI-TOF) m/z: $[M]^+$ calcd for $C_{23}H_{40}OTe$ 462,2141; found 462.2144.

*2-(Butyltelluro)resorcinol (**7a**).* 2-Bromoresorcinol (0.567 g, 3 mmol), *tert*-BuLi (1.7 M in pentane, 7.1 mL, 12 mmol), and dibutyl ditelluride (2.2 g, 4.8 mmol) were reacted in THF (21 mL) according to general procedure A. The mixture was purified by flash column chromatography (pentane/ethyl acetate = 95:5) to give the title compound as a yellow oil (0.215 g, 24%). ^{1}H NMR ($CDCl_3$): δ 7.20 (t, J = 8.0 Hz, 1H), 6.63 (d, J = 8.0 Hz, 2H), 6.07 (s, 2H), 2.60 (t, J = 7.6 Hz, 2H), 1.66 (m, 2H), 1.34 (m, 2H), 0.87 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 158.5, 133.0, 105.3, 93.5, 33.7, 24.9, 13.3, 10.1. HRMS (ESI-TOF) m/z: $[M]^+$ calcd for $C_{10}H_{14}O_2Te$ 296.0056; found 296.0046.

*2-(Octyltelluro)resorcinol (**7b**).* 2-Bromoresorcinol (0.378 g, 2 mmol), *tert*-BuLi (1.7 M in pentane, 4.7 mL, 8 mmol), and dioctyl ditelluride (1.9 g, 4 mmol) were reacted in THF (14 mL) according to general procedure A. The mixture was purified by flash column chromatography (pentane/ethyl acetate = 95:5) to give the title compound as a yellow oil (0.073 g, 10%). ^{1}H NMR ($CDCl_3$): δ 7.19 (t, J = 8.1 Hz, 1H), 6.63 (d, J = 8.1 Hz, 2H), 6.08 (s, 2H), 2.59 (t, J = 7.8 Hz, 2H), 1.68 (m, 2H), 1.23−1.33 (several peaks, 10H), 0.87 (t, J = 6.9 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 158.5, 133.0, 105.3, 93.5, 31.7 (2C), 31.6, 31.5, 29.0, 28.7, 22.6, 14.0, 10.5. HRMS (ESI-TOF) m/z: $[M]^+$ calcd for $C_{14}H_{22}O_2Te$ 352.0682; found 352.0684.

*2-(Hexadecyltelluro)resorcinol (**7c**).* 2-Bromoresorcinol (0.472 g, 2.5 mmol), *tert*-BuLi (1.7 M in pentane, 5.9 mL, 10 mmol), and dihexadecyl ditelluride (1.8 g, 2.5 mmol) were reacted in THF (14 mL) according to general procedure A. The mixture was purified by flash column chromatography (pentane/ethyl acetate = 95:5) to give the title compound as a red solid (0.111 g, 10%). Mp: 61−63 °C. ^{1}H NMR ($CDCl_3$): δ 7.19 (t, J = 8.0 Hz, 1H), 6.63 (d, J = 8.0 Hz, 2H), 6.09 (s, 2H), 2.60 (t, J = 8.0 Hz, 2H), 1.68 (m, 2H), 1.23−1.31 (several peaks, 26H), 0.89 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 158.5, 133.0, 105.3, 93.5, 31.9, 31.7, 31.6, 29.7, 29.6 (2C), 29.5, 29.4, 29.3, 28.8, 22.7, 14.1, 10.5. HRMS (ESI-TOF) m/z: $[M]^+$ calcd for $C_{22}H_{38}O_2Te$ 464.1934; found 464.1931.

*2-Bromo-3-(octyloxy)phenol (**8**).* Potassium carbonate (6.04g, 43.8 mmol) was added to a solution of 2-bromoresorcinol (5.53 g, 29.2 mmol) and 1-bromooctane (5.04 g, 29.2 mmol) in anhydrous DMF (100 mL) under nitrogen. After being stirred at 80 °C for 4 days, the solution was quenched with water (50 mL) and extracted with ether (50 mL × 3). The organic layer was dried over magnesium sulfate, filtered, and evaporated under reduced pressure. The mixture was purified by flash chromatography (pentane/ethyl acetate = 9:1) to give the title compound as a colorless oil (2.4 g, 28%). ^{1}H NMR ($CDCl_3$): δ 7.14 (t, J = 8.0 Hz, 1H), 6.66 (d, J = 8.0 Hz, 1H), 6.46 (d, J = 8.0 Hz, 1H), 5.62 (s, 1H), 4.01 (t, J = 6.4 Hz, 2H), 1.83 (m, 2H), 1.30−1.53 (several peaks, 10H), 0.89 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 156.0, 153.5, 128.5, 108.2, 104.6, 100.5, 69.2, 31.8, 29.3, 29.2, 29.1, 26.0, 22.6, 14.1. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{14}H_{22}BrO_2$ 301.0803; found 301.0791.

*2-(Butyltelluro)-3-(octyloxy)phenol (**9a**).* 2-Bromo-3-(octyloxy)-phenol (0.609 g, 2 mmol), *tert*-BuLi (1.7 M in pentane, 3.5 mL, 6 mmol), and dibutyl ditelluride (0.739 g, 2 mmol) were reacted in THF (15 mL) according to general procedure A. The mixture was purified by flash chromatography (pentane/ethyl acetate = 97.5:2.5) to give the title compound as a yellow oil (524 mg, 65%). ^{1}H NMR ($CDCl_3$): δ 7.20 (t, J = 8.0 Hz, 1H), 6.70 (dd, J = 0.8, 8.0 Hz, 1H), 6.53 (s, 1H), 6.38 (d, J = 8.0 Hz, 1H), 3.99 (t, J = 6.4 Hz, 2H), 2.68 (t, J = 7.6 Hz, 2H), 1.83 (m, 2H), 1.65 (m, 2H), 1.47 (m, 2H), 1.29−1.40 (several peaks, 10H), 0.84−0.91 (several peaks, 6H). ^{13}C NMR ($CDCl_3$): δ 161.4, 159.0, 132.0, 106.0, 102.6, 93.2, 68.8, 33.7, 31.8, 29.3 (3C), 26.2, 24.9, 22.7, 14.1, 13.3, 8.5. HRMS (ESI-TOF) m/z: $[M]^+$ calcd for $C_{18}H_{30}O_2Te$ 408.1308; found 408.1332.

*2-(Octyltelluro)-3-(octyloxy)phenol (**9b**).* 2-Bromo-3-(octyloxy)-phenol (0.609 g, 2 mmol), *tert*-BuLi (1.7 M in pentane, 3.5 mL, 6 mmol), and dibutyl ditelluride (0.963 g, 2 mmol) were reacted in THF (15 mL) according to general procedure A. The mixture was purified by flash chromatography (pentane/ethyl acetate = 97.5:2.5) to give the title compound as a yellow oil (0.490 g, 53%). ^{1}H NMR ($CDCl_3$): δ 7.20 (t, J = 8.1 Hz, 1H), 6.71 (dd, J = 0.9, 8.1 Hz, 1H), 6.54 (s, 1H), 6.38 (dd, J = 0.9, 8.1 Hz, 1H), 3.99 (t, J = 6.3 Hz, 2H), 2.68 (t, J = 7.8 Hz, 2H), 1.83 (m, 2H), 1.66 (m, 2H), 1.54 (m, 2H), 1.23−1.36 (several peaks, 20H), 0.86−0.93 (several peaks, 6H). ^{13}C NMR ($CDCl_3$): δ 161.3, 159.0, 132.0, 106.0, 102.6, 93.2, 68.8, 31.8 (3C), 31.6, 29.3 (3C), 29.1, 28.8, 26.2, 22.7, 22.6, 14.1 (2C), 8.9. HRMS (ESI-TOF) m/z: $[M]^+$ calcd for $C_{22}H_{38}O_2Te$ 464.1934; found 464.1945.

*2-(Hexadecyltelluro)-3-(octyloxy)phenol (**9c**).* 2-Bromo-3-(octyloxy)phenol (0.609 g, 2 mmol), *tert*-BuLi (1.7 M in pentane, 3.5 mL, 6 mmol), and dihexadecyl ditelluride (1.4 g, 2 mmol) were reacted in THF (15 mL) according to general procedure A. The mixture was purified by flash chromatography (pentane/ethyl acetate = 97.5:2.5) to give the title compound as a yellow oil (0.604 g, 53%). ^{1}H NMR ($CDCl_3$): δ 7.20 (t, J = 8.0 Hz, 1H), 6.70 (d, J = 8.0 Hz, 1H), 6.53 (s, 1H), 6.38 (d, J = 8.0 Hz, 1H), 3.99 (t, J = 6.4 Hz, 2H), 2.67 (t, J = 7.6 Hz, 2H), 1.83 (m, 2H), 1.65 (m, 2H), 1.40 (m, 2H), 1.22−1.34 (several peaks, 34H), 0.83−0.90 (several peaks, 6H). ^{13}C NMR ($CDCl_3$): δ 161.4, 159.1, 132.0, 106.0, 102.6, 93.2, 68.8, 31.9, 31.8 (2C), 31.6, 29.7, 29.6 (2C), 29.5, 29.4, 29.3 (4C), 28.9, 26.2, 22.7,

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14.1, 8.8. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{30}H_{54}O_2Te$ 577.3264; found 577.3258.

*2-Bromo-4,6-dimethylresorcinol (**10**).* A solution of tetrabutylammoniun tribromide (2.9 g, 6 mmol) in dichloromethane was added dropwise over the course of 15 min to a solution of 4,6-dimethylresorcinol (0.830 g, 6 mmol) in dichloromethane (75 mL). After the mixture had been stirred for 16 h at room temperature, water (30 mL) was added, and the aqueous phase was extracted with dichloromethane (30 mL × 3). The combined organic phases were dried over magnesium sulfate, filtered, and evaporated under reduced pressure. The residue was purified by flash column chromatography (pentane/ethyl acetate = 9:1) to give the title compound as a white solid (1.0 g, 77%). Mp: 120−122 °C. ^{1}H NMR ($CDCl_3$): δ 6.84 (s, 1H), 5.17 (s, 2H), 2.20 (s, 6H). ^{13}C NMR ($CDCl_3$): δ 148.2, 131.4, 116.2, 99.4, 15.7. HRMS (ESI-TOF) m/z: $[M - 2H]^+$ calcd for $C_8H_7BrO_2$ 213.9629; found 213.9608.

*2-(Butyltelluro)-4,6-dimethylresorcinol (**11a**).* 2-Bromo-4,6-dimethylresorcinol (0.542 g, 2.5 mmol), *tert*-BuLi (1.7 M in pentane, 5.9 mL, 10 mmol), and dibutyl ditelluride (1.8 g, 5 mmol) were reacted in THF (20 mL) according to general procedure A. The mixture was purified by flash chromatography (pentane/ethyl acetate = 95:5) to give the title compound as a yellow oil (0.118 g, 15%). ^{1}H NMR ($CDCl_3$): δ 6.92 (s, 1H), 5.96 (s, 2H), 2.59 (t, J = 7.6 Hz, 2H), 2.22 (s, 6H), 1.62−1.69 (m, 2H), 1.32−1.38 (m, 2H), 0.88 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 153.7, 135.3, 113.8, 93.2, 33.7, 24.9, 16.3, 13.3, 10.0. HRMS (ESI-TOF) m/z: $[M]^+$ calcd for $C_{12}H_{18}O_2Te$ 324.0369; found 324.0360.

*2-(Octyltelluro)-4,6-dimethylresorcinol (**11b**).* 2-Bromo-4,6-dimethylresorcinol (0.542 g, 2.5 mmol), *tert*-BuLi (1.7 M in pentane, 5.9 mL, 10 mmol), and dioctyl ditelluride (2.4 g, 5 mmol) were reacted in THF (20 mL) according to general procedure A. The mixture was purified by flash chromatography (pentane/ethyl acetate = 95:5) to give the title compound as a yellow oil (0.146 g, 15%). ^{1}H NMR ($CDCl_3$): δ 6.92 (s, 1H), 5.96 (s, 2H), 2.58 (t, J = 8.0 Hz, 2H), 2.22 (s, 6H), 1.68 (m, 2H), 1.24−1.31 (several peaks, 10H), 0.88 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 153.7, 135.3, 113.8, 93.2, 31.7 (3C), 29.1, 28.7, 22.6, 16.3, 14.1, 10.4. HRMS (ESI-TOF) m/z: $[M]^+$ calcd for $C_{16}H_{26}O_2Te$ 380.0995; found 380.1004.

*2-(Hexadecyltelluro)-4,6-dimethylresorcinol (**11c**).* 2-Bromo-4,6-dimethylresorcinol (0.542 g, 2.5 mmol), *tert*-BuLi (1.7 M in pentane, 5.9 mL, 10 mmol), and dihexadecyl ditelluride (1.8 g, 2.5 mmol) were reacted in THF (30 mL) according to general procedure A. The mixture was purified by flash chromatography (pentane/ethyl acetate = 95:5) to give the title compound as a yellow solid (0.060 g, 4.9%). Mp: 53−56 °C. ^{1}H NMR ($CDCl_3$): δ 6.91 (s, 1H), 5.95 (s, 2H), 2.57 (t, J = 7.6 Hz, 2H), 2.21 (s, 6H), 1.67 (m, 2H), 1.13−1.25 (several peaks, 26H), 0.88 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 153.7, 135.3, 113.8, 93.2, 31.9, 31.7 (2C), 29.7, 29.6 (2C), 29.5, 29.4 (2C), 28.8, 22.7, 16.3, 14.1, 10.4. HRMS (ESI-TOF) m/z: $[M]^+$ calcd for $C_{24}H_{42}O_2Te$ 492.2247; found 492.2212.

General Procedure B for the Preparation of Bis(alkyltelluro)-phenols. *tert*-BuLi (5 equiv) was added to a solution of 2,6-dibromophenol (1 equiv) in anhydrous THF at −78 °C under nitrogen. After the mixture had been stirred for 5 h at −78 °C and 20 min at ambient temperature, the diakyl ditelluride (2−3 equiv) was added. The solution was stirred overnight, quenched with saturated ammonium chloride (40 mL), and extracted with diethyl ether (50 mL × 3). The organic layer was dried over magnesium sulfate, filtered, and evaporated under reduced pressure. The residue was purified by flash column chromatography using pentane/ethyl acetate as an eluent.

*2,6-Bis(butyltelluro)phenol (**12a**).* 2,6-Dibromophenol (1.0 g, 4 mmol), *tert*-BuLi (1.7 M in pentane, 11.7 mL, 20 mmol), and dibutyl ditelluride (4.4 g, 12 mmol) were reacted in THF (30 mL) according to general procedure B. The crude product was purified by flash column chromatography (pentane/ethyl acetate = 92:8) to give the title compound as a yellow oil (0.409 g, 22%). ^{1}H NMR ($CDCl_3$): δ 7.57 (d, J = 7.6 Hz, 2H), 6.72 (s,1H), 6.62 (t, J = 7.6 Hz, 1H), 2.82 (t, J = 7.6 Hz, 4H), 1.76 (m, 4H), 1.39 (m, 4H), 0.90 (t, J = 7.2 Hz, 6H). ^{13}C NMR ($CDCl_3$): δ 157.9, 139.7, 122.5, 98.6, 33.6, 25.0, 13.4, 8.2. Anal. Calcd for $C_{14}H_{22}OTe_2$: C, 36.4; H, 4.8. Found: C, 36.8; H, 4.8.

*2,6-Bis(octyltelluro)phenol (**12b**).* 2,6-Dibromophenol (0.755 g, 3 mmol), *tert*-BuLi (1.7 M in pentane, 8.8 mL, 15 mmol), and dioctyl ditelluride (4.3 g, 9 mmol) were reacted in THF (30 mL) according to general procedure B. The crude product was purified by flash column chromatography (pentane/ethyl acetate = 99:1) to give the title compound as a yellow oil (0.280 g, 16%). ^{1}H NMR ($CDCl_3$): δ 7.57 (d, J = 7.6 Hz, 2H), 6.72 (s, 1H), 6.61 (t, J = 7.6 Hz, 1H), 2.81 (t, J = 7.6 Hz, 4H), 1.77 (m, 4H), 1.25−1.38 (several peaks, 20H), 0.88 (t, J = 6.8 Hz, 6H). ^{13}C NMR ($CDCl_3$): δ 157.9, 139.7, 122.5, 98.7, 31.9, 31.8, 31.5, 29.1, 28.8, 22.6, 14.0, 8.5. Anal. Calcd for $C_{22}H_{38}OTe_2$: C, 46.1; H, 6.7. Found: C, 46.0; H, 6.6.

*2,6-Bis(hexadecyltelluro)phenol (**12c**).* 2,6-Dibromophenol (0.606 g, 2.4 mmol), *tert*-BuLi (1.7 M in pentane, 7.1 mL, 12 mmol), and dihexadecyl ditelluride (3.4 g, 4.8 mmol) were reacted in THF (40 mL) according to general procedure B. The crude product was purified by flash column chromatography (pentane/ethyl acetate = 399:1) to give the title compound as a yellow solid (0.104 g, 5.4%). Mp: 42−45 °C. ^{1}H NMR ($CDCl_3$): δ 7.57 (d, J = 7.6 Hz, 2H), 6.72 (s, 1H), 6.61 (t, J = 7.6 Hz, 1H), 2.81 (t, J = 7.6 Hz, 4H), 1.76 (m, 4H), 1.25−1.36 (several peaks, 52H), 0.89 (t, J = 6.8 Hz, 6H). ^{13}C NMR ($CDCl_3$): δ 157.9, 139.7, 122.5, 98.7, 31.9, 31.5, 29.7 (2C), 29.6 (2C), 29.5, 29.4, 28.9, 22.7, 14.1, 8.5. Anal. Calcd for $C_{38}H_{70}OTe_2$: C, 57.2; H, 8.8. Found: C, 56.9; H, 8.8.

HPLC Peroxidation Assay. The experimental setup for recording inhibition time (T_{inh}) and inhibited rates of peroxidation (R_{inh}) during azo-initiated peroxidation of linoleic acid in a two-phase system was recently described.[14] The values reported in Table 1 for reactions performed in the presence of NAC are the mean ± SD's based on triplicate measurements.

Thiol Peroxidase Assay. The GPx-like activities of organotellurium compounds prepared were determined by UV spectroscopy at 21 °C following the protocol of Tomoda with slight modification.[17] The formation of diphenyl disulfide was initiated by the addition of hydrogen peroxide (3.75 M) to a solution of catalyst (0.01 mM) in the presence of thiophenol (1 mM), and the reaction was monitored by UV spectroscopy at 304 nm by using ε = 1.24 mM^{-1} cm^{-1} as the extinction coefficient for PhSSPh. Initial rates were determined for the first 10 s of the reaction, and the GPx data reported are the mean ± SD's based on triplicate measurements.

Coupled Reductase Assay. The GPx-like activities of organotellurium compounds prepared were determined by UV spectroscopy following the protocol of Wendel with slight modification.[16] The test mixture contained GSH (1 mM), ethylenediaminetetraacetic acid (EDTA, 1 mM), glutathione reductase (GR) (1 unit/mL), and β-nicotinamide adenine dinucleotide phosphate (NADPH, 0.2 mM) in a potassium phosphate buffer (100 mM) at a pH of 7.5. Catalysts (20 μM) were added to the test mixture at 21 °C, and the reaction was initiated by the addition of H_2O_2 (0.8 mM). Initial reaction rates were based on the consumption of NADPH as assessed by UV spectroscopy at 340 nm. Initial reduction rates were determined at least 3 or 4 times and calculated from the first 10 s of reaction by using ε = 6.22 mM^{-1} cm^{-1} as the extinction coefficient for NADPH. Values were corrected for the spontaneous oxidation of GSH (24 μM min^{-1}) and the maximal initial consumption of NADPH that could be attributed to the glutathione reductase reduction of telluroxide (Table S2 in the Supporting Information). The GPx data presented in Table S1 in the Supporting Information are reported as the mean ± SD's based on triplicate measurements.

■ ASSOCIATED CONTENT

Supporting Information

^{1}H and ^{13}C NMR data for all new compounds prepared; results from the coupled reductase method for assessment of glutathione peroxidase activity; and initial rates of NADPH consumption, control experiments. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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