Notes

Debrominations of *vic*-Dibromides with Diorganotellurides. 2. Catalytic Processes in Diorganotelluride

Timothy S. Butcher and Michael R. Detty*

Department of Medicinal Chemistry, School of Pharmacy, SUNY at Buffalo, Amherst, New York 14260, and Department of Chemistry, SUNY at Buffalo, Amherst, New York 14260

The protection/deprotection of olefins via bromination/debromination has been explored with a variety of different debrominating agents.[1−6] The utility of such methods is dependent upon the selectivity of the process toward *vic*-dibromides with different substituent patterns and upon other functionality in the substrates being inert to the conditions of debromination.

Several classes of organotellurium reagents have been utilized for debromination reactions[4−6] and catalytic variations have been developed for several.[5,6] The method of Engman[5] utilizing sodium 2-thienyl telluride is perhaps the most practical. As shown in Scheme 1, the Engman process uses sodium borohydride to reduce di-2-thienyl ditelluride to sodium 2-thienyl telluride. While most *vic*-dibromides are converted to olefins with this process, the method is limited to *vic*-dibromides with functional groups that do not react with sodium borohydride.

Diorganotellurides have also been useful as reagents for the debromination of *vic*-dibromides giving olefin and Te(IV) dibromide as shown in Scheme 2.[4a,b,f,6] Diorganotellurides, while nucleophilic, are unreactive toward most organic functionality. In the preceding paper, we have shown that stoichiometric variants of Scheme 2 have dibromide reactivities that parallel bromonium ion stabilities.[4f] The stoichiometric reactions are also limited by the reversibility of the process, which gives mixtures of both *vic*-dibromide and olefin.[4f] A catalytic version of
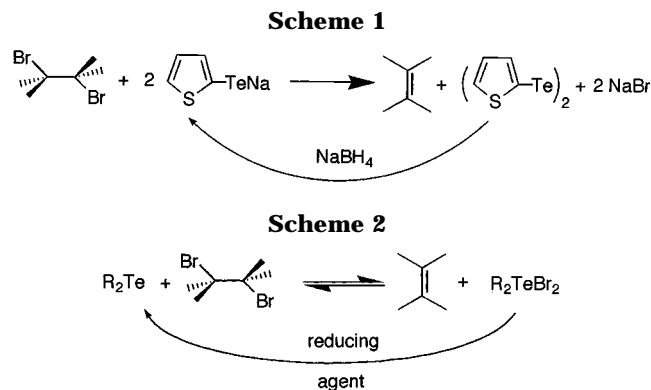
Scheme 1

Scheme 2

Scheme 2 has been described by Suzuki, Kondo, and Osuka in which 5 mol % of (*p*-CH₃OC₆H₄)₂Te can be recycled in the reaction using bisulfite as the reducing agent.[6] This variation of the reaction was reported to work only with substrates with at least one benzylic bromide (or heterocyclic equivalent). In this paper, we describe modifications to the procedure of Suzuki, Kondo, and Osuka,[6] which are more general for *vic*-dibromides.

Results and Discussion

A. Catalysis with Diorganotellurides. Catalytic reactions related to Scheme 2 are bound by certain constraints. The diorganotelluride catalyst, the *vic*-dihalide, and the olefinic substrate must be unreactive toward the reducing agent. The kinetics of the dehalogenation with a catalytic amount of diorganotelluride should be sufficiently rapid to give product in a synthetically useful time frame. The substrate, catalyst, and product should be stable to the thermal conditions of the reaction as well as to the solvents used. Finally, reduction of the Te(IV) compound should be rapid and should regenerate the diorganotelluride as the only product of reduction.
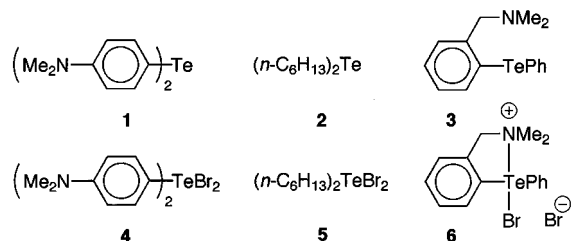
Selection of Catalysts. The procedure developed by Suzuki, Kondo, and Osuka utilized (*p*-CH₃OC₆H₄)₂Te as the catalyst for debromination reactions.[6] This catalyst only worked with *vic*-dibromides with at least one benzylic bromide (or heterocyclic equivalent). We have found that the more electron-rich diorganotellurides **1−3** are better debrominating agents than (*p*-CH₃OC₆H₄)₂Te in stoichiometric reactions.[4f] Tellurides **1−3** debrominate *vic*-dibromides to give olefins and the Te(IV) dibromides **4−6**, respectively.[4f]

(1) With iodide: (a) Plattner, P. A.; Heusser, H.; Segre, *Helv. Chim. Acta* **1948**, *31*, 249−255. (b) Solo, A. J.; Singh, B. *J. Org. Chem.* **1965**, *30*, 1658−1659. (c) Landini, D. *Synthesis* **1975**, 397−399.

(2) With Na₂S: (a) Landini, D. *J. Org. Chem.* **1984**, *49*, 152−153. (b) Nakayama, J.; Machida, H.; Hoshino, M. *Tetrahedron Lett.* **1983**, 3001−3004.

(3) With zinc and magnesium: Baciocchi, E. In *Chemistry of Functional Groups, Supplement D, Part 1*; Patai, S., Rappoport, H., Eds.; Wiley: New York, 1983.

(4) With tellurium reagents: (a) Campos, M. d. M.; Petragnani, N.; Thomé, C. *Tetrahedron Lett.* **1960**, (15) 5−8. (b) Campos, M. M.; Petragnani, N. *Chem. Ber.* **1961**, *94*, 1759−1762. (c) Ramasamy, K.; Kalyanasundarani, S. K.; Shammugan, P. *Synthesis* **1978**, 311−312. (d) Suzuki, H.; Inouye, M. *Chem. Lett.* **1985**, 225−228. (e) Huang, X.; Hou, Yu Q. *Synth. Commun.* **1988**, *18*, 2201−2205. (f) Butcher, T. S.; Zhou, F.; Detty, M. R. *J. Org. Chem.* **1997**, *63*, 167−174. D. N. *Tetrahedron Lett.* **1990**, *31*, 6291−6294. (h) Barton, D. H. R.; McCombie, S. W. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1574−1578. (i) Barton, D. H. R.; Bohe, L.; Lusinchi, X. *Tetrahedron Lett.* **1987**, *28*, 6609−6612. (j) Desilva, K. G. K.; Monsef-Mirzai, Z.; McWhinnie, W. R. *J. Chem. Soc., Dalton Trans.* **1983**, 2143-2146.

(5) Engman, L. *Tetrahedron Lett.* **1982**, *23*, 3601−3602.

(6) Suzuki, H.; Kondo, A.; Osuka, A. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 1335−1336.

Selection of Reducing Agents. Several mild procedures have been reported for the reduction of Te(IV) compounds to Te(II) derivatives.[6-10] In the one reported catalytic variation of Scheme 2, sodium bisulfite was used to reduce $(p\text{-}CH_3OC_6H_4)_2TeBr_2$ to $(p\text{-}CH_3OC_6H_4)_2Te$.[6] Telluroxides and Te(IV) dihalides have been reduced to tellurides by aromatic and aliphatic thiols, which in turn were oxidized to disulfides.[9,10] Sodium ascorbate has been utilized for the reduction of diorganotellurium(IV) dihalides to diorganotellurides under very mild conditions.[11] Most organic functional groups are unreactive toward bisulfite, thiols, and ascorbate.

The reactivity of organic functional groups toward the reducing agents can be further diminished by separating the organic substrates from the reducing agent in two-phase systems. Sodium bisulfite in aqueous benzene gave at least 20 turnovers of $(p\text{-}CH_3OC_6H_4)_2Te$ in reactive substrates.[6] A catalytic, two-phase system using 1,2-dibromotetrachloroethane as a brominating agent of Te(II) has been described in which telluroxides produced in situ are the working oxidant for the oxidation of various organic substrates.[9b] At alkaline pH, the Te(IV) dibromides were hydrolyzed to the corresponding telluroxide. Telluroxides are m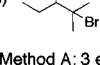ore water-soluble than the corresponding Te(IV) dibromides and Te(II) diorganotellurides.[10d,12] Hydrolysis of the Te(IV) dibromides of Scheme 2 to the corresponding telluroxides should allow reduction of the Te(IV) dibromides to occur in the aqueous phase. The Te(IV) reducing agents sodium bisulfite, sodium ascorbate, and the thiol glutathione (GSH) are water soluble and should be useful in two-phase systems.

We examined sodium bisulfite as a reducing agent for **4−6** (prepared by oxidative addition of bromine to the tellurides) but found its selectivity to be somewhat unfavorable. Although Te(IV) derivatives **4−6** are readily reduced to tellurides **1−3** with sodium bisulfite, heating **1−3** with 1.0 M aqueous sodium bisulfite (required for the slower reacting substrates) as a refluxing, two-phase mixture with $CHCl_3$ gave detelluration. A suspension of tellurium metal was produced from all three tellurides upon heating with 1.0 M aqueous sodium bisulfite ($\approx$ 3 h), and the ^{1}H NMR signals associated with **1−3** disappeared with time. Similar reactions with $(p\text{-}CH_3OC_6H_4)_2$-Te gave tellurium metal in a much slower reaction (no tellurium observed after 24 h in refluxing 1.0 M aqueous sodium bisulfite/$CHCl_3$).

The use of 1.0 M GSH or sodium ascorbate did not give observable levels of detelluration of **1−3** in two-phase mixtures with $CHCl_3$. The Te(IV) dibromides **4−6** were reduced quantitatively under these conditions. However, the rate of reduction of **4−6** was influenced by the pH of the aqueous layer. In two-phase systems with an aque-

(7) Engman, L.; Persson, J.; Andersson, C. M.; Berglund, M. *J. Chem. Soc., Perkin Trans. 2* **1992**, 1309−1314.
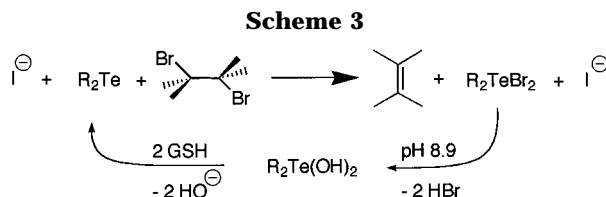
(8) (a) Petragnani, N.; Comasseto, J. V. *Synthesis* **1991**, 793−817 and 897−919. (b) Irgolic, K. J. In *Houben-Weyl Methoden der Organischen Chemie: Organotellurium Chemistry*; Klamann, D., Ed.; Georg Thieme: New York, 1990; Vol. E12b.

(9) (a) Barton, D. H. R.; Finet, J.-P.; Giannotti, C.; Thomas, M. *Tetrahedron Lett.* **1988**, *29*, 2671−2674. (b) Ley, S. V.; Meerholz, C. A.; Barton, D. H. R. *Tetrahedron* **1981**, *37*, Suppl. No. 1, 213−223.

(10) (a) Detty, M. R. *Phosphorus Sulfur Silicon* **1992**, *4*, 367−375. (b) Detty, M. R.; Gibson, S. L. *Organometallics* **1992**, *11*, 2147−2155. (c) Engman, L.; Stern, D.; Pelcman, M. *J. Org. Chem.* **1994**, *59*, 1973−1979. (d) Detty, M. R.; Friedman, A. E.; Oseroff, A. R. *J. Org. Chem.* **1994**, *59*, 8245−8250.

(11) Engman, L.; Persson, J. *Synth. Commun.* **1993**, *23*, 445−448.

(12) Detty, M. R.; Zhou, F.; Friedman, A. E. *J. Am. Chem. Soc.* **1996**, *118*, 313−318.

Table 1. Catalytic Debrominations with Diorganotellurides

entry	substrate	product	equiv	catalyst	method[a]	T, °C	time, h	% yield[b]
(1)	Ph-CHBr-CHBr-Ph	Ph-CH=CH-Ph	0.1	1	A	20	250	92 (≥99)
			0.1	1	B	20	250	97 (≥99)
			0.25	2	A	20	135	97 (≥99)
			0.1	3	A	20	250	93 (≥99)
(2)	Ph-CHBr-CHBr-CH₃	Ph-CH=CH-CH₃	0.1	1	A	80	336	89 (≥99)
			0.25	2	B	80	42	87 (≥99)
			0.1	3	A	80	336	83 (≥99)
(3)	(dibromide)	1-decene	0.25	1	A	80	536	79 (85)
			0.5	2	B	80	600	-- (66)
			0.33	2	B	80	600	-- (61)
			0.25	2	B	80	600	-- (47)
(4)	(dibromide)	trans-5-decene	0.25	1	A	80	360	81 (90)
			0.25	2	B	80	209	-- (67)
(5)	(dibromide)		0.25	1	B	80	156	-- (10)
			1.0	Bu₄NI	B	80	96	-- (20)
			0.25	1	C	80	96	-- (96)
			0.25	2	B	80	558	-- (27)
(6)	(dibromide)		0.25	1	B	80	156	-- (10)
			1.0	Bu₄NI	B	80	96	-- (23)
			0.25	1	C	80	96	-- (99)
			0.25	2	B	80	558	-- (30)
(7)	Ph-CHBr-CBr	Ph-C=CH₂	0.25	1	B	80	116	85 (99)
			0.25	2	B	80	116	85 (99)
(8)	(dibromide)		0.1	1	A	80	240	-- (95)
			0.2	2	A	80	107	-- (95)

[a] Method A: 3 equivalents of GSH in 1/1 mixture of 0.25 M phosphate buffer (pH 8.9) and $CHCl_3$; Method B: 3 equivalents of sodium ascorbate in 1/1 mixture of 0.25 M phosphate buffer (pH 8.9) and $CHCl_3$; Method C: 1.1 equivalent of Bu_4NI and 3 equivalents of GSH in 1/1 mixture of 0.25 M phosphate buffer (pH 8.9) and $CHCl_3$. [b] Isolated yield in refluxing buffer/$CHCl_3$ (% conversion by ^{1}H NMR).

ous phase at pH 8.9, reduction of **4−6** with either GSH or sodium ascorbate was faster than reduction at pH 6.0 or at pH 7.0.

Tellurides **1−3** were stable to either GSH or sodium ascorbate (initial 3-fold molar excess at 0.45 M in buffer) in a refluxing, two-phase system of $CHCl_3$ and 0.25 M phosphate buffer at pH 8.9. The corresponding Te(IV) bromides **4−6** were reduced under these same conditions to give the tellurides **1−3**, quantitatively.

Catalytic Debrominations. Two-phase mixtures of telluride and *erythro*-1,2-dibromo-1,2-diphenylethane in $CHCl_3$ with 3 equiv of either GSH or sodium ascorbate in 0.25 M phosphate buffer at pH 8.9 gave nearly quantitative conversion to *trans*-stilbene (≥98% stereoselectivity by ^{1}H NMR) after 250 h at ambient temperature (entry 1, Table 1). The diorganotelluride was used in catalytic amounts (0.1 equiv for **1** and **3**, 0.25 equiv for **2**) and was readily separated from the olefin via chromatography on silica gel. Importantly, control reactions showed no olefin products in the absence of telluride.

This procedure was applied to the other *vic*-dihalides of Table 1. The debromination reactions generated the corresponding mono-, di-, and trisubstituted olefins, which were stable to the catalysts **1−3** as well as to the reducing agents (either GSH or sodium ascorbate) in refluxing buffer/$CHCl_3$ mixtures. For precursors to 1,2-disubstituted olefins, the *erythro*-dibromides gave the corresponding *trans*-olefins in ≥98% stereoselectivity while *threo*-dibromides gave *cis*-olefins in ≥98% stereoselectivity. The *vic*-dibromides were stable to the conditions of reaction in the absence of telluride catalyst. Unlike reactions with $(p\text{-}CH_3OC_6H_4)_2Te$, catalysts **1−3** slowly gave monosubstituted olefins from 1,2-dibromoal-

Scheme 3

kanes and internal disubstituted olefins from *erythro*- and *threo*-dibromides.

Competition Experiments. To establish relative rates of reaction for various dibromide substrates, we set up competition experiments between pairs of dibromides (0.10 M) and catalytic quantities of telluride **2** (0.025 M) in CDCl$_3$ and GSH (0.30 M) in phosphate buffer at pH 8.9 The ratio of olefinic products was measured after 1 half-life for the more reactive component. Competition between 1,2-dibromo-2-methyl-1-phenylpropane and 2,3-dibromo-2-methylpentane gave 2-methyl-1-phenylpropene and 2-methyl-2-pentene, respectively, in an 82:18 ratio after 5 h. Competition between 1,2-dibromo-2-methyl-1-phenylpropane and *erythro*-1,2-dibromo-1-phenylpropane gave 2-methyl-1-phenylpropene and *trans*-1-phenylpropene, respectively, in a 52:48 ratio after 5 h. Competition between 2,3-dibromo-2-methylpentane and *erythro*-5,6-dibromodecane gave 2-methyl-2-pentene and *trans*-5-decene in an 83:17 ratio after 21 h. Competition between *erythro*-5,6-dibromodecane and 1,2-dibromodecane gave *trans*-5-decene and 1-decene, respectively, in a 87:13 ratio after 88.5 h while competition between 1,2-dibromodecane and *threo*-2,3-dibromopentane gave 1-decene and *cis*-2-pentene, respectively, in a 67:33 ratio. Nearly identical results were obtained using sodium ascorbate as reducing agent. On the basis of these results, the relative rates of reaction, which were similar to relative rates observed in stoichiometric reactions,[4f] were
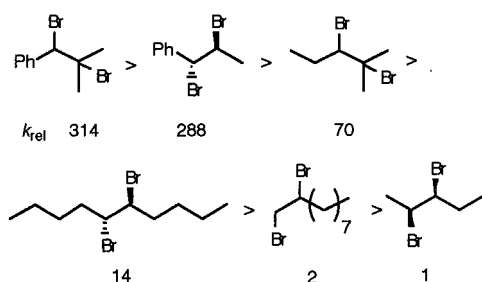
Debromination of *threo*-Dibromides. Debrominations of *threo*-2,3-dibromopentane and *threo*-2,3-dibromo-4-methylpentane (entries 5 and 6, respectively, Table 1) with catalytic or stoichiometric[4f] quantities of either **1** or **2** were slow in refluxing CHCl$_3$/buffer mixtures. Similar substrates are slow using iodide as a catalyst for debrominations.[1c] Presumably, iodide reacts with the dibromide to give IBr$_2$ and species in equilibrium with IBr$_2$.

If debrominations with iodide were reversible, then reactions might be accelerated by using the diorganotelluride as a scavenger of the IBr or Br$_2$ produced in the reaction as shown in Scheme 3. Reactions of *threo*-2,3-dibromopentane and *threo*-2,3-dibromo-4-methylpentane with telluride **1** were accelerated by the addition of 1 equiv of Bu$_4$NI to the reaction mixtures. Debrominations were complete under these conditions giving *cis*-2-pentene and *cis*-4-methyl-2-pentene, respectively, with ≥98%

stereoselectivity by ^{1}H NMR. Although iodide alone initiates debromination reactions,[1] synergy was apparent with combinations of telluride and iodide (entries 5 and 6, method C, Table 1).

The synergy between iodide and telluride for debrominations of *threo*-dibromides was not observed with other substrates. Debrominations of 1,2-dibromodecane and *threo*-5,6-dibromodecane with 1 equiv of Bu$_4$NI[1c] were not accelerated by the addition of 0.25 equiv of **1**.

Cyclic *trans*-Dibromides. The cyclic dibromides *trans*-1,2-dibromocyclohexane and *trans*-1,2-dibromocycloheptane gave no debromination with 0.25 equiv of **1**−**3** and 3 equiv of GSH or sodium ascorbate after 300 h in refluxing buffer/CHCl$_3$. These results parallel those observed in stoichiometric reactions with **1** and **2**.[4a,f]

Summary and Conclusions

We have described more efficient diorganotelluride catalysts for the conversion of *vic*-dibromides to the corresponding olefins. These catalysts, which are more electron rich than (*p*-CH$_3$OC$_6$H$_4$)$_2$Te, provide terminal olefins and *cis*- and *trans*-1,2-disubstituted olefins from appropriate precursors (although these reactions are slow). Sodium ascorbate and GSH are efficient reducing agents for the Te(IV) derivatives produced in the catalytic reaction. The catalytic reaction is similar to the stoichiometric reaction with respect to substrate reactivities, which follow bromonium ion stabilities. Of the acyclic derivatives, *threo*-2,3-dibromopentane and *threo*-2,3-dibromo-4-methylpentane were the slowest reacting substrates (perhaps due to eclipsing interactions in a bromonium ion[4f] intermediate). A combination of iodide catalysis and diorganotelluride scavenging of free halogen intermediates accelerated the debromination of these substrates to give the corresponding *cis*-olefins with high stereoselectivity.

Experimental Section

General Methods. Solvents (ethyl acetate, hexanes, chloroform, dichloromethane), deuteriochloroform, magnesium sulfate, *trans*-stilbene, *trans*-1-phenylpropene, 1-decene, *trans*-5-decene, *cis*-2-pentene, *cis*-4-methyl-2-pentene, 2-methyl-1-phenylpropene, 2-methyl-2-pentene, and mono- and dibasic salts of potassium phosphate were used as received from Aldrich Chemical Co. Catalyst **1** and dibromide **4** were prepared according to ref 7. Catalyst **3** and Te(IV) derivative **6** were prepared according to ref 13. Catalyst **2** and Te(IV) dibromide **5** were prepared according to ref 4f. The dibromide substrates were prepared from the corresponding olefins according to ref 4f. Preparative reactions were stirred magnetically. Concentration in vacuo was performed on a Büchi rotary evaporator. Nuclear magnetic resonance (NMR) spectra were recorded at 30.0 °C on a Varian Gemini-300 instrument with residual solvent signal as internal standard: CDCl$_3$ (δ 7.26 for proton, δ 77.0 for carbon).

General Procedure for Catalytic Debrominations of *vic*-Dibromides. Initial reactions on a smaller scale were monitored by ^{1}H NMR prior to larger scale preparative runs. The substrate (0.2 mmol) and the catalyst [for **1**, 18 mg (0.050 mmol) or 7.4 mg (0.020 mmol); for **2**, 15 mg (0.050 mmol); for **3**, 16 mg (0.050 mmol) or 6.5 mg (0.020 mmol)] in 2 mL of CDCl$_3$ (0.1 M in substrate) were combined with the reducing agent [GSH (0.184 g, 0.60 mmol) or sodium ascorbate (0.12 g, 0.60 mmol)] in 2 mL of 0.25 M potassium phosphate buffer (pH 8.9). The reaction mixtures were sealed in vials and were stirred at ambient temperature or in an oil bath at 80 °C (See Table 1 for

(13) Detty, M. R.; Williams, A. J.; Hewitt, J. M.; McMillan, M. *Organometallics* **1995**, *14*, 5258−5265.

details). The structures of the olefinic products were confirmed by comparison of ^{1}H and ^{13}C NMR spectra with those of authentic samples. The progress of reaction was monitored periodically by ^{1}H NMR using residual CHCl$_3$ as an internal standard. Conversions reported in Table 1 are the average of at least two runs. Blank runs were setup in an identical manner except that the telluride catalyst was omitted. The progress of reaction was monitored by ^{1}H NMR using residual CHCl$_3$ as an internal standard.

Preparative Catalytic Reactions. The substrate (3.00 mmol) and diorganotelluride **1** [(108 mg, 0.30 mmol) or (276 mg, 0.75 mmol)], **2** (232 mg, 0.75 mmol), or **3** (107 mg, 0.30 mmol) were dissolved in 20 mL of CHCl$_3$. This solution was combined with the reducing agent [glutathione (2.76 g, 9.0 mmol) or sodium ascorbate (1.80 g, 9.0 mmol)] in 20 mL of 0.25 M potassium phosphate buffer (pH 8.9). The resulting mixtures were heated at reflux for the time periods indicated in Table 1. Aliquots of the reaction mixture were sampled periodically by ^{1}H NMR. The organic layer was separated, and the aqueous phase was extracted with CH$_2$Cl$_2$. The combined organics were dried over MgSO$_4$ and carefully concentrated. *trans*-Stilbene was isolated by chromatography on a small plug of SiO$_2$ (5% EtOAc−hexanes) followed by recrystallization from hexanes. *trans*-1-Phenyl-1-propene and 2-methyl-1-phenylpropene were isolated by chromatography on SiO$_2$ (hexanes). 1-Decene (0.1 Torr, 140 °C) and *trans*-5-decene (0.1 Torr, 150 °C) were distilled from the organic residue using a molecular still. *cis*-2-Pentene, *cis*-4-methyl-2-pentene, and 2-methyl-2-pentene were not readily separated from CHCl$_3$.

General Procedure for Competition Experiments. The dibromides (0.20 mmol) and telluride **2** (15.0 mg, 0.05 mmol) were dissolved in 2.0 mL of CDCl$_3$. The resulting solution was added to 6.0 mmol of either GSH or sodium ascorbate in 2.0 mL of 0.25 M phosphate buffer at pH 8.9. The resulting mixtures were heated at reflux. After the indicated times (see text), product ratios were measured by ^{1}H NMR spectroscopy and averaged for duplicate runs.