Selenoxides as Catalysts for the Activation of Hydrogen Peroxide. Bromination of Organic Substrates with Sodium Bromide and Hydrogen Peroxide

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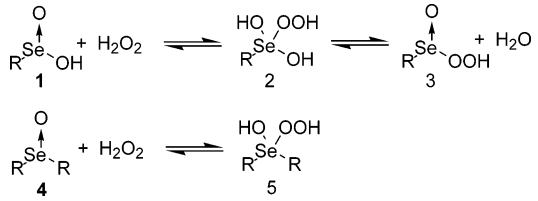
Diphenyl selenoxide (**7**), dibenzyl selenoxide (**8**), and several aryl benzyl selenoxides (**9**−**13**) are catalysts for the bromination of organic substrates in two-phase systems of CH_2Cl_2 and pH 6 phosphate buffer containing 2.0 M NaBr and 2.6 M H_2O_2. The catalysts are effective at 2.5 mol % relative to the organic substrates. In the bromination of 4-pentenoic acid, electron-donating substituents in the selenoxides accelerate the reaction, while electron-withdrawing substituents slow the reaction. Benzyl 2-((dimethylamino)methyl)phenyl selenoxide (**13**), with a chelating dimethylamino group, was the most effective catalyst and was used in the preparative bromination of 4-pentenoic acid, 2,2-diphenyl-4-pentenoic acid, 1,3,5-trimethoxybenzene, *N*,*N*-dimethylaniline, and *N*-phenylmorpholine.

Selenoxides have functioned as oxidants for a variety of substrates. Selenoxides oxidize thiols to disufides,[1,2] phosphines to phosphine oxides,[3] sulfides to sulfoxides,[3] halomethyl arenes and arene alcohols to arene aldehydes,[4,5] and catechols and hydroquinones to *o*- and *p*-quinones, respectively.[6] Selenoxides have been co-oxidants for the cis-dihydroxylation of olefins with OsO_4[7] and have been the functional oxidant for phenolic couplings.[6] In each of these reactions, oxidation of the substrate has occurred via reduction of the selenoxide to the selenide. In this process, the oxygen atom of the selenoxide is transferred to the substrate or a molecule of water is lost via the selenoxide oxygen atom and two hydrogen atoms from the substrate.

We have recently demonstrated that selenoxides are catalysts for the activation of H_2O_2 for oxidation of bromide to $HOBr/Br_2$.[8] In these reactions, the selenoxide is not reduced to the selenide during the oxidation of bromide and the selenoxide appears to be the "reduced" form of the catalyst during the catalytic cycle.

Reactions of selenoxides with H_2O_2 may parallel those of aryl seleninic acids, as shown in Scheme 1. Arylseleninic acids react with H_2O_2 to form perseleninic acids, which are the active oxidants in a variety of oxidations.[9−11] We have recently described the oxidation of bromide to $HOBr/Br_2$ with H_2O_2 using seleninic acids as catalysts.[12] The addition of H_2O_2 to the seleninic acid **1** gives the dihydroxy perhydroxyselenane intermediate **2**, which can lose water to generate the perseleninic acid **3**. The addition of H_2O_2 to the selenoxide **4** can give the hydroxy perhydroxy selenane **5**, which might function directly as an oxidant. Herein, we examine a series of selenoxides as catalysts for the bromination of organic substrates with bromide and H_2O_2.

Scheme 1



Results and Discussion

Structure−Activity Studies. The bromination of 4-pentenoic acid to give bromolactone **6** with NaBr and H_2O_2 (Scheme 2) was chosen as a model reaction to evaluate the catalytic activity of the selenoxides of Table 1. In the absence of a catalyst, the bromination of 4-pentenoic acid to bromo lactone **6** with 2 M NaBr and 2.6 M H_2O_2 in a two-phase mixture of CH_2Cl_2 and pH 6 phosphate buffer at 296 K proceeds with $k_{obs} = (2.2 \pm 0.1) \times 10^{-5}$ s^{-1}.

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(1) Hu, N. X.; Aso, Y.; Otsubo, T.; Ogura, F. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 879−884.
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Scheme 2

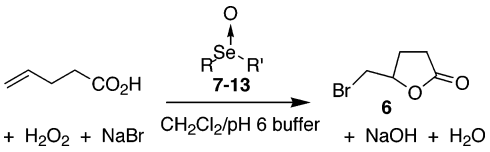


Table 1. Observed Pseudo-First-Order Rate Constants (k_{obs}) for Selenoxide-Catalyzed[a] Bromination of 4-Pentenoic Acid with 2.0 M NaBr and 2.6 M H_2O_2 and Calculated Rate Constants for Catalysis (k_{cat}) and Their Relative Magnitudes (k_{rel})

cat.	R	R′	k_{obs}, s^{-1} [b]	k_{cat}, s^{-1}	k_{rel}
control			$(2.2 \pm 0.1) \times 10^{-5}$		
7	Ph	Ph	$(3.5 \pm 0.2) \times 10^{-5}$	1.3×10^{-5}	1
8	CH_2Ph	CH_2Ph	$(1.1 \pm 0.1) \times 10^{-4}$	8.8×10^{-5}	6.8
9	Ph	CH_2Ph	$(7.7 \pm 0.3) \times 10^{-5}$	5.4×10^{-5}	4.2
10	3,5-$(CF_3)_2C_6H_3$	CH_2Ph	$(3.2 \pm 0.2) \times 10^{-5}$	9×10^{-6}	0.7
11	4-$MeOC_6H_4$	CH_2Ph	$(9.6 \pm 0.2) \times 10^{-5}$	7.3×10^{-5}	5.6
12	4-$(Me_2N)C_6H_4$	CH_2Ph	$(2.6 \pm 0.1) \times 10^{-4}$	2.4×10^{-4}	18
13	2-(Me_2NCH_2)-C_6H_4	CH_2Ph	$(3.9 \pm 0.2) \times 10^{-4}$	3.7×10^{-4}	28

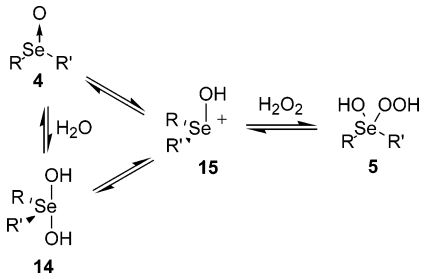
[a] Conditions: 2.5 mol % of selenoxide relative to 4-pentenoic acid in a two-phase system of pH 6 phosphate buffer and CH_2Cl_2. [b] Average of duplicate runs.

One difficulty with selenoxides is the propensity of selenoxides with β-hydrogens to undergo selenoxide elimination.[13] Diphenyl selenoxide (**7**),[14] dibenzyl selenoxide (**8**),[15] and the aryl benzyl selenoxides **9**−**13** (Table 1) have no β-hydrogen atoms and cannot undergo selenoxide elimination.

Selenoxides **10**−**12** were prepared via procedures analogous to that reported for the preparation of benzyl phenyl selenoxide **9**.[14] The arylselenide anion, prepared by $NaBH_4$ reduction of the corresponding diaryl diselenide,[10c,16−18] was treated with benzyl bromide to give the aryl benzyl selenide, which was then oxidized to the selenoxide with *N*-chlorosuccinimide in basic aqueous MeOH[14] for the preparation of **9**−**12**. Selenoxide **13** was prepared by the *m*-chloroperbenzoic acid oxidation of benzyl 2-((dimethylamino)methyl)phenyl selenide (**13**).[18]

In the model reaction of Scheme 2, 7.8 mL of 30% H_2O_2 (72 mmol) was added to a stirred mixture of 2.5 mmol of 4-pentenoic acid and 63 μmol of selenoxide (2.5 mol % relative to 4-pentenoic acid) in 20 mL of CH_2Cl_2 and 20 mL of pH 6 phosphate buffer containing 56 mmol of NaBr (final concentrations of 2.0 M NaBr and 2.6 M H_2O_2) at 296 K. The progress of the reaction over the first 2 half-lives was monitored by ^1H NMR spectroscopy of aliquots to determine the observed pseudo-first-order rate constant, k_{obs}, for bromination with each of the selenoxide catalysts. (Plots of these data are shown in the Supporting Information.) Values of k_{obs} are compiled in Table 1 and represent the average of duplicate runs.

Scheme 3



As shown in eq 1, k_{obs} consists of two terms, where k_{back} is the rate of the uncatalyzed control ($(2.2 \pm 0.1) \times 10^{-5}$ s^{-1}) and k_{cat} is the contribution from the catalyzed bromination with 2.5 mol % of the selenoxide catalyst.

$$k_{obs} = k_{back} + k_{cat} \quad (1)$$

Rearranging eq 1 gives eq 2. Values of k_{obs} and k_{cat}, as

$$k_{cat} = k_{obs} - k_{back} \quad (2)$$

well as the relative magnitudes of k_{cat} (k_{rel}), are compiled in Table 1.

All of the selenoxides **7**−**13** displayed some catalytic activity in the reaction of Scheme 2 (Table 1). Diphenyl selenoxide (**7**), with two electron-withdrawing phenyl substituents,[19] was one of the poorer catalysts in this study. Replacing one phenyl substituent with a more electron-donating benzyl substituent in **9** gave a 4-fold increase in catalytic activity, while replacing both phenyl substituents with benzyl substituents as in **8** gave a nearly 7-fold increase in catalytic activity relative to **7**. The trend observed in catalysts **7**−**9** suggested that catalytic activity was increased by electron-donating groups. Using benzyl phenyl selenoxide (**9**) as a point of comparison, the introduction of electron-donating 4-methoxy and 4-dimethylamino substituents in **11** and **12**, respectively, gave increased catalytic activity, while electron-withdrawing trifluoromethyl substituents in **10** gave decreased catalytic activity.

The most active catalyst was benzyl 2-((dimethylamino)methyl)phenyl selenoxide (**13**), which can form a five-membered intramolecular coordination complex between the amine N atom and the Se atom. Selenoxide **13** was 28 times more active as a catalyst than diphenyl selenoxide (**7**) and nearly 7 times more active than benzyl phenyl selenoxide (**9**).

Mechanistic Considerations. The substituent effects are consistent with the formation of the hydroxy perhydroxy selenane **5** perhaps being the rate-determining step in the catalytic sequence. In an aqueous environment, the selenoxide **4** is in equilibrium with its corresponding dihydroxy selenane **14**, as shown in Scheme 3.[14] In pH 6 buffer, the hydroxyselenonium species **15** is a likely intermediate that can add water to give the dihydroxy selenane **14**, can deprotonate to give the selenoxide **4**, or can add H_2O_2 to give the hydroxy perhydroxy selenane **5**. The rate of formation of **15** and its equilibrium concentration under the

(13) (a) Walter, R.; Roy, J. *J. Org. Chem.* **1970**, *36*, 2561−2563. (b) Jones, D. N.; Mundy, D.; Whitehouse, R. D. *J. Chem. Soc., Chem. Commun.* **1970**, 86−88. (c) Sharpless, K. B.; Young, M. W.; Lauer, R. F. *Tetrahedron Lett.* **1973**, 1979−1982. (d) Reich, H. J.; Reich, I. L.; Renga, J. M. *J. Am. Chem. Soc.* **1973**, *95*, 5813−5815.
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(15) Proctor, D. J.; Thornton-Pett, M.; Rayner, C. M. *Tetrahedron* **1996**, *52*, 1841−1854.
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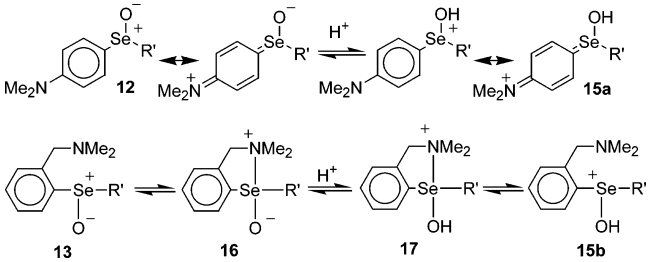
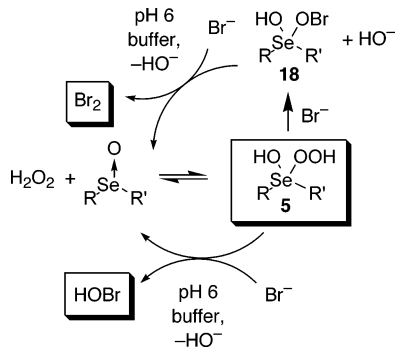
Scheme 4



Scheme 5



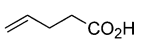
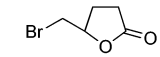
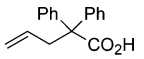
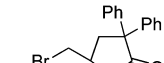
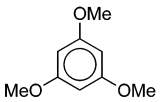
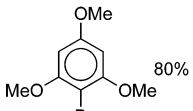
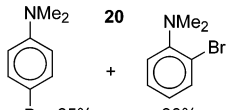
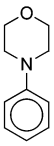
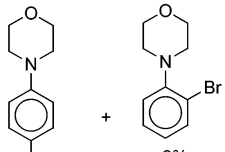
reaction conditions directly impact the rate of formation of hydroxy perhydroxy selenane **5**.

The substituents affect the basicity of the selenoxide oxygen to accept a proton and, consequently, the stability of the conjugate acid—hydroxyselenonium intermediate **15**. Electron-withdrawing substituents would decrease the basicity of the selenoxide oxygen and the stability of intermediate **15**. Conversely, electron-donating substituents would increase the basicity of the selenoxide oxygen and the stability of intermediate **15**. The benzyl substituents of **8** and **9** are more electron donating than the phenyl substituents of **7**, and the rates of catalysis reflect this trend. Resonance interactions in selenoxides **11** and **12** and the hydroxyselenonium species derived from **11** and **12** (illustrated for **12** and **15a** in Scheme 4) would give added stability to these intermediates.

The catalytic activity of benzyl 2-((dimethylamino)-methyl)phenyl selenoxide (**13**) suggests a more pronounced increase in the basicity of the selenoxide oxygen or in the stabilization of a hydroxyselenonium intermediate (Scheme 4). Chelation by the (dimethylamino)-methyl N atom in **13** would give **16**, whose selenoxide oxygen should be rendered more basic via the electron-pair donation from the chelating amine. Similar stabilization of **15b** via chelation to give **17** should provide added stability to the hydroxyselenonium intermediate. Again, these interactions provide a more rapid formation of and increased stability for **15b**/**17**, which should enhance formation of the hydroxy perhydroxy selenane **5**.

Following formation of hydroxy perhydroxy selenane **5**, two plausible mechanistic paths for the oxidation of bromide are shown in Scheme 5. Direct attack of bromide at the −OH oxygen would give HOBr, which would regenerate starting selenoxide following loss of hydroxide in pH 6 buffer. Alternatively, nucleophilic attack at the Se−O oxygen atom of **5** could lead to RR′Se(OH)OBr (**18**), which might function directly as a brominating agent or which might react directly via nucleophilic attack of bromide at the O−Br bromine atom of **18** to produce Br_2.

Table 2. Electrophilic Bromination via Selenoxide 13 Catalyzed Reactions of NaBr and H_2O_2[a]

entry	substrate	$t_{1/2}$, h (blank)	rxn time, h	product, % yield
(1)		0.5 (8.5)	8	 93% **6**
(2)		30 (>170)	170	 64% **19**
(3)		2.5 (>18)	18	 80% **20**
(4)		4.5 (>24)	24	 **21** 65% + **22** 30%
(5)		7 (>48)	48	 **23** 67% + **24** < 2%

[a] Conditions: two-phase mixture of 2.5 mmol of substrate and 0.063 mmol of **13** in 20 mL of CH_2Cl_2 and 28 mL of pH 6 phosphate buffer containing 2.0 M NaBr and 2.6 M H_2O_2. Isolated yields are the average of duplicate runs.

The intervention of either bromine or hydroxy radicals in the catalytic scheme cannot be rigorously excluded. However, methylcyclohexane was subjected to the conditions of reaction for 24 h with 2.5 mol % of selenoxide **13** and no trace of brominated, hydroxylated, or olefinic product was detected by either ^{1}H NMR spectroscopy or mass spectrometry.

Preparative Studies with Selenoxide 13. Selenoxide **13**, as the most active selenoxide catalyst, was evaluated in several preparative reactions, as shown in Table 2. The substrate (2.5 mmol) and **13** (2.5 mol % relative to substrate) were dissolved in a two-phase system of 20 mL of CH_2Cl_2 and 28 mL of pH 6 phosphate buffer containing 2.0 M NaBr and 2.6 M H_2O_2. The isolated yields of purified products are listed in Table 2 along with the half-lives, $t_{1/2}$, of the catalyzed (and uncatalyzed) reaction.

Bromolactonization of 4-pentenoic acid gave the 4-bromomethyl γ-lactone **6** in 93% isolated yield after 8 h of reaction, while $t_{1/2}$ was 8.5 h for the uncatalyzed reaction. Bromolactonization of 2,2-diphenyl-4-pentenoic acid was much slower and gave 4-bromomethyl γ-lactone **19** in 64% isolated yield after 5 days. In this example, $t_{1/2}$ of the uncatalyzed reaction was greater than 1 week.

Activated aromatic substrates were also brominated with selenoxide catalysis under the two-phase conditions. 1,3,5-Trimethoxybenzene gave 2-bromo-1,3,5-trimethoxybenzene (**20**) in 80% isolated yield after 15 h with <3% dibromination. The $t_{1/2}$ value of the uncatalyzed reaction was >18 h.

N,*N*-Dimethylaniline was brominated with selenoxide catalysis to give a 2:1 mixture of 4-bromo-*N*,*N*-dimethylaniline (**21**) and 2-bromo-*N*,*N*-dimethylaniline (**22**) in 98% yield after 24 h. The $t_{1/2}$ value of the uncatalyzed reaction was >24 h to give a 2:1 mixture of **21** to **22**.

Bromination of *N*-phenylmorpholine gave *N*-(4-bromophenyl)morpholine (**23**) in 69% isolated yield after 48 h and trace amounts (~2%) of *N*-(2-bromophenyl)-morpholine (**24**). The $t_{1/2}$ value of the uncatalyzed reaction was >48 h, and the reaction produced nearly all **23** with trace amounts of **24**.

Summary and Conclusions

The selenoxide functional group is capable of activating H_2O_2 for bromination reactions with sodium bromide and H_2O_2. Diaryl selenoxides are very robust catalysts that are free of complications from selenoxide elimination or nucleophilic displacement at the alkyl groups attached to the selenoxide, which can limit the lifetime of the catalyst.[8] Dibenzyl selenoxides and benzyl aryl selenoxides avoid the complications of selenoxide elimination reactions but are prone to eventual nucleophilic attack at the benzyl group. While the half-lives of the catalysts of this study are all >48 h under the conditions of reaction, we are searching for even more robust selenoxide catalysts that might be incorporated into dendrimers[8] or immobilized on beads.

For uncatalyzed bromination reactions using bromide and H_2O_2, the actual brominating agent is assumed to be "Br^+" from the Br_2/HOBr equilibrium. In catalyzed reactions, one can question whether "Br^+" is "free" or is bound to catalyst, in which case its reactivity might be altered. The brominations of *N*,*N*-dimethylaniline and *N*-phenylmorpholine gave essentially identical ratios of ortho- and para-substituted products in both catalyzed and uncatalyzed reactions, which suggests that some form of "free Br^+" is the actual brominating agent.

We are currently examing selenoxides as catalysts for other oxidation reactions with H_2O_2. Both epoxidation and Baeyer–Villiger oxidation may be possible using hydroxy perhydroxy selenanes **5** as oxidants.

Experimental Section

Bis(3,5-bis(trifluoromethyl)phenyl) diselenide was prepared according to ref 10c. Bis(4-methoxyphenyl) diselenide and bis-(4-(dimethylamino)phenyl) diselenide were prepared according to ref 17. Diphenyl selenoxide (**7**) and benzyl phenyl selenoxide (**9**) were prepared according to ref 14. Dibenzyl selenoxide (**8**) was prepared according to ref 15.

General Procedure for the Preparation of Aryl Benzyl Selenoxides 10–12. Sodium borohydride was added slowly in 0.2 equiv aliquots to a solution of diaryl diselenide in 1.0 M NaOEt in EtOH (0.25 mmol of diaryl diselenide/mL) heated at reflux under an Ar atmosphere until the solution became colorless and transparent. Benzyl bromide (1.1 equiv) dissolved in THF was added, and the resulting solution was heated at reflux overnight. The reaction mixture was concentrated, and the residue was slurried in water. The aqueous mixture was extracted with CH_2Cl_2 (3×). The organic extracts were combined, dried over $MgSO_4$, and concentrated. The crude aryl benzyl selenide was oxidized directly to the selenoxide.

The aryl benzyl selenide was dissolved in a 1:1 solution of MeOH/CH_2Cl_2 (10 mL/mmol) and chilled to 0 °C in an ice bath. *N*-Chlorosuccinimide (1.2 equiv) was added, and the resulting mixture was stirred for 30 min at 0 °C. The solution was diluted with an equal volume of CH_2Cl_2, and a 10% solution of NaOH was added (10 mL/mmol). The resulting mixture was stirred for 5 min, and the organic phase was separated, dried over $MgSO_4$, and concentrated. The crude selenoxides were recrystallized from hexanes/CH_2Cl_2 (4:1).

Benzyl 4-Methoxyphenyl Selenide: mp 47–47.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.79 (s, 3 H), 4.00 (s, 2 H), 6.77 (d, 2 H, J = 8.5 Hz), 7.12 (d, 2 H, J = 6.5 Hz), 7.20 (m, 3 H), 7.36 (d, 2 H, J = 8.5 Hz); ^{13}C NMR (500 MHz, $CDCl_3$) δ 33.2, 55.2, 114.6, 120.0, 126.7, 128.3, 128.8, 136.6, 139.1, 159.5; HRMS Q-TOF electrospray, m/z 279.0285 (calcd for $C_{14}H_{14}OSe + H^+$ 279.0288).

Benzyl 4-Methoxyphenyl Selenoxide (10): mp 96–100 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.85 (s, 3 H), 3.91 (d, 1 H, J = 11.2 Hz), 4.18 (d, 1 H, J = 11.2 Hz), 6.95 (m, 4 H), 7.25 (m, 3 H), 7.32 (d, 2 H, J = 8.8 Hz); ^{13}C NMR (500 MHz, $CDCl_3$) δ 55.5, 59.2, 114.8, 127.8, 128.2, 128.6, 129.8, 129.9, 130.2, 162.2; HRMS Q-TOF electrospray, m/z 317.0052 (calcd for $C_{14}H_{14}O_2Se + Na^+$ 317.0051).

Benzyl 4-(Dimethylamino)phenyl Selenide: mp 58–58.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.94 (s, 6 H), 3.96 (s, 2 H), 6.58 (d, 2 H, J = 9.0 Hz), 7.18 (m, 5 H), 7.32 (d, 2 H, J = 9.0 Hz); ^{13}C NMR (300 MHz, $CDCl_3$) δ 33.5, 40.4, 112.9, 115.0, 126.5, 128.3, 128.8, 136.6, 139.6, 150.3; HRMS Q-TOF electrospray, m/z 292.0599 (calcd for $C_{15}H_{17}NSe + H^+$ 292.0604).

Benzyl 4-(Dimethylamino)phenyl Selenoxide (11): mp 106–107 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.01 (s, 6 H), 3.93 (d, 1 H, J = 11.0 Hz), 4.17 (d, 1 H, J = 11.5 Hz), 6.69 (d, 2 H, J = 8.5 Hz), 6.99 (m, 2 H), 7.26 (m, 5 H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 40.2, 59.4, 112.1, 124.4, 127.5, 127.9, 128.6, 129.8, 130.4, 152.4; HRMS Q-TOF electrospray, m/z 308.0543 (calcd for $C_{15}H_{17}ONSe + H^+$ 308.0548).

Benzyl 3,5-Bis(trifluoromethyl)phenyl Selenide: mp 26–26.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.18 (s, 2H), 7.18–7.29 (m, 5H), 7.71 (s, 1H), 7.76 (s, 1H); fluorine splitting in the ^{13}C NMR spectrum made unambiguous assignment of signals difficult; HRMS Q-TOF electrospray, m/z 384.9923 (calcd for $C_{15}H_{11}F_6Se + H^+$ 384.9930).

Benzyl 3,5-Bis(trifluoromethyl)phenyl Selenoxide (12): mp 137–139 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.93 (d, 1 H, J = 11.2 Hz), 4.33 (d, 1 H, J = 11.6 Hz), 6.88 (d, 2 H, J = 6.8 Hz), 7.25 (t, 2 H, J = 7.0 Hz), 7.32 (t, 1 H, J = 6.6 Hz), 7.70 (br s, 2 H), 7.94 (br s, 1 H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 59.1, 121.4, 125.0, 126.6, 128.3, 128.8, 128.9, 129.7, 132.4, 142.4; HRMS Q-TOF electrospray, m/z 422.9698 (calcd for $C_{15}H_{10}OF_6Se + Na^+$ 422.9693).

Preparation of Benzyl 2-(Dimethylaminomethyl)phenyl selenoxide.[18] *N*,*N*-Dimethylbenzylamine (3.0 mL, 20 mmol) was dissolved in 150 mL of anhydrous ether under an Ar atmosphere. A 1.6 M solution of *n*-BuLi (13.6 mL, 22 mmol) was added dropwise, and the resulting solution was stirred under Ar for 24 h at ambient temperature. After 24 h, Se powder (1.58 g, 20 mmol) was added rapidly and the resulting mixture was stirred under Ar for 3 h at ambient temperature. The reaction mixture was cooled to 0 °C in an ice bath. A solution of benzyl bromide (3.42 g, 20 mmol) in 20 mL of anhydrous ether was added dropwise. The resulting solution was stirred under Ar at 0 °C for 2 h and was then warmed to ambient temperature. The reaction mixture was washed with 250 mL of water. The aqueous wash was extracted with ether (3 × 50 mL). The organic phases were combined, dried over $MgSO_4$, and concentrated to give 4.86 g (80%) of the crude benzyl 2-((dimethylamino)methyl)phenyl selenide as a pale yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.17 (s, 6 H), 3.41 (s, 2 H), 4.09 (s, 2 H), 7.16–7.31 (m, 8 H), 7.48–7.51 (m, 1 H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 31.2, 43.9, 44.7, 45.3, 64.3, 126.0, 126.6, 127.0, 127.6, 128.4, 128.9, 129.6, 131.3.

To a solution of the selenide (1.52 g, 5.0 mmol) in 50 mL of CH_2Cl_2 was added 50 mL of saturated K_2CO_3. A solution of *m*-chloroperbenzoic acid (6.0 mmol) in 25 mL of CH_2Cl_2 was

added dropwise, and the resulting mixture was stirred at ambient temperature for 3 h. An additional 100 mL of water was added. The organic phase was separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were dried over $MgSO_4$ and concentrated. The crude **13** was recrystallized in hexanes/CH_2Cl_2 (4:1) to give 1.28 g (80%) of **13**, whose spectral properties were identical with reported values:[18] mp 48−51 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.30 (s, 6 H), 3.32 (d, 1 H, J = 13.0 Hz), 3.83 (d, 1 H, J = 11.5 Hz), 3.85 (d, 1 H, J = 13.5 Hz), 4.19 (d, 1 H, J = 11.5 Hz), 7.19 (m, 3 H), 7.29 (m, 3 H), 7.37 (m, 2 H), 7.78 (m, 1 H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 44.6, 57.6, 63.1, 126.8, 127.9, 128.0, 128.4, 128.5, 129.9, 130.4, 131.6, 138.4, 141.8.

General Procedure for Kinetic Studies of the Bromination of 4-Pentenoic Acid with Hydrogen Peroxide and Sodium Bromide. The appropriate selenoxide (0.063 mmol) and 4-pentenoic acid (0.250 g, 2.5 mmol) were dissolved in 20 mL of CH_2Cl_2. Twenty milliliters of 0.23 M pH 6.0 phosphate buffer was added, followed by NaBr (5.77 g, 56 mmol). Hydrogen peroxide (30 wt %, total volume of 7.8 mL, 72 mmol) was added via syringe in one portion. Small aliquots of the reaction mixture were quenched with sodium bisulfite and acidified with 10% HCl, and the progress of bromination was determined by ^{1}H NMR spectroscopy. Rates of bromination, k_{obs}, are based on the average of duplicate runs, which agreed within 10%.

General Procedure for Preparative Brominations. Preparation of 5-(Bromomethyl)dihydrofuran-2-one (6) (Entry 1, Table 1). Hydrogen peroxide (30%, 7.8 mL, 72 mmol) was added dropwise to a mixture of 2.5 mmol of substrate (4-pentenoic acid, 0.250 g), **13** (0.029 g, 0.063 mmol, 2.5 mol %), NaBr (5.77 g, 56 mmol), 20 mL of CH_2Cl_2, and 20 mL of 0.23 M pH 6.0 phosphate buffer. After the indicated time (8 h for pentenoic acid), the reaction mixture was acidified with 10% HCl and the products were extracted with CH_2Cl_2 (4 × 25 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated at reduced pressure. The crude product mixture was purified via chromatography on SiO_2 (ether) followed by Kugelrohr distillation to give **6** (0.412 g, 93%) as a colorless oil with spectral properties identical with literature values:[20] ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.70−4.76 (m, 1 H), 3.49−3.57 (m, 2 H), 2.51−2.69 (m, 2 H), 2.38−2.47 (m, 1 H), 2.06−2.15 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.14, 77.63, 34.28, 28.07, 25.69; IR (film, NaCl) 1775 cm^{-1}.

Preparation of 5-(Bromomethyl)-3,3-diphenyldihydrofuran-2-one (19) (Entry 2, Table 1). 2,2-Diphenyl-4-pentenoic acid (0.631 g, 2.50 mmol) was treated as described above for 120 h. The crude product was purified via chromatography on SiO_2 (CH_2Cl_2/hexanes, 4/1) and then recrystallized from EtOH to give 0.524 g (64%) of **19** as a white solid: mp 87.0−88.5 °C (lit.[21] mp 88−90 °C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30−7.36 (m, 10 H), 4.51−4.59 (m, 1 H), 3.61 (d × d, 1 H, J = 5, 10 Hz), 3.51 (d × d, 1 H, J = 6.6, 10 Hz), 3.16 (d × d, 1 H, J = 5, 13.1 Hz), 2.81 (d × d, 1 H, J = 10, 13.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.02, 141.34, 139.11, 128.79, 128.24, 127.70, 127.42, 127.17, 127.01; IR (KBr) 1757 cm^{-1}.

Preparation of 1-Bromo-2,4,6-trimethoxybenzene (20) (Entry 3, Table 2). 1,3,5-Trimethoxybenzene (0.421 g, 2.50 mmol) was treated as described for 15 h. The crude product was passed through a short plug of SiO_2 and eluted with CH_2Cl_2 and was then recrystallized from hexanes to give **20** (0.485 g, 80%) as a white solid: mp 93.5−95.0 °C (lit.[22] mp 98−99 °C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.15 (s, 2 H), 3.86 (s, 6 H), 3.80 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.43, 157.42, 91.60, 56.30, 55.46.

Preparation of 2-Bromo-*N*,*N*-dimethylaniline (21) and 4-Bromo-*N*,*N*-dimethylaniline (22) (Entry 4, Table 2). *N*,*N*-Dimethylaniline (0.303 g, 2.50 mmol) was treated as described above for 24 h. The products were separated by chromatography on SiO_2 (CH_2Cl_2) followed by vacuum-drying of **21** to give 0.333 g (66%) of a white solid, mp 51.5−53.0 °C (lit.[23] mp 53−54 °C) and Kugelrohr distillation of **22** to give 0.16 g (32%) of a colorless oil.

21:[23] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28 (d, 2 H, J = 9 Hz), 6.57 (d, 2 H, J = 9 Hz), 2.90 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.40, 131.57, 113.99, 108.35, 40.43.

22:[24] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53 (d × d, 1 H, J = 8 Hz), 7.24 (d × t, 1 H, J = 1.5, 7.5 Hz), 7.07 (d × d, 1 H, J = 1.5, 8 Hz), 6.87 (d × t, 1 H, J = 1.5, 7.5 Hz), 2.79 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.79, 133.80, 128.01, 123.82, 120.42, 119.09, 44.13.

Preparation of *N*-(4-Bromophenyl)morpholine (23) (Entry 5, Table 2). *N*-Phenylmorpholine (0.408 g, 2.50 mmol), was treated as described above for 48 h. The crude product was purified by chromatography on SiO_2 (CH_2Cl_2) to give *N*-(4-bromophenyl)morpholine (0.420 g, 70%) as a white solid: mp 112−115 °C (lit.[25] mp 114.5−115.5);[26] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (d, 2 H, J = 9 Hz), 6.75 (d, 2 H, J = 9 Hz), 3.83 (t, 4 H, J = 4.8 Hz), 3.10 (t, 4 H, J = 4.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.20, 131.80, 117.14, 111.96, 66.61, 48.98.

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Supporting Information Available: Plots of the natural logarithm of the remaining fraction of 4-pentenoic acid as a function of time in the presence and absence of selenoxide catalysts **7**−**13**. This information is available free of charge via the Internet at http://pubs.acs.org.

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