JOC*Note*

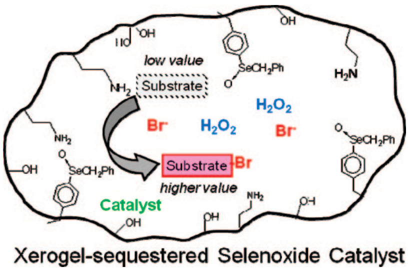
A Xerogel-Sequestered Selenoxide Catalyst for Brominations with Hydrogen Peroxide and Sodium Bromide in an Aqueous Environment

Stephanie M. Bennett, Ying Tang, Danielle McMaster,
Frank V. Bright, and Michael R. Detty*

Department of Chemistry, University at Buffalo, The State University of New York, 627 Natural Sciences Complex, North Campus, Buffalo, New York 14260-3000

mdetty@buffalo.edu

Received June 8, 2008

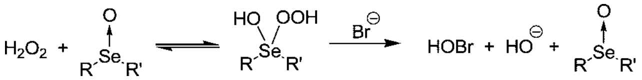


4-(Hydroxymethyl)phenyl benzyl selenoxide (**4**) sequestered in a halide-permeable, Class II xerogel formed from 10/90 (mol/mol) 3-aminopropyltriethoxysilane/tetraethoxysilane catalyzes the bromination of organic substrates (4-pentenoic acid, 3,5-dihydroxybenzoic acid, 1,3,5-trimethoxybenzene, *N*-phenylmorpholine, and *N*,*N*-dimethylaniline) with NaBr and H_2O_2. Catalyst performance (reaction rate) when sequestered within the halide-permeable xerogel is 23-fold greater in comparison to xerogel-free catalyst in solution. The catalyst is easily separated from the reaction mixture via filtration and the recovered catalyst can be reused without loss of activity through formation of the first 80 mol of product per mole of catalyst.

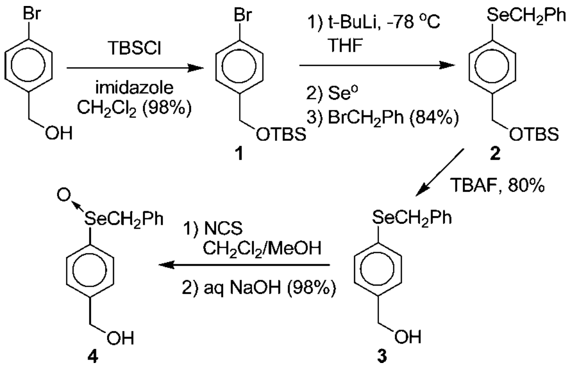
In a "green" future, synthetic transformations that minimize the use of organic-based solvents and reagents will contribute to a low-carbon-use economy. Water is a carbon-free solvent, H_2O_2 is a carbon-free, inexpensive oxidant, and aqueous oxidations with H_2O_2 have the potential to minimize solvent waste and organic byproducts. The bromination of organic substrates with NaBr and H_2O_2 is one such reaction.[1] An easily recovered and recycled catalyst for the activation of H_2O_2 would further contribute to value-added organic transformations while making the use of aqueous H_2O_2 more practical.

Selenoxides are excellent catalysts for a variety of oxidations with H_2O_2 including bromination with NaBr as shown in Scheme 1.[2–4] However, the catalyst is only recovered following time-consuming extractive workup and chromatography. Recent studies have shown that catalytic groups can be sequestered within xerogels or bulk silica by "imprinting" to give spatially arranged functionality on the nanoscale.[5] The reactivity of the imprinted functionality and the transport of reagents from bulk solution into pores can be modified by end-capping hydrophilic and acidic silanol functionality with various groups.[6] Enhanced rates have been observed for the sequestered catalysts relative to similar catalyst structures used as homogeneous catalysts.[7] Xerogel-sequestered selenoxide catalysts offer an environmentally benign, porous solid platform for using H_2O_2 as an oxidant and simultaneously provide simple filtration as a means to isolate and recycle the catalyst.

SCHEME 1. Oxidation of Bromide with H_2O_2 and a Selenoxide Catalyst



SCHEME 2. Synthesis of Selenoxide Catalyst 4



Synthesis of the Selenoxide Catalyst. Aryl benzyl selenoxides have excellent catalytic activity with H_2O_2[3] and avoid the complication of selenoxide elimination[8] by having no β-hydrogens. Covalent attachment of the catalyst within the xerogel requires suitable functionality (alcohol, amine) on the catalyst. A selenoxide with benzyl alcohol functionality was prepared as shown in Scheme 2. 4-Bromobenzyl alcohol was protected as its TBS ether **1** by using TBSCl and imidazole and **1** was then treated with 2.2 equiv of *t*-BuLi. The resulting anion was then reacted with Se powder and benzyl bromide to give selenide **2**. The TBS protecting group was removed with Bu_4NF to give selenide **3**, which was then

---

* To whom correspondence may be sent. Phone:(716)-645-6800 × 2200. Fax: (716)-645-6963.

(1) Mohammed, A.; Liebhafsky, H. A. *J. Am. Chem. Soc.* **1934**, *56*, 1680.

(2) Drake, M. D.; Bright, F. V.; Detty, M. R. *J. Am. Chem. Soc.* **2003**, *125*, 12558.

(3) Goodman, M. A.; Detty, M. R. *Organometallics* **2004**, *23*, 3016.

(4) Goodman, M. A.; Detty, M. R. *Syn. Lett.* **2006**, 1100.

(5) (a) Katz, A.; Davis, M. E. *Nature* **2000**, *403*, 286. (b) Notestine, J.; Katz, A. *Chem. Eur. J.* **2006**, *12*, 3954.

(6) (a) Bass, J. D.; Katz, A. *Chem. Mater.* **2003**, *15*, 2757. (b) Bass, J. D.; Anderson, S. L.; Katz, A. *Angew. Chem., Int. Ed.* **2003**, *42*, 5219. (c) Bass, J. D.; Solovyov, A.; Pascall, A. J.; Katz, A. *J. Am. Chem. Soc.* **2006**, *126*, 3737.

(7) Notestein, J. M.; Solovyov, A.; Andrini, L. R.; Requejo, F. G.; Katz, A.; Iglesia, E. *J. Am. Chem. Soc.* **2007**, *129*, 15585.

(8) (a) Walter, R.; Roy, J. *J. Org. Chem.* **1970**, *36*, 2561. (b) Jones, D. N.; Mundy, D.; Whitehouse, R. D. *J. Chem. Soc., Chem. Commun.* **1970**, 86. (c) Sharpless, K. B.; Young, M. W.; Lauer, R. F. *Tetrahedron Lett.* **1973**, 1979. (d) Reich, H. J.; Reich, I. L.; Renga, J. M. *J. Am. Chem. Soc.* **1973**, *95*, 5813.

10.1021/jo801234e CCC: $40.75

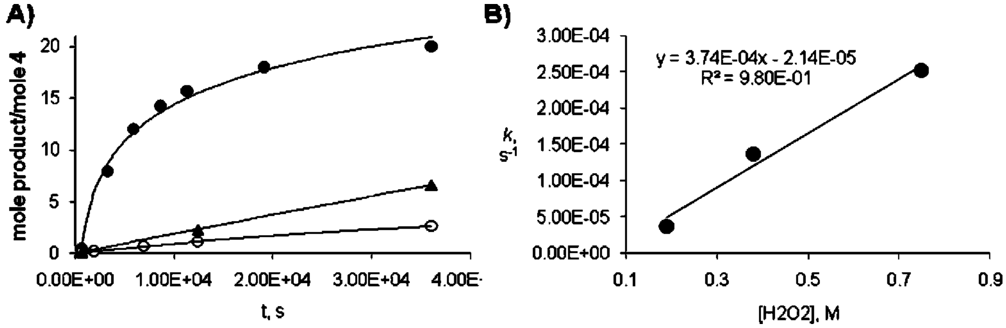


FIGURE 1. (A) Moles of brominated products **5** and **6** per mole of **4** as a function of time for 5 mol % **4** sequestered in APTES/TEOS (filled circles), sequestered in C3TriMOS/TMOS (filled triangles), and dissolved in D_2O (open circles) with 0.38 M H_2O_2 and 1.4 M NaBr at 301.5 ± 0.4 K. Lines represent first-order fits of the data. (B) Rate dependence on H_2O_2 concentration for the APTES/TEOS-sequestered **4** catalyzed reactions at 301.5 ± 0.4 K.

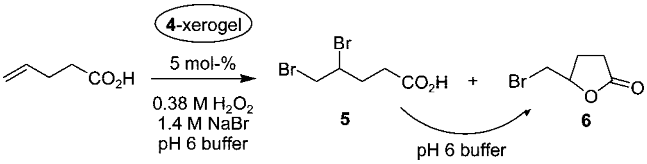
oxidized to selenoxide **4** with *N*-chlorosuccinimide in MeOH/CH_2Cl_2 followed by hydrolysis with aqueous NaOH.[9]

Sequestered Catalysts. As described in the Supporting Information, halide permeability was determined in a series of xerogels by investigating the I^- quenching of sequestered tris(4,7′-diphenyl-1,10′-phenanathroline)ruthenium(II) chloride. A xerogel based on 10/90 (mol/mol) 3-aminopropyltriethoxysilane/tetraethoxysilane xerogel (APTES/TEOS) was permeable to halide ions and had mechanical properties suitable for use as a powdered support for catalyst **4**. A second xerogel based on 50/50 (mol/mol) *n*-propyltrimethoxysilane/tetramethoxysilane (C3TriMOS/TMOS) was much less permeable to halides (Supporting Information) and was used as a control. Monoliths of both APTES/TEOS and C3TriMOS/TMOS with and without 0.015 mM **4** were prepared and crushed into a fine powder by using a mortar and pestle (particle diameter = 30−90 μm). Theoretically, each gram of APTES/TEOS contained 0.057 g (1.9×10^{-4} mol) of selenoxide **4** while each gram of C3TriMOS/TMOS contained 0.037 g (1.3×10^{-4} mol). Atomic absorption analysis of Se content was consistent with the theoretical values.

The importance of covalent attachment of the catalyst was demonstrated by preparing monoliths of APTES/TEOS containing 0.015 M benzyl phenyl selenoxide.[3] Ether extraction of the crushed powder removed >90% of the selenoxide catalyst from the xerogel.

Kinetic Studies of the Bromination of 4-Pentenoic Acid with NaBr/H_2O_2 and APTES/TEOS-Sequestered 4. Bromination of 4-pentenoic acid with 1.4 M NaBr and 0.38 M H_2O_2 at pH 6 with 5 mol % APTES/TEOS-sequestered **4** at 296 ± 1 K gives 4,5-dibromopentanoic acid (**5**) and bromolactone **6** as shown in Scheme 3.[10] At pH 6, **5** is converted to **6** upon standing. The ^1H NMR chemical shifts of the olefinic protons of 4-pentenoic acid are distinct from the bromomethine proton of **5** and the lactone methine proton of **6** (Figure S11, Supporting Information), allowing product ratios to be determined as a function of time. As shown in Figure S12 (Supporting Information), pseudo-first-order behavior was observed with rate constants, k_{obs}, of $(8.9 \pm 0.1) \times 10^{-5}$ s^{-1} ($R^2 = 0.99$) for the catalyzed process and $(6.7 \pm 0.3) \times 10^{-7}$ s^{-1} ($R^2 = 0.98$) for the catalyst-free APTES/TEOS control. The uncatalyzed, xerogel-free bromination of 4-pentenoic acid under identical conditions gave k_{obs} of $(4.8 \pm 0.3) \times 10^{-7}$ s^{-1}.

SCHEME 3. Bromination Products of 4-Pentenoic Acid



In D_2O as Solvent. The bromination of 4-pentenoic acid was also followed by ^1H NMR spectroscopy in D_2O at pH/D 6 with suppression of the HOD/H_2O signal. As shown in Figure 1A, bromination of 4-pentenoic acid (0.13 M) with 5 mol % APTES/TEOS-sequestered **4**, 0.38 M H_2O_2, and 1.4 M NaBr followed excellent pseudo-first-order behavior [$k = (1.38 \pm 0.03) \times 10^{-4}$ s^{-1}, $R^2 = 0.99$, Table 1] and the reactions went to completion (20 mol of product per mole of catalyst). A first-order dependence on H_2O_2 was observed over the range of 0.19−0.75 M with a second-order rate constant of 3.8×10^{-4} M^{-1} s^{-1} with respect to H_2O_2 concentration (Figure 1B). Bromination appeared to be independent of Br^- concentration at the concentrations (0.7 to 2.8 M NaBr) employed in these studies (Table 1).

The bromination of 4-pentenoic acid using 5 mol % C3TriMOS/TMOS-sequestered **4** or for xerogel-free **4** dissolved in buffered D_2O is also shown in Figure 1A. Bromination was nearly 10-fold slower [$k = (1.48 \pm 0.03) \times 10^{-5}$ s^{-1}, Table 1] with C3TriMOS/TMOS-sequestered **4** relative to APTES/TEOS-sequestered **4**. Bromination with 5 mol % **4** dissolved in D_2O gave k_{obs} of $(6.06 \pm 0.04) \times 10^{-6}$ s^{-1} while the catalyst-free APTES/TEOS powder as a control reaction was much slower with k_{obs} of $(5.45 \pm 0.09) \times 10^{-7}$ s^{-1} (Table 1).

The bromination of 4-pentenoic acid with 5 mol % C3TriMOS/TMOS-sequestered **4** or for xerogel-free **4** dissolved in buffered D_2O is also shown in Figure 1A. Bromination was nearly 10-fold slower [$k = (1.48 \pm 0.03) \times 10^{-5}$ s^{-1}, Table 1] with 5 mol % C3TriMOS/TMOS-sequestered **4**. Bromination of 4-pentenoic acid with 5 mol % **4** dissolved in D_2O gave k_{obs} of $(6.06 \pm 0.04) \times 10^{-6}$ s^{-1} while bromination in the presence of catalyst-free APTES/TEOS powder was much slower with k_{obs} of $(5.45 \pm 0.09) \times 10^{-7}$ s^{-1} (Table 1).

Preparative Bromination of Organic Substrates with Xerogel-Sequestered Catalyst 4. Bromination of 4-pentenoic acid was complete within 15 h at ambient temperature with 1.4 M NaBr, 0.25 M H_2O_2 (2 equiv), and 5 mol % APTES/TEOS-

---

[9] Detty, M. R. *J. Org. Chem.* **1980**, *45*, 274.

[10] (a) Francavilla, C.; Bright, F. V.; Detty, M. R. *Org. Lett.* **1999**, *1*, 1043. (b) Francavilla, C.; Drake, M. D.; Bright, F. V.; Detty, M. R. *J. Am. Chem. Soc.* **2001**, *123*, 57.

[11] (a) Dave, B. C.; Soyez, H.; Miller, J. M.; Dunn, B.; Valentine, J. S.; Zink, J. I. *Chem. Mater.* **1995**, *7*, 1431. (b) Avnir, D. *Acc. Chem. Res.* **1995**, *28*, 328. (c) Ingersoll, C. M.; Bright, F. V. *CHEMTECH* **1997**, *27*, 26.

[12] Jaber, N.; Gelman, D.; Schumann, H.; Dechert, S.; Blum, J. *Eur. J. Org. Chem.* **2002**, 1628.

[13] Fischer, A.; Henderson, G. N. *Can. J. Chem.* **1983**, *61*, 1045.

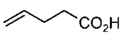
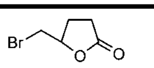
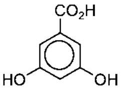
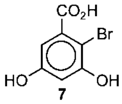
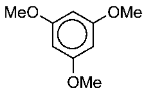
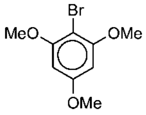
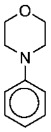
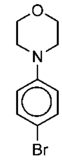
[14] (a) Effenberger, F.; Steinbach, A.; Epple, G.; Hanauer, J. *Chem. Ber.* **1983**, *116*, 3539. (b) Cheng, Y.; Zhan, Y.-H.; Meth-Cohn, O. *Synthesis* **2002**, *1*, 34.

TABLE 1. Rate Constants for the Bromination of 4-Pentenoic Acid with Various Concentrations of H_2O_2 and NaBr in the Presence or Absence of 5 mol % Selenoxide 4 (Relative to 4-Pentenoic Acid) Sequestered in 10/90 APTES/TEOS or 50/50 C3TriMOS/TMOS or Dissolved in D_2O

catalyst/xerogel combination	[H_2O_2], M	[NaBr], M	k_{obs},[a] s^{-1}	k_{rel}
APTES/TEOS-sequestered **4**	0.19	1.4	$(3.81 \pm 0.22) \times 10^{-5}$	6.3
	0.38	1.4	$(1.38 \pm 0.03) \times 10^{-4}$	23
	0.38	2.8	$(1.13 \pm 0.02) \times 10^{-4}$	19
	0.38	0.7	$(1.23 \pm 0.03) \times 10^{-4}$	22
	0.75	1.4	$(2.53 \pm 0.26) \times 10^{-4}$	42
5 mol % **4** in D_2O	0.38	1.4	$(6.06 \pm 0.04) \times 10^{-6}$	1
C3TriMOS/TMOS- sequestered **4**	0.38	1.4	$(1.48 \pm 0.18) \times 10^{-5}$	2.4
APTES/TEOS (no **4**)	0.38	1.4	$(5.45 \pm 0.09) \times 10^{-7}$	0.09

[a] Average of duplicate runs at 301.5 ± 0.4 K.

TABLE 2. Bromination of Organic Substrates with 1.4 M NaBr, 0.25 M H_2O_2 with and without 5 mol % Selenoxide 4 (Relative to 4-Pentenoic Acid) Sequestered in 10/90 APTES/TEOS in pH 6 Phosphate Buffer (Entry 1) or 1/1 (v/v) Dioxane/pH 6 Phosphate Buffer (Entries 2−4)

entry	substrate	product	time,[a] h	isolated yield %[b]	% conversion xerogel only[b]
(1)	 	 **6**	24	87 ± 1	5.6 ± 0.1
(2)	 	 **7**	19	89 ± 2	< 1.0
(3)	 	 **8**	24	96 ± 1	8 ± 3
(4)	 	 **9**	24	89 ± 2	8 ± 1

[a] No starting material detected at this point. [b] Average of duplicate runs.

sequestered **4** (relative to 4-pentenoic acid at 0.125 M) to give bromolactone **6** in (87 ± 1)% isolated yield (average of duplicate runs) after a total reaction time of 24 h (entry 1, Table 2). The APTES/TEOS-sequestered **4** was separated via filtration from the reaction mixture. Control reactions in the presence of catalyst-free APTES/TEOS gave approximately 5% conversion to products after 24 h.

Brominations of 3,5-dihydroxybenzoic acid (entry 2), 1,3,5-trimethoxybenzene (entry 3), and *N*-phenylmorpholine (entry 4) were also examined with 5 mol % **4** sequestered in APTES/TEOS as summarized in Table 2. These substrates were less soluble in phosphate buffer and a 1/1 mixture of dioxane and pH 6 phosphate buffer was used as solvent in these reactions. Bromination of 3,5-dihydroxybenzoic acid was complete after 19 h to give a 94:6 mixture of two products from which 2-bromo-3,5-dihydroxybenzoic acid (**7**) was isolated in 89% yield. The 4-bromo isomer was the minor product. Bromination of 1,3,5-trimethoxybenzene was complete after 24 h to give a 98:2 mixture of 2-bromo-1,3,5-trimethoxybenzene (**8**) as the major product, isolated in 96% yield, and trace amounts of the dibrominated product. Bromination of *N*-phenylmorpholine was complete after 24 h to give a 97:3 mixture of *N*-(4-bromophenyl)morpholine (**9**) and the 2-isomer as the minor component in 89% isolated yield for the two products.

As a control reaction, the preparative brominations were also conducted with an equivalent weight of catalyst-free xerogel. After 24 h, <1% bromination was observed with 3,5-dihydroxybenzoic acid and approximately 8% bromination was observed with 1,3,5-trimethoxybenzene and *N*-phenylmorpholine (Table 2).

Recycling APTES/TEOS-Sequestered 4. The APTES/TEOS-sequestered **4** from the bromination of 4-pentenoic acid was recovered by filtration, washed with water and ether, dried, and recycled. Complete conversion of 4-pentenoic acid to bromolactone **6** was observed after 24 h for three additional runs with the same catalyst (total of 80 mol of product per mole of **4**) with **6** isolated in 86% yield (average of four runs, each run in duplicate). When the catalyst was used for a fifth time, only 69% conversion to bromolactone **6** was observed after 24 h. However, the selenium content [(1.4 ± 0.3)% Se by atomic absorption analysis] was essentially unchanged from that of the virgin catalyst [(1.5 ± 0.3)% Se].

Summary and Discussion. We have developed a recyclable catalyst for bromination of organic substrates with NaBr and H_2O_2 based on xerogel-sequestered selenoxide **4**. When used at 5 mol % catalyst, the APTES/TEOS-sequestered catalyst can be recovered by filtration and recycled without apparent loss of activity through 80 mol of product per mole of catalyst. The xerogel-sequestered catalyst works well in water and aqueous dioxane as solvents. The system appears to be first order in H_2O_2 and independent of Br^- at the concentrations employed here.

The relative rate of bromination of pentenoic acid with the APTES/TEOS-s*equ*estered selenoxide **4** was 23× faster in comparison to the homogeneous reaction with **4** dissolved in D_2O. This difference is even more remarkable when one considers that only a fraction of the total catalytic sites are likely accessible within the xerogel matrix in comparison to 100% in bulk solution.[11] There is precedent for reactions with silica-sequestered catalysts being faster relative to homogeneous catalysis with soluble analogues of the same catalyst.[7] Local concentrations of reagents within the xerogel pores would be higher in comparison to bulk solution leading to faster reaction rates. The enhanced rate of catalysis observed with APTES/TEOS-sequestered **4** is another example of active-site/surface cooperativity[5b] and is the first example of this in an aqueous environment with use of either organically modified xerogels or imprinted silica.

The importance of hydrogen-bond donors and acceptors in the xerogel support can be gleaned from catalysis with the C3TriMOS/TMOS-sequestered **4**. In this material the surface is more hydrophobic from the *n*-propyl groups and lacks the amino functionality of the APTES. This xerogel is also much less permeable to halides (Figure S8, Supporting Information), which suggests that catalysis, if any, will come from catalytic sites at the surface and near-surface pores and not from deeper pores within the xerogel bulk. The consequence is that catalysis with the APTES/TEOS-sequestered **4** is nearly 10× faster than catalysis with C3TriMOS/TMOS-sequestered **4**.

The catalyst, while effective, has a somewhat limited lifetime. The catalyst is not leaching from the xerogel during reaction based on selenium content. Solution studies have shown that aryl benzyl selenoxides remain intact at the completion of reaction.[3,4] The local concentrations of reagents within the xerogel pores may be sufficiently high that the benzyl carbon of the catalyst becomes a site for nucleophilic attack with loss of the selenoxide functionality and loss of catalytic activity. Diaryl selenoxides with appropriate reactivity may be more robust catalysts for sequestering in xerogels in future studies.

Experimental Section

Preparation of the TBS Ether 1.[10] Imidazole (4.73 g, 69.5 mmol), TBSCl (10.5 g, 69.5 mmol), and 4-bromobenzyl alcohol (10.0 g, 53.5 mmol) were stirred 15 h in CH_2Cl_2 (100 mL). Aqueous workup and extraction with CH_2Cl_2 (3 × 25 mL) gave 15.7 g (98%) of **1** as a colorless oil following SiO_2 chromatography eluting with CH_2Cl_2.

Preparation of Selenide 2. Silyl ether **1** (9.63 g, 32.0 mmol) in anhydrous THF (200 mL) was treated sequentially with *t*-BuLi (1.7 M solution, 41 mL, 70 mmol) at −78 °C, Se powder (2.52 g, 32.0 mmol) at room temperature until Se was consumed, and benzyl bromide (6.01 g, 32.0 mmol) at −78 °C. The mixture was stirred 15 h at ambient temperature followed by an aqueous workup and extraction with ether (3 × 30 mL) to give 10.5 g (84%) of selenide **2** as an orange oil following SiO_2 chromatography eluting with hexanes (R_f 0.4).

Preparation of 4-(Hydroxymethyl)phenyl Benzyl Selenide (3). A mixture of Bu_4NF (1 M in THF, 77 mmol) and silyl ether **2** (15.0 g, 38.3 mmol) was stirred 2 h at room temperature in anhydrous THF (150 mL). Saturated NH_4Cl (200 mL) was added and products were extracted with EtOAc (3 × 40 mL) to give 8.52 g (80%) of selenide **3** as a white solid, mp 76−78 °C, following SiO_2 chromatography eluting with CH_2Cl_2 (R_f 0.4).

Preparation of Selenoxide 4. *N*-Chlorosuccinimide (1.40 g, 10.5 mmol) and selenide **3** (2.42 g, 8.7 mmol) in 20 mL of 1/1 (v/v) $MeOH/CH_2Cl_2$ were stirred for 0.5 h at 0 °C.[9] The reaction mixture was diluted with CH_2Cl_2 (20 mL) and 10% aq NaOH (20 mL) followed by stirring for 5 min. The organic layer was separated, dried over $MgSO_4$, and concentrated to a yellow oil, which was crystallized form CH_2Cl_2/hexanes to give selenoxide **4** (2.15 g, 94%) as a white solid: mp 126−126.5 °C. Anal. Calcd for $C_{14}H_{14}O_2Se$: C, 57.35; H, 4.81. Found: C, 57.26; H, 4.95.

Preparation of the Sol APTES/TEOS. Sol TEOS: TEOS (12.5 g, 60.1 mmol), water (2.16 mL), EtOH (13.6 mL), and 60 μL of 0.1 N HCl sealed in a glass vial were stirred at room temperature for 6 h. **Sol APTES:** APTES (2.544 g, 11.49 mmol), 6.67 N HCl (2.00 g), and EtOH (10.56 mL) sealed in a glass vial were sonicated at room temperature for 40 min. **Sol APTES/TEOS:** Sol APTES (5.000 mL, 3.83 mmol of APTES) and Sol TEOS (16.77 mL, 33.54 mmol of TEOS) were sonicated at room temperature for 20 min to give 20 mL of Sol APTES/TEOS.

APTES/TEOS-Sequestered 4. Sol APTES/TEOS (20.00 mL) and **4** (0.176 g, 0.58 mmol) in a glass vial were sonicated at room temperature for 1 h, allowed to gel for 1 week covered, and then placed uncovered under vacuum at room temperature for 1 week. The resulting xerogel (3.09 g) was ground into a fine powder (mortar and pestle), stirred with several portions of ether (3 × 100 mL, 4 h each), and dried. The combined ether washes were concentrated to give <0.010 g of residue, suggesting >95% of **4** was sequestered. Theoretically, each gram of xerogel contains 0.057 g (1.9×10^{-4} mol) of selenoxide **4**. Atomic absorption analysis indicated (1.5 ± 0.3)% Se in the powdered xerogel. (Calcd for 1.9×10^{-4} mol of Se per g: 1.5%.)

Stock Solutions for Kinetics Experiments. K_2HPO_4 (1.75 g, 10.0 mmol) and KH_2PO_4 (4.80 g, 35.2 mmol) were dissolved in 200 mL of distilled H_2O or D_2O to give pH 6.0 ± 0.2 buffer (0.23 M in phosphate). 4-Pentenoic acid (2.56 g, 2.56 mmol) and NaBr (28.6 g, 0.28 mol) were added and the mixture was stirred until they dissolved. Benzoic acid (0.61 g, 0.5 mmol) was added to the D_2O stock.

Kinetic Studies of the Bromination of 4-Pentenoic Acid. APTES-TEOS-sequestered **4** [0.65 g, 0.037 g (1.3×10^{-4} mol) of selenoxide **4**] or selenoxide-free APTES-TEOS (0.65 g) was added to 20 mL of stock pH 6 phosphate buffer. H_2O_2 (8.8 M, 0.81 mL, 7.5 mmol) was added via micropipette in one portion. Small aliquots of the reaction mixture (0.5 mL) were quenched with sodium bisulfite, acidified with 10% HCl, and extracted with $CDCl_3$ (1.0 mL). The progress of bromination was determined by ^1H NMR spectroscopy by integration of the olefinic proton at C4 of 4-pentenoic acid (δ 5.82) with the methine protons of **5** (δ 4.75) and **6** (δ 4.25). Rates of bromination, k_{obs}, are based on the average of duplicate runs, which agreed within 10%.

Kinetic Studies in Buffered D_2O. Selenoxide **4** (0.018 g, 6.1×10^{-5} mol), APTES/TEOS-sequestered **4** (0.32 g, 6.1×10^{-5} mol of **4**), C3TriMOS/TMOS-sequestered **4** (0.50 g, 6.5×10^{-5} mol of **4**), or catalyst-free APTES/TEOS (0.32 g) was added to 10 mL of stock phosphate-buffered D_2O. H_2O_2 (8.8 M, 0.405 mL, 3.8 mmol; 0.81 mL, 7.5 mmol; or 0.203 mL, 1.9 mmol) was added in one portion via micropipette. One milliliter aliquots of the reaction mixture were removed, filtered through a cotton plug, and analyzed by ^1H NMR spectroscopy by integration of the olefinic proton at C4 of 4-pentenoic acid and the methine protons of **5** (δ 4.75) and **6** (δ 4.25). The aliquot was returned to the reaction vessel immediately after acquisition of ^1H NMR spectral data. The benzoic acid doublet at δ 7.94 was used as an internal standard. Rates of bromination, k_{obs}, are compiled in Table 1 and are based on the average of duplicate runs.

General Procedure for the Bromination of Organic Substrates. Hydrogen peroxide (0.56 mL, 30% by wt, 8.8 M, 5.0 mmol) was added dropwise to a mixture of NaBr (2.86 g, 28.0 mmol), substrate (2.50 mmol), and 5 mol % APTES/TEOS-sequestered **4** [0.65 g containing 0.037 g (1.3×10^{-4} mol) of selenoxide **4**] in 20 mL of a 1:1 (v/v) mixture of pH 6 phosphate buffer (0.23 M in phosphate) and dioxane. After 19 or 24 h (Table 2), the catalyst was removed via filtration, and products were extracted with EtOAc (3 × 20 mL). The combined organic extracts were washed with 5% sodium bisulfite (10 mL) and brine (10 mL), dried over $MgSO_4$, and concentrated. Products were purified by SiO_2 chromatography eluted with EtOAc/hexanes to give 0.530 g (91%) of 2-bromo-3,5-dihydroxybenzoic acid (**7**),[12] 0.562 g (96%) of 1-bromo-2,4,6-trimethoxybenzene (**8**), mp 93.5−95.0 °C (lit.[13] mp 98−99 °C), or 0.545 g (90%) of *N*-(4-bromophenyl)morpholine (**9**), mp 112−115 °C (lit.[14] mp 114.5−115.5 °C).

Acknowledgment. We thank the Office of Naval Research (Grant No. N00014021-0836) and the U.S. Department of Energy (Grant No. DE-FG02-90ER14143) for support of this work.

Supporting Information Available: General experimental statement; xerogel permeability studies; spectral characterization of compounds **1**−**4** and **6**−**9**; ^1H and ^{13}C NMR spectra for compounds **3** and **4**; ^1H NMR spectrum of a mixture of 4-pentenoic acid, **5**, and **6**; and kinetics plots of the bromination of 4-pentenoic acid with catalyst-doped and undoped APTES/TEOS. This material is available free of charge via the Internet at http://pubs.acs.org.

JO801234E