mmol) to the NMR tube. The solution was vortex stirred for 10 min before recording the NMR spectra of the solution containing a 2:1:1 ratio of $PhMe_2SiLi$, MeLi, and CuCN.

Typical Procedure for Reactions of $PhMe_2SiLi$/MeLi/CuCN Solutions with 2-Cyclohexen-1-one. $PhMe_2SiLi$ (3.00 mL, 3.0 mmol) was added dropwise at -78 °C to a solution of MeCu(CN)Li [(3.0 mmol, prepared from the addition of MeLi in Et_2O (2.14 mL, 3.0 mmol) and CuCN (0.269 g, 3.0 mmol in THF (20 mL) at -50 °C)] in THF (22.14 mL) under argon. The resulting deep red solution was stirred for 0.5 h after which cyclohexenone (0.29 mL, 3.0 mmol) was added via a syringe. Reactions were stirred for a further 0.5 h and then quenched with 2 N HCl. Workup involved extraction of the organic phase with Et_2O (3 × 15 mL). The combined extracts were dried over anhydrous $MgSO_4$ and concentrated in vacuo. Flash column chromatography (5:1 hexanes:EtOAc) yielded 3-(dimethylphenylsilyl)cyclohexanone in 82% isolated yield and >95% purity as judged by gas chromatographic analysis. The ^1H NMR and IR data for the 1,4-adduct matched those reported by Fleming et al.[1] for this compound: ^{13}C ($CDCl_3$) δ 212.5, 136.6, 133.8, 129.2, 127.8, 42.3, 41.8, 29.7, 27.5, 26.0, -5.4, -5.5; MS *m/e* (rel intensity) 232 (M^+, 20), 217 (15), 189 (5), 156 (22), 135 (100).

Typical Procedure for Reactions of $(PhMe_2Si)(CH_3)Cu(CN)Li_2$ (2) with Organic Substrates. $PhMe_2SiLi$ (3.00 mL, 3.0 mmol) was added dropwise at -78 °C to a solution of MeCu(CN)Li [prepared as above] in THF (22.14 mL) under argon. The resulting deep red solution was stirred for 0.5 h after which 3.0 mmol of the organic substrate dissolved in 5.0 mL of THF was added via cannula. Reactions were stirred for a further 1.5 h at -78 °C and then quenched with saturated NH_4Cl. Workup involved extraction of the organic phase with Et_2O (3 × 15 mL). The combined extracts were dried over anhydrous $MgSO_4$ and concentrated in vacuo. Compounds were purified by flash column chromatography (10:1 hexanes:EtOAc).

Reaction of $(PhMe_2Si)(CH_3)Cu(CN)Li_2$ (2) with 1,2-Epoxyoctane. Methyl transfer product (nonan-3-ol): ^1H NMR ($CDCl_3$) δ 3.5 (m, 1 H, CHOH), 1.56-1.34 (m, 5 H, CH_2), 1.28 (m, 7 H, CH_2), 0.93 (t, J = 7.83 Hz, 3 H, CH_3), 0.87 (t, J = 6.96 Hz, 3 H, CH_3); ^{13}C NMR ($CDCl_3$) δ 73.23, 36.87, 31.74, 30.04, 29.28, 25.52, 22.50, 13.93, 9.72; GC/MS, *m/e* (rel intensity) 126 (M^+ - 18, 6.4), 115 (30.6), 97 (76.1), 69 (20.6), 59 (100.0); HRMS *m/e* (M - 18) calcd 126.2412, obsd 126.1412 (96% pure by GC). Phenyldimethylsilyl transfer product (1-(phenyldimethylsilyl)-octan-2-ol): ^1H NMR ($CDCl_3$) δ 7.58-7.32 (m, 5 H, Ar), 3.78 (m, 1 H, CHOH), 1.48-1.33 (m, 2 H, CH_2), 1.33-1.16 (m, 8 H, CH_2's), 1.16-1.02 (m, 2 H, CH_2), 0.88 (t, J = 8.00 Hz, 3 H, CH_3), 0.35 (s, 6 H, $SiCH_3$); ^{13}C NMR ($CDCl_3$) δ 139.33, 133.55, 128.92, 127.82, 69.91, 40.86, 31.79, 29.19, 25.76, 25.63, 22.56, 14.03, -2.26; GC/MS *m/e* (rel intensity) 262 (M^+ - 2, 9.9), 247 (63.5), 185 (59.3), 137 (100.0), 101 (16.5); HRMS *m/e* (M - 2) calcd 262.4663, obsd 262.1762 (98% pure by GC).

Reaction of $(PhMe_2Si)(CH_3)Cu(CN)Li_2$ (2) with 2-Methyl-2-(3-bromopropyl)-5,5-dimethyl-1,3-dioxane. Phenyldimethylsilyl transfer product (2-methyl-2-(3-(phenyldimethylsilyl)propyl)-5,5-dimethyl-1,3-dioxane): ^1H NMR ($CDCl_3$) δ 7.57-7.27 (m, 5 H, Ar), 3.52 (d, J_{gem} = 11.30 Hz, 2 H, ring CH_2), 3.41 (d, J_{gem} = 11.30 Hz, 2 H, ring CH_2), 1.72 (m, 2 H, CH_2), 1.47 (m, 2 H, CH_2), 1.33 (s, 3 H, CH_3), 0.99 (s, 3 H, CH_3), 0.90 (s, 3 H, CH_3), 0.78 (m, 2 H, CH_2), 0.28 (s, 6 H, $SiCH_3$); ^{13}C NMR ($CDCl_3$) δ 139.59, 133.54, 128.73, 127.69, 98.92, 70.30, 41.77, 29.93, 22.71, 20.45, 17.82, 16.10, -2.98; GC/MS *m/e* (rel intensity) 307 (M^+, 70.1), 229 (13.9), 143 (100.0), 129 (20.1), 105 (14.0); HRMS *m/e* (M^+) calcd 306.5193, obsd 306.2000 (90% pure by GC).

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Photochemistry of Benzophenone-Capped β-Cyclodextrin

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The photochemistry of $6^A,6^C$-(3,3'-benzophenonedisulfonyl)-β-cyclodextrin (1) is explored. Irradiation of 1 in H_2O or aqueous CH_3CN results in regioselective oxidation of a glucose C6 hydroxymethyl group, giving **2a** and **2b** via intramolecular H-abstraction by the excited benzophenone group. Molecular mechanics calculations suggest that the photooxidation occurs at the E and F glucose residues. In contrast, irradiation of 1 in aqueous *i*-PrOH gives rise to pinacol coupling products **3a-c**.

Introduction

Cyclodextrins (CDs) are well-known host molecules that find extensive use in complexation and catalysis studies.[1] Their well-defined cavities, small size, and ease of functionalization make them ideal enzyme models.[2] A number of interesting catalysts have been synthesized from CDs.[3] Cyclodextrins also have been used to modify photochemical reactions;[4] however, only a few photochemically active, derivatized CDs have been created. Among the photoreactive groups attached to CDs are benzophenone, rose bengal, and porphyrin moieties.[5-7] We have recently reported the photochemistry of several anthraquinone-substituted β-CDs[8] and found that they undergo facile intramolecular H-abstraction upon irradiation. On the other hand, Tabushi and co-workers report that benzophenone-capped β-CD is an effective triplet sensitizer in frozen solutions.[5] Since photoexcited benzophenone also

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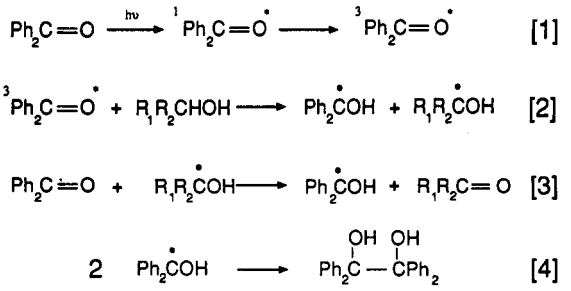
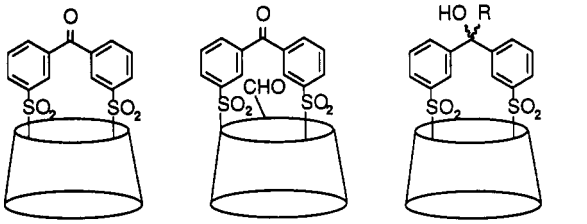
Scheme I



is known to abstract hydrogen, we decided to examine the photochemistry of benzophenone-derivatized β-CD in fluid solution. Although Tabushi used a *p,p'*-dicarboxyl linking group in his energy-transfer study, we opted to use the *m,m'*-disulfonylbenzophenone-capped β-CD (1) because it is readily synthesized in relatively large quantities. It also is produced as mainly one regioisomer: A,C.[9] The regioselectivity is good enough that 1 is often used as an intermediate in the production of other selectively substituted β-CDs.

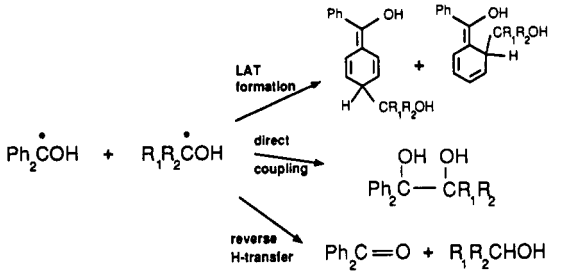


1 (A,C-capped) **2a,b** **3a,b,c** R=4a,b-H **4a,b** R=H

The photochemistry of benzophenone in alcohol solutions has been examined thoroughly. In fact, by 1900 Ciamician and Silber had established benzopinacol as the major product from photolysis in ethanol.[10] The basic mechanism for benzopinacol formation is shown in Scheme I.[11] The hydrogen atom exchange in [3] is driven by formation of a more stable radical, and it allows for quantum yields greater than unity for benzophenone consumption. Indeed, the quantum yield approaches two, its theoretical limit, when the photolysis is conducted with low intensity light and in the absence of oxygen.[12]

Other products became more pronounced under high intensity irradiation. Large light fluxes increase the steady-state concentration of the radical intermediates, and radical–radical reactions become more likely.[12] In particular, the two ketyl radicals couple both directly and at the ortho and para positions of the aromatic ring. The former reaction gives the cross-pinacol product, whereas the latter gives rise to light-absorbing transients (LATs, Scheme II).[12] Both LATs react in the presence of O_2; the ortho isomer reacts faster than the para isomer, and both produce benzophenone and the alkyl ketone. However, some of the para isomer can react without scission of the C–C bond, producing the para-substituted benzophenone.[13]

Scheme II



Both LATs are quenchers of triplet benzophenone. Also of interest are the reactions that do not occur with appreciable yield: coupling of the alkyl ketyl radicals and disproportionation of the two ketyl radicals, either to form benzhydrol or to regenerate benzophenone. On the other hand, the latter reverse H-transfer must occur to some extent in the geminate radical pair to explain the observed CIDNP effects.[14]

Experimental Section

Commercially available β-cyclodextrin (Amaizo) was dried under vacuum (0.05 mm, LN_2 trap) at 100 °C for 12 h. Pyridine was fractionally distilled; the fraction boiling between 114 and 115 °C was collected and stored over activated 4A molecular sieves. ^1H and ^{13}C NMR spectra were obtained with a GE QE-300 spectrometer. Typically, 20–30-mg samples were dissolved in DMSO-d_6 and treated with 2–3 drops of D_2O. UV/vis spectra were measured on a Beckman DU-70 spectrophotometer. TLC was carried out on 0.25-mm (60F-254) precoated silica plates (Baker); spot detection was done with UV and staining with vanillin (Fisher). Reverse-phase column chromatography was done with Baker RP-18 silica gel. High performance liquid chromatography was performed on a Waters 600E system equipped with a variable wavelength absorption detector set at 254 nm. The analysis of the product mixtures was carried out with a Whatman ODS-3 analytical column, using a linear gradient program (15 to 25% aqueous CH_3CN, 30 min). Relative mole % compositions were calculated from peak areas, using response factor adjustments. Reported retention times are the average of several chromatograms. Preparative HPLC was performed on a Waters 244 system equipped with a UV absorption detector (254 nm), using a Whatman Magnum 20 ODS column. Melting points were taken on a Thomas-Hoover capillary mp apparatus and are uncorrected. Irradiations were carried out with a Hanovia 450-W medium pressure lamp, using a uranium glass filter sleeve. Combustion analysis was performed by Desert Analytics, using a heated block technique. Percentage composition for elements other than C and H are adjusted by the mass loss on drying observed for the C and H determination.

Benzophenone-3,3'-disulfonyl Chloride.[15] Benzophenone (4.60 g, 25.2 mmol) was added in portions to freshly distilled chlorosulfonic acid (50 mL, 752 mmol). The solution was heated to 120 °C for 20 h under $CaCl_2$ drying. The solution was cooled and poured carefully into ice. The resulting solid was collected by filtration, washed with water, and dissolved in CH_2Cl_2 (75 mL). The solution was washed with saturated aqueous $NaHCO_3$, H_2O, and saturated aqueous NaCl. The organic phase was dried over Na_2SO_4 and concentrated in vacuo. The resulting solid was recrystallized once from hexane/CH_2Cl_2 to afford the disulfonyl chloride (2.67 g, 7.04 mmol, 28%), mp 140–141 °C: ^1H NMR ($CDCl_3$) δ 8.45 (br s, 2 H), 8.33 (br d, J = 7.7 Hz, 2 H), 8.17 (br d, J = 7.8 Hz, 2 H), 7.86 (dd, J = 7.7, 7.8 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 191.2, 145.1, 137.6, 135.8, 131.0, 130.6, 128.2; UV (CH_2Cl_2) λ (log ε) 344 nm (2.1).

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$6^A,6^C$-(Benzophenone-3,3′-disulfonyl)-β-cyclodextrin (1).[9] β-Cyclodextrin (3.82 g, 3.37 mmol) was added to pyridine (105 mL), and the mixture was sonicated until the β-cyclodextrin dissolved completely. The solution was heated under N_2, and pyridine (ca. 10 mL) was distilled to remove traces of H_2O. The solution was cooled to 60 °C, and benzophenone-3,3′-disulfonyl chloride (1.23 g, 3.24 mmol) was added slowly. The mixture was stirred until the solid dissolved completely, and then it was stirred at 60 °C for 1 h. The mixture was cooled, and the solution was decanted from viscous oligomeric precipitates. The pyridine was removed by vacuum distillation (0.2 mm, $T < 40$ °C). The residue was washed with acetone, filtered, and dried in vacuo overnight. The resulting solid (5.05 g) was divided into 3 portions and subjected to reverse-phase chromatography using a gradient elution (0 to 60% aqueous CH_3CN). Fractions containing the desired compound (R_f = 0.71, 5:4:3 *n*-BuOH/EtOH/H_2O) were concentrated in vacuo, affording the capped β-CD derivative (900 mg, 0.65 mmol, 20%). Final purification was accomplished through preparative HPLC using CH_3CN–H_2O gradient elution (20% to 29%). Approximately 33% of the injected material was recovered in this step, affording an overall yield of 7% HPLC-purified material: ^1H NMR (D_2O) δ 8.23 (d, J = 7.8 Hz, 2 H), 8.15 (d, J = 8.0 Hz, 1 H), 8.06 (d, J = 8.0 Hz, 1 H), 7.94 (s, 1 H), 7.90 (s, 1 H), 7.86 (dd, J = 7.8, 8.0 Hz, 1 H), 7.82 (dd, J = 7.8, 8.0 Hz, 1 H), 5.35 (d, J = 3.4 Hz, 1 H), 5.23 (d, J = 3.7 Hz, 1 H), 4.94 (d, J = 3.7 Hz, 1 H), 4.92 (d, J = 3.7 Hz, 1 H), 4.86 (d, J = 3.8 Hz, 1 H), 4.85 (d, J = 3.3 Hz, 1 H), and β-CD resonances; ^{13}C NMR (D_2O) δ 194.8, 137.7, 137.6, 136.3, 135.4, 135.2, 133.2, 133.1, 132.4, 132.1, 130.5, 130.2, 102.7, 102.4, 101.4, 101.1, 99.6, 81.8, 81.6, 81.3, 80.7, 79.5, 78.9, 78.8, 78.2, 78.1, 74.6, 74.1, 74.0, 73.8, 73.5, 73.0, 72.8, 72.7, 72.5, 72.3, 72.2, 71.6, 71.3, 70.1, 70.0, 69.9, 60.7, 60.8; UV (1:1 CH_3CN/H_2O) λ (log ε) 334 nm (2.1).

Photolysis of 1. In Aqueous CH_3CN. Compound 1 (102.4 mg, 71.1 mmol) was dissolved in H_2O and CH_3CN (5.0 mL each), and the solution was placed in a Pyrex tube and deaerated with N_2 for 10 min. A balloon filled with N_2 was attached to the tube, and the apparatus was placed in an ice bath, which was situated next to a Hanovia 450-W medium pressure mercury arc lamp in a uranium glass filter sleeve. Aluminum foil was placed around the immersion well, and an elliptical hole was cut out of the wrap. The solution was irradiated for 1.5 h; it was allowed to stand for 30 min, and then air was bubbled through the solution overnight. Analysis of the reaction mixture by HPLC showed the following composition (compound, t_R, relative mol %): **6**,[16] 2.3 min, 14%; **5**, 2.6 min, 1%; **3a**, 21.6 min, 2%; **3b**, 24.7 min, 8%; **3c**, 25.8 min, 18%; **2a** + **2b**, 29.6 min, 20%; **1**, 33.9 min, 37%. Compound 1 (2.5 mg, 1.8 mmol) was dissolved in H_2O/CH_3CN (1 mL each), and the solution was transferred to a 1-cm quartz UV cell and degassed with N_2 gas for 15 min. The solution was irradiated as above for 60 min. The reaction mixture was monitored by UV and HPLC. The behavior by HPLC was similar to that of the above reaction. UV monitoring gave the results shown in Figure 3.

Preparative Scale. In Aqueous CH_3CN. Crude 1 (1.32 g, 0.916 mmol) from reverse-phase chromatography was dissolved in CH_3CN and H_2O (250 mL each), and the flask was immersed in an ice bath and evacuated (0.05 Torr, 10 min). The solution was irradiated at 0 °C for 3.5 h and then left to stand in the dark for 1.5 h. The vacuum was broken, and the solution was stirred for 2 days. The solvent was removed in vacuo, and the remaining solid was subjected to HPLC, affording **1** (190 mg, 14%) and **2a** and **2b** (100 mg, 8%, **2a**/**2b** ca. 1:4). The proportion of **2a** and **2b** was estimated by peak areas in the HPLC chromatogram (17% aqueous CH_3CN, 1 mL/min, t_R = 35.8 and 38.1 min, respectively). **2b**: ^1H NMR (CD_3CN/D_2O) δ 9.65 (s, 0.2 H), 8.26 (m, 4 H), 8.14 (s, 1 H), 8.08 (s, 1 H), 7.93 (m, 2 H), and β-CD resonances; ^{13}C NMR (DMSO-d_6/D_2O) δ 193.2, 138.0, 137.7, 135.9, 135.8, 134.7, 134.6, 131.7, 131.1, 130.5, 130.2, 129.2, 129.1, 102.4, 102.3, 102.0, 101.9, 101.4, 87.6, 83.2, 82.0, 81.8, 81.5, 80.9, 80.5, 73.3, 73.2, 73.1, 73.0, 70.9, 69.1, 69.0, 68.3, 60.2, 60.0, 59.9, 59.8, 59.2; UV (H_2O) λ (log ε) 322 nm (2.0).

Anal. Calcd for $C_{55}H_{74}O_{40}S_2$: C, 45.90; H, 5.18; S, 4.45. Found: C, 45.89; H, 5.43; S, 4.44.

(16) The counterion is H^+ not K^+ for **5** and **6** in this case.

Preparative Scale. In H_2O. Crude 1 (870 mg, 0.60 mmol) from reverse-phase chromatography was dissolved in H_2O (300 mL), and the solution was irradiated as above for 5 h and stirred open to air for 3 days. HPLC provided 1 (92 mg, 11%) and **2a** and **2b** (29 mg, 3%, **2a**/**2b** ca. 9:1). **2a**: ^1H NMR (CD_3CN/D_2O) δ 9.62 (s, 0.1 H), 8.26 (m, 4 H), 8.13 (s, 1 H), 8.08 (s, 1 H), 7.93 (m, 2 H), and β-CD resonances; ^{13}C NMR (DMSO-d_6/D_2O) δ 193.2, 138.0, 137.7, 135.9, 135.8, 134.7, 134.6, 131.7, 130.5, 130.3, 129.2, 129.1, 128.1, 102.4, 102.3, 102.2, 102.1, 102.0, 101.9, 101.4, 87.6, 82.0, 81.9, 81.7, 81.5, 73.2, 72.8, 72.6, 72.5, 72.4, 72.1, 71.8, 71.0, 70.5, 70.3, 69.1, 69.0, 68.3, 60.1, 60.0, 59.9, 59.8, 59.5, 59.1; UV (H_2O) λ (log ε) 318 nm (2.1).

Anal. Calcd for $C_{55}H_{74}O_{40}S_2 \cdot H_2O$: C, 45.33; H, 5.25; S, 4.40. Found: C, 45.38; H, 5.36; S, 4.17.

Preparative Scale. In Aqueous *i*-PrOH. Pure 1 (214 mg, 0.148 mmol) from preparative HPLC was dissolved in *i*-PrOH (13 mL) and H_2O (9 mL), and the solution was deaerated with N_2, placed under a balloon filled with N_2, and irradiated as above for 2.5 hrs. The balloon was removed, air was bubbled into the solution for several min, and it was left to stand exposed to air for 3 days and then concd in vacuo. An analytical HPLC of the reaction mixture showed the following composition (compound, t_R, relative mol %): **6**, 2.3 min, 1%; **4a**, 21.3 min, 3%; **3a**, 21.6 min, 24%; **4b**, 22.4 min, 4%; **3b**, 24.7 min, 24%; **3c**, 25.8 min, 44%; **1**, 33.9 min, 1%. The residue was separated into 5 fractions by HPLC (gradient: 15 to 28% aqueous CH_3CN, 35 min) (compound, mass): **3a**, 18.4 mg; **4a**, 3.5 mg; **4b**, 4.5 mg; **3b**, 34.2 mg; **3c**, 60.6 mg (combined yield 57%). **3a**: ^1H NMR (1:1 CD_3CN/D_2O) δ 8.23 (d, J = 7.8 Hz, 2 H), 8.07 (br s, 2 H), 7.85 (d, J = 8.1 Hz, 2 H), 7.80 (d, J = 8.1 Hz, 2 H), 7.74 (d, J = 7.8 Hz, 2 H), 7.46–7.57 (m, 6 H); ^{13}C NMR (1:1 CD_3CN/D_2O) δ 146.0, 144.8, 136.3, 136.1, 135.6, 134.5, 130.0, 129.8, 129.0, 128.6, 128.1, 127.5, 103.2, 103.1, 102.9, 102.8, 102.0, 83.7, 82.2, 81.7, 81.4, 74.3, 74.2, 73.9, 73.2, 72.9, 72.4, 70.9, 70.4, 70.2, 69.3, 61.2, 60.8, 60.5; UV (H_2O) λ (log ε) 270 nm (3.6), 278 (3.6).

Anal. Calcd for $C_{110}H_{154}O_{80}S_4 \cdot 4H_2O$: C, 44.69; H, 5.52; S, 4.34. Found: C, 44.68; H, 5.60; S, 4.13.

3b: ^1H NMR (2:5 CD_3CN/D_2O) δ 8.24 (br s, 2 H), 7.75–7.81 (m, 8 H), 7.62 (d, J = 7.9 Hz, 2 H), 7.56 (dd, J = 8.0, 7.9 Hz, 2 H), 7.47 (dd, J = 7.9, 7.8 Hz, 2 H); ^{13}C NMR (2:5 CD_3CN/D_2O) δ 146.1, 145.6, 135.2, 134.5, 134.4, 130.2, 129.4, 129.2, 127.4, 127.3, 102.6, 102.1, 101.1, 83.5, 81.5, 81.2, 80.6, 73.9, 73.8, 73.6, 73.1, 72.7, 72.5, 72.3, 71.9, 70.7, 70.3, 70.1, 69.4, 60.8, 60.6, 60.5, 60.4, 59.9; UV (H_2O) λ (log ε) 270 nm (3.6), 278 (3.6).

Anal. Calcd for $C_{110}H_{154}O_{80}S_4 \cdot 3H_2O$: C, 44.96; H, 5.49; S, 4.36. Found: C, 45.27; H, 5.65; S, 3.81.

3c: ^1H NMR (1:1 CD_3CN/D_2O) δ 8.24 (d, J = 8.0 Hz, 2 H), 8.07 (br s, 2 H), 7.72–7.86 (m, 6 H), 7.46–7.57 (m, 6 H), and β-CD resonances; ^{13}C NMR (5:2 D_2O/CD_3CN) δ 145.6, 145.5, 145.4, 145.3, 145.2, 144.6, 135.1, 135.0, 134.9, 134.8, 134.4, 134.2, 133.2, 130.3, 129.9, 129.7, 129.4, 129.3, 129.2, 129.1, 129.0, 127.5, 127.3, 126.9, 126.8, 102.6, 102.4, 102.3, 102.2, 102.0, 101.5, 101.4, 101.3, 101.0, 83.4, 83.3, 81.5, 81.4, 81.3, 81.2, 81.1, 74.0, 73.8, 73.7, 73.6, 73.5, 73.4, 72.7, 72.6, 72.3, 72.1, 72.0, 70.8, 70.7, 70.6, 70.5, 70.4, 70.1, 69.6, 69.5, 69.4, 69.1, 60.7, 60.6, 60.5, 60.3, 60.2; UV (H_2O) λ (log ε) 270 nm (3.6), 278 (3.6).

Anal. Calcd for $C_{110}H_{154}S_4 \cdot 10H_2O$: C, 43.11; H, 5.72; S, 4.18. Found: C, 42.94; H, 5.34; S, 3.91.

$NaBH_4$ Reduction of 2a and 2b. The mixture of **2a** and **2b** from irradiation in CH_3CN/H_2O (5.0 mg) was treated with 1% aqueous $NaBH_4$ (2 mL), and the solution was analyzed by HPLC (17% aqueous CH_3CN, 1 mL/min). Two peaks at 20.7 and 21.1 min were observed. The same peaks are produced when the above reaction is carried out on 1, and they are ascribed to the two isomeric benzhydrol β-CD derivatives **4a** and **4b**.

Benzophenone-3,3′-disulfonic Acid Dipotassium Salt (5). Benzophenone-3,3′-disulfonyl chloride (1.00 g, 2.6 mmol) and KOH (0.46 g, 8.2 mmol) were combined with EtOH (50 mL). The mixture was heated to boiling, and it turned opaque after several minutes. Water was added dropwise until the solution cleared. The mixture was allowed to cool to room temperature, and then it was refrigerated for 5 days. The resulting solid was collected by filtration to afford the disulfonic acid dipotassium salt (0.94 g, 2.2 mmol, 85%): ^1H NMR (CD_3CN/D_2O) δ 8.15 (br s, 2 H), 8.07 (d, J = 7.8 Hz, 2 H), 7.89 (d, J = 7.7 Hz, 2 H), 7.67 (dd, J = 7.8, 7.8 Hz, 2 H); ^{13}C NMR (CD_3CN/D_2O) δ 197.9, 144.4, 137.5,

Table I. Lowest Energy Conformers of 1

structure	rel energy[a]	dihedral angles along cap					
		C5–C6	C6–O	O–SO_2	SO_2–O	O–C6	C6–C5
1A	0.0	164	−84	87	−174	174	71
1B	3.8	52	73	177	169	73	−81
1C	5.2	157	−60	−157	180	178	64
1d	5.5	177	−78	−75	−179	−178	65

[a] Kcal/mol.

133.2, 130.8, 130.0, 127.3; UV (H_2O) λ (log ε) 254 nm (4.2), 320 nm (sh, 2.2).

Anal. Calcd for $C_{13}H_8O_7S_2K_2$: C, 37.31; H, 1.93; S, 15.32; K, 18.68. Found: C, 37.62; H, 1.91; S, 14.78; K, 20.86.[17]

1,2-Dihydroxyethane-1,2-diylidene-1,1,2,2-tetrakis(benzene-3-sulfonic acid potassium salt) (6). Benzophenonedisulfonic acid dipotassium salt (0.50 g, 1.2 mmol) was dissolved in *i*-PrOH and H_2O (30 mL each). The solution was deaerated with N_2 for 15 min, placed under a balloon filled with N_2, and irradiated as above for 2 h. The solution was dried in vacuo, and the resulting solid was recrystallized from EtOH (11 mL) and H_2O (6 mL) to afford the pinacol (0.36 g, 0.43 mmol, 72%); ^1H NMR (CD_3CN/D_2O) δ 7.78 (br s, 4 H), 7.60 (br d, J = 7.7 Hz, 4 H), 7.51 (br d, J = 7.8 Hz, 4 H), 7.29 (dd, J = 7.8, 7.7 Hz, 4 H); ^{13}C NMR (CD_3CN/D_2O) δ 146.4, 144.0, 132.3, 128.6, 127.3, 125.4, 84.3; UV (H_2O) λ (log ε) 268 nm (3.4), 275 nm (3.3).

Anal. Calcd for $C_{26}H_{18}O_{14}S_4K_4 \cdot 1H_2O$: C, 36.44; H, 2.35; S, 14.96; K, 18.64. Found: C, 36.58; H, 2.75; S, 14.78; K, 19.49.[17]

Calculations. Molecular modeling was carried out with use of Alchemy II (Tripos Associates) and PCMODEL (Serena Software). Molecular mechanics calculations were performed with MMX (Serena Software) as described previously.[8]

Results

Benzophenone-capped β-CD 1 was synthesized according to the procedure of Tabushi and co-workers.[9] It was purified by liquid chromatography followed by HPLC. Although the crude product from liquid chromatography could be used in some preparative photochemical reactions, most of the photolyses required HPLC-purified material in order to obtain reasonable mass balances and well-defined reaction products. Since the photolysis of 1 shows solvent dependency (vide infra), it is relevant that the NMR spectra of 1 are also solvent dependent. For example, its ^{13}C NMR spectra in D_2O shows all seven C4 resonances of glucose, whereas in DMSO-d_6 only four C4 resonances are distinct. The separation of all seven C1–H doublets in the ^1H NMR spectrum in D_2O is more dramatic. The solvent effects most likely result from different average solution conformations. In particular, the hydrophobic effect may force the benzophenone group within the CD cavity.

Molecular mechanics calculations were employed to probe the ground-state conformational energy surface of 1. Although these calculations cannot deal well with solvation effects, strain considerations should largely determine the conformations of 1 because the benzophenone group is anchored to the CD at two points, making it part of a ring structure. Since 1 possesses many atoms, its conformations could be mapped only through trial and error. Initial structures were created by changing the torsional angles about the C5–C6, C6–O, and O–SO_2 bonds of the benzophenone cap. A total of 63 structures were created and minimized. The four best structures are shown in Figure 1, and their torsional angles and relative enthalpies are given in Table I. Three of these (**1A**, **1C**, and **1D**) are related to each other by a rotation about the O–SO_2 bond nearest the A glucose ring; whereas **1B** must be altered by rotations about at least three bonds to interconvert with the others. The gross structural feature common to **1A**, **1C**, and **1D** is that one benzene ring is "included" in the CD cavity. As a result, the carbonyl group is directed toward and is in close proximity to the E and F glucose rings. It is reasonable to believe that this self-solvation is present and may be even exaggerated in water solution, and it would be consistent with the distinction in chemical shifts observed for the anomeric hydrogens and the C4 glucose carbons.

Table II. Comparison of ^{13}C NMR Resonances of the Pinacol Products

pinacol	aromatic resonances						C–OH
6[a]	148.2	145.9	134.1	130.5	129.1	127.2	86.2
3a[a,c]	146.0	144.8	135.6	129.9	128.8	127.8	83.7
3b[b,c]	146.1	145.6	134.8	130.2	129.3	127.4	83.5
3c[b,c]	145.4	144.6	134.2	130.2	129.2	127.2	83.4

[a] In 1:1 D_2O/CD_3CN. [b] In 5:2 D_2O/CD_3CN. [c] Average chemical shifts values are reported.

The photochemistry of 1 was examined and found to be solvent dependent. In aqueous *i*-PrOH, irradiation results in the formation of several products that have much shorter retention times by HPLC than 1. The three major products (**3a–c**) have been assigned as isomeric pinacol products of 1, whereas the two very minor products (**4a,b**) are the isomeric benzhydrol derivatives of 1. The first assignment is based largely upon the ^{13}C NMR spectra (Table II) through comparison with that of a suitable model compound: the pinacol of benzophenone-*m,m'*-disulfonate (**6**). Both **6** and the major photoproducts show two sets of aromatic resonances around 145 ppm, whereas 1 does not show any resonance greater than 140 ppm. More critical is the presence of pinacol carbon resonances around 84 ppm in both **6** and **3a–c** and the absence of carbonyl resonances. Unexpected evidence for the pinacol structure came from attempts to record the ^{13}C NMR spectrum of **3c** in DMSO-d_6. Under these mild conditions, **3c** decomposed cleanly to 1 and **4a** and **4b**, even though it is stable in aqueous acetonitrile. The cleavage of a pinacol into its corresponding carbonyl and alcohol has been documented, but the reaction usually proceeds under strongly basic conditions.[18] The benzophenone carbonyl has an endo and exo face, so three pinacol products are possible (Figure 2): the endo-endo, exo-exo, and endo-exo coupled isomers. The major pinacol product, **3c**, must be the endo-exo isomer since it would show two pinacol resonances, whereas the symmetrical endo-endo and exo-exo isomers would show only one resonance for these atoms.

(17) Percent compositions for K are high even after repeated recrystallization.

(18) Cohen, S. G.; Ramsay, G. C.; Stein, N. M.; Weinstein, S. Y. *J. Am. Chem. Soc.* **1974**, *96*, 5124–5130.

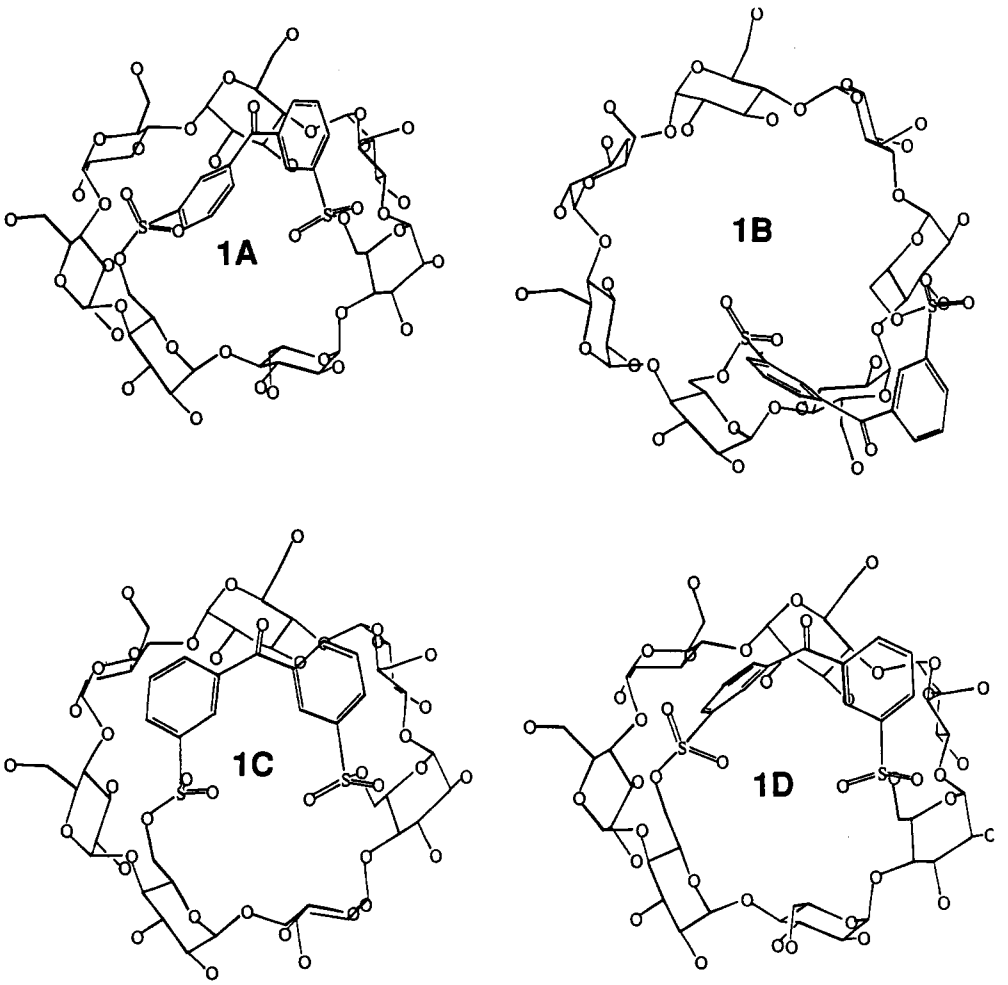


Figure 1. Lowest energy conformers of 1.

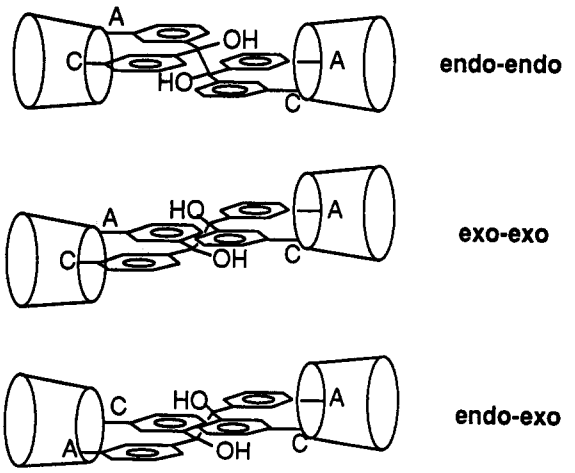


Figure 2. Possible pinacol products.

The pinacol isomers are formed in essentially a statistical distribution.

In water or aqueous acetonitrile solution, irradiation results in two major monomeric products, **2a** and **2b**; however, most of the mass balance consists of a complex mixture of pinacols including **6** and **3a–c**. Photoproducts **2a** and **2b** were determined to be regioisomeric C6-oxidized derivatives of 1 based on the following evidence. Borohydride reduction of the photoproducts gives the same binary mixture as does reduction of 1. Since borohydride should only reduce the carbonyl group in 1, the reduced mixture is assigned as the isomeric benzhydrol-capped β-CDs **4a** and **4b**. The photoproducts still possess a benzophenone group according to ^{13}C NMR (Table III), so they must contain at least one more oxidation site than 1. The carbon spectrum of both also reveals a resonance at 87.6 ppm which is not present in 1. An attached proton test (gated broad-band decoupling) indicates that this carbon bears 1 (or 3) H atom(s). The chemical shift is consistent with a saturated carbonyl derivative, either a hydrate or hemiacetal; therefore, the carbonyl group must be an aldehyde. The ^1H NMR spectra confirm the fractional (<25% in aldehyde form) presence of a mixture of aldehydes (ca. 9.6 ppm) in the ratio indicated by HPLC. An aldehyde can only result from oxidation of a C6-glucose carbon in β-CD. The regioisomer ratio depends dramatically on the solvent. In water **2b** is formed almost exclusively (9:1 ratio), whereas in aqueous acetonitrile **2a** dominates (4:1 ratio).

The photochemistry is dependent on the oxygen concentration. When air is present during the irradiation, compounds **2a** and **2b** are formed immediately, probably from the reaction of O_2 with the ketyl radicals. But if air is excluded, the products take several days of exposure to air to form fully. Also under these conditions, 1 reappears on the same time scale as the products **2**. Following the reaction by UV/vis spectrophotometry reveals that LATs are formed under anaerobic conditions (Figure 3). These LATs disappear over the same time scale as for the for-

Table III. Comparison of the ^{13}C NMR Resonances of the Benzophenone Derivatives

compd	C=O	aromatic resonances					
5[a]	197.9	144.4	137.5	133.2	130.8	130.0	127.3
1[b,d]	193.1	137.9	135.8	134.6	131.5	130.4	129.1
2a[c-e]	193.2	137.8	135.8	134.6	131.7	130.4	128.8
2b[c-e]	193.2	137.8	135.8	134.6	131.4	130.4	129.2

[a] In 1:1 D_2O/CD_3CN. [b] In DMSO-d_6. [c] In DMSO-d_6/D_2O (2 drops). [d] Average chemical shift values are reported. [e] An additional acetal resonance at 87.6 ppm is also observed.

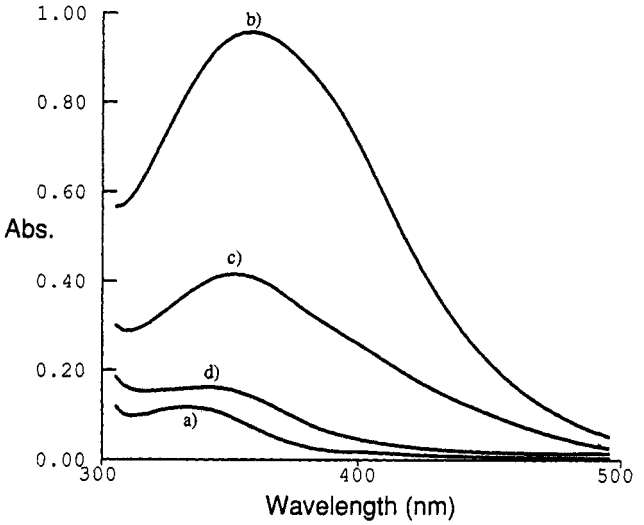


Figure 3. UV/vis monitoring of the photolysis of 1: (a) before irradiation, (b) after irradiation for 1 h, (c) after standing for 1 h, (d) after standing for 1 day.

mation of 1 and 2. Preparative photolysis was carried out under anaerobic conditions in order to limit the extent of oxidation.

Molecular mechanics calculations were used to compare transition-state enthalpies for intramolecular H-abstractions involving the benzophenone group and various remote C6-methylene groups. The enthalpy portion of the free energy should be critical because the entropy should be similar for the various transition states. Most of the low-energy, ground-state conformations that place the carbonyl oxygen close to an abstractable H-atom were used to create initial transition-state structures. As in our previous work, we examined the effect of the "solvent" dielectric constant and the torsional force constant that enforces the in-plane H-abstraction (V2 term).[8] The lowest energy H-abstraction transition states are reported in Table IV. The results show that abstraction is most favorable at the E and F glucose residues. Abstraction at the B and G rings is particularly unfavorable, whereas abstraction at the D glucose is not as unfavorable. Comparing these data with the experimental results suggests that the photoproducts **2a** and **2b** are oxidized at the E and F positions, but the exact assignment is still uncertain. The calculations fail to show the dramatic change in regioisomer ratio observed in water vs aqueous acetonitrile, although the last line of Table IV does show a reversal in preference when a distance-dependent dielectric and a smaller V2 term is used.

Discussion

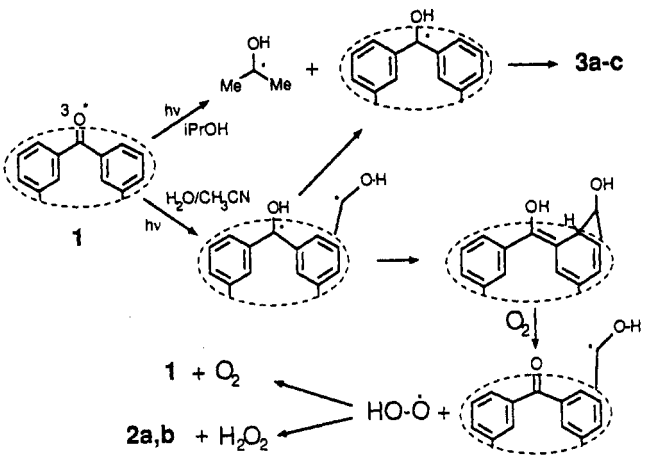
The photochemistry of 1 can be explained in terms of the basic mechanism for irradiation of benzophenone in

Table IV. Transition-State Enthalpy Differences (kcal/mol) for H-Abstraction at Various Glucose Residues

dielectric constant	V2 term	glucose residue				
		B[a]	D[b]	E[c]	F[d]	G[d]
59	7.5	25.7	10.8	4.4	0	21.9
1.5	7.5	25.6	11.4	4.3	0	21.0
−1	7.5	26.3	12.6	5.7	0	20.4
59	2.7	25.0	6.6	0.9	0	23.0
1.5	2.7	26.9	7.7	2.0	0	19.5
−1	2.7	24.5	5.1	0	0.1	23.6

[a] The initial structure was created from 1B. [b] Created from a conformation 8.6 kcal/mol higher than 1A. [c] From 1D. [d] From 1A.

Scheme III



alcohol solution (Scheme III). Irradiation of 1 ultimately produces the excited triplet state of the benzophenone moiety. The carbonyl oxygen then abstracts a hydrogen atom. In aqueous 2-propanol solution the 2-propanol serves as the hydrogen source, whereas in aqueous acetonitrile the CD is the hydrogen donor. Pinacol isomers form from coupling of the benzophenone ketyl radicals. In aqueous 2-propanol the pinacol coupling gives **3a–c** in good yield; however, in aqueous acetonitrile, pinacol coupling is neither as efficient nor as clean since many regioisomeric pinacols with a remote glucose C6 aldehyde group are possible. Obviously, ketyl radicals are able to encounter each other in spite of the fact that the β-CD structures can encapsulate the ketyls and otherwise obstruct the coupling. The formation of the C6 oxidation products, **2a** and **2b**, from aqueous acetonitrile requires an involved explanation but raises interesting mechanistic questions. The abstraction of the H-atom from the CD is likely to be intramolecular rather than intermolecular. Molecular mechanics calculations show that the lowest energy conformations place the benzophenone carbonyl oxygen close to several transannular C6 hydrogens. The principle of least motion suggests that abstraction of these hydrogens is favored. Transition-state calculations point to the E and F glucose rings as the reaction sites. In this analysis the relative reaction rates of various conformers are compared, so the ramifications of the Curtin–Hammett principle must be considered.[19] The differences in transition-state enthalpies should predict the product distribution if conformational interconversion is fast with respect to H-abstraction. However, since 1 has a relatively rigid structure, the reverse probably is true, in which case the product

(19) Seeman, J. I. *Chem. Rev.* **1983**, *83*, 83–134.

distribution is under "ground-state control" (i.e., the product ratio derives from the ground-state distribution of reactive conformations).[20] Fortunately, this problem is moot since the lowest transition-state enthalpies derive from the lowest energy ground-state conformers; specifically, **1A** leads to abstraction from the F residue and **1D** leads to abstraction from the E residue. Supporting the idea that the photochemistry is under ground-state control is the observation that the benzophenone moiety dissociates from the β-CD portion to a much larger extent in aqueous CH_3CN than in aqueous *i*-PrOH. In the latter solution most all conformers should be close to a 2-propanol molecule, whereas in the former solution those conformers that are not close to a C6 methylene may rid themselves of their excitation energy through bond cleavage.

The mechanism leading from the diradical to **2a** and **2b** is unclear. The fact that **1** and **2** appear as the LATs disappear suggests that **1** and **2** are formed from an LAT. Other precursors of **1** and **2** can be postulated, but their existence is not consistent with experimental results. Long-lived radicals are unlikely because the benzophenone ketyl portions would undergo coupling to pinacols, which are stable under the reaction conditions. Direct coupling of the radicals giving the cross-pinacol product is another possibility, but this *vic*-diol should not decompose in the presence of O_2 nor would it give rise to an LAT. Intermolecular coupling to form an LAT (C6-ketyl/benzophenone ketyl) seems unlikely because the process encounters too much steric encumbrance and violates the principle of least motion. We assign the intermediate as the ortho-coupled isomer instead of the para isomer because the atoms that would bond together are too distant in the latter case and because the *p*-LAT should give some para-coupled product.[12] The *o*-LAT should be favored since the in-plane H-abstraction places the hydroxymethyl radical very close to an ortho position. *o*-LATs do not lead to coupled products, rather, they suffer C–C bond scission, regenerating the benzophenone.[13] This intermediate can explain the formation of both **1** and **2**: O_2-induced scission results in formation of the benzophenone and an alkyl ketyl radical. The latter can lose or gain an H-atom, resulting in **2** or **1**, respectively.

(20) Wagner, P. J. *Acc. Chem. Res.* **1983**, *16*, 461-467.

Conclusions

Attachment of a benzophenone group to β-CD does not alter the typical benzophenone photochemical pathways. Pinacol formation is efficient when **1** is irradiated in aqueous *i*-PrOH. Without a good H-atom source, the benzophenone abstracts a hydrogen atom from across the β-CD from either the E or F glucose methylene leading to the C6-oxidized products **2** and to a complex mixture of pinacols. Light-absorbing transients (LATs), possibly the intramolecular, ortho-coupled isomers, are observed under anaerobic conditions. They decompose slowly in the presence of air to give **2** and to regenerate **1**.

Acknowledgment is made to the Thomas F. and Kate Miller Jeffress Memorial Trust for the support of this research.

Registry No. **1**, 76700-69-1; **2a**, 133322-44-8; **2b**, 133294-74-3; **3a**, 133322-45-9; **3b**, 133398-17-1; **3c**, 133398-18-2; **4a**, 133294-75-4; **4b**, 133397-41-8; **5**, 82125-70-0; **6**, 133294-76-5; β-CD, 7585-39-9; benzophenone-3,3′-disulfonyl chloride, 17619-15-7; benzophenone, 119-61-9.

Oxidation of Bis(*tert*-butylthio) Selenide at Low Temperatures: Search for a Bis(alkylthio) Selenoxide[1a]

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Oxidation of bis(*tert*-butylthio) selenide, *t*-BuSSeSBu-*t* (**1a**), by peracetic acid at −40 °C leads to a monooxidation product (**1a**-O) whose ^1H (two singlets) and ^{13}C NMR spectra (four resonances) show that the two *tert*-butyl groups in **1a**-O are magnetically nonequivalent. It cannot therefore be the bis(alkylthio) selenoxide, *t*-BuSSe(O)SBu-*t* (**3a**), and is either *t*-BuS(O)SeSBu-*t*, **5a** (oxidation of **1a** at S rather than Se), or *t*-BuSSeOSBu-*t*, **4a** (formed by rapid isomerization of initially formed **3a**). The fact that δ ^{77}Se for **1a**-O is 289 ppm downfield from δ ^{77}Se for **1a** is inconsistent with structure **5a** and indicates that **1a**-O has structure **4a**, *t*-BuSSeOSBu-*t*. Reaction of *t*-BuSH with **1a**-O gives **1a** plus *t*-BuSOH, in accord with what would be expected for nucleophilic attack of the thiol on the selenium of **4a**. While oxidation of **1a** by peracid is thought to result initially in **3a**, this thioselenoxide apparently isomerizes to **4a** so rapidly, even at −40 °C, that **4a** is the first oxidation product detectable by NMR. These results are of significance with regard to several steps in the previously proposed (ref 4) mechanism (Scheme I) for the formation of bis(alkylthio) selenides from the reaction of thiols with selenite.

The reaction of selenite with the thiol groups in cysteine residues, glutathione, or coenzyme A to form bis(alkylthio) selenides, RSSeSR (**1**), is known[2,3] to be an important pathway by which inorganic selenium is initially incorporated into living systems. Ganther[2a] established that the usual combining ratio of thiol to selenite was 4:1 and proposed that the stoichiometry of the reaction was as shown in eq 1.

$$4RSH + H_2SeO_3 \rightarrow \underset{\mathbf{1}}{RSSeSR} + RSSR + 3H_2O \quad (1)$$

0022-3263/91/1956-3520$02.50/0