3b: IR 1740 (s), 1585 (w) cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 7.45 (m, 2 H), 7.31 (m, 3 H), 5.31 (m, 2.5 H), 4.99 (m, 0.5 H), 4.79 (s, 2 H), 4.72 (AB, J = 12 Hz), 4.11 (m, 1 H), 3.8–3.5 (m), 3.68 (s), 3.64 (s) [9 H, overall], 3.39 (s, 3 H), 2.15 (s, 3 H), 2.05 (s), 1.98 (s), [3 H, overall], 2.2–1.2 (m, 14 H), 1.13 (d, J = 6 Hz, 3 H). Anal. Calcd for $C_{31}H_{48}O_8S_2$: 612.2791. Found: 612.2791.

4(*R*),1′(*R*),2′(*S*),4′(*S*),6′(*S*)-Methyl 4-Acetoxy-4-(2-(6-hydroxy-1-(*E*)-heptenyl)-4-[(methoxyethoxy)methoxy]cyclopentyl)-2-(phenylsulfinyl)butanoate. NCS (93 mg, 0.70 mmol) and AgNO$_3$ (119 mg, 0.70 mmol) in 0.5 mL of 5:1 v/v acetonitrile–water was added to 106 mg (0.173 mmol) of **3b** in 0.25 mL of 5:1 v/v acetonitrile–water using an additional 0.25 mL of solvent to aid transfer. The mixture (immediate silver chloride precipitate on mixing) was stirred at room temperature for 1.3 h. Saturated aqueous solutions of sodium sulfite, sodium carbonate, and sodium chloride (0.2 mL each) were added successively. The mixture was stirred vigorously with 3 × 10 mL of 1:1 hexane/methylene chloride with decantation of the organic layer each time. The organic layer was then dried (Na$_2$SO$_4$) and concentrated. Flash chromatography (4:1 ethyl acetate/hexane) gave 121 mg of an oil, obviously contaminated by succinimide. The mixture was dissolved in 25 mL of 1:1 hexane/methylene chloride, washed with 2 × 5 mL of water, dried (Na$_2$SO$_4$), and concentrated to give 74 mg (75%) of a clear oil: IR (neat) 3700–3200 (m), 2930 (s), 1740 (s), 1450 (m), 1375 (m), 1245 (s), 1050 (s) cm^{-1}; partial ^{1}H NMR (CDCl$_3$) δ 7.5 (m, 5 H), 5.46–5.02 (m, 2.4 H), 4.93 (m, 0.6 H), 4.68 (s, 2 H), 4.09 (m, 1 H), 3.84–3.42 (m), 3.56 (s), 3.47 (s) [9 H, overall], 3.38 (s, 3 H), 1.97 (s), 1.80 (s), 1.16 (d), 1.15 (d). Anal. Calcd for $C_{29}H_{44}O_9S$: C, 61.24; H, 7.80. Found: C, 61.34; H, 7.88.

4(*R*),1′(*R*),2′(*S*),4′(*S*),6′(*S*)-Methyl 4-Acetoxy-4-(2-(6-hydroxy-1-(*E*)-heptenyl)-4-[(methoxyethoxy)methoxy]cyclopentenyl)-2-(*E*)-butenoate, 2c, and 7-MEM-secobrefeldinoic Acid, 2d. The above sulfoxide (65 mg, 0.11 mmol) and 3.25 mL of BSA were heated in 13.5 mL of dry toluene at 80 °C for 4.5 h. The solution was evaporated to a yellow solid which was dissolved in 3 mL of methanol. Silica gel was added and the mixture stirred for 1 h. Flash chromatography (3:2 ethyl acetate/hexane) gave 37 mg (73% yield) of **2c** and 9 mg of its silyl ether. The latter was dissolved in 1 mL of ether and stirred with 1 mL of 1 N aqueous sulfuric acid for 0.5 h. The ether layer was dried (MgSO$_4$) and concentrated. Preparative layer chromatography gave an additional 4 mg (total yield 81%) of **2c**: $[\alpha]^{22}_D$ −6.44°; IR (neat) 3600–3200 (m), 2920 (s), 1740 (s), 1725 (s), 1710 (m); ^{1}H NMR (CDCl$_3$) (partial) δ 6.83 (dd, J = 15, 6 Hz, 1 H), 5.87 (d, J = 15 Hz, 1 H), 5.5–5.1 (m, 3 H), 4.68 (s, 2 H), 4.15 (m, 1 H), 3.73 (s), 3.87–3.47 (m), [overall, 9 H], 3.39 (s, 3 H), 2.10 (s, 3 h), 1.09 (d, J = 7 Hz, 3 H). Anal. Calcd for $C_{23}H_{38}O_8$: C, 62.42; H, 8.66. Found: C, 61.91; H, 8.55. The diester **2c** (5.60 mg, 0.0013 mmol) was dissolved in 0.15 N LiOH in 0.30 mL (0.045 mmol) of a 3:1 methanol/water solution of 0.15 N lithium hydroxide at room temperature. After stirring 16 h, 30 mg (0.2 mmol) of sodium bisulfate in 0.5 mL of water was added. The solution was extracted with 4 × 2 mL of ethyl acetate and the combined extract was washed with 3 mL of brine, dried (MgSO$_4$), and concentrated to 4.84 mg (99% yield) of **2d** as a clear oil: partial ^{1}H NMR (CDCl$_3$) 7.05 (dd, J = 16, 5 Hz, 1 H), 6.04 (d, J = 16 Hz, 1 H), 5.2–5.5 (m, 3 H), 4.80 (s, 3.4 H), 3.40 (s, 6 Hz), 1.2 (d, J = 7 Hz).

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Communications to the Editor

Microheterogeneous Photooxidation

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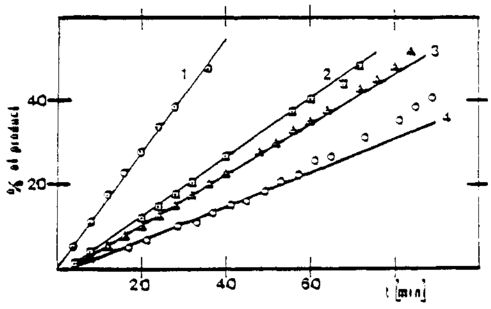
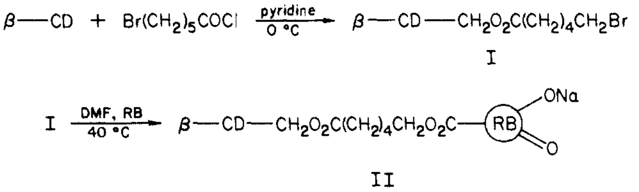
Singlet oxygen lifetimes vary from 1 μs in water to several hundred microseconds in halocarbon solvents. This work demonstrates that one can enhance the reactivity of an acceptor or quencher of singlet oxygen by covalently bonding a sensitizer to a ligand which complexes the acceptor.[†] We call this effect a microheterogeneous photochemical effect, for the reagents are prevented from being freely dispersed in fluid solution by the ligand and the covalent bonding of the ligand to the sensitizer, respectively.[6] Microheterogeneous effects in photosensitized processes enhance the observed reactivity of an excited state with an acceptor by increasing the effective local concentration of the acceptor.



1. RB (2.9 x 10^{-4} m)
2. RB (2.9 x 10^{-4} m) + β-cyclodextrin (2.9 x 10^{-4} m) + β-carotene (9.0 x 10^{-6} m)
3. II (RB = 2.9 x 10^{-4} m) + β-carotene
4 II (RB = 2.9 x 10^{-4} m) + β-carotene (9.0 x 10^{-6} m)
- 1,2-dipnenyl-p-dioxene added directly before photooxidation

Figure 1. Photooxidation of 1,2-diphenyl-*p*-dioxene (4.0 × 10^{-3} M) in EtOH.

Scheme I



To illustrate the principle, we modified rose bengal[7] through its tethering to β-cyclodextrin. This has been made possible by the work of Lamberts and Neckers,[8-10] who showed that the C-2′

[†] The key role of distance in electron transfer has been studied between porphyrins and quinones as photosynthetic models. See ref 2–5 and citations therein.

(1) Technical and Agricultural University, Department of Chemistry and Chemical Engineering, Bydgoszcz, Poland.

(2) Clayton, R. K. "The Photosynthetic Bacteria"; Clayton, R. K., Sistrom, W. R., Eds.; Plenum Press: New York, 1978; pp 387–396.

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(6) See, for example: Scott, H., Ed. *Chromatogr. Sci.* **1984**, *27*. Herbert Scott, Ed., Dekker, 1984.

(7) The chemistry of rose bengal has been reviewed. See: Paczkowski, J.; Lamberts, J. J. M.; Paczkowska, B; Neckers, D. C. *Free Radicals in Biology and Medicine*, in press.

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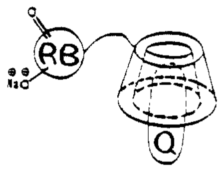
Scheme II



carboxylate of rose bengal was the more nucleophilic of the two anionic sites in the molecule and that it could be selectively functionalized (Scheme I).[11]

Two experiments were carried out. In the first, the rate of photooxidation of 1,2-diphenyl-*p*-dioxene using II was measured in the presence and in the absence of β-carotene[12] (Figure 1). II shows enhanced efficiency of singlet oxygen quenching by β-carotene when compared with the solution containing rose bengal and β-cyclodextrin as independent, dissolved entities. The results indicate that since β-carotene has a very high rate of singlet oxygen quenching in fluid solution (3.0×10^{10} M^{-1} s^{-1} in benzene),[13,14] the singlet oxygen source is closer to the quencher than it would be in fluid solution, and Forster effects of distance take over. Though singlet oxygen quenching occurs by the exchange mechanism, microheterogeneous organization causes a higher local concentration of β-carotene. The probability of collision between donor and acceptor is thus higher than it would be in solution and physical quenching is enhanced by the proximate quenchers, Scheme II.

The concentration of β-carotene used in our experiments was much smaller than the concentration of the sensitizer employed to form singlet oxygen. Even when all β-carotenes in solution are complexed by the β-cyclodextrin cavities, however, some intermolecular quenching also must occur. Thus, the observed photopromixity effect is that of the sum of both the intra- and intermolecular quenching processes. An artifically enhanced local concentration of β-carotene quenches singlet oxygen from sensitizer II as it is formed. That singlet oxygen that escapes is quenched by the β-carotene complexed in a neighboring cyclodextrin cavity.

To test whether 1,2-diphenyl-*p*-dioxene is also captured by II as an inclusion complex, all reagents were added to the solvent immediately save 1,2-diphenyl-*p*-dioxene, which was added just before measurement of the oxidation rate, Figure 1, line 4. The rate of quenching by β-carotene is much greater than in the case when both the physical quencher and the chemical trap are allowed to compete for the carbohydrate's hydrophobic cavity. When no competition is allowed, the maximum concentration of β-carotene is complexed by the cavity by preequilibration and the quenching effect is the greatest. In other words, the microheterogeneous photocatalytic effect is maximized. Importantly with II, quenching by β-carotene decreases with reaction time. Thus the product of photooxidation of 1,2-diphenyl-*p*-dioxene is more easily accommodated in the hydrophobic cavity of the carbohydrate than is 1,2-diphenyl-*p*-dioxene itself; and the dibenzoate displaces some of the β-carotene in the inclusion complex's center cavity as its concentration builds up during the course of the reaction.

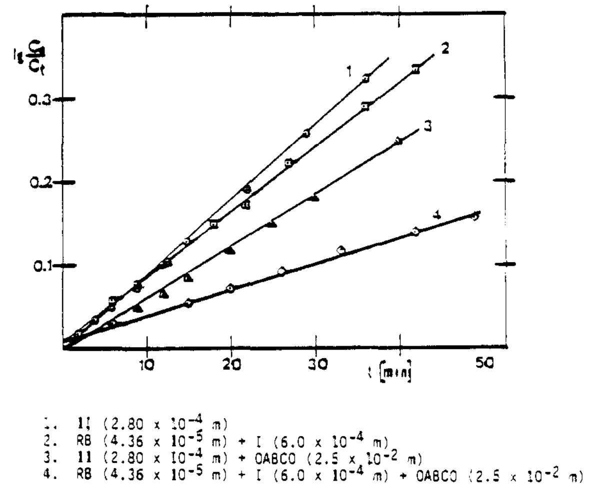


Figure 2. First-order photooxidation of anthracene (3.51×10^{-6} M) in water.

The difference between the rate of oxidation of anthracene by II and the rate of oxidation of anthracene by rose bengal in the presence of β-cyclodextrin in water presents a more favorable situation for the acceptor molecule as the inclusion complex than in solution. The difference in oxidation rates is not large, since anthracene reacts slowly with singlet oxygen. In the presence of a water soluble physical quencher, the difference between the rate of sensitizer oxidation using the immobilized sensitizer II and the dissolved sensitizer/cyclodextrin pair becomes significant. This is shown by the effect of DABCO (1,4-diazobicyclo[2.2.0]octane) (Figure 2) on the photooxidation of anthracene sensitized by II. DABCO dramatically decreases the rate of oxidation of anthracene in the control using rose bengal and free β-cyclodextrin, but it has much less effect in the case of II. II organizes the reluctant water insoluble acceptor, anthracene, into a much enhanced concentration at the source of the singlet oxygen. In fluid solution the water soluble physical quencher reacts with singlet oxygen more frequently. It is clear that the organization of the anthracene into the proximity of the sensitizer is very important, and thermal diffusion of the excited molecule to the physical quencher is slower than is that process enhanced by the affinity effect.

These experiments suggest that chemical organization in a photochemical system must have a significant effect on the rate of a photosensitized process. The implications in biochemical systems such as those of photosynthesis and the possibility of enhancing the reactivity in photochemical processes with the substrates of enzymes by similar effects are suggested and are under active investigation.†

Acknowledgment. This work has been supported by the National Science Foundation, Division of Materials Research (DMR 8404001). We are grateful for this financial support. Many helpful discussions with Professor J. C. Dalton and with Dr. Peter Gottschalk are also acknowledged.

Registry No. II, 99377-23-8; DABCO, 280-57-9; RB, 11121-48-5; β-CD, 7585-39-9; 1,2-diphenyl-*p*-dioxene, 4344-45-0; β-carotene, 7235-40-7; anthracene, 120-12-7; oxygen, 7782-44-7.

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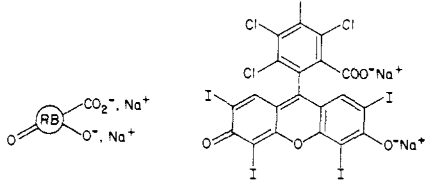
(11) β-Cyclodextrin (5.65 mmol) was dissolved in 75 mL of dry pyridine. To an ice cold water bath containing the cyclodextrin/pyridine solution, 3.2 g (15 mmol) of 6-bromohexanoyl chloride was added. The reaction mixture was stirred and after 4 h the modified cyclodextrin was precipitated with acetone. It was next reprecipitated twice from a DMF–H_2O (3:1) solution with acetone. I (3.95 g) was dissolved in 50 mL of DMF and rose bengal (2.16 g, 2 mmol) was added. The mixture was stirred for 20 h at 70 °C after which the red product was precipitated with acetone and reprecipitated twice from a DMF/water solution (3:1) with acetone. The product was dried in a vacuum. The rose bengal nucleus is abbreviated.



(12) A solution of β-carotene (9.0×10^{-6} M), 24.5 mg of II, and 23.8 mg of 1,2-diphenyl-*p*-dioxene (4.0×10^{-3} M) in 25 mL of ethanol was allowed to equilibrate for 48 h, and the rate of oxidation of the chemical quencher was measured. The results were compared with control systems in which (1) rose bengal, disodium salt (2.9×10^{-4} M), and 1,2-diphenyl-*p*-dioxene (4.0×10^{-3} M), (2) rose bengal, disodium salt (2.9×10^{-4} M), 1,2-diphenyl-*p*-dioxene (4.0×10^{-3} m), and β-carotene (9.0×10^{-6} m), and (3) rose bengal (2.9×10^{-4} M), 1,2-diphenyl-*p*-dioxene (4.0×10^{-3} m), β-cyclodextrin (2.9×10^{-4} M), and β-carotene (9.0×10^{-6} M) were employed under identical experimental conditions.

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