

Photooxidation of *N,N'*-Diacylindigo Dyes

Bradley D. Smith,* David E. Alonso,*[†] Jeffrey T. Bien, Elise C. Metzler, Maoyu Shang, and John M. Roosenberg, II[†]

Department of Chemistry and Biochemistry, University of Notre Dame, Notre Dame, Indiana 46556, and Department of Chemistry, Andrews University, Berrien Springs, Michigan 49104

Received August 19, 1994[⊗]

Irradiation of *N,N'*-diacylindigo dyes in the presence of oxygen resulted in an unusual oxygen insertion/acyl transfer reaction. While this process occurred over many weeks at room temperature, at 100 °C it was complete in a few hours. In some cases the yield of photooxidized product was virtually quantitative. The product structures were proved by spectroscopic methods and in one example by X-ray analysis. A series of mechanistic experiments led to the conclusion that at least the oxygen insertion part of the photooxidation process proceeded via a radical mechanism. The evidence included the following observations: (1) When the photooxidation was conducted in toluene, large amounts of benzyl hydroperoxide were produced; (2) the photooxidation could be achieved in the dark with a radical initiator; (3) attempts to generate the photooxidized product using singlet oxygen chemistry failed. The postulated radical mechanism is described.

We have recently reported on the structure and photochemistry of *N,N'*-diacylindigo dyes, **1**.¹ In the absence of oxygen three photochemical reactions are known to occur: photochromic cis/trans isomerization (path A in Scheme 1),² photoreduction (path B),³ and photochemical [1,3] alkyl migration (path C).^{1c} We now describe the photochemistry observed in the presence of oxygen, namely, a remarkable oxygen insertion/acyl transfer process (path D).

As shown in Scheme 2, the photooxidation reaction (path D) occurred with *N,N'*-diacylindigo derivatives containing alkyl or aryl side chains. Starting compounds **1a–f** were prepared from indigo and the appropriate acid chloride by known methods.⁴ Upon photooxidation their solutions became colorless. ¹H NMR and EI mass spectral patterns of the major product isolated from each reaction indicated they were analogous. In each case the product showed a parent peak in the EI mass spectra 16 mass units higher than the respective starting material. In addition, an abundant fragment at *m/z* = 278 was observed for the products with alkyl side chains. Fortunately, product **5a** was obtained as single crystals suitable for analysis by X-ray diffraction. Its structure is shown in Figure 1.⁵ By analogy, the structures of the other products were assigned as **5b,c**, and the ion at *m/z* = 278 was assigned as the fragment **6**.

Typically, the photooxidations were achieved using the following reaction conditions. Solutions of compounds

1a–f in toluene were heated to reflux and irradiated with light selective for the trans absorption band ($\lambda > 530$ nm). Every few hours the solutions were saturated with oxygen gas and for the remaining time they were left exposed to the atmosphere. After 12–36 h the solvent was evaporated and the product purified by preparative TLC and/or recrystallization. The virtually quantitative yields for products **5a** and **5b** are notable. Similar conversions were observed in refluxing benzene solutions, but the reaction times were longer. Remarkably, the photooxidations could be achieved with solutions simply left standing on a laboratory window ledge and exposed to the atmosphere. Under these conditions the reaction took many weeks; nonetheless, the yields were only slightly lower than those indicated in Scheme 2. In the case of product **5c** these conditions were the preparative conditions of choice, as the compound decomposed at elevated temperatures.

Previous studies by other groups on the photofading of indigo and *N,N'*-dimethylindigo have identified isatin and *N*-methylisatin as the respective major products.⁶ A dye-sensitized singlet oxygen mechanism has been proposed with a dioxetane intermediate. In contrast, our studies with *N,N'*-diacylindigo compounds have produced no evidence for isatin products. Moreover, the following observations suggest that at least the oxygen insertion part of the photooxidation process proceeds via a radical mechanism.

1. When the photooxidation was conducted in toluene, large amounts of benzyl hydroperoxide were generally obtained. The identity of this side-product was confirmed by comparison of its NMR, IR, and mass spectra with that of authentic material.⁷ Control experiments showed that both the dye and light were necessary for benzyl hydroperoxide production.

2. A dark, oxygen-saturated solution of **1a**, and AIBN (1 mol equiv) in refluxing benzene, produced significant

[†] Andrews University.

[⊗] Abstract published in *Advance ACS Abstracts*, November 15, 1994.

(1) (a) Smith, B. D.; Paugam, M. -F.; Haller, K. J. *J. Chem. Soc., Perkin Trans. 2* **1993**, 165–169. (b) Smith, B. D.; Haller, K. J.; Shang, M. *J. Org. Chem.* **1993**, *58*, 6905–6908. (c) Smith, B. D.; Alonso, D. E.; Bien, J. T.; Zielinski, J.; Smith, S. L.; Haller, K. J. *J. Org. Chem.* **1993**, *58*, 6493–6396.

(2) Ross, D. L.; Blanc, J. In *Photochromism*; Brown, G., Ed.; Wiley: New York, 1971; Chapter 5.

(3) Ci, X.; Whitten, D. G. In *Photoinduced Electron Transfer*; Fox, M. A., Chanon, M., Eds.; Elsevier: Amsterdam, 1988; Chapter 4.9 and references therein.

(4) Setsune, J.; Wakemoto, H.; Matsueda, T.; Tajima, H.; Kitao, T.; Ishihara, S.; Yamamoto, R.; *J. Chem. Soc. Perkin Trans. 1* **1984**, 2305–2309.

(5) The author has deposited atomic coordinates for this structure with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

(6) (a) Kuramoto, N.; Kitao, T. *J. Soc. Dyers Colour.* **1979**, *95*, 257–261. (b) Miehe, G.; Süssle, P.; Kupeik, V.; Egert, E.; Nieger, M.; Kunz, G.; Gerke, R.; Knieriem, B.; Niemeier, M.; Lüttke, W. *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 964–967.

(7) Cookson, P. G.; Davies, A. G.; Roberts, B. P. *J. Chem. Soc., Chem. Commun.* **1976**, 1022–1023.

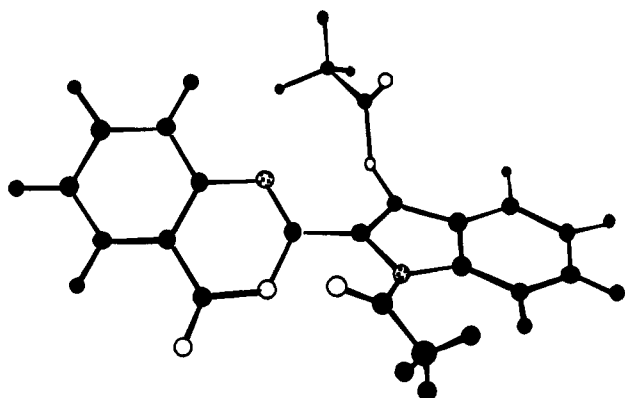
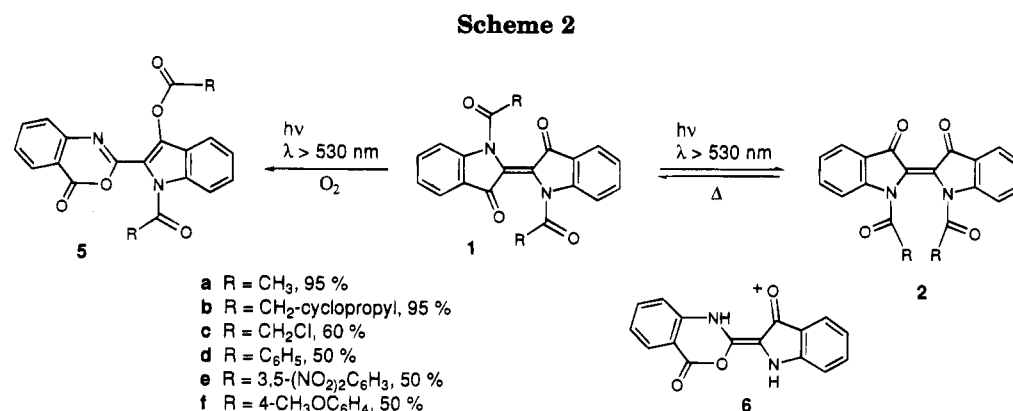
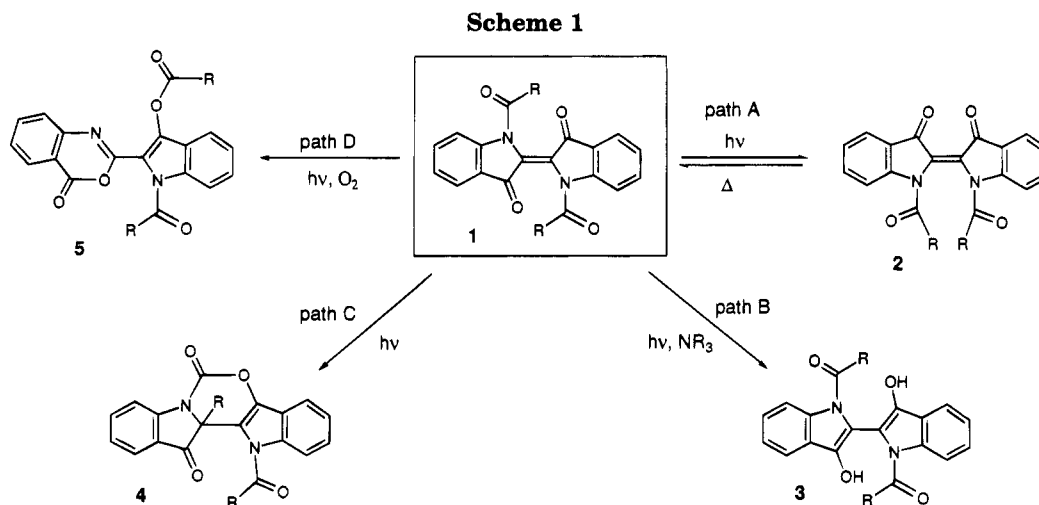


Figure 1. Ball and stick representation of the X-ray structure of **5a**.

amounts of oxygenated product **5a**. In the absence of AIBN no reaction occurred.

3. Attempts to detect the presence of singlet oxygen using classical chemical trapping compounds such as 2,5-dimethylfuran,⁶ 1,3-cyclohexadiene,⁸ and 1,3-diphenylisobenzofuran⁹ all failed. In addition, a previous qualitative study on the photofading of a *N,N'*-diacylindigo derivative reported that the use of photosensitizing dyes to generate singlet oxygen had no effect on the rate of photofading.¹⁰

All these observations can be accommodated by the following mechanistic picture. Irradiation of a toluene

solution of *N,N'*-diacylindigo, **1**, results in photochromic trans to cis isomerization ($\phi_{t-c} = 0.10$).¹¹ The cis isomer, **2**, is thermally unstable and slowly reverts back to **1**. In the presence of oxygen, the oxygenation/acyl transfer mechanism shown in Scheme 3 is postulated as a competing process ($\phi_{ox} \sim 0.01$).¹² Upon photoexcitation, triplet **1** reacts with ground state triplet oxygen to form a peroxy biradical, **7**, which is trapped as the peroxide radical, **8** (the group R' in **8** could be hydrogen, a second molecule of **1**, or benzyl). Fission of the peroxy bond results in diradical **9** or possibly its isomeric epoxide **10**. (Attempts to generate **10** independently by treatment of **1** with dimethyl dioxirane failed to produce **10** or **5**). Subsequent rearrangement of **9** (or **10**) gives the O-inserted diradical **11** which undergoes an N to O acyl transfer via **12** (a similar intermediate to that proposed for the alkyl migration, path C^{1c}) to provide **5** as the surprisingly stable final product. Alternatively, the final rearrangement (**10** to **5**) could occur as a polar transformation.

Why indigo and *N,N'*-dimethylindigo react with oxygen to form a dioxetane, whereas *N,N'*-diacylindigo compounds undergo oxygen insertion, is an interesting question. A rationalization based on steric differences seems unlikely because the molecular structures of *N,N'*-dimethylindigo and **1** are very similar.^{1b,6b} In terms of the mechanism in Scheme 3, a plausible argument based on

(11) Blanc, J.; Ross, D. L. *J. Phys. Chem.* **1973**, *77*, 831–2823.

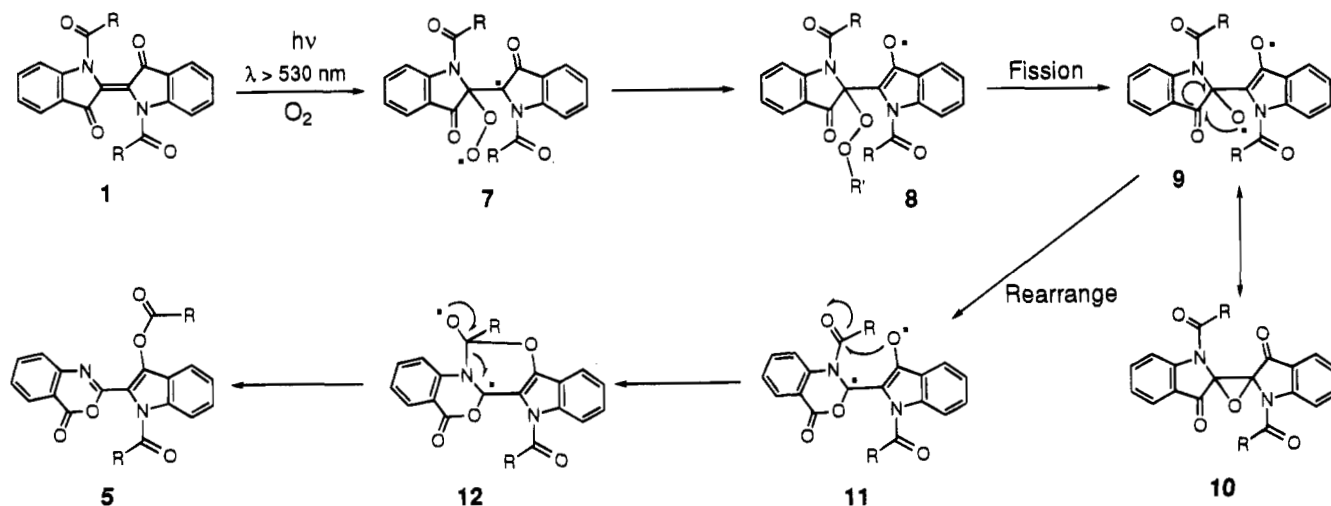
(12) The photooxidation process in Scheme 3 is a bimolecular reaction, thus ϕ_{ox} is dependent on oxygen concentration. The value of $\phi_{ox} \sim 0.01$ is estimated for a reaction performed under the representative conditions described in the Experimental Section, where the refluxing aromatic solvent is saturated with oxygen gas at atmospheric pressure.

(8) Kaneko, C.; Sugimoto, A.; Tanaka, S. *Synthesis* **1974**, 876–877.

(9) Akasaka, T.; Nakagawa, M.; Ando, W. *J. Org. Chem.* **1986**, *51*, 4477–4479.

(10) Fukishi, K.; Shigenawa, Y.; Kuwabara, M.; Yamanaka, H.; Nomura, M. *Chem. Express* **1987**, *6*, 325–328.

Scheme 3



substituent effects on diradical **7** can be developed. The *N*-acyl group in **7** stabilizes the adjacent carbon-centered radical well enough that bimolecular trapping of the peroxy-centered radical is the observed pathway. In the case of NCH_3 or NH groups, the analogous carbon centered radical is less stabilized, and intramolecular closure to form a dioxetane is sufficiently enhanced to become the favored pathway.

Experimental Section

General Methods. All solvents were purchased as reagent grade and were used without further purification. Flash chromatography was conducted with silica gel (60–200 mesh) as the solid support and preparative TLC with 20×20 cm plates of silica gel (500 μ M thickness). NMR spectra were acquired on General Electric GN 300 MHz and Varian VXR 500 MHz instruments. Coupling constants (J) are quoted in hertz and are ± 0.3 Hz. Visible spectra were recorded on a Hewlett Packard 8452A diode array spectrophotometer. Infrared spectra were recorded on a Nicolet Magna 550 FT-IR spectrophotometer.

***N,N'*-Diacylindigo Derivatives 1a,c,d.** These compounds were prepared during a previous study.^{1c}

***N,N'*-Bis(cyclopropylacetyl)indigo (1b)** was prepared by following the procedure of Setsune.⁴ Indigo was reduced to leucoindigo and then acylated with cyclopropylacetyl chloride (prepared by treating cyclopropylacetic acid with thionyl chloride). The resulting *O,O'*-diacylated derivative was converted to the desired product **1b** by treatment with DDQ. The product was purified by preparative TLC (eluent, 1:3 ethyl acetate/hexanes): $R_f = 0.74$; mp = 180–182 °C (not corrected); 1H NMR ($CDCl_3$) 8.26 (2H, br d, $J = 7.5$), 7.76 (2H, d, $J = 7.5$), 7.66 (2H, m), 7.26 (2H, t, $J = 7.5$), 2.74 (4H, br s), 1.15 (2H, m), 0.57 (4H, d, $J = 8.0$), 0.17 (4H, br d, $J = 4.0$) ppm; ^{13}C NMR ($CDCl_3$) 184.1, 173.0, 149.4, 136.9, 125.8, 125.0, 124.3, 121.8, 117.0, 41.1, 7.6, 4.3 ppm; MS (EI) m/z 426 (M), 360, 344, 289, 278, 262; UV (benzene) $\lambda_{max} = 568$ nm.

***N,N'*-Bis(3,5-dinitrobenzoyl)indigo (1e)** was prepared by the method of Omote.¹³

***N,N'*-Bis(4-methoxybenzoyl)indigo (1f)** was prepared by the method of Görner.¹⁴

Irradiation Experiments. The following is a representative procedure. A refluxing solution of the appropriate *N,N'*-diacylindigo **1a–f** in toluene (10 mL, 1 mM) was irradiated with a Xe 150 W arc lamp equipped with a housing unit to

collimate the beam and an Oriel 51272 filter to allow $\lambda > 530$ nm. Oxygen was bubbled into the solution prior to heating and 2–3 additional times throughout the reaction. The top of the reflux condenser was left open to the atmosphere. When TLC indicated consumption of the starting material (12–36 h), the solvent was evaporated and the extent of conversion to the major rearranged product determined by 1H NMR. The major product was then isolated by preparative TLC to give in each case:

5a (95% conversion): Recrystallized from hexane/methylene chloride. TLC (eluent, 1:8 ethyl acetate/hexanes): $R_f = 0.4$; 1H NMR ($CDCl_3$) 8.25 (1H, d, $J = 8.4$), 8.10 (1H, d, $J = 8.4$), 7.86 (1H, t, $J = 8.4$), 7.65 (1H, d, $J = 8.4$), 7.55 (2H, m), 7.36 (2H, m), 2.65 (3H, s), 2.45 (3H, s); MS (EI) m/z 362 (M), 278. Crystal data: $C_{20}H_{14}N_2O_5$, $M = 362.34$, triclinic $P1$ (No. 2), $a = 8.274(2)$, $b = 9.123(2)$, $c = 12.341(2)$ Å, $\alpha = 98.56(1)^\circ$, $\beta = 90.44(1)^\circ$, $\gamma = 108.67(1)^\circ$, $V = 871.2(5)$ Å³, $Z = 2$, $D_c = 1.381$ g/cm³ (293 K), $\mu(Mo K\alpha) = 0.944$ cm⁻¹, $R_{merge}(I) = 0.019$, 3054 unique reflections, 2461 with $F_o^2 > 3\sigma(F_o)^2$, coordinates of all hydrogen atoms refined, $R_1 = 0.034$, $R_2 = 0.056$, gof = 1.57.

5b (95% conversion): TLC (eluent, 1:6 ethyl acetate/hexanes): $R_f = 0.7$; 1H NMR ($CDCl_3$) 8.23 (1H, dd, $J = 8.0, 1.5$), 7.98 (1H, d, $J = 8.5$), 7.83 (1H, ddd, $J = 8.0, 7.7, 1.5$), 7.61 (1H, dd, $J = 8.0, 0.5$), 7.55 (1H, ddd, $J = 8.0, 7.5, 1.0$), 7.50 (1H, ddd, $J = 8.0, 7.0, 1.0$), 7.33 (1H, t, $J = 7.5$), 7.25–7.26 (1H, m), 2.83 (2H, d, $J = 6.5$), 2.68 (2H, d, $J = 7.0$), 1.15–1.19 (1H, m), 1.22–1.31 (1H, m), 0.65 (2H, ddd, $J = 8.0, 6.0, 4.5$), 0.53 (2H, ddd, $J = 8.0, 5.0, 5.0$), 0.33 (2H, q, $J = 5.0$), 0.133 (2H, q, $J = 5.0$) ppm; MS (FAB) m/z 443 (M + 1), 391, 307, 278; HRMS (FAB) calcd for $C_{26}H_{22}O_5N_2$ (M + 1) 443.1607, found 443.1602.

5c: The photooxygenated product was obtained at room temperature in the presence of laboratory light over 2 months. Oxygen was periodically bubbled into the solution (60% conversion). TLC (eluent, 1:3 ethyl acetate/hexanes): $R_f = 0.6$; 1H NMR ($CDCl_3$) 8.24 (1H, d, $J = 8.4$), 8.04 (1H, d, $J = 8.4$), 7.87 (1H, t, $J = 8.4$), 7.60 (3H, m), 7.39 (2H, m), 4.65 (2H, s), 4.63 (2H, s) ppm; MS (FAB) m/z 431 (M + 1), 355, 278; HRMS (FAB) calcd for $C_{20}H_{12}O_5N_2Cl_2$ (M + 1) 431.0202, found 431.0204.

5d (50% conversion): TLC (eluent, 1:4 ethyl acetate/hexanes): $R_f = 0.5$; 1H NMR ($CDCl_3$) 8.29 (2H, d, $J = 9.0$), 7.94 (1H, d, $J = 9.0$), 7.85 (2H, d, $J = 9.0$), 7.80 (4H, m), 7.64 (2H, t, $J = 9.0$), 7.55 (2H, t, $J = 9.0$), 7.46 (2H, d, $J = 9.0$), 7.42 (2H, d, $J = 9.0$), 7.23 (1H, d, $J = 9.0$) ppm; MS (CI) 487 (M + 1); HRMS (EI) calcd for $C_{30}H_{18}N_2O_5$ 486.1216, found 486.1175.

5e (50% conversion): TLC (eluent, 1:3 ethyl acetate/hexanes): $R_f = 0.6$; 1H NMR ($CDCl_3$) 9.46 (2H, d, $J = 2.1$), 9.39 (1H, t, $J = 2.1$), 9.05 (1H, t, $J = 2.1$), 8.88 (2H, d, $J = 2.1$), 7.96 (1H, d, $J = 8.4$), 7.77 (1H, d, $J = 8.4$), 7.66 (2H, m), 7.49 (1H, t, $J = 8.4$), 7.41 (2H, m), 7.18 (1H, d, $J = 8.4$) ppm; MS (FAB) m/z 667 (M + 1).

5f (50% conversion): TLC (eluent, 1:3 ethyl acetate/hex-

(13) Omote, Y.; Tomotake, A.; Aoyama, H.; Nishio, T.; Kashima, C. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 470–472.

(14) Görner, H.; Pouliquen, J.; Wintgens, V.; Toscano, V.; Jaafar, B. B.; Tripathi, S.; Kossanyi, J.; Valat, P. *Can. J. Chem.* **1984**, *62*, 2478–2486.

anes): $R_f = 0.6$; $^1\text{H NMR}$ (CDCl_3) 8.28 (2H, d, $J = 8.7$), 8.01 (1H, d, $J = 8.1$), 7.81 (2H, d, $J = 8.7$), 7.71 (1H, t, $J = 8.1$), 7.63 (2H, m), 7.41 (2H, m), 7.32 (1H, t, $J = 8.1$), 7.18 (1H, d, $J = 8.1$), 7.04 (2H, d, $J = 8.7$), 6.85 (2H, d, $J = 8.7$), 3.93 (3H, s), 3.76 (3H, s) ppm; HRMS (EI) m/z calcd for $\text{C}_{32}\text{H}_{22}\text{N}_2\text{O}_7$ 546.1427, found 546.1440.

Benzyl hydroperoxide⁷(isolated from photooxygenation product mixtures): $^1\text{H NMR}$ (CDCl_3) 7.39 (5H, m), 5.01 (2H, s) ppm; IR (neat) 3385, 3109, 3091, 3064, 3032, 2923, 2879, 1696, 1545, 1496, 1454, 1344, 746, 731, 697 cm^{-1} ; MS (EI) m/z 124 (M), 119, 105, 91, 77, 51.

Acknowledgment. B.D.S. acknowledges the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research. D.E.A. was an ACS-PRF Summer Faculty Fellow.

Supplementary Material Available: $^1\text{H NMR}$ spectra of **1b** and **5a-f**; all spectra of benzyl hydroperoxide (9 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.