J. Org. Chem. 1986, 51, 4477-4479

Anal. Calcd for $C_{25}H_{43}NO$: C, 80.36; H, 11.60; N, 3.75. Found: C, 80.13; H, 11.18; N, 3.94.

The more polar compound *cis*-**12** (0.093 g, 27% yield) was also obtained as a colorless oil: MS (IC), *m/z* 374 (MH^+); ^1H NMR ($CDCl_3$, 400 MHz) δ 0.87 (t, J = 6.5 Hz, 3 H, CH_3), 1.13 (d, J = 6 Hz, 3 H, CH_3), 1.1–1.7 (m, 26 H, piperidine and side chain CH_2), 2.75 (dq, J = 9, 6 Hz, 1 H, H-2), 3.16 (m, 1 H, H-6), 3.72 (dd, J = 6, 10 Hz, 1 H, H-8a), 3.85 (dd, J = 7, 10 Hz, 1 H, H-8b), 3.98 (dd, J = 6, 7 Hz, 1 H, H-9), 7.35 (m, 5 H, Ar); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 14.1 (CH_3), 16.0, 20.9 (CH_3), 22.8, 27.9, 28.4, 29.5, 29.7, 30.0, 30.7, 32.0, 33.8 (piperidine and side chain CH_2), 47.8 (C-2), 56.7 (C-6), 62.3 (C-8), 66.3 (C-9), 127.5, 128.4, 128.5, 140.8 (Ar). Anal. Calcd for $C_{25}H_{43}NO$: C, 80.36; H, 11.60; N, 3.75. Found: C, 80.37; H, 11.59; N, 4.16.

(2*S*,6*S*)-(+)-Solenopsin A (1). A solution of alcohol **11** (0.115 g, 0.3 mmol) in methanol (15 mL) was hydrogenated over 5% Pd/C at atmospheric pressure for 15 h. The reaction mixture was then filtered through a Celite bed and the filtrate concentrated after addition of a few drops of concentrated HCl. The resultant white residue was then dissolved in water (10–15 mL) and extracted with ether to remove phenylethanol. The aqueous solution was then made alkaline with sodium carbonate and extracted with CH_2Cl_2. The combined CH_2Cl_2 layers were dried over Na_2SO_4 and concentrated to give a colorless oil.

The crude product was purified by filtration through a short column of silica gel [CH_2Cl_2–MeOH (95/5)]. By collection and acidification of the appropriate column fractions (+)-solenopsin A (**1**) was isolated as its HCl salt (0.072 g, colorless crystals, 81% yield): **1**·HCl: mp 146 °C (CH_2Cl_2–ether) (lit. mp 114 °C[8]); $[\alpha]^{20}{}_D$ +7.5° ($CHCl_3$, *c* 1.3), $[\alpha]^{20}{}_D$ −1° (MeOH, *c* 1.7). The ^1H and ^{13}C NMR spectra for **1** were identical with those reported in the literature.[8]

Registry No. **1**, 35285-25-7; **1**·HCl, 104713-87-3; **4**, 88056-92-2; **5**, 104713-83-9; **6** (isomer 1), 104713-84-0; **6** (isomer 2), 104713-88-4; **8** (isomer 1), 104642-00-4; **8** (isomer 2), 104713-85-1; **10**, 104642-01-5; **11**, 104642-02-6; **12**, 104713-86-2; $C_{11}H_{23}Br$, 693-67-4.

---

[8] Moriyama, Y.; Doan-Huynh, D.; Monneret, C.; Khuong-Huu, Q. *Tetrahedron Lett.* **1977**, 825.

Quenching of Singlet Oxygen by 4-[2-(*N*,*N*-Dimethylhydrazono)ethylidene]-2,6-diphenyl-4*H*-pyran

Takeshi Akasaka, Masaru Nakagawa, and Wataru Ando*

Department of Chemistry, University of Tsukuba, Sakura-mura, Ibaraki 305, Japan

Received April 25, 1986

It is well-known that singlet oxygen is an active oxygen species and it may be involved in photodegradation of cells by pigments, light, and oxygen in biological systems.[1] Efficient quenchers of $^1O_2$[2] might, therefore, have practical importance. Carotenes,[3] the most efficient quenchers, show protective action against photobleaching of chlorophyll *a* but are not very stable to oxidation. Several tertiary aliphatic amines are capable of inhibiting oxidations by $^1O_2$[4] and DABCO (1,4-diazabicyclo[2.2.2]octane)[5] is often used as convenient quencher in photosensitized oxygenations, but the quenching rates appear to be somewhat lower than with other quenchers. Recently, we found that 1,3,5-triaryl-2-pyrazolines with relatively low oxidation potential are not oxidized by $^1O_2$ but capable of quenching $^1O_2$ efficiently.[6] We now wish to report a novel $^1O_2$ quencher, 4-[2-(*N*,*N*-dimethylhydrazono)ethylidene]-2,6-diphenyl-4*H*-pyran (**1**, first oxidation potential; E_p(anodic) = +0.24 V and E_p(cathodic) = +0.13 V vs. SCE, reversible), which quenches $^1O_2$ efficiently. In preliminary quenching experiments, dye-sensitized photooxidation of 6.3 × 10^{-2} M of diethyl sulfide (k_r = 7 × 10^6 M^{-1} s^{-1} [7]) (rose bengal (RB)/CH_3COCH_3, tetraphenylporphine (TPP)/C_6H_6, and methylene blue (MB)/CH_2Cl_2) was carried out in the presence of 6.3 × 10^{-3} M of pyran **1** and their results obtained are shown in Figure 1.

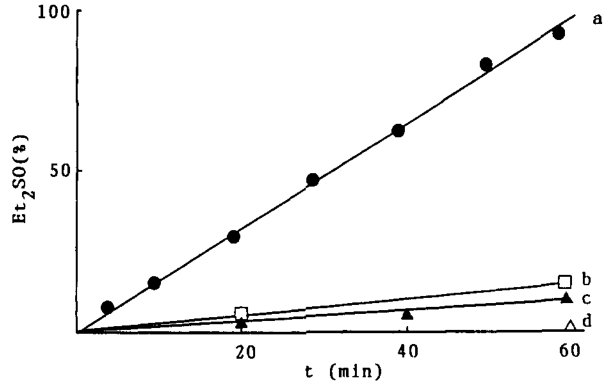
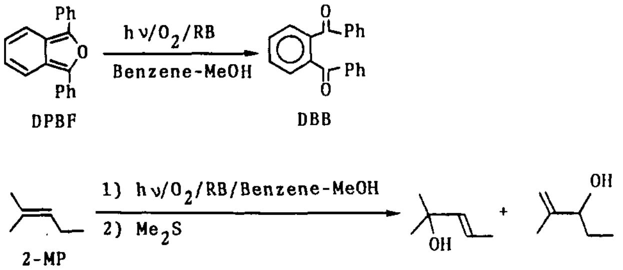
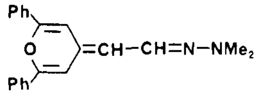


Figure 1. Photosensitized oxygenation of diethyl sulfide in the presence of **1**. Conditions: [Et_2S] = 6.3 × 10^{-2} M; [**1**] = 6.3 × 10^{-3} M; (a) MB/CH_2Cl_2; (b) **1**/RB/CH_3COCH_3; (c) **1**/TPP/C_6H_6; (d) **1**/MB/CH_2Cl_2.

Scheme I





1

The data indicate that the formation of diethyl sulfoxide was apparently suppressed by addition of pyran **1**. These findings encouraged us to carry out an exploratory quenching experiment of $^1O_2$. The quenching efficiency of pyran **1** was determined by measuring the inhibition rate for the oxidation of 1,3-diphenylisobenzofuran (DPBF)[8]

---

[1] (a) Foote, C. S. *Free Radical in Biology*; Pryor, W. A., Ed.; Academic: New York, 1976; p 85. (b) Bellus, D. *Singlet Oxygen, Reactions with Organic Compounds and Polymers*; Ranby, B., Rabek, J. F., Eds.; Wiley: New York, 1978; p 61.

[2] For reviews, see: (a) Foote, C. S. *Singlet Oxygen*; Wasserman, H. H., Murray, R. W., Eds.; Academic: New York, 1979; p 139. (b) Ogryzlo, E. A., ref 1b, p 17. Young, R. H.; Brewer, D. R., ref 1b, p 36. Garner, A.; Wilkinson, F., ref 1b, p 48.

[3] (a) Foote, C. S.; Denny, R. W. *J. Am. Chem. Soc.* **1968**, *90*, 6233. (b) Foote, C. S.; Young, Y. C.; Denny, R. W. *J. Am. Chem. Soc.* **1970**, *92*, 5216, 5218.

[4] (a) Ogryzlo, E. A.; Tang, C. W. *J. Am. Chem. Soc.* **1970**, *92*, 5034. Young, R. H.; Martin, R. L. *J. Am. Chem. Soc.* **1972**, *94*, 5183. (b) Matheson, I. B. C.; Lee, J. *J. Am. Chem. Soc.* **1972**, *94*, 3310. Furukawa, K.; Ogryzlo, E. A. *J. Photochem.* **1972**, *1*, 163. Young, R. H.; Martin, R. L.; Feriozi, D.; Brewer, D. R.; Kayser, R. *Photochem. Photobiol.* **1973**, *17*, 233. Monroe, B. M. *J. Phys. Chem.* **1977**, *81*, 1861.

[5] Quannes, C.; Wilson, T. *J. Am. Chem. Soc.* **1968**, *90*, 6527.

[6] Ando, W.; Sato, R.; Yamashita, M.; Akasaka, T.; Miyazaki, H. *J. Org. Chem.* **1983**, *48*, 542.

[7] Foote, C. S.; Peters, J. W. *Proc. Int. Congr. Pure Appl. Chem., Spec. Lect., 23rd* **1971**, *4*, 129. Cited in ref 1a.

0022-3263/86/1951-4477$01.50/0

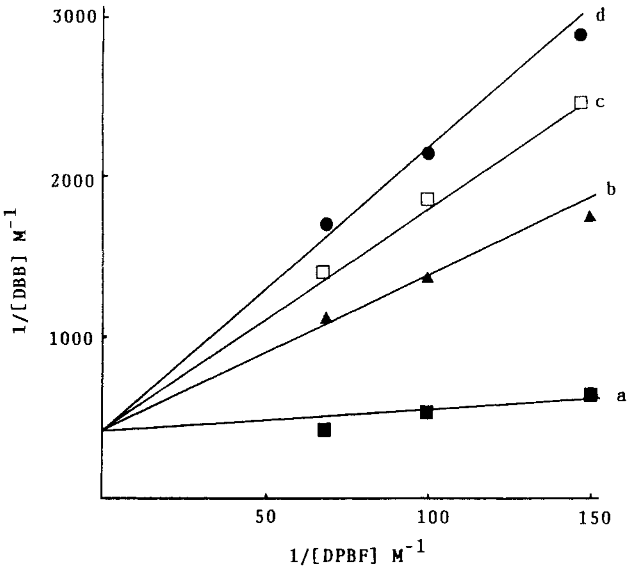


Figure 2. Photosensitized oxygenation of DPBF quenched by 1. Concentration of added 1: (a) none; (b) 5.0×10^{-4} M; (c) 1.0×10^{-3} M; (d) 2.0×10^{-3} M.

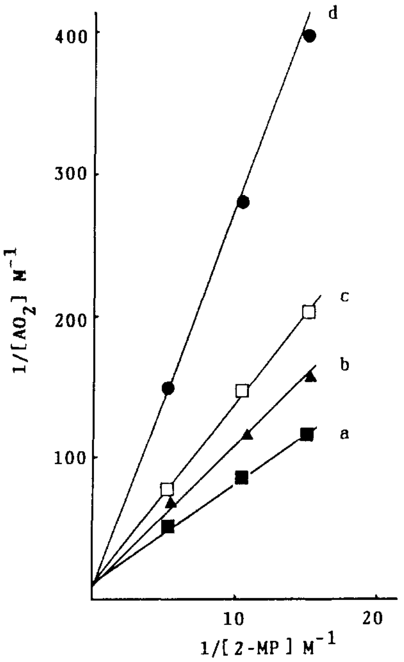


Figure 3. Photosensitized oxygenation of 2-MP quenched by 1. Concentration of added 1: (a) none; (b) 5.0×10^{-4} M; (c) 1.0×10^{-3}; (d) 2.0×10^{-3} M.

Scheme II

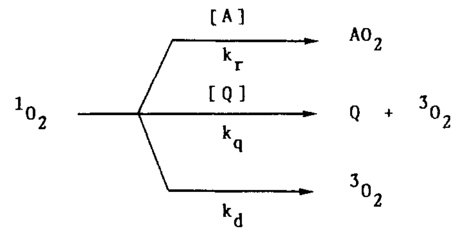


Table I. Kinetic Parameters Determined in Quenching Experiments of 1

DPBF		2-MP	
k_q/k_r[a]	k_q, $M^{-1}\,s^{-1}$[b]	k_q/k_r[a]	k_q, $M^{-1}\,s^{-1}$[c]
34.5	$2.2\ (\pm 0.3) \times 10^{10}$ $[3.5\ (\pm 0.5) \times 10^{10}]$	3660	$3.0\ (\pm 0.3) \times 10^{9}$ $[2.3\ (\pm 0.2) \times 10^{9}]$

[a] $k_d = 1.8 \times 10^5\ s^{-1}$ was used for methanol.[11] [b] Determined by the photosensitized oxygenation of DPBF. k_q was calculated from the value, $6.3 \times 10^8\ M^{-1}\,s^{-1}$ for k_r of DPBF.[12] Values in brackets are k_q calculated from the value $k_r = 1.0 \times 10^9\ M^{-1}\,s^{-1}$ in methanol.[12] [c] Determined by the photosensitized oxygenation of 2-MP. k_r was taken to be $8.1 \times 10^5\ M^{-1}\,s^{-1}$.[12] Values in brackets are k_q calculated from the value $k_r = 6.2 \times 10^5\ M^{-1}\,s^{-1}$ in methanol.[12]

Table II. Quenching Rate Constants (k_q) of Several Quenchers[13]

quenchers	k_q, $M^{-1}\,s^{-1}$
1	2.2×10^{10}
β-carotene	$>10^{10}$
Ni^{II} chelate	$>10^{10}$
aliphatic amines	$(1-100) \times 10^{6}$
DABCO	$>10^{7}$
2-pyrazolines[6]	$>10^{9}$

and 2-methyl-2-pentene (2-MP)[9] with $^1O_2$. DPBF is known as the most reactive compound toward $^1O_2$. Quenching rate constants were determined kinetically by the method of Zweig and Henderson,[10] a modification of the Foote method[2a] (see Experimental Section). Conversions of the substrate were kept to less than 10%. Under the reaction conditions, pyran 1 was not oxidized at all. After irradiation, DPBF gave a sole product, *o*-dibenzoylbenzene (DBB), which was analyzed directly by gas chromatography (Scheme I). In the case of 2-MP, the amounts of hydroperoxides formed in photooxygenation were determined by gas chromatography after reduction to alcohols with an excess of dimethyl sulfide. Results for photosensitized oxygenation of DPBF and 2-MP in the presence of pyran 1 are shown in Figures 2 and 3, respectively.

Scheme II holds for photooxygenation of a substrate, A, in the presence of quencher, Q, where k_d, k_q, and k_r are the decay rate constant of $^1O_2$, the quenching rate constant by the quencher, and the reaction rate constant with the acceptor, respectively. $[^1O_2]$ is the total amount of $^1O_2$ generated in the reaction time. The steady-state kinetic equation for the formation of product AO_2 is given by eq 1.

$$1/[AO_2] = 1/[^1O_2] + ((k_q[Q] + k_d)/k_r)(1/[^1O_2])(1/[A]) \quad (1)$$

The best fit of the data gives $k_q/k_r = 34.5$ and 3660 for the photosensitized oxygenation of DPBF and 2-MP in the presence of pyran 1, respectively (Table I). These values depend critically on the value of intercepts of each of the lines are shown in Figures 2 and 3. We assume that quenching of the excited sensitizer by the quencher (1) was not involved in the reaction. If such a process is involved, the only parameter in the equation that will be affected is $[^1O_2]$, which decreases with increasing concentration of the quencher. If the quenching of $^1O_2$ is only involved, the intercept of the plot does not change. The quenching rate constants obtained are compared with those of other quenchers are shown in Table II. The k_q value is remarkably large compared with those of other known $^1O_2$ quenchers and is comparable to the rate constant of β-carotene.[2] A plausible mechanism for the quenching of $^1O_2$ by pyran 1 could involve a charge-transfer process or weak molecular complexes, similar to those of electron-rich

---

(8) Wilson, T. *J. Am. Chem. Soc.* **1966,** *88,* 2898.

(9) Foote, C. S. *Acc. Chem. Res.* **1968,** *1,* 104.

(10) Zweig, A.; Henderson, W. A. *J. Poly. Sci., Polym. Chem. Ed.* **1975,** *13,* 717.

(11) Young, R. H.; Wehrly, K.; Martin, R. L. *J. Am. Chem. Soc.* **1971,** *93,* 5774.

(12) Wilkinson, F.; Brummer, J. G. *J. Phys. Chem. Ref. Data* **1981,** *10,* 809.

(13) Foote, C. S., ref 2a, references cited therein.

compounds such as amines[2,4] and pyrazolines.[6]

Experimental Section

Melting points are uncorrected. IR spectra were recorded with a Hitachi 26-50 spectrometer, ^{1}H NMR spectra with a Varian EM 360A spectrometer, and ^{13}C NMR with a JEOL JNM FX100 spectrometer (solvent, deuteriochloroform; tetramethylsilane as internal standard), and UV spectra with a Shimazu UV 365 spectrometer. GLC analysis was performed by using a Hitachi 164 gas chromatograph with a FID detector. Cyclic voltammograms of substrates were obtained in 0.1 M n-Bu$_4$NClO$_4$/CH$_3$CN solution (vs. SCE; scan rate, 200 mV/s; Hokuto Denko Ltd., Potentiostat/galvanostat HA-301). The light source was a Xenon lamp (λ > 460 nm) through a glass filter (Y-48, HOYA Co.). Irradiations were carried out through a 2-mm slit while passing oxygen.

Diphenylisobenzofuran (DPBF, Tokyo Kasei) was used as received. Its purity was confirmed by the lack of a carbonyl absorption in the IR spectrum, and GLC analysis showed that no trace of *o*-dibenzoylbenzene (DBB) was present. 2-Methyl-2-pentene (2-MP, Wako Pure Chemicals) was distilled from sodium hydride to remove alcoholic impurities, and its purity was confirmed by GLC analysis.

Pyran 1 was prepared as follows: 200 mL of ethanol solution of 4-(formylmethylidene)-2,6-diphenyl-4*H*-pyran[14] (1.8 mmol) and *N*,*N*-dimethylhydrazine (18 mmol) was refluxed for 30 min under an nitrogen atmosphere. The deposited precipitates after cooling were collected and recrystallized from ethanol: 84% yield; mp 279–280 °C; UV λ_{max} 406 nm (log ϵ 4.53); ^{1}H NMR δ 2.93 (s, 6 H), 5.83 (d, 1 H), 6.41 (d, 1 H), 6.79 (d, 1 H), 7.42–8.0 (m, 11 H); ^{13}C NMR δ 43.27 (q), 101.51 (d), 108.03 (d), 112.19 (d), 150.3 (s), 151.56 (s). Anal. Calcd for $C_{21}H_{20}N_2O$: C, 79.71; H, 6.37; N, 8.85. Found: C, 79.73; H, 6.34; N, 8.75.

Quenching of Photosensitized Oxygenation of Diethyl Sulfide. A solution of diethyl sulfide (6.3×10^{-2} M) and a sensitizer (6.3×10^{-5} M) in the absence or presence of the quencher (6.3×10^{-3} M) was saturated with oxygen and the system closed and irradiated. At regular intervals, the yield of diethyl sulfoxide was measured by GLC (4 mm × 1 m glass tube, 10% PEG-20M on Uniport HP; column temperature, 150 °C). The results obtained are shown in Figure 1.

Photosensitized Oxygenation of DPBF. A stock solution of RB (2 mL, 4×10^{-4} M) in methanol and 2 mL of freshly prepared DPBF with pyran 1 (variable concentrations of DPBF to constant concentrations of 1) in methanol–benzene (3:2) were mixed in Pyrex reaction tubes. After irradiation for a constant time (1 min) under constant oxygen bubbling, the internal standard, 9,10-diphenylanthracene (DPA), was added, and the reaction mixture was immediately analyzed by GLC (4 mm × 1 m glass column, 10%-SF 96 on Chromosorb; column temperature, 220 °C). The yields of DBB produced were determined by the comparison of the peak areas with that of the internal standard (DPA).

Photosensitized Oxygenation of 2-MP. A stock solution of RB (2.5 mL, 4×10^{-4} M) in methanol, 2.5 mL of freshly prepared 2-MP, and 2.5 mL of pyran 1 (variable concentrations of 2-MP to constant concentrations of 1) in methanol–benzene (3:2) were mixed in Pyrex reaction tubes. After irradiation for 20 min under a constant oxygen flow, the reaction mixture was reduced with an excess of dimethyl sulfide, allowed to stand for 6 h, and the internal standard (cyclohexanone) was added and the reaction mixture analyzed by GLC (4 mm × 2 m glass column, 10% Carbowax 20M on Celite 545; column temperature, 80 °C). The yields of alcohols[6] were determined by the comparison of the peak areas with that of the internal standard.

Acknowledgment. This work was supported by a Grant-in-Aid for Developmental Scientific Research (No. 59850137) from the Ministry of Education, Science and Culture of Japan.

Registry No. 1, 104549-50-0; DPBF, 5471-63-6; 2-MP, 625-27-4; $^1O_2$, 7782-44-7.

---

[14] Reynolds, G. A.; Vanallan, J. A. *J. Org. Chem.* **1969**, *34*, 2734.

On the Reaction of α-Methylene-β-peroxy Lactones with Olefins

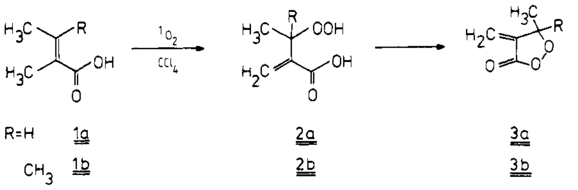
Waldemar Adam,* Axel Griesbeck, and Dag Kappes†

Institut für Organische Chemie der Universität Würzburg
Am Hubland, D-8700 Würzburg, Federal Republic of Germany

Received May 12, 1986

In a previous paper[1] we reported the synthesis of the novel α-methylene-β-peroxy lactone **3a** via photooxygenation of tiglic acid (**1a**) and subsequent treatment of the initially formed β-hydroperoxy acid **2a** with catalytic amounts of mineral acid. Here we report the synthesis of derivative **3b**, another member of this new class of substances, and the reaction of such β-peroxy lactones with olefins.

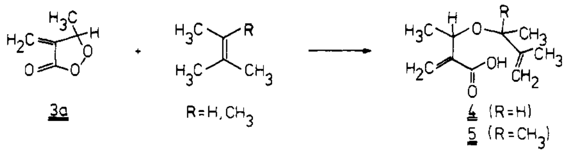
Trimethylacrylic acid (**1b**)[2] was allowed to react with singlet oxygen, generated by tetraphenylporphine (TPP) photosensitization in chlorinated solvents. The initially formed hydroperoxy acid **2b** was acidic enough to catalyze its own cyclization to the α-methylene-β-peroxy lactone **3b** (eq 1). However, **2b** could be detected by means of ^{1}H NMR and IR spectra, taken directly after completion of the photooxygenation. Characteristic for the structure of **2b** is its carbonyl absorption at 1696 cm^{-1}, which on standing becomes replaced by the 1780-cm^{-1} C=O absorption of the β-peroxy lactone **3b**.



(1)

3b was isolated in high yield (>90%) by Kugelrohr distillation. The reaction of **1b** with singlet oxygen, therefore, shows the same surprising regioselectivity observed already for the (*Z*)- and (*E*)-2-methyl-2-butene carboxylic acids.[1] For **1b** the degree of regio control was even higher as for its methyl ester, where an 88% preference for hydrogen abstraction from the methyl group proximate to the carbonyl functionality was observed.[3]

We were interested in using the α,β-unsaturated carbonyl moiety of the α-methylene-β-peroxy lactones **3a**,**b** in Diels–Alder reactions with electron-rich olefins as a potential route to vinylic peroxides. Although the novel β-peroxy lactone **3a** reacted readily with olefins such as 2,3-dimethyl-2-butene or 2-methyl-2-butene at 0 °C, instead of the desired Diels–Alder adducts, the ene-type products **4** and **5** were generated quantitatively (eq 2).



(2)

Formally, this transformation can be considered as a [(σ^2 + π^2) + σ^2]-ene reaction, in which the peroxy lactone **3a** serves as the σ^2-enophile. The reaction of phthaloyl peroxide with olefins serves as precedent,[4] leading to the phthalate half-esters as ene-type products. Astounding is the fact that for the unsymmetrical 2-methyl-2-butene, the ene reaction with **3a** proceeded perfectly regioselectively.

---

† Undergraduate research participant, winter semester, 1986.

0022-3263/86/1951-4479$01.50/0