starting material being subjected to a preliminary exchange of the amide hydrogen with D_2O. In these experiments, the aluminum amalgam was prepared by using a 0.5% solution of mercuric chloride in D_2O, rinsed twice with THF moistened with D_2O, and finally with dry THF. The mass spectra of the isomers of 5-d_1 showed m/z 199, 171, 129, and 101.

(±)-2-Amino-3-butenoic Acid (1). A mixture of 5 (1.2 g, 50 mmol), 6 N HCl (10 mL), and methanol (10 mL) was heated under reflux for 4 h. The reaction mixture was concentrated to dryness in vacuo, and the residue was applied to an ion-exchange column (Dowex-50, H^+ form), which was eluted with 1% aqueous pyridine to provide 1 (0.4 g, 80%): ^1H NMR (D_2O, pD 5.0) δ 4.40 (d, J = 8 Hz, 1 H), 5.58 (dd, J = 17 and 10 Hz, 2 H), 5.9-6.4 (td, J = 17, 10, and 8 Hz, 1 H). For ^1H NMR spectra of 1, (*E*)- and (*Z*)-[4-$^2H_1$]-1, and (*Z*)-[3,4-$^2H_2$]-1, see supplementary material.

Registry No. 1, 52773-87-2; (*E*)-[4-$^2H_1$]-1, 103384-16-3; (*Z*)-[3,4-$^2H_2$]-1, 103384-17-4; 2, 32501-93-2; 3, 1068-90-2; 3 (deuterium exchanged), 14341-56-1; (*E*)-4, 103384-10-7; (*Z*)-4, 103384-11-8; (*E*)-[3,4-$^2H_2$]-4, 103384-12-9; (*Z*)-[3,4-$^2H_2$]-4, 103384-13-0; 5, 70562-47-9; (*E*)-[3,4-$^2H_2$]-5, 103384-14-1; (*Z*)-[3,4-$^2H_2$]-5, 103384-15-2.

Supplementary Material Available: NMR spectra of 1, (*E*)- and (*Z*)-[4-$^2H_1$]-1, and (*Z*)-[3,4-$^2H_2$]-1 (2 pages). Ordering information is given on any current masthead page.

Singlet Oxygen Production from the Reactions of Alkylperoxy Radicals. Evidence from 1268-nm Chemiluminescence

Jeffrey R. Kanofsky

Medical Service, Edward Hines Jr., Veterans Administration Hospital, Hines, Illinois 60141, and Loyola University Stritch School of Medicine, Maywood, Illinois 60153

Received March 21, 1986

Substantial evidence obtained over the last three decades demonstrates that alkylperoxy radicals react via a tetraoxide intermediate which decomposes to give radical or nonradical products.[1-10] For primary and secondary

$$2RR'R''COO^{\bullet} \rightleftharpoons RR'R''COOOOCRR'R'' \quad (1)$$

$$RR'R''COOOOCRR'R'' \rightarrow RR'R''COOCRR'R'' + O_2 \quad (2)$$

$$RR'R''COOOOCRR'R'' \rightarrow 2RR'R''CO^{\bullet} + O_2 \quad (3)$$

$$RR'HCOOOOCRR'H \rightarrow RR'CO + RR'CHOH + O_2 \quad (4)$$

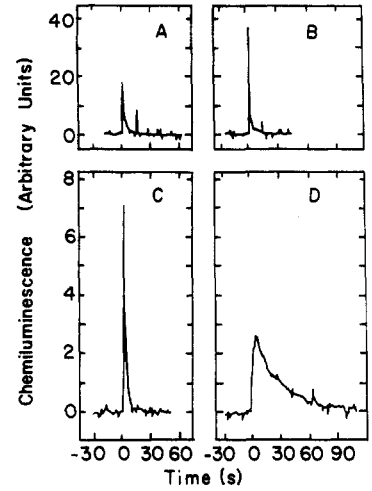

Figure 1. Chemiluminescence at 1268 nm in the reaction of ceric ion with hydroperoxides. Conditions, 1 mM ceric ammonium nitrate, 1 mM hydroperoxide, 20 mM hydrochloric acid, deuterium oxide solvent: (A) cumyl hydroperoxide; (B) 13-hydroperoxylinoleic acid; (C) ethyl hydroperoxide; (D) *tert*-butyl hydroperoxide.

alkylperoxy radicals, reaction 4 is the favored route of decomposition for the tetraoxide intermediate.[4] Reaction 4 may generate either an electronically excited oxygen molecule or an electronically excited ketone.[5] Spin restriction requires that excited singlet oxygen be produced if the ketone product is in its ground state.[5] Alternatively, an electronically excited triplet ketone and ground-state triplet oxygen may be the products.[5] Considerable experimental support for the production of singlet oxygen by reaction 4 comes from the chemical trapping study of Howard and Ingold,[5] the spectroscopically resolved chemiluminescence demonstrated by Bogan et al.,[6] and the data of Hawco et al. from chemiluminescence and chemical trapping experiments.[7] Nakano et al. and Inaba et al. have also reported visible chemiluminescence in the reaction of peroxy radicals, but the spectral analysis of the emission they observed had little correlation with dimolecular singlet oxygen chemiluminescence.[8] Reaction 4 does not occur with tertiary alkylperoxy radicals,[5,9] but Thomas has pointed out that reaction 2 should also produce singlet oxygen.[10] Howard and Ingold were unable to detect the characteristic endoperoxide product from 9,10-diphenylanthracene in the reaction of *tert*-butyperoxy radicals, but they felt this result may have been due to the destruction of the expected endoperoxide product by the *tert*-butylperoxy radicals.[5]

Studies in this laboratory have recently demonstrated characteristic singlet oxygen emission at 1268 nm in the reaction of 13-peroxylinoleic acid radicals.[11] In view of the high sensitivity and high specificity of 1268-nm emission for singlet oxygen in complex systems,[12] I undertook studies of singlet oxygen production from the bimolecular reactions of alkylperoxy radicals.

Results and Discussion

The reaction of ceric ion with hydroperoxides was used to produce peroxy radicals in aqueous solution.[5,7-8] As

(1) Bennett, J. E.; Brown, D. M.; Mile, B. *Trans. Faraday Soc.* **1970**, *66*, 397-405. Bennett, J. E.; Brown, D. M.; Mile, B. *Chem. Commun.* **1969**, 504-505. Adamic, K.; Howard, J. A.; Ingold, K. U. *Chem. Commun.* **1969**, 505-506. Bartlett, P. D.; Traylor, T. G. *J. Am. Chem. Soc.* **1963**, *85*, 2407-2410. Hiatt, R.; Clipsham, J.; Visser, T. *Can. J. Chem.* **1964**, *42*, 2754-2757. Bennett, J. E., Brown, D. M.; Mile, B. *Trans. Faraday Soc.* **1970**, *66*, 386-395. Blanchard, H. S. *J. Am. Chem. Soc.* **1959**, *81*, 4548-4552.

(2) Thomas, J. R. *J. Am. Chem. Soc.* **1967**, *89*, 4872-4875.

(3) Traylor, T. G.; Russell, C. A. *J. Am. Chem. Soc.* **1965**, *87*, 3699-3706. Howard, J. A.; Ingold, K. U. *Can. J. Chem.* **1968**, *46*, 2655-2660.

(4) Russell, G. A. *J. Am. Chem. Soc.* **1957**, *79*, 3871-3877.

(5) Howard, J. A.; Ingold, K. U. *J. Am. Chem. Soc.* **1968**, *90*, 1056-1058.

(6) Bogan, D. J.; Celii, F.; Sheinson, R. S.; Covaleskie, R. A. *J. Photochem.* **1984**, *25*, 409-417.

(7) Hawco, F. J.; O'Brien, C. R.; O'Brien, P. J. *Biochem. Biophys. Res. Commun.* **1977**, *76*, 354-361.

(8) Nakano, M.; Takayama, K.; Shimizu, Y.; Tsuji, Y.; Inaba, H.; Migita, T. *J. Am. Chem. Soc.* **1976**, *98*, 1974-1975. Inaba, H.; Shimizu, Y.; Tsuji, Y.; Yamagishi, A. *Photochem. Photobiol.* **1979**, *30*, 169-175.

(9) Ingold, K. U. *Acc. Chem. Res.* **1969**, *2*, 1-9.

(10) Thomas, J. R. *J. Am. Chem. Soc.* **1965**, *87*, 3935-3940.

(11) Kanofsky, J. R.; Axelrod, B. *J. Biol. Chem.* **1986**, *261*, 1099-1104.

(12) Kanofsky, J. R. *J. Biol. Chem.* **1983**, *258*, 5991-5993. Kanofsky, J. R. *J. Photochem.* **1984**, *25*, 105-113.

0022-3263/86/1951-3386$01.50/0

Table I. Spectral Analysis of Near-Infrared Emission in the Reaction of Peroxy Radicals

filter[a]	H_2O_2 + HOCl[b]	*tert*-butyl hydroperoxide[c]	cumyl hydroperoxide[c]	13-hydroperoxylinoleic acid[d]	ethyl hydroperoxide, ^2H_2O[c]	ethyl hydroperoxide, H_2O[e]	ethyl hydroperoxide, ^2H_2O, 2 mM azide ion[f]
1070	0.000 ± 0.002	0.01 ± 0.01	0.01 ± 0.01	0.00 ± 0.04	−0.08 ± 0.05	0.02 ± 0.12	−0.03 ± 0.08
1170	0.002 ± 0.002	0.00 ± 0.01	0.01 ± 0.0	0.00 ± 0.02	−0.03 ± 0.08	0.09 ± 0.05	−0.05 ± 0.02
1268	1.00 ± 0.02	1.0 ± 0.02	1.00 ± 0.03	1.00 ± 0.03	0.95 ± 0.03	1.0 ± 0.07	1.0 ± 0.06
1377	0.59 ± 0.01	0.51 ± 0.04	0.48 ± 0.02	0.55 ± 0.03	1.00 ± 0.03	0.54 ± 0.08	0.79 ± 0.08
1475	0.14 ± 0.02	0.04 ± 0.02	0.09 ± 0.02	0.16 ± 0.05	0.74 ± 0.06	0.04 ± 0.26	0.02 ± 0.05
1580	0.03 ± 0.004	0.01 ± 0.01	0.01 ± 0.02	0.00 ± 0.03	0.09 ± 0.08	−0.3 ± 0.1	−0.07 ± 0.14

[a] Emission intensities have been corrected for filter transmission and detector response. All systems were normalized to give a peak emission of 1. [b] Singlet oxygen standard; 0.5 mM hydrogen peroxide, 0.5 mM hypochlorous acid, p^{2}H 7.0, 50 mM sodium phosphate, deuterium oxide solvent. [c] 1 mM ceric ammonium nitrate, 1 mM hydroperoxide, 20 mM hydrochloric acid, deuterium oxide solvent. [d] 0.5 mM ceric ammonium nitrate, 0.5 mM 13-hydroperoxylinoleic acid, 20 mM hydrochloric acid, 0.8% ethanol (v/v), deuterium oxide solvent. [e] 1 mM ceric ammonium nitrate, 1 mM ethyl hydroperoxide, 20 mM hydrochloric solvent, light water solvent, average of nine experiments. [f] 1 mM ceric ammonium nitrate, 1 mM ethyl hydroperoxide, 20 mM hydrochloric acid, 2 mM sodium azide, deuterium oxide solvent, average of nine experiments.

Table II. Effect of Azide Ion and Light Water on 1268-nm Chemiluminescence in the Reaction of Ceric Ion with Hydroperoxide

hydroperoxide	control[a]	2 mM sodium azide added	10% light water (v/v)	100% light water
tert-butyl hydroperoxide	1.00 ± 0.04	0.05 ± 0.006	0.48 ± 0.03	0.03 ± 0.01
cumyl hydroperoxide	1.00 ± 0.03	0.03 ± 0.02	0.46 ± 0.05	0.05 ± 0.01
13-hydroperoxylinoleic	1.00 ± 0.03	0.15 ± 0.01	0.59 ± 0.08	0.16 ± 0.03
ethyl hydroperoxide	1.00 ± 0.07	0.64 ± 0.06	0.73 ± 0.07	0.43 ± 0.03

[a] 1 mM ceric ammonium nitrate, 1 mM hydroperoxide, 20 mM HCl, deuterium oxide solvent.

shown in Figure 1, this reaction was accompanied by near-infrared chemiluminescence for all of the organic hydroperoxides studied. Spectral analysis of the light emission (Table I) and strong quenching of the chemiluminescence by light water and by azide ion (Table II) support the assignment of this emission to singlet oxygen for the tertiary hydroperoxides, *tert*-butyl hydroperoxide and cumyl hydroperoxide.[12,13]

Analysis of the near-infrared emission in the ethyl hydroperoxide system, which produced primary radicals, was more complex. The emission in deuterium oxide solvent extended to longer wavelengths than that of singlet oxygen. Emission quenching by azide ion and by light water was limited, but the spectra obtained in light water or in deuterium oxide with azide present were consistent with singlet oxygen, since they lacked the longer wavelength emission. One explanation for this phenomenon was that singlet oxygen was produced in the ceric ion + ethyl hydroperoxide system and that some of it reacted to produce a second excited species which emitted at longer wavelengths. In deuterium oxide, where the half-life of singlet oxygen was long, much of the singlet oxygen was consumed by this process, limiting the intensity of the 1268-nm emission and producing chemiluminescence at longer wavelengths. In light water or in deuterium oxide with azide ion present, most of the singlet oxygen was quenched before it could react to produce the second emitting species, thus giving an emission spectrum due almost entirely to singlet oxygen. Singlet oxygen chemiluminescence alone was sufficient to explain the emission spectrum in the ceric ion + 13-hydroperoxylinoleic acid system. The decreased quenching effects of light water and of azide ion suggested that other processes in addition to solvent quenching limited the half-life of singlet oxygen in deuterium oxide. No 1268-nm emission was seen in the ceric ion–hydrogen peroxide system. This result was consistent with most past studies and demonstrated that singlet oxygen was not a product of the reaction of hydroperoxy radicals.[14]

Table III. Yield of Singlet Oxygen in the Reaction of Ceric Ion with Hydroperoxides

hydroperoxide[a]	singlet oxygen yield, μM	% of predicted yield[d]
ethyl hydroperoxide	23 ± 6[b]	4.6 ± 1.2
13-hydroperoxylinoleic acid	62 ± 11[b]	12.4 ± 2.2
tert-butyl hydroperoxide	12.2 ± 0.4[c]	2.4 ± 0.1
cumyl hydroperoxide	8.4 ± 0.3[c]	1.7 ± 0.1
hydrogen peroxide	0.04 ± 0.07[c]	0.008 ± 0.014

[a] 1 mM ceric ammonium nitrate, 1 mM hydroperoxide, 20 mM hydrochloric acid. [b] Light water solvent. [c] Deuterium oxide solvent. [d] Assuming one singlet oxygen molecule is produced from two peroxy radicals.

Estimates of the total yield of singlet oxygen were made by using the hydrogen peroxide + hypochlorous acid reaction as a calibration standard[12,15] and appear as Table III. Hydrogen peroxide, *tert*-butyl hydroperoxide, and cumyl hydroperoxide were studied in deuterium oxide, since the long singlet oxygen half-life permitted more accurate measurements. Ethyl hydroperoxide and 13-hydroperoxylineoleic acid were studied in light water because, as discussed earlier, the half-life of singlet oxygen in these systems failed to increase appropriately when detuerium oxide solvent was used. The yields of singlet oxygen were substantially below that predicted if reaction 2 or reaction 4 was the predominant reaction.

(13) Hasty, N.; Merkel, P. B.; Radlick, P.; Kearns, D. R. *Tetrahedron Lett.* **1972**, 49–52. Foote, C. S.; Fujimoto, T. T.; Chang, Y. C. **1972**, 45–48. Rodgers, M. A. J.; Showden, P. T. *J. Am. Chem. Soc.* **1982**, *104*, 5541–5543.

(14) Foote, C. S.; Shook, F. C.; Abakerli, R. A. *J. Am. Chem. Soc.* **1980**, *102*, 2503–2504. Aubry, J. M.; Rigaudy, J. *J. Am. Chem. Soc.* **1981**, *103*, 4965–4966. Nilsson, R.; Kearns, D. R. *J. Phys. Chem.* **1974**, *78*, 1681–1683. Nanni, E. J., Jr.; Birge, R. R.; Hubbard, L. M.; Morrison, M. M.; Sawyer, D. T. *Inorg. Chem.* **1981**, *20*, 737–741. Foote, C. S., Abakerli, R. B.; Clough, R. L.; Shook, F. C. *Biological and Clinical Aspects of Superoxide and Superoxide Dismutase*; Bannister, W. H., Bannister, J. W., Eds.; Elsevier: New York, 1980; pp 222–230. Barlow, G. E.; Bisby, R. H.; Cundall, R. B. *Radiat. Phys. Chem.* **1979**, *13*, 73–75. Arudi, R. L.; Bielski, B. H. J.; Allen, A. O. *Photochem. Photobiol.* **1984**, *39*, 703–706. Nagano, T.; Fridovich, I. *Photochem. Photobiol.* **1985**, *41*, 33–37. Kanofsky, J. R. *J. Am. Chem. Soc.* **1986**, *106*, 2977–2979.

(15) Kanofsky, J. R.; Wright, J.; Miles-Richardson, G. E.; Tauber, A. I. *J. Clin. Invest.* **1984**, *74*, 1489–1495.

This study demonstrates singlet oxygen production in the intermolecular reaction of two tertiary alkylperoxy radicals and confirms earlier studies of singlet oxygen production in the reactions of primary and of secondary alkylperoxy radicals. Under the conditions studied, singlet oxygen constitutes only a minor reaction product, being only 1.68–12.4% of the amount predicted by reaction 2 or reaction 4. The data presented are not sufficient to identify a particular reaction mechanism, but a review of the literature does suggest mechanisms which can rationalize the data and thermochemical considerations exclude some mechanisms. Reaction 3 is not sufficiently exothermic to directly form singlet oxygen.[6] Further, it is not clear that the solvent cage effects suggested by Mendenhall and Quinga[16] can overcome this objection. Reaction 4 remains a good explanation for the singlet oxygen production by primary and secondary peroxy radicals. Singlet oxygen may be a direct product of reaction 4 or it may be produced as a consequence of the reaction of ground-state oxygen with an excited triplet ketone produced by reaction 4. For the cumylperoxy radical, two mechanisms likely

$$R_2CO^* + O_2\ (^3\Sigma_g) \rightarrow R_2CO + O_2\ (^1\Delta_g) \qquad (5)$$

account for the singlet oxygen produced. Reaction 2 is the most obvious mechanism. A more complex reaction sequence for the production of singlet oxygen is initiated by the fragmentation of cumylalkoxy radicals produced in reaction 3 to give methyl radicals and acetophenone.[2,3] The methyl radicals rapidly react with oxygen to give methylperoxy radicals which then react via reaction 4 to give singlet oxygen. For *tert*-butyl peroxy radicals the singlet oxygen most likely results from reaction 2, since β-scission of *tert*-butylalkoxy radicals produced in reaction 3 is less favored than is the fragmentation of cumylalkoxy radicals.[3]

Experimental Section

Chemiluminescent Spectrometer. The infrared chemiluminescene spectrometer used and the method of calibration of singlet oxygen yields using the hydrogen peroxide + hypochlorous acid reaction have been described previously.[11,12,15] Spectral analysis was done by using a series of interference filters.[15]

Chemicals and Reagents. Ceric ammonium nitrate, *tert*-butyl hydroperoxide, cumyl hydroperoxide, and deuterium oxide, 99.8%, were obtained from Sigma Chemical Co. Ethyl hydroperoxide, 10% aqueous solution, was obtained from Polysciences, Inc. Hydrogen peroxide, 30% stabilized reagent, was a product of J.T. Baker Chemical Co. Ethyl hydroperoxide and hydrogen peroxide were assayed by using the method of Cotton and Dunford.[17] Cumyl hydroperoxide and *tert*-butyl hydroperoxide were assayed by iodide ion oxidation in acetic acid using hydrogen peroxide as a standard. The excess iodide ion was complexed with cadmium ion prior to the measurement of absorbance at 358 nm.[18] Hydroperoxylinoleic acid was enzymatically synthesized from linoleic acid by using soybean lipoxygenase at 0 °C in the presence of excess oxygen.[19] About 90% of the hydroperoxide produced was the 13-hydroperoxy isomer.[19] The product had no discrete absorption band at 280 nm. The hydroperoxide was assayed by absorbance at 234 nm by using an extinction coefficient of $2.5 \times 10^4\ M^{-1}\ cm^{-1}$.[20] Hypochlorous acid was purified and assayed as previously described.[15] Other inorganic chemicals were reagent grade. Water was glass distilled.

Reaction Conditions. All experiments were done at 25 °C in air-saturated solutions. Many experiments were done in deuterium oxide, which greatly enhanced the singlet oxygen emission. Ceric ammonium nitrate in 1.5 mL of 20 mM hydrochloric acid solution was placed in the spectrometer. The reaction was then initiated by the rapid injection of an additional 1.5 mL of hydrochloric acid solution containing the hydroperoxide to be studied.

Statistical Analysis. Unless otherwise specified, all experiments were done in triplicate and were reported as the mean ± the standard error.

Acknowledgment. I thank William Wardman for technical assistance in performing experiments and Shirley Zwiesler for assistance in preparation of the manuscript. This work is supported by Grant GM-32974 from the National Institutes of Health and the Veterans Administration Research Service.

Registry No. O_2, 7782-44-7; ethyl hydroperoxide, 3031-74-1; 13-hydroperoxylinoleic acid, 23017-93-8; *tert*-butyl hydroperoxide, 75-91-2; cumyl hydroperoxide, 80-15-9; hydrogen peroxide, 7722-84-1; ceric ammonium nitrate, 16774-21-3.

(16) Mendenhall, G. D.; Quinga, E. M. Y. *Int. J. Chem. Kinet.* **1985**, *17*, 1187–1190.
(17) Cotton, M. L.; Dunford, H. B. *Can. J. Chem.* **1973**, *51*, 582–587.
(18) Takagi, T.; Mitsuno, Y.; Masumara, M. *Lipids* **1978**, *13*, 147–151.
(19) Christopher, J. P.; Pistorius, E. K.; Regnier, F. E.; Axelrod, B. *Biochim. Biophys. Acta* **1972**, *289*, 82–87.
(20) Johnston, A. E.; Zilch, K. T.; Selke, E.; Dutton, H. J. *J. Am. Oil Chem. Soc.* **1961**, *38*, 367–371.

A Convenient Procedure for the Monosilylation of Symmetric 1,*n*-Diols

Patrick G. McDougal,* Joseph G. Rico, Young-Im Oh, and Brian D. Condon

School of Chemistry, Georgia Institute of Technology, Atlanta, Georgia 30332

Received March 4, 1986

Bifunctional reagents are important synthons for the organic chemist. Many of these reagents (**3**) have as their starting material symmetric 1,*n*-diols (**1**). The crucial step in the production of the bifunctional reagent (**3**) is often the monoprotection of the diol (**1** → **2**). While numerous

$$\underset{\mathbf{1}}{HO(CH_2)_nOH} \rightarrow \underset{\mathbf{2}}{HO(CH_2)_nOR} \rightarrow \underset{\mathbf{3}}{X(CH_2)_nY}$$

methods have been developed for the selective protection of unsymmetric diols, for example, protection of a primary alcohol in the presence of a secondary alcohol, the selective monoprotection of symmetric diols can still present a problem.[1] In general if stoichiometric equivalents of protecting reagent to diol are utilized, a statistical mixture of unprotected, monoprotected, and diprotected products result in which the yield of the desired monoprotected material is only 50%.[2] To date this statistical pitfall has been circumvented most easily by employing a large excess of the starting diol relative to the protecting reagent. This produces an acceptable yield of the monoprotected product based on the protecting reagent as the limiting reagent.[3] The excess diol, if inexpensive, is simply discarded or, if expensive, can be recycled via chromatography. Other more esoteric solutions to the problem of selective protection include the use of polymer supports[1] and the use of continuous solvent extraction to remove the desired monoprotected product.[4] In this paper we wish to report

(1) For a discussion of this problem, see: Leznoff, C. C. *Acc. Chem. Res.* **1978**, *11*, 327 and references therein.
(2) Reaction of symmetrical diols with thallium alkoxide in a Williamson ether synthesis have shown some selectivity toward monoprotected material, see: Kalinowski, H. O.; Crass, G.; Seebach, D. *Chem. Ber.* **1981**, *114*, 477.
(3) For some applications of this methodology, see: (a) Sheehan, M.; Spangler, R. J.; Djerassi, C. *J. Org. Chem.* **1971**, *36*, 3526. (b) Trost, B. M.; Verhoeven, T. R. *J. Am. Chem. Soc.* **1980**, *102*, 4743. (c) Ikeda, J.; Ikeda, N.; Yamamoto, H. *Tetrahedron Lett.* **1984**, *25*, 5177.

0022-3263/86/1951-3388$01.50/0