Without detracting from the importance of many experiments involving the use of dipyrromethanes[3,4,22,23] and bilanes[3,19] which have provided excellent probes for the overall process via ^{13}C-labeling, it is now clear that the deaminase/cosynthetase enzymes can deal with both "normal" and rearranged species of bilane[3,19,24] and pyrromethane[4,22,23] which bear sufficient chemical reactivity to insinuate themselves into the biochemical machinery. We submit that the NMR method using the known, physiological substrate, PBG, provides an unequivocal, non-invasive view of the true enzyme process at work.

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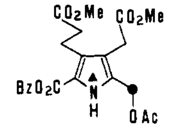
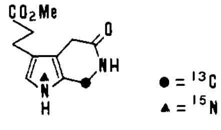
References and Notes

(1) G. Burton, P. E. Fagerness, S. Hosozawa, P. M. Jordan, and A. I. Scott, *J. Chem. Soc., Chem. Commun.*, 202 (1979).
(2) P. M. Jordan, G. Burton, H. Nordlöv, M. M. Schneider, L. M. Pryde, and A. I. Scott, *J. Chem. Soc., Chem. Commun.*, 204 (1979).
(3) Review: A. R. Battersby and E. McDonald, *Acc. Chem. Res.*, **12**, 14 (1979).
(4) Review: A. R. Battersby and E. McDonald in "Porphyrins and Metalloporphyrins", K. M. Smith, Ed., Elsevier, Amsterdam, 1975, p 61.
(5) Review: A. I. Scott, *Acc. Chem. Res.*, **11**, 29 (1978). See also A. I. Scott, A. J. Irwin, L. M. Siegel, and J. N. Shoolery, *J. Am. Chem. Soc.*, **100**, 316, 7978 (1978); A. R. Battersby, E. McDonald, M. Thompson, and V. Ya. Bykhovsky, *J. Chem. Soc., Chem. Commun.*, 150 (1978); R. Deeg, H.-P. Kriemler, H.-H. Bergmann, and G. Müller, *Hoppe Seyler's Z. Physiol. Chem.*, **358**, 339 (1977).
(6) A. I. Scott, *Tetrahedron*, **31**, 2639 (1975).
(7) The sample of [11-^{13}C:1-^{15}N]-PBG was prepared by modification of a published method[8] in which the pyrrole (i), synthesized from $Na^{15}NO_2$ and



i



ii

[^{13}C]-DMF, had the following: ^1H NMR δ 5.01 (dd, $-CH_2OAc$, $^1J_{^1H-^{13}C}$ = 149.2, $^2J_{^1H-^{15}N}$ = 2.8 Hz), 9.22 (d, NH, $^1J_{^1H-^{15}N}$ = 98.0 Hz); ^{13}C NMR δ 56.90 (d, $-^{13}CH_2OAc$, $^2J_{^{13}C-^{15}N}$ = 1.9 Hz). i was converted to PBG lactam methyl ester (ii), *m/e* 224 (97%, M^+), 223 (100%, $M^+ - 1$), to give a pure sample of PBG 99% in ^{15}N and 90% in ^{13}C.
(8) Kevin M. Smith in ref **4**, p 757.
(9) All incubations were carried out under argon and in absolute darkness.
(10) This broad line corresponds to the superposition of the resonances of the four meso carbons of uro'gen I (**2**) and the three bridge methylene carbons of bilane **5** (X = NH_2), the relative amounts depending on the incubation time, as described below. Similar considerations apply to the ^{15}N NMR spectra.
(11) D. F. Wiemer, D. I. C. Scopes, and N. J. Leonard, *J. Org. Chem.*, **41**, 3051 (1976).
(12) C. S. Irving and A. Lapidot, *J. Chem. Soc., Chem. Commun.*, 184, (1977).
(13) R. B. Woodward and R. Hoffmann, *Angew Chem., Int. Ed. Engl.*, **8**, 781 (1969).
(14) J. Pluscec and L. Bogorad, *Biochemistry*, **9**, 4736 (1970).
(15) R. Radmer and L. Bogorad, *Biochemistry*, **11**, 904 (1972).
(16) R. C. Davies and A. Neuberger, *Biochem. J.*, **133**, 471 (1973).
(17) A. R. Battersby et al., *J. Chem. Soc., Chem. Commun.*, in press. We warmly thank Professor Battersby for a preprint of his work on the identification of another trapped species of the deaminase reaction, the hydroxy bilane (**5**, X = OH), and its enzymatic incorporation into uro'gen III.
(18) B. Frydman et al., *J. Am. Chem. Soc.*, in press.
(19) A. R. Battersby, C. J. R. Fookes, E. McDonald, and M. J. Meegan, *J. Chem. Soc., Chem. Commun.*, 185 (1978).
(20) H. Matsumoto and S. Hosozawa, unpublished work in this laboratory.
(21) Determined by cellulose TLC electrophoresis, by reaction with Ehrlich reagent and by ^{13}C NMR spectroscopy[1] of the appropriate incubations using authentic samples of bilane **5** (X = NH_2) as standard in these assays.
(22) B. Frydman and R. B. Frydman, *Acc. Chem. Res.*, **8**, 201 (1975).
(23) A. I. Scott, K. S. Ho, M. Kajiwara, and T. Takahashi, *J. Am. Chem. Soc.*, **98**, 1589 (1976).
(24) A. R. Battersby, C. J. R. Fookes, G. W. J. Matcham, and E. McDonald, *J. Chem. Soc., Chem. Commun.*, 1064 (1978).
(25) R. T. Pajer and I. M. Armitage, *J. Magn. Reson.*, **21**, 485 (1976).
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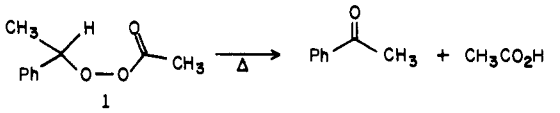
Investigation of the Mechanism of the Unimolecular and the Electron-Donor-Catalyzed Thermal Fragmentation of Secondary Peroxy Esters. Chemiluminescence of 1-Phenylethyl Peroxyacetate by the Chemically Initiated Electron-Exchange Luminescence Mechanism

Sir.

Our interest in highly exergonic thermal reactions of organic peroxides led us to the investigation of 1-phenylethyl peroxyacetate (**1**). Thermolysis of **1** in benzene solution gives a quantitative yield of acetic acid and acetophenone,[1] a small fraction of which is electronically excited. The reaction of **1** is catalyzed by a wide range of easily oxidized substances. In this case, the electronically excited state of the catalyst (activator) is formed apparently by the recently described chemically initiated electron-exchange (CIEEL) mechanism.[2] We report herein our examination of the mechanism of both the unimolecular and catalyzed reaction of **1**.



(1)

Perester **1** was prepared by the acid-catalyzed reaction of ketene with 1-phenylethyl hydroperoxide in CH_2Cl_2 and purified by distillation.[3] The thermolysis of **1** in argon purged benzene can be followed conveniently by the indirect or activated[4] chemiluminescence that results upon addition of biacetyl or any one of several easily oxidized fluorophores (see below), respectively. The rate at which the perester reacted showed apparent first-order kinetic behavior. However, the observed rate constants and derived activation parameters for solutions 1×10^{-2} M and above are dependent upon the initial perester concentration, indicating the likely involvement of a radical induced homolysis path.[5] At low initial perester concentration (1×10^{-5} to 1×10^{-3} M) the rate of reaction is independent of concentration. Moreover, the activation parameters for the reaction, $\Delta H^{\ddagger} = 33.2 \pm 0.7$ kcal/mol, $\Delta S^{\ddagger} = 11.0 \pm 1.9$ eu (see Figure 1), under these conditions indicate a unimolecular process.[6]

In contrast to the modified Russell mechanism[7] suggested by Hiatt and co-workers[8] for the thermolysis of secondary peresters, our findings are more consistent with a stepwise process in which oxygen-oxygen bond homolysis is followed by rapid in-cage hydrogen atom abstraction. In particular, the activation enthalpy indicates a transition state in which bond cleavage is uncompensated by bond formation,[6] and the quantitative yield of acetic acid rules out escape from the solvent cage of a significant amount of the so formed acetyloxy radical.[9] The calculated heat of reaction for the process shown in eq 1 is −58 kcal/mol.[10] Thus, the transition state for this reaction lies some 94 kcal/mol above ground-state products. Sufficient energy is released therefore to populate electronically excited states of acetophenone.[11] Indeed, we detect a low

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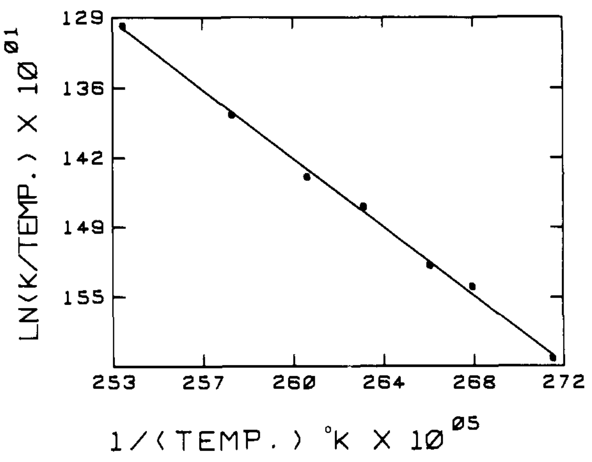


Figure 1. Eyring plot for the unimolecular thermolysis of perester **1** in argon saturated benzene. The perester concentration was 3 × 10^{-4} M. Rate constants were determined by measuring the decrease in 9,10-diphenylanthracene chemiluminescence intensity which was shown to be directly proportional to the concentration of the perester.

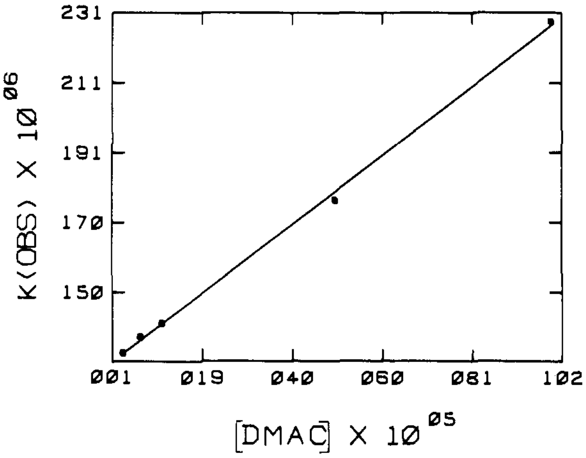


Figure 2. Catalysis of perester **1** by DMAC. The observed rate constants were determined by monitoring the DMAC activated chemiluminescence in argon purged benzene solution at 99.9 °C and were first order for 3 or more half-lives. The perester concentration was 3 × 10^{-4} M.

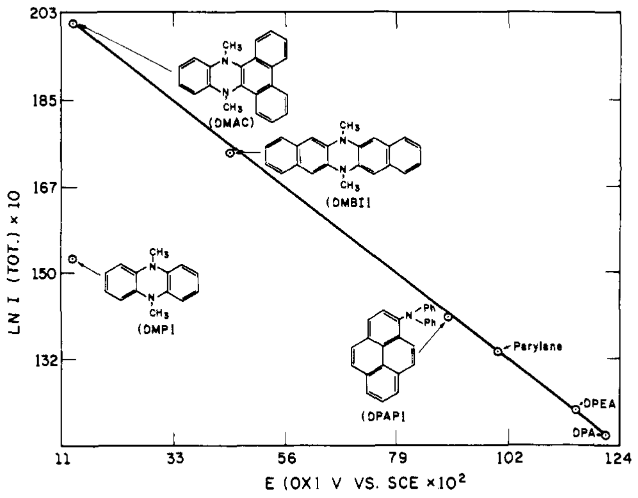
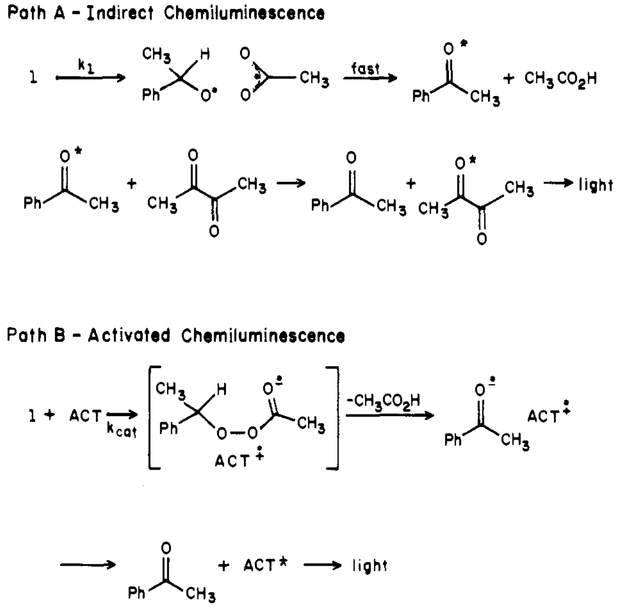


Figure 3. Correlation of total chemiluminescence intensity with activator oxidation potential (E_{ox}). Measured in argon purged benzene with activator at 1 × 10^{-4} M and perester at 1 × 10^{-3} M at 99.5 °C.

Scheme I



yield of excited state product as indirect chemiluminescence from added biacetyl.[12] The emission spectrum of the chemiexcited biacetyl is composed entirely of the phosphorescence, thus implicating acetophenone triplet as its precursor. This mechanism is shown as path A in Scheme I.

When a small amount of an easily oxidized substance is added to benzene solutions of perester **1** the thermolysis reaction is somewhat different. For example, *N*,*N*-dimethyldihydrodibenzo[*ac*]phenazine (DMAC)[13] accelerates the rate of reaction of **1** (Figure 2) without itself being consumed. The products of this reaction are acetic acid and acetophenone, formed in quantitative yield as they were in the uncatalyzed case. Electronically excited states are formed by the catalytic reaction as well, and in contrast to the unimolecular transformation are detected as the fluorescence of the excited singlet state of the activator. The DMAC is not unique in its catalytic ability. Similar observations were made for other phenazines, *N*,*N*-diphenyl-1-aminopyrene (DPAP),[14] rubrene, perylene, 9,10-diphenylethynylanthracene (DPEA), 9,10-diphenylanthracene (DPA), and others.

The quantum efficiency for light generation by the various activators was determined by measuring the total chemiluminescence intensity under conditions where essentially all of **1** reacts by the unimolecular path (i.e., low activator concentration so that $k_1 \gg k_{cat}$[ACT]; the rate constants are defined in Scheme I). After correcting for differences in fluorescence quantum yield and photomultiplier tube and monochromator spectral efficiency, it is apparent that the only predictor of activator chemiluminescence efficiency in its reaction with perester **1** is its one-electron oxidation potential, *except* for *N*,*N*-dimethyldihydrophenazine (DMP); see Figure 3 and Table I. The failure of the DMP oxidation potential to predict its chemiluminescence efficiency is in fact a remarkable triumph of the CIEEL mechanism.

The CIEEL mechanism applied to the reaction of perester **1** is shown as path B in Scheme I where ACT represents the catalytic chemiluminescence activator. The first step in the proposed mechanism is rate-limiting endergonic one-electron transfer from the activator to the perester. This reaction is rendered irreversible by rapid cleavage of the oxygen-oxygen bond of the reduced perester. This sequence of events gives rise to the prediction that log k_{cat} will be inversely proportional to activator oxidation potential,[15] a prediction which is borne out by experiment (Table I). Transfer of a hydrogen atom simultaneously with, or subsequent to, oxygen-oxygen bond cleavage generates acetophenone radical anion in a solvent cage with the activator radical cation. In the general case annihilation of these radical-ion intermediates leads to the observed excited singlet-state activator. The exception is DMP. To generate

Table I

activator	E_s,[a] kcal/mol	E_{ox},[b] V vs. SCE	ϕ_{fl}[c]	k_{cat},[d] $M^{-1}\ s^{-1}$
DMAC	58	0.14	0.04	9.73×10^{-2}
DMP	72	0.14	0.18	3.42×10^{-1} [e]
DMBI	68	0.46	0.88	7.07×10^{-3}
rubrene	54	0.82	0.56	1.40×10^{-4} [f]
DPAP	68	0.90	1.00	2.35×10^{-4}
perylene	65	1.00	0.84	1.19×10^{-4}
DPEA	62	1.16	0.96	3.58×10^{-5}
DPA	72	1.22	1.00	2.22×10^{-5}

[a] Assigned from the 0–0 band of the fluorescence spectrum. [b] Determined by cyclic voltammetry in CH_3CN solution with tetrabutylammonium perchlorate supporting electrolyte. [c] At 90 °C in argon saturated benzene solution. [d] Calculated by comparing relative total intensity with that of DMAC. [e] Measured by determining the apparent first-order rate constant for reaction of deuterated **1** at varying DMP concentration. [f] Unavoidable self-absorption by rubrene apparently leads to the observed low calculated value for k_{cat}.

light the energy released by the ion annihilation reaction must be at least as great as the lowest singlet-state energy of the emitter. This requirement is apparently fulfilled by all of the activators of Figure 3 *except* DMP. In this case, the ion annihilation is calculated[16] to release ~59 kcal/mol and the singlet energy of DMP is 72 kcal/mol. Thus, DMP is still a powerful catalyst for the reaction of perester **1** (Table I), but it generates less than 1% of the expected chemiluminescence because of the energy deficit in the excitation step. This observation provides convincing evidence for the radical-ion intermediates proposed in the CIEEL mechanism.

This is the fourth well-documented case of an electron-transfer initiated reaction of a peroxide that leads to electronically excited-state product.[2] As in the previously described examples, the major evidence is the correlation of rate constant and oxidation potential, i.e., Figure 3. Comparison among the various peroxides reveal that the catalytic rate constant is strongly dependent upon structure. The diacyl peroxides, for example, react much more rapidly than do the more difficulty reduced peresters.[17] However, the magnitude of the slope of the line resulting from the semilog plot of rate constant against activator oxidation potential is essentially constant and equal to ca. $-0.3/RT$ for the systems investigated to date. This result is consistent with rate-limiting irreversible electron transfer from activator to peroxide occurring with a transfer coefficient of ~0.3.[15,18]

In summary, we have observed two distinct reaction paths for thermolysis of secondary perester **1**. The unimolecular reaction appears to proceed by a stepwise route, the bimolecular reaction with electron donors by an electron-transfer mechanism. The electron-transfer mechanism in particular may serve as a model for the excitation step in the bacterioluminescence reaction.[19] We are continuing our investigation of this and other aspects of the chemistry of these peresters.

Acknowledgment. We thank Professor Faulkner of this department for many helpful discussions. The authors gratefully acknowledge financial support for this work by the Office of Naval Research, The National Science Foundation, and the donors of the Petroleum Research Fund, administered by the American Chemical Society. We also thank Mr. Steven P. Schmidt for preparing and purifying the DMAC, DPAP, DMP, and DMBI.

References and Notes

(1) The products were identified by comparison with authentic material. The yield of acetic acid was determined by gas chromatography on a Poropak Q column at 245 °C, the yield of acetophenone by gas chromatography on a 3% SE-30 on Chromasorb Q column at 100 °C.

(2) Koo, J.-y.; Schuster, G. B. *J. Am. Chem. Soc.* **100**, 4496 (1978); Schmidt, S. P.; Schuster, G. B. *ibid.* **100**, 1966 (1978); Smith, J. P.; Schuster, G. B. *ibid.*, **100**, 2564 (1978); Koo, J.-y.; Schuster, G. B. *ibid.* **99**, 6107 (1977).

(3) Peroxy ester **1** was characterized as follows: IR (CCl_4) 3000, 1785, 1500, 1285 cm^{-1}; ^1H NMR (CCl_4 internal Me_4Si) δ 1.50 (d, **3** H, $J = 7$ Hz), 1.9 (s, 3 H), 5.17 (q, 1 H, $J = 7$ Hz), 7.3 (s, 5 H) Anal. Calcd for $C_{10}H_{12}O_3$: C, 66.64; H, 6.73. Found: C, 66.98; H, 6.66. In addition perester **1** was reduced with triethyl phosphite to 1-phenylethyl acetate which was characterized by comparison with authentic material.

(4) We propose the following definitions. (i) Direct chemiluminescence: the emission of light is from the excited state formed as a direct result of a unimolecular thermal chemical reaction. (ii) Indirect chemiluminescence: the emission of light is from an excited state formed as a result of energy transfer from the initially generated excited state. (iii) Activated chemiluminescence: the emission of light is from an excited state directly formed from a bimolecular reaction between substrate and catalyst.

(5) Wolf, R. A.; Migliore, M. J.; Fuery, P. H.; Gagnier, P. R.; Sabeta, I. C.; Trocino, R. J. *J. Am. Chem. Soc.* **100,** 7967 (1978). Nozaki, K.; Bartlett, P. D. *ibid.* **68**, 1686 (1946).

(6) Pryor, W. A.; Smith, K. *Int. J. Chem. Kinet.* **3,** 387 (1971). Bartlett, P. D.; Hiatt, R. R. *J. Am. Chem. Soc.* **80,** 1398 (1958). Lorand, J. P.; Bartlett, P. D. *ibid.* **88,** 3294 (1966).

(7) Russell, G. A. *J. Am. Chem. Soc.* **79**, 3871 (1957).

(8) Hiatt, R. R.; Glover, L. C.; Mosher, H. S. *J. Am. Chem. Soc.* **97,** 1556 (1975).

(9) Martin, J. C.; Taylor, J. W.; Drew, E. H. *J. Am. Chem. Soc.* **89,** 129 (1967), and references cited therein.

(10) Benson, S. "Thermochemical Kinetics", 2nd ed., Wiley: New York, 1976.

(11) Wilson, E. B. *J. Am. Chem. Soc.* **98,** 3387 (1976). Lissi, E. *ibid.* **98,** 3386 (1976).

(12) Biacetyl is useful because it has a much higher phosphorescence efficiency than acetophenone under these conditions.

(13) Smith, J. G.; Levi, E. M. J. *Organomet. Chem.* **36,** 215 (1972).

(14) Prepared by reaction of 1-aminopyrene with bromobenzene and lithium tetramethylpiperidide in THF. Anal. Calcd for $C_{28}H_{19}N$: C, 91.02; H, 5.18; N, 3.79. Found: C, 90.77; H, 4.99; N, 3.78.

(15) The details of the kinetic analysis will be presented in a forthcoming publication.

(16) The amount of energy released is calculated by taking the difference between the oxidation potential of the activator and the reduction potential of acetophenone after correction for the change in these values that result from change of solvent and the absence of electrolyte.

(17) For the series diphenoyl peroxide, dimethyldioxetanone, and perester **1**, we estimate that k_{cat} for DMAC is $\sim 7 \times 10^3$, 180, and 0.1 $M^{-1}\ s^{-1}$, respectively.

(18) Delahay, P. "Double Layer and Electrode Kinetics", Wiley-Interscience: New York, 1965; Chapter 7.

(19) Hastings, J. W.; Nealson, K. H. *Annu. Rev. Microbiol.* **31,** 549 (1977).

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Silver-Catalyzed 1,2-Acyl Migration in an Optically Active Chlorohydrin. Evidence for Neighboring-Group Participation by Carbonyl Carbon

Sir:

Molecular rearrangements where the migrating substituent stabilizes the transition state by becoming bonded to an adjacent reaction center in the rate-limiting step is by definition a concerted process. A classic example of such neighboring-group participation (NGP)[1] is the phenonium ion which was introduced by Cram in his studies on stereospecific tosylate solvolyses.[2] The substrates used in these experiments usually required assistance by the migrating phenyl group to effect ionization of the leaving group and the results were best explained by a bridged-ion intermediate.

In contrast, stereochemical studies by Collins[3] on deamination reactions of amino alcohols have elegantly demonstrated that 1,2-phenyl shifts may also be nonconcerted, involve discrete carbenium-ion intermediates, and proceed with both inversion and retention at the migration terminus.[4] In fact, if steric interactions are involved in the transition state for 1,2 migration, retention may predominate.[5] Similarily, the pinacol rearrangement[6] has been shown to involve a carbenium-ion intermediate. However, if water leaves from a primary or secondary carbon, then a more concerted pathway is antici-