the formation of an acid chloride or carboxylic acid. And the observation that **10** is not formed from **2** would also argue against **9** being responsible for inhibition of serine proteases by **1**.

Evidence presented here indicates that **1** and **2** are mechanism-based irreversible inhibitors of serine proteases. These are the first demonstrated examples of enzyme-activated inhibitors of HL elastase and cathepsin G. These enzymes have been noted to be major contributors to elastin destruction observed in emphysema.[11] These inhibitors and similar structures may have considerable pharmacologic potential as inhibitors in vivo. Studies leading to a clearer understanding of these inhibition processes are now in progress.

Acknowledgment. This work was supported by grants from the National Institutes of Health (HL 29307) and from the Council for Tobacco Research. We are grateful to Dr. Jim Travis at the University of Georgia for supplying the leukocyte proteases.

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(11) Powers, J. C. *Am. Rev. Respir. Dis.* **1983**, *127*, S54–S58.

Chemiluminescence from Hyponitrite Esters. Excited Triplet States from Dismutation of Geminate Alkoxyl Radical Pairs[1]

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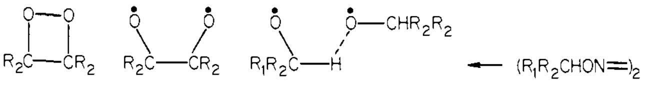
Received May 18, 1983

Numerous studies have focussed attention on chemiluminescence from excited states produced by thermal decomposition of dioxetanes.[2-5] There is general agreement[6-8] that a bialkoxyl 1,4-biradical intermediate (I′) is consistent with the production



I I′ II′ II

a, $R_1 = CH_3$, $R_2 = Ph$; b, $R_1R_2 = (CH_3)_2CH$; c, $R_1R_2 = (CH_2)_5$; d, $R_1 = H_1$, $R_2 = Ph$

of these excited states, and spin inversion in the intermediate to a triplet biradical is a convenient way to rationalize the high triplet yields commonly realized from these compounds. We wish to present preliminary results of a study of the quantum yields arising from alkoxyl radical pairs, in which the assumed transition state (II′) exhibits a formal similarity to I′. In the latter, one σ bond is subsequently lost and two π bonds are formed, while in the former, one σ bond is lost with a gain of one π and one σ bond. The exothermic self-reaction of alkoxyl pairs provide one way to assess the relative importance of cyclic structures and ring strain for efficient generation of excited states from oxygenated precursors.[9,10]

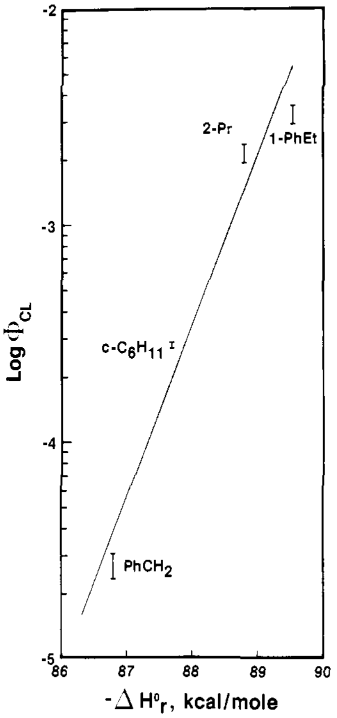


Figure 1. Quantum yields from alkyl hyponitrites in *tert*-butylbenzene as a function of enthalpy for disproportionation to ground-state products. The ordinate values were obtained as described in the text at 43.7 °C.

The chemiluminescence intensity from 5.0×10^{-3} to 5.0×10^{-4} M solutions of hyponitrites (HN; IIa–d) or dioxetane (D; I (R = CH_3)) was measured as a function of 7.0×10^{-4}–3.0×10^{-3} M 9,10-dibromoanthracene (DBA, triplet acceptor) or 9,10-diphenylanthracene (DPA, singlet acceptor).[3,11] The data for every case showed linear relationships ($r > 0.98$) when $1/(\mathrm{d}(h\nu)/\mathrm{d}t)$ was plotted against 1/[acceptor], but the ratios of intercept to slope[12] ($=k_f/(k_d + k_0[^3O_2])$) for the hyponitrite solutions were about 1000–5000 for both aromatic sensitizers. This suggested that the enhanced chemiluminescence from the DPA-sensitized solutions arose from an inefficient triplet–singlet energy-transfer process and that the same, relatively long-lived triplet precursor was responsible for exciting both aromatic fluorescers. In subsequent experiments, addition of piperylene[8] was shown to strongly quench the emission from solutions of DPA and IIa, but not from DPA and dioxetane. Extrapolation to infinite diene concentration gave limiting values of singlet emission that were comparable to the background signal. The singlet yield was 3.7×10^{-6} at the upper limit from 1-phenylethyl hyponitrite at 48.6 °C, corresponding to $^3T/^1S > 1500$.

The intercepts of the Stern–Volmer plots gave values of I_∞^{-1}, from which triplet quantum yields were calculated from the relation in eq 1, in which k's are the first-order rate constants for

$$\Phi_{HN} = (k_D[D]\Phi_D/k_{HN}[HN])(I_\infty^{HN}/I_\infty^{D}) \qquad (1)$$

decomposition, and the bracketed terms refer to initial concentrations. The values of k were obtained from the decay of chemiluminescence from the same solutions over long time periods, which follows the relation $I_t = I_0e^{-kt}$ or by extrapolation of k's obtained at elevated temperatures.[13a] The value of Φ_D was taken as 0.31.[14]

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(1) Mendenhall, G. D.; Quinga, E. M. Y. *Abstr. Pap.–Am. Chem. Soc.* **1983**, *185th*, ORGN 51.

(2) Kopecky, K. R.; Filby, J. E.; Mumford, C.; Lockwood, P. A.; Ding, J-Y. *Can. J. Chem.* **1975**, *53*, 1103–1122.

(3) Wilson, T.; Golan, D. E.; Harris, M. S.; Baumstark, A. L. *J. Am. Chem. Soc.* **1976**, *98*, 1086 and references therein.

(4) Turro, N. J.; Chow, M.-F. *J. Am. Chem. Soc.* **1980**, *102*, 5058–5064.

(5) Adam, W. *Adv. Heterocycl. Chem.* **1977**, *21*, 438–481.

(6) Richardson, W. H.; Anderegg, J. H.; Price, M. E.; Tappan, W. A.; O'Neal H. E. *J. Org. Chem.* **1978**, *43*, 2236–2241.

(7) Koo, J.; Schuster, G. B *J. Am. Chem. Soc.* **1977**, *99*, 5403–5408.

(8) Baumstark, A. L.; Wilson, T. E. *Tetrahedron Lett.* **1979**, 2569–2570.

(9) Hart, R. C.; Cormier, M. J. *Photochem. Photobiol.* **1979**, *29*, 209–215.

(10) Adam, W. *Acc. Chem. Res.* **1979**, *12*, 390–396.

(11) Vassil'ev, R. F. *Prog. React. Kinet.* **1967**, *4*, 305–350.

(12) For a sequence where hyponitrite gives triplets (^3P) which undergo quenching ($k_d + k_0[^3O_2]$) or energy transfer (k_f) to fluorescer (F) we derive $1/[\mathrm{d}(h\nu)/\mathrm{d}t] = (k_d + k_0[^3O_2])/fk_f[F][\mathrm{d}(^3P)/\mathrm{d}t] + 1/f[\mathrm{d}(^3P)/\mathrm{d}t]$, where f is a proportionality constant and the derivatives refer to rates of production.

(13) (a) Ogle, C. A.; Martin, S. W.; Dzioback, M. P.; Urban, M. W.; Mendenhall, G. D. *J. Org. Chem.*, in press. (b) Gas-phase chemiluminescence from mixtures of ethyl hyponitrite and acetaldehyde has been ascribed to a different process: Holden, H. W.; Kutschke, K. O. *Can. J. Chem.* **1961**, *39*, 1552–1553.

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Scheme I

$$\begin{array}{l} \mathrm{RON{=}NOR} \xrightarrow{\Delta} [\mathrm{RO\cdot}\uparrow + \mathrm{N_2} + \mathrm{RO\cdot}\downarrow] \xrightarrow{k_s} \mathrm{ROH} + \mathrm{R'R''CO}\ (^{\circ}\mathrm{S}) \\ \qquad\qquad\qquad\qquad \upharpoonleft\!\downharpoonright \text{ fast} \\ \qquad\qquad\quad\;\; [\mathrm{RO\cdot}\uparrow + \mathrm{N_2} + \mathrm{RO\cdot}\uparrow] \xrightarrow{k_t} \mathrm{ROH} + \mathrm{R'R''CO}\ (^{3}\mathrm{T}) \end{array}$$

The triplet yields in *tert*-butylbenzene are presented in Figure 1 as a function of the gas-phase exothermicities of the alkoxyl disproportionations to give *ground state* products.[15,16] The use of a log scale for the ordinate is a matter of convenience, and the points are not corrected for the cage effect (ca. 30–70%)[13,17] or solvation energies. A linear relation may be assumed *tentatively*, since the error in ΔH_r is at least ±1 kcal/mol. The plot is consistent with our qualitative observation that methyl hyponitrite ($-\Delta H_r^\circ$ = 79 kcal) gives much less light than the other esters. Linear extrapolation of the four points leads to a prediction of a quantum efficiency of about 0.5 above $-\Delta H_r \cong 92$ kcal, an exothermicity accessible with suitable derivatives now under synthesis.

The ordering of triplet yields in Figure 1 is interesting for two reasons. First, the quantum yields do not appear to be a function of triplet energies of the excited-state carbonyl species formed or of the exothermicities of triplet production. Thus IIa, giving acetophenone (E_T = 74.0 kcal/mol,[18] $-\Delta H_{r,\mathrm{triplet}}$ = 15.5 kcal/mol), is at the opposite end of the scale from IId, which gives benzaldehyde (E_T = 71.0 kcal/mol,[18] $-\Delta H_{r,\mathrm{triplet}}$ = 14.9 kcal/mol). Second, an exothermicity relationship of the sort shown in Figure 1 would be consistent with larger activation energies for rate constants k_t than k_s (Scheme I) as the source of the differences in quantum yields. The activation energies, obtained by temperature-jump methods for DBA-enhanced chemiluminescence from IId, IIc, and IIa were 20.4 ± 1.1, 23.3 ± 0, and 21.5 ± 0.6 kcal/mol, respectively. The respective activation energies for disappearance of hyponitrite ester were 26.0 ± 0.4, 27.1 ± 0.0, and 25.2 ± 0.0 kcal/mol in the same solvent system. The differences of −5.6 ± 1.2, −3.8, and −3.7 kcal/mol increase in the opposite direction than expected and are largely due to an activation energy of about −4 kcal/mol for DBA fluorescence.[3]

It is possible that the anticipated differences (≅3 kcal/mol) are overwhelmed by an increase of solvent fluidity with temperature, which would decrease the fraction of alkoxyl pairs that undergo cage reaction.[19] Such an explanation, however, would require us to assume that cage escape for benzyloxyl pairs increases to a greater extent with fluidity than for the other radical pairs.

A more promising explanation may be in quantum-mechanical tunneling[20] of the H atom in II′, particularly if the thickness of the tunneling barrier for k_t resembled k_s and the resemblance were more so with increasing exothermicity of the latter process.

The following experiments indicate that the CL from hyponitrites arises from the mechanism of Scheme I and not from a related or adventitious process: (a) *tert*-butyl hyponitrite, which lacks α-protons, does not give significant CL under our conditions, (b) the extrapolated yield of triplets from 10^{-3} M benzyl hyponitrite in *tert*-butylbenzene with DBA was unchanged in the presence of 0.02 M 2,6-di-*tert*-butyl-4-methylphenol, a free radical scavenger, and (c) the decay of CL from solutions of hyponitrite and fluorescers at elevated temperatures gave the same first-order rate constants as those determined by following the loss of the hyponitrite by HPLC.[13a]

These results may have implications for the mechanism of hydrocarbon oxyluminescence, which heretofore has been ascribed almost exclusively to excited states from peroxyl radical termination.[11,21]

Acknowledgment. This work was supported by a graduate fellowship from the 3M Co. to E.M.Q.

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(14) (a) Adam, W.; Cheng, C.-C.; Cueto, O.; Sakanishi, K.; Zinner, K. *J. Am. Chem. Soc.* **1979**, *101*, 1324–1325. (b) Lechtken, P. *Chem. Ber.* **1976**, *109*, 2862–2870.

(15) For the calculations we assumed DH°(RO–H) = 103 kcal/mol, from which the equation $\Delta H_r = \Delta H_f^\circ(\mathrm{R'R''CO}) - \Delta H_f^\circ(\mathrm{ROH}) - 102$ can be derived. The heat of formation of 1-phenylethanol was estimated from group additivity[15b] while values for other compounds were taken from the literature.[15c] (b) Benson, S. W. "Thermochemical Kinetics"; Wiley: New York, 1968; p 23. (c) Cox, J. D.; Pilcher, G. "Thermochemistry of Organic and Organometallic Compounds"; Academic Press: New York, 1970.

(16) A marked solvent effect was noted in 95% ethanol, which reduced Φ_{triplet} from IIa to 1.9×10^{-5}. The measurements of Φ_{CL} in $\mathrm{CClF_2CFCl_2}$ and in *tert*-butyl alcohol was frustrated by the insolubility of DBA and in isooctane by nonlinear Stern–Volmer plots.

(17) Nair, S.; DeSousa, J. B. *J. Chem. Soc.* **1962**, 4464–4467. We measured a 70% yield of acetophenone and a 78% yield of 1-phenylethanol from decomposition of IIa.

(18) Engel, P. S.; Monroe, B. M. *Adv. Photochem.* **1970**, *8*, 245.

(19) Neumann, R. C.; Bussey, R. J. *J. Am. Chem. Soc.* **1970**, *92*, 2440–2445.

(20) (a) Brunton, G.; Griller, D.; Barclay, L. R. C.; Ingold, K. U. *J. Am. Chem. Soc.* **1976**, *98*, 6803–6811. (b) Platz, M. S.; Senthilnathan, V. P.; Wright, B. B.; McCurdy, D. W., Jr. *Ibid.* **1982**, *104*, 6494–6501 and references therein.

(21) (a) Lundeen, G.; Livingston, R. *Photochem. Photobiol.* **1965**, *4*, 1085–1096. (b) Kellogg, R. E. *J. Am. Chem. Soc.* **1969**, *91*, 5433–5436. (c) Beutel, J.; *Ibid.* **1971**, *93*, 2615–2621.

Thermal Generation of the [16]Annulene Anion Radical from the [8]Annulene Anion Radical

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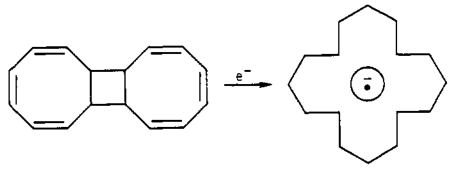
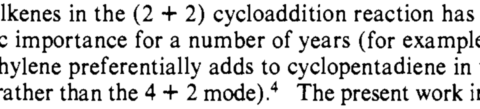
The anion radical of [16]annulene was first generated by Schröder and co-workers[1] via the reduction of the neutral molecule with alkali metal. Later Vincow and Concepcion[2] found that this anion radical could be generated without the laborious synthesis of neutral [16]annulene by simply reducing the (2 + 2) dimer of [8]annulene in tetrahydrofuran (THF) or in hexamethylphosphoramide (HMPA) (reaction 1).[3]



(1)

We now wish to report the generation of the [16]annulene anion radical directly from that of [8]annulene (COT). This reaction represents the first example of a (2 + 2) anion radical–neutral molecule combination.

The high reactivity of electron-rich alkenes with electron-deficient alkenes in the (2 + 2) cycloaddition reaction has been of synthetic importance for a number of years (for example, tetrafluoroethylene preferentially adds to cyclopentadiene in the 2 + 2 mode rather than the 4 + 2 mode).[4] The present work indicates that the very electron-rich COT anion radical reacts readily with the electron-deficient [8]annulene to yield the anion radical of [16]annulene (reaction 2).



(2)

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(1) Oth, J. F. M.; Bauman, H.; Giles, J. M.; Schröder, G. *J. Am. Chem. Soc.* **1972**, *94*, 3498.

(2) Concepcion, J. G.; Vincow, G. *J. Phys. Chem.* **1975**, *79*, 2037.

(3) Stevenson, G. R.; Sedgwick, J. B.; Miller, R. *J. Phys. Chem.* **1982**, *86*, 2441.

(4) Carey, F. A.; Sundberg, R. J. "Advanced Organic Chemistry"; Plenum Press: New York, 1977; Part B, p 221.

0002-7863/83/1505-6521$01.50/0