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Fluoride-Triggered Decomposition of *m*-Sililoxyphenyl -Substituted Dioxetanes by an Intramolecular Electron Transfer (CIEEL) Mechanism

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Abstract: *The synthesis of the protected phenolate-substituted 1,2-dioxetanes 1 and 2, containing the substituent directly linked to the peroxidic ring or separated by a methylene group, is reported. The activation parameters and chemiluminescence quantum yields upon unimolecular and catalyzed decomposition of 1 and 2 are in agreement with the occurrence of an intramolecular CIEEL mechanism in the catalyzed decomposition of these dioxetanes.* © 1999 Elsevier Science Ltd. All rights reserved.

The chemiluminescent reaction most investigated over the past 30 years is the decomposition of 1,2-dioxetanes.[1] Well before they were actually prepared and isolated by Kopecky and Mumford in 1969,[2] 1,2-dioxetanes were proposed as key intermediates in several chemi- and bioluminescent reactions.[3] The thermal cleavage of such compounds generate two carbonyl fragments, one of which can be formed in an electronically excited state. The excited carbonyl product is formed predominantly in the triplet state,[1, 4-6] except for dioxetanes containing electron-rich substituents, for which excited singlet state formation may prevail.[5] In the latter case, such dioxetanes become labile and their decomposition may envolve "chemically initiated electron exchange luminescence" (CIEEL), an electron transfer mechanism originally proposed by Schuster for diphenoylperoxide[7, 8] and in the meantime abundantly reported for α-peroxylactones and various other peroxides.[9-11] However, more recently doubts arose with respect to the quantum yields obtained in intermolecular systems[12] and the validity of the CIEEL sequence has been questioned.[13] On the other hand, intramolecular CIEEL systems proved to be highly efficient.[14] The most successful design utilizes thermally persistent spiroadamantane-substituted dioxetanes with a protected phenolate ion. The decomposition of these dioxetanes can be achieved on treatment with an appropriate reagent (trigger) to induce phenolate ion release. These phenolate-initiated intramolecular CIEEL processes provide the basis for numerous commercial applications, most prominently in chemiluminescence imunoassays.[15] Thus, the search for more effective triggerable CIEEL-active dioxetanes continues attracting the interest of many research groups.[16]

In this communication we report the synthesis and chemiluminescence properties of the 1,2-dioxetanes **1** and **2**. These compounds were treated with fluoride to generate the corresponding phenolate ion either directly bond to the peroxide ring (**1**) or separated from it by a methylene bridge (**2**), in order to verify the occurrence of an intramolecular CIEEL mechanism. In this respect, the distinction between a "resonance" (**1**) and a "through space" (**2**) electron transfer from the generated phenolate to the dioxetane moiety appeared of special interest to us, due to the fact that there is no example in the literature of an intramolecular CIEEL where the electron donor is not directly bond to the peroxide ring.

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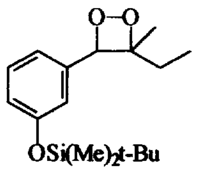

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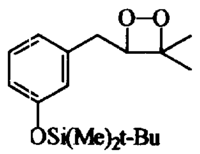

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The dioxetanes 1 and 2 were prepared from the corresponding olefins using the classical Kopecky route.[2] They were purified by low temperature (–35 °C) silica-gel column chromatography and unequivocally characterized on the basis of their spectral data (^{1}H- and ^{13}C-NMR). The thermal decomposition of 1 and 2 leads exclusively to the formation of the expected carbonyl cleavage products. Upon unimolecular decomposition, the dioxetanes show activation parameters and chemiexcitation yields within the expected range for trissubstituted 1,2-dioxetanes, relatively high stability ($\Delta G^{\neq} \approx$ 25 kcal.mol^{-1}) and preferential formation of triplet excited states are observed (table 1). The activation parameters were obtained from the temperature dependence of the decomposition rate constants and the chemiexcitation quantum yields, by utilization of the sensitizers 9,10-diphenylantracene (DPA) for singlet and 9,10-dibromoantracene (DBA) for triplet state counting.[5]

Upon deprotection of the silyloxy-substituted phenyl moiety by treatment of 1 and 2 with tetrabutylammonium fluoride (1,0 mol.L^{-1} solution in THF), which generates the corresponding phenolates, a yellow flash of light is observed. The catalyzed reactions are about 10^4 times faster than the unimolecular ones and, in both cases, a strong direct emission with a maximum around 550 nm is observed. The decomposition rate constant shows a linear dependence on the [F$^-$] at low concentrations ([F$^-$] < 5 mM) for both dioxetanes and proved to be independent of the catalyst concentration at high concentrations ([F$^-$] > 20 mM). Moreover, the fluoride triggered decomposition of 1 and 2 leads to the preferential formation of singlet excited species with high quantum yields, 100 and 1.0%, respectively (table 1). The singlet quantum yields were determined by direct chemiluminescence measurements, utilizing the fluorescence quantum yields of the decomposition products, determined under identical experimental conditions.

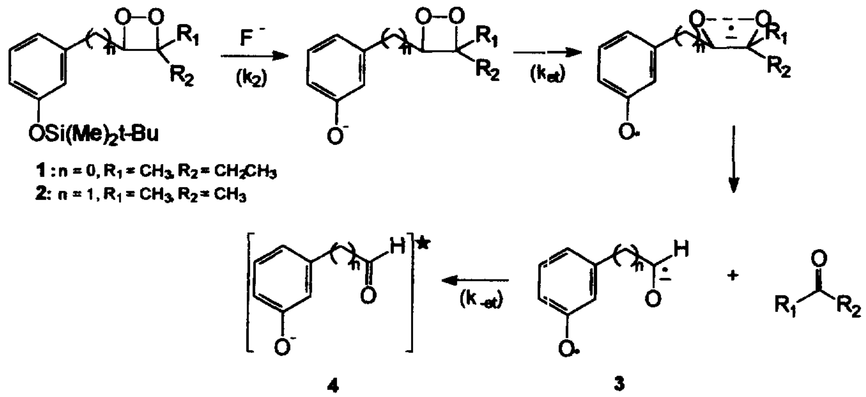
Table 1: Activation Parameters and Quantum Yields for the Unimolecular and Catalyzed Decomposition of Dioxetanes 1 and 2.[a]

	$\Delta H^{\neq}$	$\Delta S^{\neq}$	$\Delta G^{\neq}$ (25°C)	$t_{1/2}$ (25°C)	Φ^T x10^2	Φ^S x10^2
1	24.9 ± 0.7	-0.54 ± 0.02	25.1 ± 0.6	2.9 x 10^5 s	6.8 ± 1.8	0.36 ± 0.10
1 + F$^-$	20.6 ± 0.2	5.0 ± 0.07	19.2 ± 0.2	11 s	___	100 ± 30
2	22.6 ± 0.9	-5.8 ± 0.1	24.1 ± 1.1	8.7 x 10^4 s	6.6 ± 0.6	0.022 ± 0.01
2 + F$^-$	17.6 ± 0.8	-5.9 ± 0.4	19.4 ± 1.0	16 s	___	1.0 ± 0.3

a. $\Delta H^{\neq}$ e $\Delta G^{\neq}$ in kcal.mol^{-1}, $\Delta S^{\neq}$ in cal.mol^{-1}.K^{-1}, Φ^T e Φ^S in E.mol^{-1}; unimolecular decomposition: [1]=(1.0±0.2)x10^{-4}mol.L^{-1}, [2]=(2.1±0.4)x10^{-5} mol.L^{-1}, toluene, 65-85°C; catalyzed decomposition: [1]=(2.0±0.4)x10^{-5} mol.L^{-1}, [2]=(4.2±0.8)x10^{-5} mol.L^{-1}, THF, [F$^-$]=32 x 10^{-3} mol.L^{-1}, 0-25°C, Φ^S obtained under the same conditions at 25^{0}C.

The chemiluminescence spectra of 1 and 2 match the fluorescence spectra of the respective phenolate substituted decomposition products, generated by the addition of tetrabutylammonium fluoride to the corresponding silyl substituted carbonyl compounds. The activation parameters obtained for the catalyzed decomposition are considerably lower than in the unimolecular one (table 1). Although the values for the activation enthalpy ($\Delta H^{\neq}$) and activation entropy ($\Delta S^{\neq}$) in the catalyzed decomposition of **1** and **2** are quite different, the $\Delta G^{\neq}$ at 25°C proved to be similar. These results have led us to propose a mechanism analogous to the CIEEL sequence, which involves the removal of the silyl protective group by fluoride treatment. The released phenolate anion acts as an intramolecular electron donor to the dioxetane moiety inducing dioxetane cleavage and formation of an electronically excited singlet state, which emits fluorescence (Scheme 1).

Scheme 1:



Interestingly, the values obtained for $\Delta S^{\neq}$, positive for **1** and highly negative for **2**, may be attributed to a better charge delocalization in the transition state of the rate limiting electron transfer step, causing a loss of solvatation, in the case of **1**, and to the necessity of a specific conformation for the occurrence of the electron transfer from the phenolate not directly linked to the dioxetane ring, in the case of **2**. It should be pointed out here that the rate limiting step in the catalyzed decomposition of **1** and **2** in our experimental conditions (high $[F^-]$) was proved to be the electron transfer initiated dioxetane decomposition, as both rate constants are independent of the $[F^-]$ in this concentration range (see above).

The first electron transfer from the phenolate to the peroxide ring, which is supposed to be accompanied by the peroxide cleavage, occurs with similar rate constants in both cases. Therefore, the observed difference in the singlet quantum yields of **1** and **2** must be related to the back electron transfer step (k_{-et}). In the case of **1**, the carbonyl radical anion **3**, generated after the peroxide cleavage, represents directly the excited state of **4**. Moreover, this hypothesis can be supported by the so-called *meta*-effect,[17] which predicts that the excited specie generated in the case of **1** can be stabilized by "resonance structures". In the case of **2** this stabilization is not possible, turning excited state formation by back electron transfer less efficient.

In summary, we report the first example of an induced dioxetane decomposition, where the intramolecular catalyst is not directly bond to the peroxide ring. Our experimental results, specifically the quantum yields for **1** and **2**, can be perfectly explained on basis of the proposed CIEEL pathways. Hence, this work supplies direct evidence for the occurrence of an electron transfer in the phenolate induced dioxetane decomposition and for the validity of the widely cited but still polemic CIEEL mechanism.

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References

[1] Wilson,T. *Int. Rev. Sci.: Phys. Chem. Ser. Two* **1976**, 9, 265.

[2] **a)** Kopecky, K. R.; Mumford, C. *Can. J. Chem.* **1969**, 47, 709, **b)** Kopecky, K. R.; Mumford, C. **1968**, *Abstracts, 51st Annual Conference of Chemical Institute of Canada*, Vancouver (B C), p. 41.

[3] **a)** Staudinger, H. *Chem. Ber.* **1925**, 58, 1075, **b)** Staudinger, H.; Dyckerhoff, K.; Klever, H. W.; Ruzicka, L. *Chem. Ber.* **1925**, 58, 1079.

[4] Bechara, E. J. H.; Wilson, T. *J. Org. Chem.* **1980**, 45, 5261.

[5] Adam, W.; Cilento, G. "Chemical and Biological Generation of Excited States", Academic Press, NY **1982**.

[6] Wilson, T.; Halpern, A. M. *J. Phys. Org. Chem.* **1995**, 8, 359.

[7] Koo, J. -Y.; Schuster, G. B. *J. Am. Chem. Soc.* **1978**, 100, 4496.

[8] Schuster, G. B.; Dixon, B.; Koo, J.-Y; Schmidt, S. P.; Smith, J. P. *Photochem. Photobiol.* **1979**, 30, 17.

[9] Schuster, G. B. *Acc. Chem. Res.* **1979**, 12, 366.

[10] Schmidt, S. P.; Schuster, G. B. *J. Am. Chem. Soc.* **1980**, 102, 306.

[11] **a)** McCapra, F.; Beheshti, I.; Burford, A.; Hann, R. A.; Zaklika, K. A. *J. Chem. Soc. Chem. Comm.* **1977**, 944, **b)** Lee, C.; Singer, L. A. *J. Am. Chem. Soc.*, **1980**, 102, 3823, **c)** Zaklika, K. A.; Kissel, T.; Thayer, A. L.; Burns, P. A.; Schaap, A. P. *Photochem. Photobiol.* **1979**, 30, 35, **d)** Schaap, A. P.; Gagnon, S. D. *J. Am. Chem. Soc.* **1982**, 104, 3504, **e.** Nakamura, H.; Goto, T. *Photochem. Photobiol.* **1979**, 30, 27.

[12] Catalani, L. H.; Wilson, T. *J. Am. Chem. Soc.* **1989**, 111, 2633.

[13] **a)** Wilson, T. *Photochem. Photobiol.* **1995**, *62*, 601, **b)** McCapra, F. *Bioluminescence and Chemiluminescence: Molecular Reporting with Photons*, eds J. W. Hastings, L. J. Kricka & P. E. Stanley, John Wiley & Sons, Chichester **1997**, p.7.

[14] **a)** Schaap, A. P.; Chen, T.-S.; Handley, R. S.; DeSilva, R.; Giri, B. P. *Tetrahedron Lett.* **1987**, 28, 1155, **b)** Schaap, A. P.; Handley, R. S.;Giri, B. P. *Tetrahedron Lett.* **1987**, 28, 935, **c)** Schaap, A. P.; Sandison, M. D.; Handley, R. S. *Tetrahedron Lett.* **1987**, 28, 1159.

[15] **a)** Bronstein, I.; Voyta, J. C.; Lazzari, K. G.; Murphy, O.; Edwards, B.; Kricka, L. J. *Biotechniques* **1990**, 8, 310, **b)** Bronstein, I.; Edwards, B.; Voyta, J. C. *J. Biolum. Chemilum.* **1989**, 4, 99, **c)** Bronstein, I.; Voyta, J. C.; Edwards, B. *Anal. Biochem.* **1989**, 180, 95, **d)** Schaap, A. P.; Akhavan, H.; Romano, L. J. *Clin. Chem.* **1989**, 35, 1863, **e)** Bronstein, I.; Voyta, J. C.; Vant Erve, Y.; Kricka, L.J. *Clin. Chem.* **1991**, 37, 1526, **f)** Thorpe, G. H. G.; Bronstein, I.; Kricka, L. J.; Edwards, B.; Voyta, J. C. *Clin. Chem.* **1989**, 35, 2319.

[16] **a)** Adam, W.; Reinhardt, D.; Saha-Möller, C. R. *Analyst* **1996**, 121, 1527, **b)** Adam, W.; Reinhardt, D. *Liebigs Ann.* **1997**, 1359, **c)** Imanishi, T.; Ueda, Y.; Tainaka, R.; Miyashita, K. *Tetrahedron Lett.* **1997**, 38, 841, **d)** Matsumoto, M.; Watanabe, N.; Kobayashi, H.; Azami, M.; Ikawa, H. *Tetrahedron Lett.* **1997**, 38, 411.

[17] Fleming, S. A.; Jensen, A. J. *J. Org. Chem.* **1996**, 61, 7040.