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Hydrogen Bonding Affects the Persistency of Alkyl Peroxy Radicals

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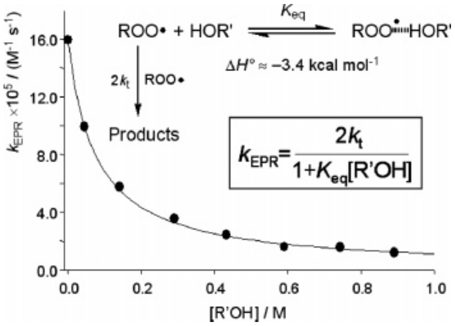
ABSTRACT



The effect of 1,1,1,3,3,3-hexafluoro-2-phenylpropan-2-ol (HFPP) on the persistency of *sec*-alkyl peroxy radicals has been investigated. The formation of a hydrogen-bonding complex between HFPP and the radical resulted in a large increase in the lifetime of the radical. This variation was accompanied by a decrease in the *g*-value. An enthalpy change of -3.4 kcal mol^{-1} was estimated for the formation of the hydrogen-bonded complex.

It is well-established that hydrogen-bonding effects are important in modulating free-radical properties.[1] As an example, phenoxy and semiquinone radicals are known to significantly change their spectroscopic, kinetic, and thermochemical properties upon formation of a hydrogen-bonded complex on the oxygen atom retaining the unpaired electron.[2] Similarly, the possibility of nitroxide radicals to accept a hydrogen bond at the nitroxidic oxygen has been exploited to modulate their reactivity[3] or to control their molecular arrangement in the solid state.[4]

Ab initio calculations and matrix studies have shown that the hydroperoxy radical ($HOO^{\bullet}$) is able to form very stable seven-member-ring complexes with sulfuric[5] and carboxylic acids[6] in which the $HOO^{\bullet}$ radical acts as both a hydrogen-bond donor and a hydrogen-bond acceptor at the terminal oxygen.[7]

Alkyl peroxy radicals, $ROO^{\bullet}$, in which the hydrogen atom is replaced by an alkyl group, are expected to behave only as hydrogen-bond acceptors. Nevertheless, direct evidence of their possibility to accept a hydrogen bond in solution is still missing.[8,9]

As a part of our current studies on the interaction between closed-shell and open-shell molecules,[10] we report here a study on the interaction between alkyl peroxy radicals and

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[1] Chipman, D. M. *J. Phys. Chem. A* **2000**, *104*, 11816−11821.

[2] See for examples: (a) Maki, T.; Araki, Y.; Ishida, Y.; Onomura, O.; Matsumura, Y. *J. Am. Chem. Soc.* **2001**, *123*, 3371−3372. (b) Lucarini, M.; Pedulli, G. F.; Mugnaini, V. *J. Org. Chem.* **2002**, *67*, 928−931. (c) Lucarini, M.; Mugnaini, V.; Pedulli, G. F.; Guerra, M. *J. Am. Chem. Soc.* **2003**, *125*, 8318−8329. (d) Lucarini, M.; Pedulli, G. F.; Guerra, M. *Chem. Eur. J.* **2004**, *10*, 933−939. (e) Thomas, F.; Jarjayes, O.; Jamet, H.; Hamman, S.; Saint-Aman, E.; Duboc, C.; Pierre, J.-L. *Angew. Chem., Int. Ed.* **2004**, *43*, 594−597. (f) Yuasa, J.; Yamada, S.; Fukuzumi, S. *Angew. Chem., Int. Ed.* **2007**, *46*, 3553−3555.

[3] (a) Beckwith, A. L. J.; Bowry, V. W.; Ingold, K. U. *J. Am. Chem. Soc.* **1992**, *114*, 4983−4992. (b) Marque, S.; Fischer, H.; Baier, E.; Studer, A. *J. Org. Chem.* **2001**, *66*, 1146−1156.

[4] Ahrens, B.; Davidson, M. G.; Forsyth, V. T.; Mahon, M. F.; Johnson, A. L.; Mason, S. A.; Price, R. D.; Raithby, P. R. *J. Am. Chem. Soc.* **2001**, *123*, 9164−9165.

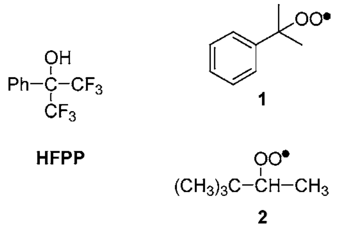
[5] Miller, C. H.; Francisco, J. S. *J. Am. Chem. Soc.* **2001**, *123*, 10387−10388.

[6] (a) Aloiso, S.; Francisco, J. S. *J. Am. Chem. Soc.* **2000**, *122*, 9196−9200. (b) Parreira, R. L. T.; Galembeck, *J. Am. Chem. Soc.* **2003**, *125*, 15614−15622.

[7] Nelander, B. *J. Phys. Chem. A* **1997**, *101*, 9092−9096.

10.1021/ol071059e CCC: $37.00

Scheme 1



hydrogen-bond donors (HBD), interpreted for the first time in terms of formation of a hydrogen-bonded (HB) complex. As HBD we used a fluorinated alcohol such as 1,1,1,3,3,3-hexafluoro-2-phenylpropan-2-ol (HFPP),[11] which is characterized by a very large α_2^H value,[12] indicative of an extremely strong hydrogen-bond donor character, and by a β_2^H value very close to zero, implying that no interaction with the oxygen of OH groups should occur.

Evidence of formation of a HB complex between the cumyl peroxy radical (**1**) and HFPP was obtained by following with EPR spectroscopy the variation in the *g*-value of **1** induced by the addition of the fluorinated alcohol to the solution of cumyl peroxy radicals (see Figure 1).[13] The substantial decrease of the *g*-value ($\Delta g = -0.0004$) observed when increasing amounts of HFPP, up to 1 M, were added to the solution was attributed to the formation of a HB complex between the terminal oxygen atom of the cumyl peroxy radical and the hydroxylic hydrogen of the fluorinated alcohol.

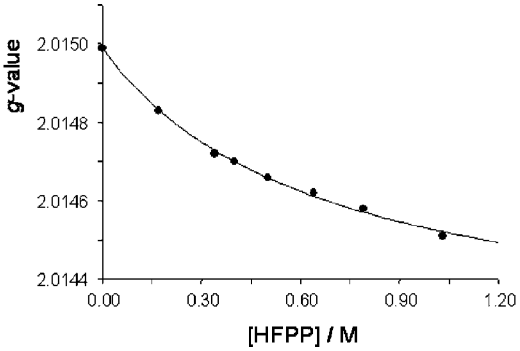


Figure 1. Experimental dependence of the *g*-value of radical **1** at 293 K. The curve is a best fit to eq 2 with the equilibrium constant for the hydrogen-bonded complex of 1.4 M^{-1}.

Peroxy radicals are known to have very large *g*-values.[14] This large positive *g*-value shift from the free electron value mainly originates from the small energy gap between πx^* and πy^* orbitals. Accordingly, any factor increasing the energy difference between these two orbitals should lead to a reduction in the *g*-value. In the case under study, we can hypothesize that the observed decrease in the *g*-value is a consequence of the increase in the energy gap between πx^* and πy^* orbitals, caused by a different perturbation of the *x*- and *y*-levels as a result of hydrogen bonding formation between the terminal oxygen of the peroxy radical and the hydroxylic hydrogen of the alcohol.

This variation of the *g*-value can be used to estimate the strength of hydrogen bonding. The simplest model for the effect of hydrogen bonding formation on the *g*-value assumes an equilibrium of the form

$$\mathrm{ROO}^{\bullet} + \mathrm{H{-}OR} \overset{K_1}{\rightleftharpoons} \mathrm{ROO}^{\bullet}\cdots\mathrm{H{-}OR} \qquad (1)$$

Because the rate of formation and breaking of the hydrogen bonds is very large in the time scale of EPR spectroscopy, the observed averaged *g*-value (g_{obs}) is given by

$$g_{\mathrm{obs}} = \frac{g_{\mathrm{free}} + g_{\mathrm{bound}}K_1[\mathrm{HFPP}]}{1 + K_1[\mathrm{HFPP}]} \qquad (2)$$

where g_{free} and g_{bound} represent the *g*-values for the free and hydrogen-bonded peroxy radicals, respectively, and K_1 is the equilibrium constant.[15] Numerical fitting of the experimental data with this simple model afforded at room temperature an equilibrium constant of 1.4 M^{-1}.

The effect of HFPP on the self-decay of peroxy radicals was also investigated. As a representative species we studied the behavior of the *sec*-alkyl peroxy radical **2** for which the self-reaction above −80 °C has been shown to be a simple bimolecular reaction.[16,17] Radical **2** was produced directly inside the EPR cavity by photolysis of oxygen-saturated

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[8] Hydrogen bonding by water molecules has sometimes been invoked to justify the reduction in the termination rate constant of alkyl peroxyl, $ROO^{\bullet}$, observed in microenvironments such as micelles and phosholipid bilayers compared to nonaqueous homogenous solvents. (a) Barclay, L. R. C.; Baskin, K. A.; Locke, S. J.; Vinquist, M. R. *Can. J. Chem.* **1989**, *67*, 1366−1369. (b) Boyd, S. L.; Boyd, R. J.; Barclay, L. R. C. *J. Am. Chem. Soc.* **1990**, *112*, 5724−5730.

[9] Hydrogen bonding between $ROO^{\bullet}$ and *N*-hydroxyphtalimide has been suggested to justify the low energy barrier found in the corresponding hydrogen transfer reaction. (a) Hermans, I.; Vereecken, L.; Jacobs, P. A.; Peeters, J. *Chem. Commun.* **2004**, 1140−1141. (b) Hermans, I.; Jacobs, P.; Peeters, J. *Phys. Chem. Chem. Phys.* **2007**, *9*, 686−690.

[10] (a) Franchi, P.; Lucarini, M.; Pedrielli, P.; Pedulli, G. F. *ChemPhysChem* **2002**, *3*, 789−793. (b) Mugnaini, V.; Punta, C.; Liantonio, R.; Metrangolo, P.; Recupero, F.; Resnati, G.; Pedulli, G. F.; Lucarini, M. *Tetrahedron Lett.* **2006**, *47*, 3265−3269.

[11] Eberson, L.; Hartshorn, M. P.; Persson, O.; Radner, F. *Chem. Commun.* **1996**, 2105−2111 and references cited therein.

[12] A value of $\alpha_2^H = 0.771$ has been reported for 1,1,1,3,3,3-hexafluoropropan-2-ol (Abraham, M. H.; Grellier, P. L.; Prior, D. V.; Duce, P. P.; Morris, J. J.; Taylor, P. J. *J. Chem. Soc., Perkin Trans 2* **1989**, 699−711).

[13] Radical **1** was produced directly inside the EPR cavity by UV photolysis of oxygen-saturated solutions of cumene (1 M) in benzene containing *tert*-butyl peroxide (0.05 M) and increasing amounts of HFPP. The EPR spectra were recorded on a Bruker ESP 300 spectrometer equipped with a HP 5350B microwave frequency counter for the determination of the *g*-values, which were corrected with respect to that of perylene radical cation in concentrated H_2SO_4 ($g = 2.00258$).

[14] For an exhaustive discussion on the effects determining the *g*-value in the peroxy radical see: Rhodes, C. J. Electron Spin Resonance Studies of Peroxy Radicals in Solid Matrices. In *Peroxy Radicals*; Alfassi, Z. B., Ed.; John Wiley & Sons Ltd: New York, 1997; Chapter 11, pp 335−354.

[15] The reported equation is valid only by assuming that the presence of a small quantity of HFPP does not alter significantly the contribution of the general medium effect on the *g*-value.

[16] Howard, J. A.; Bennett, J. E. *Can. J. Chem.* **1972**, *50*, 2374−2377.

solutions of *tert*-butyl peroxide in 2,2-dimethylbutane containing different amounts of HFPP. Self-decay was studied by analysis of the EPR decay traces recorded after stopping the irradiation of the sample (see Figure 2).[18]

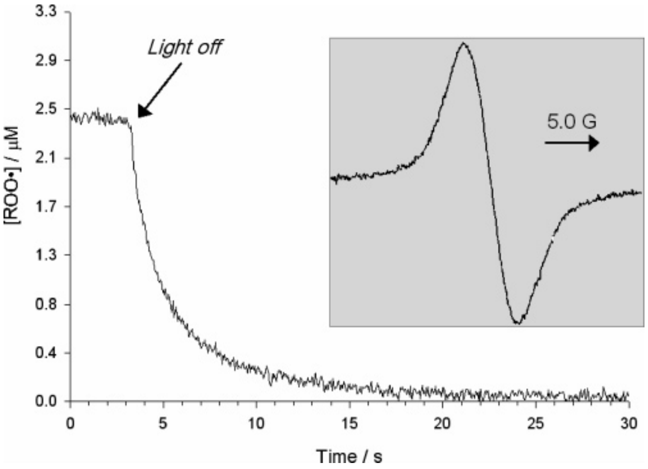


Figure 2. EPR trace of the decay of peroxy radical **2** photolytically generated from a 0.29 M solution of HFPP in oxygen-saturated 2,2-dimethylbutane in the presence of 0.05 M *tert*-butyl peroxide at −70 °C. Insert: Steady-state EPR signal of radical **2** observed during irradiation.

In all cases the EPR decay traces followed good second-order kinetics. In the absence of fluorinated alcohol the measured second-order kinetic constant, $2k_t$ (1.6×10^6 M^{-1} s^{-1} at −70 °C), was in good agreement with the value calculated at the same temperature by using the activation parameters reported by Howard et al. for the same reaction (1.3×10^6 M^{-1} s^{-1}).[16] Addition of HFPP to the solution resulted in a dramatic decrease of the experimental second-order rate constants, k_{EPR}, for peroxy radical **2** (see Figure 3).

On examining Figure 3, it is immediately apparent that k_{EPR} decreases more than 1 order of magnitude on going from pure 2,2-dimethylbutane to a solution containing 0.89 M HFPP. As a consequence of the reduction in the apparent $2k_t$ value, the steady-state concentration of the EPR signals is much higher when radical **2** is produced in the presence of HFPP.

To explain the progressive reduction in the rate of termination by peroxy radical **2** as the concentration of HFPP increased we can invoke the simple kinetic model advanced by Ingold and co-workers to justify the solvent effect observed in the rate of hydrogen abstraction from phenol by alkoxy radicals.[19] According to this model, the EPR decay traces are due to the self-reaction of non-hydrogen-bonded peroxy radical in rapid equilibrium with nonreactive hydrogen-bonded radicals. Under these conditions the measured EPR termination rate is given by the equation reported in Scheme 2, where K_{eq} is the equilibrium constant for hydrogen bond formation between the peroxy radical and HFPP.

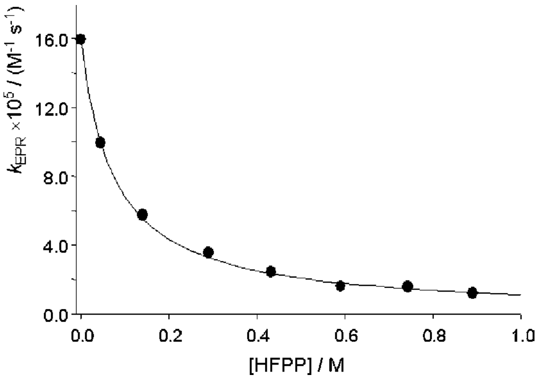
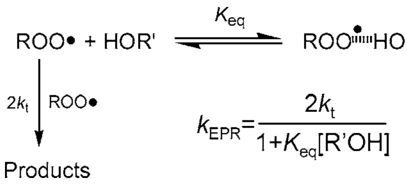


Figure 3. Dependence of k_{EPR} on HFPP concentration at −70 °C for the radical **2**. The curve is a best fit to the equation reported in Scheme 2 with the equilibrium constant for the HB complex of 13.4 M^{-1}.

Scheme 2



Nonlinear fitting of the experimental termination rate constant against the concentration of HFPP afforded a value of 13.4. M^{-1} for K_{eq} at −70 °C.

An estimation of $\Delta H°$ for the formation of the HB complex from the equilibrium constant determined at −70 °C requires knowledge of the corresponding $\Delta S°$. If we make the crude assumption that the entropy change in the present case is comparable to that measured to form the analogous complex between a nitroxide radical (2,2,6,6-tetramethylpiperidine-*N*-oxyl, TEMPO) and 1,1,1,3,3,3-hexafluoropropan-2-ol (HFP)[20] ($\Delta S° = -11.5$ eu),[10a] $\Delta H°$ becomes ca. −3.4 kcal/mol.[21]

Comparison of the $\Delta H°$ value found in this work with that reported for the HB complex between TEMPO and HFP

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(17) The decay of tertiary alkyl peroxyl radical is more complex because of β-scission of the alkoxy radicals generated in the termination reaction. For a review on the argument see: Howard, J. A. Reactions of Organic Peroxyl Radicals in Organic Solvents. In *Peroxy Radicals*; Alfassi, Z. B., Ed.; John Wiley & Sons Ltd: New York, 1997; Chapter 10, pp 319−334.

(18) The contribution of the eventually formed primary peroxy radicals to the EPR signal can be discarded because of their much shorter lifetime.

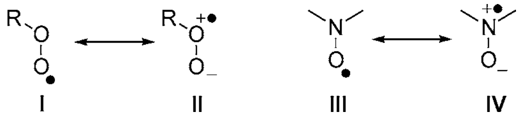
(19) (a) Avila, D. V.; Ingold, K. U.; Lusztyk, J.; Green, W. H.; Procopio, D. R. *J. Am. Chem. Soc.* **1995**, *117*, 2929−2930. (b) Valgimigli, L.; Banks, J. T.; Ingold, K. U.; Lusztyk, J. *J. Am. Chem. Soc.* **1995**, *117*, 9966−9971. (c) Banks, J. T.; Ingold, K. U.; Lusztyk, J. *J. Am. Chem. Soc.* **1996**, *118*, 6790−6791.

(20) Hydrogen-bond acidity of HFP and HFPP can safely be considered in a similar fashion. See ref 12.

(21) Adopting the same entropy change and the K_{eq} determined by following the dependence of the *g*-value at 293 K, $\Delta H°$ becomes −3.5 kcal/mol. This value is in excellent agreement with that found at −70 °C by kinetic experiments.

(−5.45 kcal/mol)[10a] proves that alkyl peroxy radicals are weaker hydrogen bond acceptors than dialkylnitroxides. These two types of radicals are isoelectronic and considered structurally similar (see Scheme 3). However, EPR experiments on ^{17}O-enriched peroxy and nitroxide radicals have shown that the spin density on the terminal oxygen is approximately twice that on the inner oxygen for the former ones[22] and almost identical with that on the nitrogen atom for the latter ones.[23] According to this, the dipolar structure, in which the terminal oxygen possessing more electron density behaves as a better hydrogen-bond acceptor, is expected to be more important in nitroxide radicals (**IV**) than in peroxy radicals (**II**).

Scheme 3



In conclusion, we have estimated for the first time the strength of a hydrogen-bonded complex between a alkyl peroxy radical and a strong hydrogen-bond donor. Although the magnitude of such supramolecular interaction is smaller with respect to those reported for other oxygen-centered radicals, its occurrence can appreciably change the kinetic behavior of peroxy radicals when dissolved in HBD solvents.

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[22] Adamic, K.; Ingold, K. U.; Morton, J. R. *J. Am. Chem. Soc.* **1970**, *92*, 922−923.

[23] (a) Improta, R.; Barone, V. *Chem. Rev.* **2004**, *104*, 1231−1253. (b) Aurich H. G. Nitroxides. In *The Chemistry of Amino, Nitroso and Nitro Compounds and Their Derivatives. Part 1*; Patai, S., Ed.; John Wiley & Sons Ltd: Chichester, UK, 1982; pp 565−622.