ChemComm
www.rsc.org/chemcomm

Greatly attenuated reactivity of nitrile-derived carbon-centered radicals toward oxygen

Enrique Font-Sanchis, Carolina Aliaga, K.-S. Focsaneanu and J. C. Scaiano*
Department of Chemistry, University of Ottawa, Ottawa, Ontario, Canada K1N6N5.
E-mail: tito@photo.chem.uottawa.ca

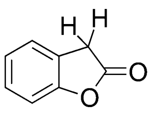
Received (in Cambridge, UK) 3rd April 2001, Accepted 7th June 2002
First published as an Advance Article on the web 20th June 2002

Several cyanoalkyl radicals are reported to be unreactive toward oxygen; spin delocalization on nitrogen is proposed to be the most important factor to explain this unusual behaviour.

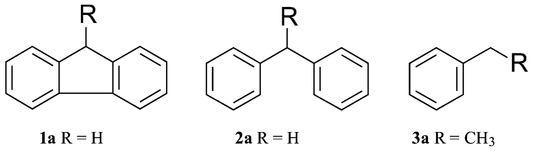
Chain breaking antioxidants are molecules that react with peroxyl radicals by hydrogen transfer processes stopping oxidative chains and generating stabilized radicals unreactive toward oxygen. Thus, phenols are good antioxidants because they meet this criterion.[1–3] However, most carbon centered radicals are highly reactive towards oxygen, and as result hydrogen atom donors bearing labile C–H bonds are not antioxidants;[4] thus, molecules such as diphenylmethane are not antioxidants in spite of being moderately efficient hydrogen donors. Surprisingly, cyanobis(pentachlorophenyl)methyl and α-isopropoxycarbonylbis(pentamethylphenyl)methyl radicals, the substituted analogues of the diphenylmethyl radical, are persistent and do not react with oxygen.[5] The stability of these radicals has been ascribed mainly to steric factors more than electronic effects.

Remarkably, the radicals derived from lactones such as 2-coumaranone do not react with oxygen. Some of these lactones have found commercial applications. We note that in the context of this communication, the reactivity toward oxygen is based on laser photolysis studies and, in this context, ′unreactive radicals′ are those with oxygen quenching rate constants $\leq 5 \times 10^3$ M^{-1}s^{-1}. This represents at least a one million attenuation by comparison with typical radical reactivities. Five parameters have been proposed to explain the diminished reactivity towards oxygen: (a) benzylic resonance stabilization; (b) favorable stereoelectronic effects; (c) unpaired spin delocalization on heteroatoms, *e.g.*, oxygen; (d) electron withdrawing effects, and (e) steric effects.[6,7]

In order to gain further insight into the parameters that can make carbon centered radicals unreactive toward oxygen we have studied the nitriles and esters of Scheme 1. These molecules represent an attempt to address this issue where only criteria (a–d) above are important. As part of this work, we have also examined the reactivity of these substrates towards alkoxyl radicals. We note that for the 9-*tert*-butyl-9-fluorenyl radical, oxygen quenching is only *ca.* five times slower than for the parent 9-fluorenyl, suggesting that steric effects do not play a major role in the compounds studied here.



2-coumaranone



1a R = H
1b R= COOMe
1c R = CN

2a R = H
2b R = COOMe
2c R = CN

3a R = CH$_3$
3b R = COOMe
3c R = CN

Scheme 1

The reactivity towards alkoxyl radicals was determined by studying their reaction with *tert*-butoxyl radicals using laser flash photolysis techniques.[8] The radicals produced in these reactions have convenient absorptions that can be used to monitor their formation directly. Thus, the *tert*-butoxyl radicals were produced by 355 nm laser excitation of a deaerated solution of the peroxide in benzene (50%) (reaction 1, Scheme 2). The growth of the radical signal reflects reaction 2 (k_2) and other forms of decay of *tert*-butoxyl (k_0), such as reaction with the solvent and β-cleavage. The experimental rate constant for the growth is given by equation 3. The rate constants determined from plots of k_{exptl} *vs.* [RH] are given in Table 1.

$$\mathrm{Bu^tOOBu^t} \xrightarrow{h\nu} 2\ \mathrm{Bu^tO\bullet} \qquad (1)$$

$$\mathrm{Bu^tO\bullet} + \mathrm{R\text{-}H} \longrightarrow \mathrm{Bu^tOH} + \mathrm{R\bullet} \qquad (2)$$

$$k_{\text{exptl}} = k_0 + k_2\,[\text{R-H}] \qquad (3)$$

Scheme 2

The enhancement in the rate constants for the hydrogen abstraction of nitrile compounds shows a stabilizing effect of the cyano group on the benzyl radical generated. It seems that the contribution of the resonance form centered on nitrogen is decisive to explain the stability of **1–3c** radicals. In fact, spin density calculation[9] data for these radicals show that about 50% of the unpaired electron is located on the benzylic carbon atom. However, radicals generated from nitrile compounds show a ~20% contribution of the unpaired electron on the nitrogen atom of the cyano group due to resonance delocalization, (*e.g.*, 26% for **3c**) and some double bond character in the C–C(N) bond.

Laser flash photolysis studies of di-*tert*-butyl peroxide at 355 nm in the presence of the substrates were carried out in order to generate the corresponding radicals and to study their reactivity with oxygen (maxima absorption are shown in Table 1). The **1b**

Table 1 Rate constants for the reactions of *tert*-butoxyl radicals with hydrogen donors, absorption of radicals and radical reactivity towards oxygen

Radical from	k_2 (10^6 M^{-1}s^{-1})	$\lambda_{\max}$/nm for radicals	Radical reacts with oxygen?[a]
HP-136[7]	12.4	340	No
2-Coumaranone[7]	51	400	No
1a	6.2	500	Yes
1b	7.4	550	No
1c	26.9	540	No
2a[10]	0.91	340	Yes
2b	0.78	330	Yes
2c	4.21	340	No
3a[8]	1.05	309	Yes
3b	0.62	470	Yes
3c	1.08	470	No

[a] Based on laser flash photolysis work in a 100 μs time scale, see text.

DOI: 10.1039/b203158b

and **1c** radicals generated bands at 550 and 540 nm respectively. The visible band in fluorenyl radical (500 nm) is red-shifted and its intensity is enhanced due to the stabilization of the carboxy or cyano group (Fig. 1, bottom). On the other hand, the visible bands in the cases of **2b**, **2c** (Fig. 1, top), **3b** and **3c** radicals are more intense than in the case of the benzyl radical, enhancement being due to the presence of heteroatoms.[11]

The comparison of nitrogen and oxygen saturated samples showed that both radical growth and decay were not affected by oxygen for **1b** (growth showed in Fig. 2, top), **1c**, **2c** (decay showed in Fig. 2, bottom), and **3c** radicals. However, in oxygen saturated samples, the radicals from **1–3a** and **2,3b** were totally quenched, with barely a fast spike indicating their presence in the early stages following the laser pulse.

The esters methyl diphenylacetate **2b** and methyl phenyl acetate **3b** present flexible structures. However, in methyl 9-fluorene-9-carboxylate **1b**, the five membered ring of the fluorene structure provides forced planarity between the aromatic rings. The lack of reactivity of the **1b** radical with oxygen suggests that electron delocalization in the fluorene structure plays a key role. Moreover, the resonance delocalization of the unpaired electron on the carbonyl oxygen atom in **1b** and **2b** radicals is not important according to ESR data, demonstrating that the preferred resonance structure is as a carbon centered-radical. Furthermore, the mode of dimerization for these radicals shows only C–C coupling.[12]

The lack of reactivity towards oxygen of radicals generated from nitrile compounds is surprising, especially for radicals derived from **2c** and **3c**. On the other hand, it is clear that a high spin delocalization on the cyano group, as it has been demonstrated by spin density calculations, contributes to the stability of these radicals.

Finally, the reactivity enhancements toward alkoxyl radicals caused by nitrile substitution are even more remarkable when one considers that alkoxyl radicals are electrophilic. The dramatic effect of –CN on radical reactivity toward oxygen, while unexpected, can be rationalized on the basis of the same five parameters as for other radicals, with spin density on nitrogen and electron withdrawing effects adding to stabilization achieved by benzylic delocalization.

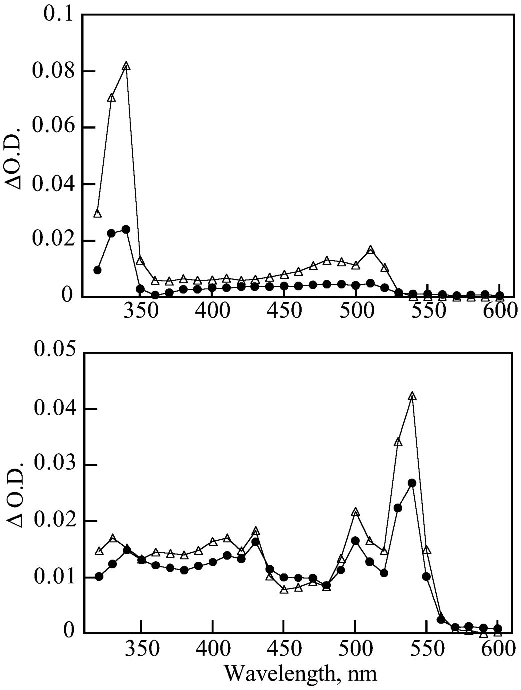


Fig. 1 Top: transient absorption spectra recorded following 355 nm laser excitation of a sample of 0.184 M containing diphenylacetonitrile **2c** in benzene–di-*tert*-butyl peroxide (50:50) under nitrogen, (●) 0.20 μs and (△) 3.48 μs after the laser pulse. Bottom: transient absorption spectra recorded following 355 nm laser excitation of a 0.01 M sample containing 9-cyanofluorene **1c** in benzene–di-*tert*-butyl peroxide (50:50) under nitrogen, (●) 0.72 μs and (△) 8.40 μs after the laser pulse.

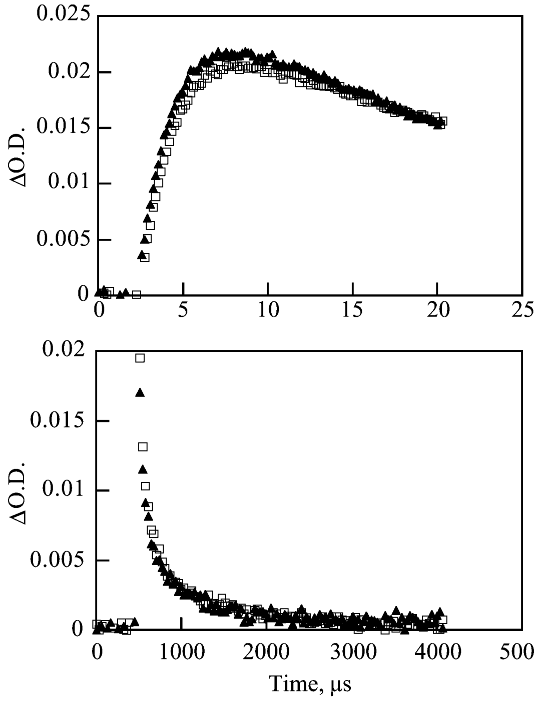


Fig. 2 Top: transient kinetic trace recorded at 550 nm recorded following 355 nm laser excitation of a sample containing 0.134 M of methyl 9-fluorene-9-carboxylate **1b** in benzene–di-*tert*-butyl peroxide (50:50). Bottom: transient kinetic trace recorded at 510 nm recorded following 355 nm laser excitation of a sample containing 0.15 M of diphenylacetonitrile **2c** in benzene–di-*tert*-butyl peroxide (50:50). Traces in both panels recorded under nitrogen (□) and oxygen (▲).

J. C. S. thanks the Natural Sciences and Engineering Research Council of Canada for generous support. E. F. S. thanks Spanish Ministry of Education for a grant.

Notes and references

1 G. W. Burton, T. Doba, E. J. Gabe, L. Hughes, F. L. Lee, L. Prasad and K. U. Ingold, *J. Am. Chem. Soc.*, 1985, **107**, 7053.
2 G. W. Burton and K. U. Ingold, *Acc. Chem. Res.*, 1986, **19**, 194.
3 P. K. Das, M. V. Encinas, S. Steenken and J. C. Scaiano, *J. Am. Chem. Soc.*, 1981, **103**, 4162.
4 B. Maillard, K. U. Ingold and J. C. Scaiano, *J. Am. Chem. Soc.*, 1983, **105**, 5095.
5 L. F. Clarke, A. F. Hegarty and P. O′Neill, *J. Org. Chem.*, 1992, **57**, 362.
6 J. C. Scaiano, A. Martin, G. P. A. Yap and K. U. Ingold, *Org. Lett.*, 2000, **2**, 899.
7 E. V. Bejan, E. Font-Sanchis and J. C. Scaiano, *Org. Lett.*, 2001, **3**, 4059.
8 H. Paul, R. D. Small and J. C. Scaiano, *J. Am. Chem. Soc.*, 1978, **100**, 4520.
9 Spin density calculations were calculated by Density Functional Theory. Electronic structures of the radical molecules were calculated using the Spartan software package (V.5.0.3, Wavefunction, Inc. Irvine). The molecular structures were optimized employing a split-valence basis with a single set of polarization functions added to each atom (DN**). A gradient-corrected functional combining Becke-Perdew as exchange-correlation functional (BP86) was chosen.
10 I. W. C. E. Arends, P. Mulder, K. B. Clark and D. D. M. Wayner, *J. Phys. Chem.*, 1995, **99**, 8182.
11 C. Chatgilialoglu, in *Handbook of Organic Photochemistry*, ed. J. C. Scaiano, CRC Press, Boca Raton, FL, 1989, Vol. II; p. 3.
12 W. P. Neumann and R. Stapel, *Chem. Ber.*, 1986, **119**, 3422.