

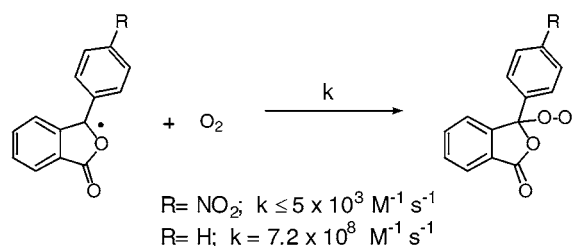
Reactivity toward Oxygen of Isobenzofuranyl Radicals: Effect of Nitro Group Substitution

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ABSTRACT



The presence of a nitro group in the *p*-phenyl position dramatically slows down the oxygenation of isobenzofuranyl radicals. However, both unsubstituted and *m*-substituted phenyl rings have no appreciable influence on the reactivity toward oxygen. Spin delocalization on the nitro group is proposed to explain the stability of the carbon-centered radical generated.

Benzofuranones and isobenzofuranones (phthalides) have been used as stabilizers to prevent thermal and oxidative decomposition during the processing of polymers at high temperatures.^{1,2} In fact, some of these benzofuranones have been found to be relatively good hydrogen donors, and the carbon-centered radicals generated from them present low reactivity toward oxygen, showing typical properties of chain breaking antioxidants.

We have proposed that five parameters can be used to rationalize the attenuated reactivity of carbon-centered radicals toward oxygen: (a) benzylic resonance stabilization; (b) favorable stereoelectronic effects; (c) unpaired spin delocalization on heteroatoms (particularly oxygen); (d) electron-withdrawing effects; and (e) steric effects.^{3,4}

We have recently reported on the importance of electronic effects on some nitrile-derived carbon-centered radicals to explain their low reactivity with oxygen.⁵ In fact, spin

delocalization on nitrogen has been proposed to be the most important factor to explain this unusual behavior.

On the other hand, it is known that the reactivity of benzylic radicals toward oxygen is influenced by the presence of substituents in the aromatic ring.⁶ Thus, the presence of para electron-donating groups such as methoxy or methyl increases slightly the reactivity with oxygen in comparison with the parent benzyl radical. However, in the presence of strong para electron-withdrawing groups such as cyano or nitro, the reactivity with oxygen can be attenuated by a factor of 3. Further, depending on the position of the substituent in the aromatic ring the reactivity of carbon-centered radicals with oxygen can be altered. For example, *m*-cyanobenzyl radical is as reactive as the benzyl radical.

An interesting example is the diphenylpicryl hydrazyl radical (DPPH), a commercially available nitrogen-centered radical that is stabilized by an aromatic ring that bears three nitro groups in the ortho and para positions. It is clear that steric and electronic effects due to the presence of the nitro groups play a role in determining the stability of this radical.

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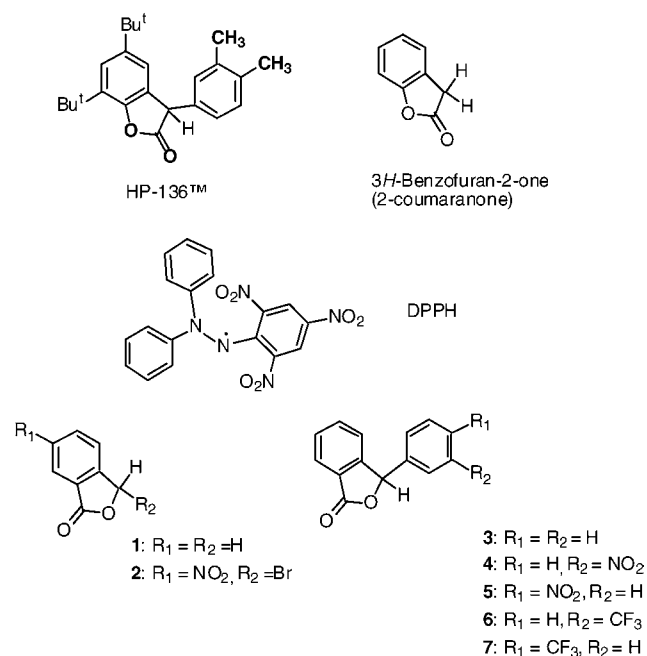
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In this context, we now report the generation and reactivity with oxygen of the radicals derived from isobenzofuranone compounds in Scheme 1. We selected these molecules to

Scheme 1. Isobenzofuranones Studied and Related Compounds



compare their reactivity toward oxygen with those previously reported for benzofuranones⁴ and to establish the importance of electron-withdrawing effects due to the presence of nitro or trifluoromethyl groups.

The radicals were generated from the corresponding precursors by laser excitation of di-*tert*-butyl peroxide in benzene 50% (v/v), using 355-nm laser pulses (radical absorption maxima are given in Table 1). The *tert*-butoxyl radicals abstract the benzylic hydrogen to produce carbon-centered radicals and *tert*-butyl alcohol. The growth of the radical signal reflects the H-abstraction and other forms of decay of *tert*-butoxyl such as reaction with the solvent and β -cleavage.⁷

Under a nitrogen atmosphere the radical generated from 3H-isobenzofuran-1-one (**1**) absorbs at 360 and 525 nm. The visible band is more intense than in the case of the benzyl radical; this enhancement is probably due to the presence of heteroatoms. A similar behavior has been previously described for the 2-coumaranone radical; however, in this case the maximum was detected at 400 nm and the intensity of the band was far greater than that in the case of the radical from **1**. When the same experiments are carried out in oxygen-saturated samples the transient is totally quenched.

The photolysis of di-*tert*-butyl peroxide under nitrogen in the presence of 3-phenyl-3H-isobenzofuran-1-one (**3**) (0.05 M) yields a transient with maximum at 340 nm; this band is quite similar to that for the diphenylmethyl radical.⁸ No other

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Table 1. Absorption of the Radicals, Rate Constants for the Reactions of Cumyloxyl/*tert*-Butoxyl Radicals with Hydrogen Donors, and Reactivity toward Oxygen

substrate	alkoxy radical rate constant (10 ⁶ M ⁻¹ s ⁻¹)	radical wavelength max, nm	reactivity with oxygen ^a
HP-136 ⁴	12.4 ^b	340	no
2-coumaranone ⁴	51 ^c	400	no
1	2.07 ^c	360, 525	yes
2		360	(no) ^d
3	5.35 ^e	340	yes
4	2.83 ^e	340, 380	yes
5	3.77 ^e	340, 580	no
6	3.01 ^e	340	yes
7	2.70 ^e	340	yes

^a Based on laser flash photolysis work in a 100- μ s time scale. ^b Obtained by laser flash photolysis of dicumyl peroxide. ^c Obtained by laser flash photolysis of di-*tert*-butyl peroxide. ^d These measurements are difficult due to potential interference of Br₂⁻ at 360 nm. There are also poorly resolved absorbances in the 500–600 nm range; these are normal for a radical with this structure. ^e Obtained from product studies with cumyl hyponitrite as the source of cumyloxyl radicals.

bands were detectable between 300 and 700 nm, indicating a low contribution of the carbonyl group to the absorption of the radical. Further, the signal for the radical from **3** was quenched by oxygen with a rate constant of 7.2×10^8 M⁻¹ s⁻¹. This is about a million times faster than the isomeric radical from 2-coumaranone.

Benzyl radicals are readily quenched by paramagnetic substrates such as nitroxide radicals (the rate constants for these reactions are frequently $\sim 10^8$ M⁻¹ s⁻¹ in acetonitrile).⁹ Thus, the rate constants of the radicals generated from **3** and the HP-136 toward 2,2,5,5-tetramethylpiperidin-1-oxyl (TEMPO) were obtained from the transient decay at different TEMPO concentrations in mixtures of benzene/di-*tert*-butyl peroxide (1/1 v/v). The values obtained are 1.77×10^7 and 1.35×10^5 M⁻¹ s⁻¹, respectively. Clearly, the benzofuranone structure leads to a more stable, and therefore less reactive radical.

From the above results, it seems that the contribution of the resonance form centered on oxygen is decisive to explain the lack of reactivity of the benzofuranone structure toward oxygen. In fact, spin density calculation data¹⁰ for the radical from phthalide **1** show higher spin density located on the benzylic carbon atom (52.4%) than for the radical from 2-coumaranone (45.3%).

If we assume that the spin density at the benzylic position is key to the coupling reaction of benzyl radical and

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(10) Spin density calculations were calculated by Density Functional Theory. Electronic structures of the radical molecules were calculated with use of 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 the exchange-correlation functional (BP86) was chosen. For more details see the Supporting Information.

molecular oxygen, the introduction of electron-withdrawing groups could reduce the reactivity with oxygen of the carbon-centered radical. With this aim, we generated and studied the radicals from molecules **2** and **4–7**.

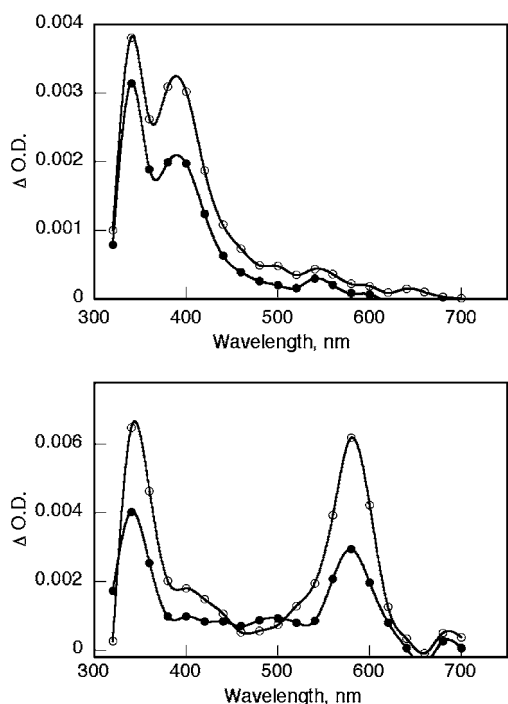


Figure 1. Top: Transient absorption spectra recorded following 355-nm laser excitation of a 0.004 M sample containing 3-(3-nitrophenyl)-3H-isobenzofuran-1-one (**4**) in benzene/di-*tert*-butyl peroxide (50/50) under nitrogen, (●) 7.84 μ s and (○) 31 μ s after the laser pulse. Bottom: Transient absorption spectra recorded following 355-nm laser excitation of a 0.004 M sample containing 3-(4-nitrophenyl)-3H-isobenzofuran-1-one (**5**) in benzene/di-*tert*-butyl peroxide (50/50) under nitrogen, (●) 1.08 μ s and (○) 7.60 μ s after the laser pulse.

The photolysis of di-*tert*-butyl peroxide in the presence of 6-nitrothalide does not produce good signals that might be used to monitor its formation. On the other hand, it is known that photolysis of benzylhalide compounds leads to the homolytic cleavage of the C–X bond to generate benzylic radicals.¹¹ Thus, the radical from 6-nitrothalide is generated by laser flash photolysis (LFP) of **2** (0.001 M) at 355 nm in benzene or acetonitrile. The radical generated in acetonitrile shows a broad band around 360 nm that does not decay completely after 100 μ s. Monitoring at 360 nm,¹² the comparison of nitrogen- and oxygen-saturated samples shows that the signal decay is not influenced by oxygen. When the

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(12) These signals may be somewhat contaminated by $\text{Br}_2^{\cdot-}$ that absorbs in the same region. It is clear, however, that the dominant contribution is from the phthalide radical, since $\text{Br}_2^{\cdot-}$ is shorter lived, and the 360-nm signal is also observed in benzene, where bromine atoms have a different fate: Hug, G. L. *Optical Spectra of Nonmetallic Inorganic Transient Species in Aqueous Solution*; National Bureau of Standards: Washington, DC, 1981; Vol. NSRDS-NBS 69.

photolysis is carried out in benzene, together with the band at 360 nm we observed a second band at 550 nm with a lifetime around 2 μ s. This transient can be assigned to the well-known bromine radical–benzene complex.¹³ Further, spin density calculations for the radical from 6-nitrothalide (**2**) show less spin density located on the benzylic carbon atom than for the radical from **1**.

In the presence of a nitrogen atmosphere, the abstraction of the benzylic hydrogen by *tert*-butoxyl radicals in the case of 3-(3-nitrophenyl)-3H-isobenzofuran-1-one (**4**) (0.004 M) produces a transient with maxima at 340 and 380 nm (Figure 1, top); this transient is readily quenched by oxygen.

However, LFP of the peroxide in the presence of 3-(4-nitrophenyl)-3H-isobenzofuran-1-one (**5**) (0.004 M) generates a transient with maxima at 340 and 580 nm (Figure 1, bottom) that is not affected by the presence of oxygen (Figure 2). The intense band observed at 580 nm might indicate the

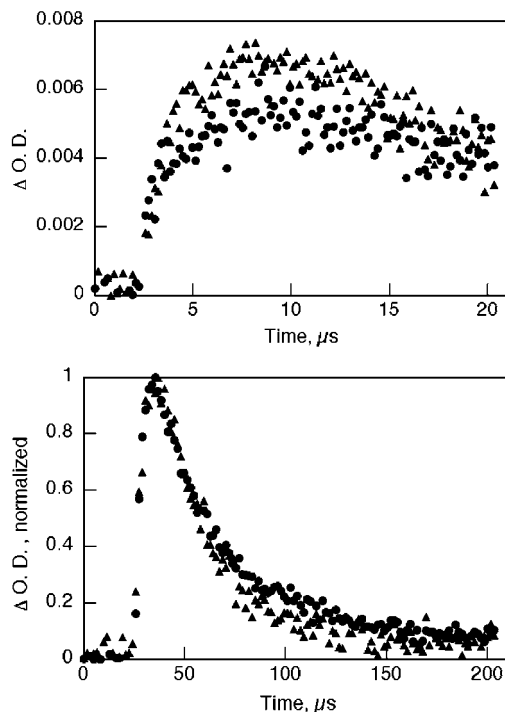


Figure 2. Transient kinetic trace recorded following 355-nm laser excitation of a sample containing a 0.004 M sample of 3-(4-nitrophenyl)-3H-isobenzofuran-1-one (**5**) in benzene/di-*tert*-butyl peroxide (50/50) under nitrogen (●) and oxygen (▲) at 340 (top) and 580 nm (bottom).

contribution of the nitro group to the chromophore. A similar absorption spectrum has been previously reported for the *p*-nitrobenzyl radical.¹⁴

The absorption spectra and reactivity toward oxygen of the radicals generated from the trifluoromethyl compounds **6** and **7** are similar to that observed for the radical from **3**.

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A good antioxidant needs to be a good hydrogen donor. Thus, we also examined the reactivity of **3–7** toward cumyloxyl radicals by the thermolysis of di- α -cumyl hyponitrite, where the rate constants are based on product studies (acetophenone vs cumyl alcohol).^{15,16} The isobenzofuranones studied are good hydrogen donors, but their reactions are somewhat slower than in the case of benzofuranones (e.g., HP-136 and 2-coumaranone). From an oversimplified approach, in the latter case one can write resonance structures placing the spin on oxygen without affecting ring aromaticity, something that is also reflected in the spin density calculations.

In summary, it is clear that the presence of a nitro group in the *p*-phenyl position slows down the oxygenation of isobenzofuranyl radicals. However, meta substituents have no appreciable influence on the reactivity toward oxygen. These results, together with the fact that the radicals derived from trifluoromethyl compounds **6** and **7** react with oxygen,

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show the importance of spin delocalization on a heteroatom (oxygen in this case) to explain the stability of the carbon-centered radical generated. Clearly the benzofuranone structure is better than the isobenzofuranone in stabilizing the carbon radical center toward reaction with oxygen. This should be attributed to resonance stabilization effects, since steric and electron-withdrawing effects should be comparable. Even addition of a phenyl ring (as in **3**) is not enough to prevent reaction, but rather the strong electron-withdrawing effect from a *p*-nitro substituent is needed.

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

Supporting Information Available: Experimental details, methodology used for determining H-abstraction constants, and spin density distribution for radicals. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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