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Mechanistic Studies of Radical-Based Processes. Use and Misuse of EPR Spectroscopy

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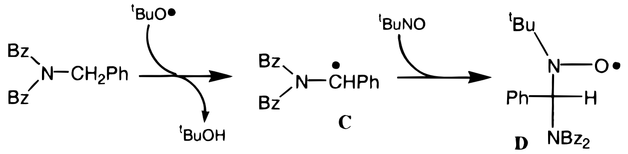
ABSTRACT



The identification of the species observed by EPR spectroscopy in the SmI$_2$-promoted coupling of *N*-(*N*′,*N*′-dialkylaminoalkyl)benzotriazoles as substituted benzyl radicals is disputed on the basis of results obtained studying the model radical derived from tribenzylamine.

Organic free radicals and radical ions are in most cases very labile transient species, often difficult to reveal and characterize. EPR spectroscopy is by far the technique of choice for studying these species: indeed, it represents a very sensitive tool for their detection while the spectral parameters of the detected radicals may provide a unique route to their identification, the hyperfine splitting (hfs) constants and *g*-factor being a sort of fingerprint of these species.[1]

On the other hand, intercepting radical species in the course of chemical processes is often made difficult by the fact that these species hardly reach a steady-state concentration high enough to allow a direct EPR detection. To overcome this impasse the spin trapping technique was devised some 30 years ago,[2] which consists of adding to the system under examination a small amount of a substance capable of readily reacting with the transient radicals thus converting them to spin adducts characterized by a higher persistence and therefore easier to detect. Although this technique only provides a "second-hand" information of the investigated radicals, it has nevertheless proved very useful and has been largely exploited by EPR spectroscopists since its introduction.[3,4]

When investigating radical processes through EPR spectroscopy, the utmost care must be exerted in the interpretation of the spectral parameters, a clear-cut identification of the paramagnetic species detected being essential in deriving a correct reaction mechanism. A significant example of the ambiguity that may arise is provided by the case of the phenyldiazotate radical, Ph−N═N−O•;[5] in fact, back in the late 1960s this species was initially postulated, subsequently refuted, and eventually proved as a key intermediate in the phenylation with aromatic diazo compounds mainly on the basis of the spectra detected when running the reaction inside the cavity of an EPR spectrometer.

A paper recently published in this journal[6] reported on the direct as well as indirect (spin trapping) EPR detection and characterization of radicals in the SmI$_2$ promoted coupling of *N*-(*N*′,*N*′-dialkylaminoalkyl)benzotriazoles. The

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(1) Wertz, J. E.; Bolton, J. R. *Electron Spin Resonance, Elementary Theory and Practical Applications*; McGraw-Hill: New York, 1972.

(2) Janzen, E. G.; Blackburn, B. J. *J. Am. Chem. Soc.* **1968**, *90*, 5909.

(3) Perkins, M. J. *Adv. Phys. Chem.* **1980**, *17*, 1.

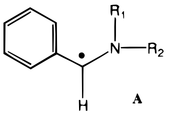
(4) Tordo, P. In *Electron Spin Resonance. A Specialist Periodical Report*; Gilbert, B. C., Atherton, N. M., Davis, M. G., Eds.; The Royal Society of Chemistry: London, 1998; p 116.

(5) Binsch, G.; Rüchardt, C. *J. Am. Chem. Soc.* **1966**, *88*, 173. Binsch, G.; Merz, E.; Rüchardt, C. *Chem. Ber.* **1967**, *100*, 247. Chalfont, G. R.; Perkins, M. J. *J. Am. Chem. Soc.* **1967**, *89*, 3054. Chalfont, G. R.; Hey, D. H.; Liang, K. S. Y.; Perkins, M. J. *J. Chem. Soc., Chem. Commun.* **1967**, 367. Cadogan, J. I.; Paton, R. M.; Thomson, C. *J. Chem. Soc., Chem. Commun.* **1969**, 614.

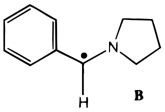
(6) Katritzky, A. R.; He, H.-Y.; Qiu, G.; Bratt, P. J.; Parrish, S. H., Jr.; Angerhofer, A. *Org. Lett.* **1999**, *1*, 1755.

10.1021/ol005741j CCC: $19.00

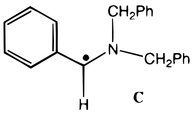
radicals involved were in all cases identified as α-dialkylamino benzyl radicals having the general structure **A**.



A



B



C

It occurred to us that both the EPR spectrum shown in the paper and attributed to radical **B** as well as the very low *g*-factor values (2.0007−2.0009) reported for that and the other detected species were totally inconsistent with the proposed α-dialkylaminobenzyl radicals **A**. Actually the vast majority of organic radicals have *g*-factor values equal to or larger than that of the free electron, i.e., 2.0023.[7] Only σ-radicals such as acyl, thioacyl, or vinyl radicals exhibit values lower than that of the unpaired electron, in a few cases as low as 2.0006.[8] Benzyl radicals are π species where, in the absence of unfavorable steric situations, the unpaired electron is delocalized onto the aromatic ring. They have *g*-factors ≥ 2.0023, the values becoming even larger when sulfur-, oxygen-, or nitrogen-centered substituents are linked to the radical center.[9] Besides, in addition to couplings with the aromatic hydrogen atoms, their spectra exhibit in all cases a doublet splitting of ca. 1.3−1.7 mT due to the α-hydrogen atom; thus, even under high modulation conditions, the spectra of radicals **A** cannot consist of a single line narrower than 1 mT. To verify this point we photolyzed inside the cavity of an EPR spectrometer an argon-purged benzene solution of tribenzylamine containing a small amount of di-*tert*-butyl peroxide. The photogenerated *tert*-BuO• radicals abstract one of the six equivalent methylenic hydrogen atoms affording radical **C**, which exhibits a very weak and rather complex spectrum that has a *g*-factor of 2.0031, and whose overall splitting largely exceeds 3.0 mT (see Figure 1).

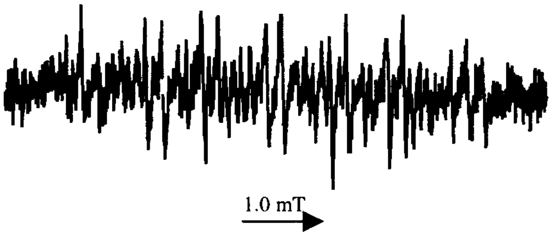


Figure 1. EPR spectra observed upon photolysis of a benzene solution of $(PhCH_2)_3N$ and di-*tert*-butyl peroxide at 278 K (32 scans).

Despite the poor S/N ratio, the spectral pattern could be rationalized by assuming coupling of the unpaired electron with two *ortho* (a_{Ho} = 0.525, 0.586 mT), two *meta* (a_{Hm} = 0.14, 0.159 mT), one *para* (a_{Hp} = 0.742 mT), and one α ($a_{H\alpha}$ = 1.709 mT) hydrogen atoms, the magnetic unequivalence of the two *meta* and *ortho* hydrogen atoms resulting from restricted rotation of the phenyl ring about the phenyl−C_α bond. This set of parameters is fully consistent with those of several α-substituted benzyl radicals. In our opinion, the single line signals with *g*-factors 2.0007−2.0009 erroneously assigned[5] to the benzyl radicals are more likely to be due to a samarium-centered paramagnetic species of some sort. We could not find in the literature any spectral data for samarium radicals, but found that the *g*-factor values of the two radicals •YbH and •YbF centered at ytterbium, an element that like Samarium belongs to the lanthanide family, had *g*-factors of 2.0000 and 1.9997, respectively,[10] i.e., very low values similar to those reported in ref 5.

Photolysis of a sample to which a small amount of the spin trap 2-methyl-2-nitrosopropane (MNP) had been added[11] led to the spectrum shown in Figure 2a, which is dominated by the signals from two radicals: the di-*tert*-butyl nitroxide

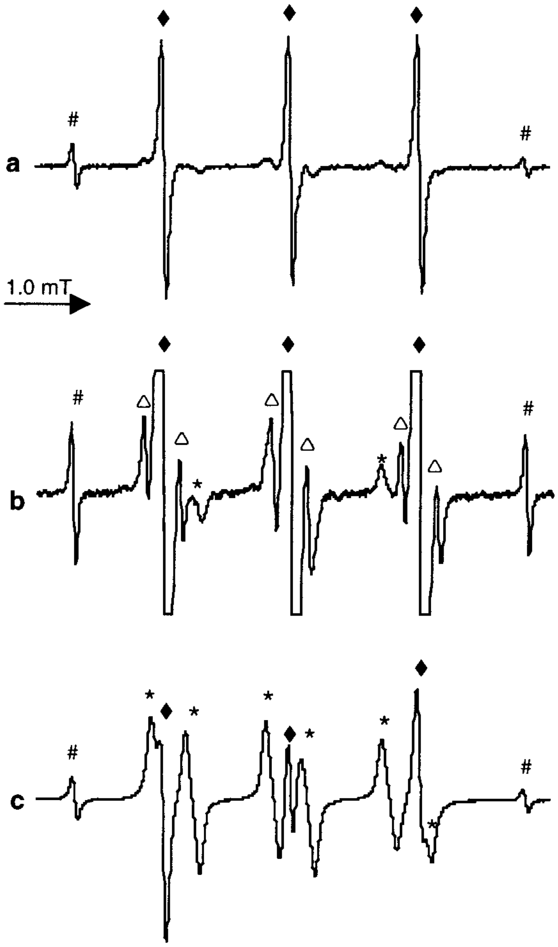


Figure 2. EPR spectra observed upon photolysis of a benzene solution of $(PhCH_2)_3N$, $(CH_3)_3COOC(CH_3)_3$, and MNP. Signals derive from di-*tert*-butyl nitroxide (◆), nitroxide **D** ($*$), and *tert*-butyl *tert*-butoxy nitroxide (#). (a) Spectrum after a flash of light. (b) Spectrum evidencing ^{13}C satellites (△) of lines (◆). Spectrum after prolonged photolysis.

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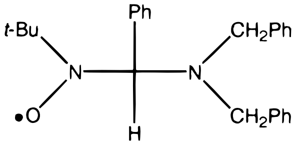
(7) Landolt-Börnstein, New Series. *Magnetic Properties of Free Radicals*; Fischer, H., Hellwege, K.-H., Eds., Springer-Verlag: Heidelberg, 1977; Group II, Vol. 9, Part b. Landolt-Börnstein, New Series. *Magnetic Properties of Free Radicals*; Fischer, H., Ed., Springer-Verlag: Heidelberg, 1987; Group II, Vol 17, Part c.

(1:1:1 triplet, $a_N = 1.545$ mT, $g = 2.0059_5$), always present in MNP solutions but whose amount decreases upon continuous UV irradiation, and the *tert*-butoxy *tert*-butyl nitroxide (1:1:1 triplet, $a_N = 2.717$ mT, $g = 2.0054_1$) resulting from addition of photogenerated *tert*-BuO• radicals to MNP. Upon prolonged irradiation a third species (1:1:1 triplets of 1:1 doublet, $a_N = 1.397$ mT, $a_H = 0.441$ mT, $g = 2.0059_7$) became dominant (see Figure 2c).



D

We identify this last radical, whose amount increases in time with respect to the other two species, with the spin adduct **D** resulting from the trapping of radical **C** by MNP.

In this light we believe that the spectrum shown in Figure 2 in ref 5 cannot be due to the superimposition of the spectra of **D** and t-$Bu_2N(O•)$, but is instead that of the latter nitroxide alone, the small doublets being the satellites due to the ^{13}C-isotopes of the eight carbon atoms of the two butyl groups ($a_{13C\beta} = 0.495$ mT, $a_{13C\gamma} = 0.45$ mT),[12] as evidenced in Figure 2b.

Before concluding we wish to stress that it is not our intention to dispute the proposed radical mechanism in the SmI_2-promoted reductive coupling of *N*-(*N′*,*N′*-dialkylaminoalkyl)benzotriazoles, and that the present results do not actually exclude it. On the other hand, despite the fact that the probable detection of a samarium radical supports the occurrence of the hypothesized SET reaction,[5] the previous EPR investigation does not provide any evidence of the involvement of benzyl-like radicals.

From the above explanation emerges the necessity of identifying without any ambiguity the radicals responsible for the observed spectra when outlining a radical-based mechanism following EPR observations. Besides, it should be emphasized that EPR spectroscopy, because it exclusively detects paramagnetic species, is a very delicate technique whose results are to be handled with great caution. Indeed, the EPR observation of radicals in the course of a reaction does not definitely imply that a radical-based process is taking place, and conversely the failure to detect radical species does not definitely exclude the occurrence of a radical-based process.

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(9) Miertus, S.; Hysel, O. *Chem. Phys*. **1977**, *21*, 33. Sylvander, L.; Stell, L.; Korth, H.-G.; Sustmann, R. *Tetrahedron Lett.* **1985**, *26*, 749.

(10) Van Zee, R. J.; Seely, M. L.; Weltner, W. *J. Chem. Phys*. **1977**, *67*, 861.

(11) **EPR Experiments**. EPR spectra were recorded on an upgraded Bruker ER 200D/ESP 300 X-band spectrometer with built-in gaussmeter (field calibration), frequency counter (*g*-factor determination), and variable temperature controller. Samples consisted of thoroughly argon-purged 10^{-2} M benzene solutions of tribenzylamine containing some di-*tert*-butyl peroxide (10^{-2} M). For the spin trapping experiments, some 2-methyl-2-nitrosopropane, MNP, was also present (10^{-3} M). Samples were irradiated inside the cavity of the spectrometer with the direct light from a Hanovia high pressure 1 kW Mercury lamp at a temperature just above the freezing point of the solvent (278 K). All the chemicals were purchased from Fluka and used as received, with the exception of benzene that was dried via standard procedures.

(12) Brière, R.; Chapelet-Letourneux, G.; Lemaire, H., Rassat, A. *Mol. Phys*. **1971**, *20*, 684.