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EPR Studies on the SmI_2-Promoted Coupling of *N*-(*N*′,*N*′-Dialkylaminoalkyl)benzotriazoles

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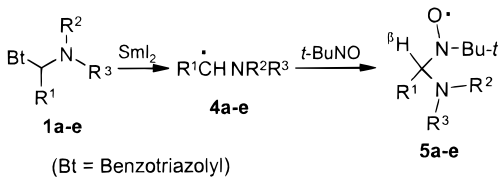
ABSTRACT



Radicals generated in the SmI_2-promoted coupling of *N*-(*N*′,*N*′-dialkylaminoalkyl)benzotriazoles 1 have been detected using the EPR spin-trapping technique. Single electron transfer (SET) between 1 and SmI_2 is discussed as a mechanism for the formation of the radicals.

In 1992, Aurrecoechea and Fernandez-Acebes[1] reported the SmI_2-promoted reductive coupling of *N*-(*N*′,*N*′-dialkylaminoalkyl)benzotriazoles **1** to furnish *tertiary* vicinal diamines **2** (Scheme 1). The mechanism for the SmI_2-promoted reductive coupling of **1** is considered to involve the initial formation of immonium cations **3**,[2] which are reduced by SmI_2 to generate α-aminoalkyl radicals **4**.[3] The coupling of two such radicals produces the vicinal diamines (route A). We have now found direct evidence (previously lacking) for the existence of radical intermediates using the electron paramagnetic resonance (EPR) technique.

N-(*N*′,*N*′-Dialkylaminoalkyl)benzotriazoles **1a**−**e** were prepared by the condensations of benzotriazole with aliphatic or aromatic aldehydes and secondary amines as previously described.[4a−d]

Using the EPR technique to observe the reactions of **1a**−**d** with SmI_2 at −70 °C, one EPR peak was obtained (e.g., Figure 1 for **4b**). The *g* values (2.0007−2.0009) for the EPR

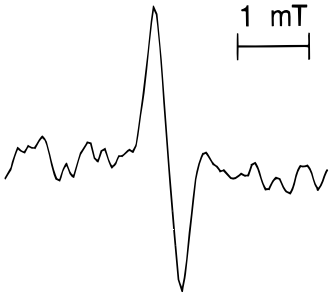


Figure 1. EPR signal of the radical **4b**.

signals indicate that they are carbon-centered radicals. This provides direct evidence that the coupling reactions of **1a**−**d**

(1) Aurrecoechea, J. M.; Fernandez-Acebes, A. *Tetrahedron Lett.* **1992**, *33*, 4763.
(2) Katritzky, A. R.; Rachwal, S.; Hitchings, G. J. *Tetrahedron* **1991**, *47*, 2683.
(3) Martin, S. F.; Yang, C. P.; Laswell, W. L.; Rueger, H. *Tetrahedron Lett.* **1988**, *29*, 6685.

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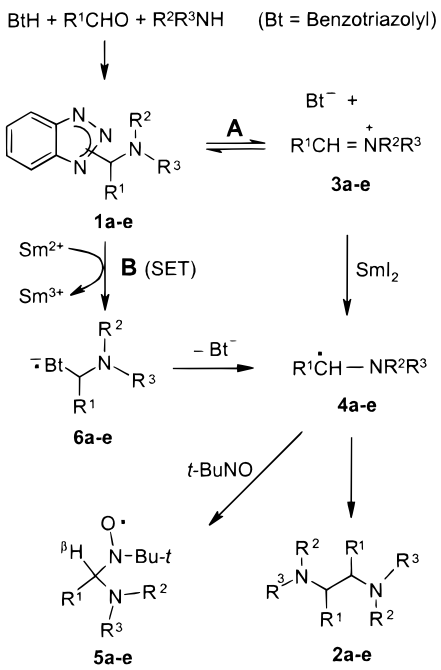
Scheme 1



Compd	R1	R2	R3
2a	Ph	$PhCH_2$	$PhCH_2$
2b	Ph	$-CH_2CH_2CH_2CH_2-$	
2c	Ph	$PhCH_2$	CH_3
2d	Ph	$PhCH_2$	Ph
2e	*i*-Pr	$PhCH_2$	$PhCH_2$

involve radicals. We believe that the radicals detected are **4a**−**d**, but the signal−noise ratios are remarkably low and the signals disappear within 8−15 min. This is probably due to the instability of carbon-centered radicals bearing α-hydrogens.

No EPR signal was observed for the SmI_2-promoted coupling of **1e**. Since the radical intermediate **4e** has no phenyl group attached to the carbon-centered radical, no EPR signal was to be expected.

As the instability of the radicals **4a**−**e** precludes obtaining well-resolved spectra, the spin-trapping technique was applied. In spin-trapping, unstable, short-lived carbon-centered radicals react with spin-trapping agents, such as nitroso compounds, to form more stable, longer-lived nitroxides which are easier to detect by EPR. *N*-*tert*-Butyl-α-phenylnitrone (PBN) when used as a spin-trapping agent gave no EPR signal, presumably because sterically hindered PBN does not efficiently trap the radicals **4a**−**e**. However, nitroso-*tert*-butane (*t*-BuNO) as a spin-trapping agent gave similar EPR signals for each substrate (cf. Figure 2). The strong triplet peaks are attributed to di-*tert*-butyl nitroxide [*t*-Bu-N(O•)-Bu-*t*], which is always present in the *t*-BuNO solution.

(4) (a) Katritzky, A. R.; Yannakopoulou, K.; Lue, P.; Rasala D.; Urogdi, L. *J. Chem. Soc., Perkin Trans. 1* **1989**, 225. (b) Katritzky A. R.; Fan, W. Q. *J. Fluorine Chem.* **1991**, *51*, 33. (c) Katritzky, A. R.; Latif, M.; Urogdi, L. *J. Chem. Soc., Perkin Trans. 1* **1990**, 667. (d) Katritzky, A. R.; Chang, H. X.; Wu, J. *Synthesis* **1994**, 907.

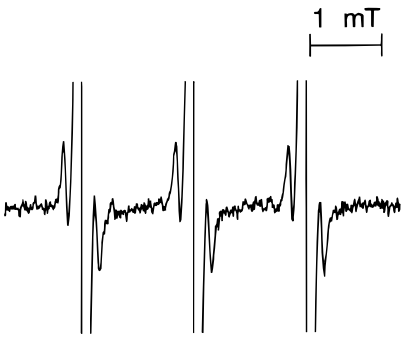


Figure 2. EPR signal of the spin-adduct **5a** and $(t\text{-Bu})_2$N(O**i**).

The six other smaller EPR peaks (cf. Figure 2) possess the typical nitroxides *g* values (2.0063−2.0065),[5a,b] which are consistent with spin adducts **5a**−**e**, generated from the spin-trapping of **4a**−**e** with *t*-BuNO (Scheme 1). The six-line pattern is caused by the hyperfine splitting of the EPR signal with one nitrogen (triplet) and one hydrogen at the β-position (doublet).[6] The a_N (triplet) and a_H^β (doublet) values vary little among spin adducts **5a**−**e**; thus, the a_N value ranges from 15.4 G (for **5c**) to 15.5 G (for **5b**) and the a_H^β value ranges from 4.4 G (for **5a**) to 4.5 G (for **5e**).

Different molar ratios of **1a**−**e** to SmI_2 (e.g., 1.5:1, 1:1, 1:1.3) were used but were found to have little influence on the *g* values or the a_N and a_H^β values. However, adding more SmI_2/THF solution did adversely affect the EPR signals, because the solvent THF strongly absorbs microwaves due to its high polarity. In addition, different temperatures (rt or −70 °C) in the EPR cavity were also utilized. The final EPR signals were unaffected, although the formation of the spin adducts **5a**−**e** was slower at −70 °C.

(5) (a) He, R. H. Y.; Zhao, C. X.; Zhou, C. M.; Jiang, X. K. *Tetrahedron* **1999**, *55*, 2263. (b) Kojima, T.; Tsuchiya, J.; Nakashima, S.; Ohya-Nishiguchi, H.; Yano, S.; Hidai, M. *Inorg. Chem.* **1992**, *31*, 2333.

(6) Janzen, E. G.; Davis, E. R.; Dubose, C. M. *Magn. Reson. Chem.* **1995**, *33*, S166.

(7) Katritzky, A. R.; Lan, X.; Yang, J. Z.; Denisko, O. V. *Chem. Rev.* **1998**, *98*, 409.

(8) **General Experimental Details.** SmI_2 (0.1 M in THF) was purchased from Aldrich and used directly without further treatment. Nitroso-*tert*-butane (*t*-BuNO) and *N*-*tert*-butyl-α-phenylnitrone (PBN) were also purchased from Aldrich. CH_2Cl_2 was distilled from sodium−benzophenone prior to use. In a typical experiment, the substrate **1** (0.1 M in CH_2Cl_2, 0.2 mL) was added into a deoxygenated EPR tube (2 mm in diameter) and cooled in a dry ice−acetone bath (−70 °C). Then previously cooled SmI_2 solution (0.2 mL) was injected into the tube using a syringe. After being shaken rigorously several times, the EPR tube was inserted into the EPR cavity (−70 °C) and the EPR spectra for radical intermediates were recorded immediately. An Oxford Instruments (CF900) helium flow cryostat was used to keep the sample below −70 °C. For the spin-trapping experiment, the substrate **1** (0.1 M in CH_2Cl_2, 0.15 mL) and the spin trapper (*t*-BuNO, 0.1 M in CH_2Cl_2, 0.15 mL; or PBN, 0.1 M in CH_2Cl_2, 0.15 mL) were added to a deoxygenated EPR tube and cooled in a dry ice−acetone bath (−70 °C). An SmI_2 solution (0.10, 0.15, or 0.20 mL) was then injected into the tube using a syringe. After being shaken rigorously several times, the EPR tube was inserted into the EPR cavity and the EPR spectra for radical intermediates were recorded immediately. The spectra were recorded at −70 °C as well as at room temperature. EPR spectra were recorded by a Bruker EPR Elexsys 580 spectrometer in CW mode using a rectangular cavity (TE_{102}). The conditions employed were as follows: modulation, 100 kHz; frequency, 9.764 GHz; microwave power, 2 mW; modulation amplitude, 1− 5 G; time constant, 0.04 s; sweep width, 100 G. The magnetic field was determined by a Hall probe and the microwave frequency by the built-in frequency counter of the Bruker Bridge model E580-1010.

Although the radicals **4a**−**e** were postulated to be formed by the reduction of the immonium cations **3a**−**e** with SmI_2,[1] another mode of generation is also possible. Single electron transfer (SET) of **1** and SmI_2 could be competitive with the previously proposed mechanism (Scheme 1). Since the benzotriazole group is a good electron acceptor as well as a good electron donor,[7] compound **1** could receive one electron from Sm^{2+} to form the benzotriazolyl radical anion **6**, while Sm^{2+} is oxidized to Sm^{3+}. Subsequent elimination of the benzotriazolyl anion from **6** would generate the radical **4** (route B).[8]

In conclusion, the EPR studies on the SmI_2-promoted coupling of *N*-(*N*′,*N*′-dialkylaminoalkyl)benzotriazoles support the involvement of a radical mechanism.

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