New Method for Preparation of Isolable *N-tert*-Alkoxyarylaminyl Radicals

Yozo Miura* and Yoshikazu Muranaka
Department of Applied Chemistry, Graduate School of Engineering, Osaka City University,
Sumiyoshi-ku, Osaka 558-8585

(Received December 28, 2004; CL-041617)

Stable *N-tert*-alkoxy-2,4-diphenyl-6-*tert*-butylphenylaminyl radicals were prepared by heating 2,4-diphenyl-6-*tert*-butylphenylnitrosobenzenes and azo compounds in refluxing benzene and isolated as radical crystals. Their structures were confirmed by the elemental analyses, ESR, and X-ray crystallography.

Although a vaiety of *N*-alkoxyalkylaminyls and *N*-alkoxyarylaminyls have widely been investigated by ESR,[1] their isolation has been unsuccessful for a long period. In quite recently, however, we have succeeded in the first isolation of *N-tert*-butoxy-2,4,6-triarylphenylaminyls (**1**), *N-tert*-butoxy-2,4-diaryl-6-*tert*-butylphenylaminyls (**2**), *N-tert*-butoxy-2,6-diaryl-4-*tert*-butylphenylaminyls (**3**), and their analogues (Chart 1).[2–5] In recent years, isolable stable free radicals have attracted much attention as spin sources in molecule-based magnetism[6] and as mediators in the controlled/living radical polymerization.[7] However, in spite of their increasing importance, a family of isolable stable free radicals are still rare.[8]

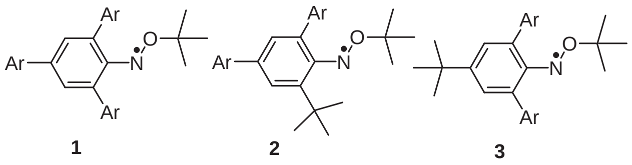
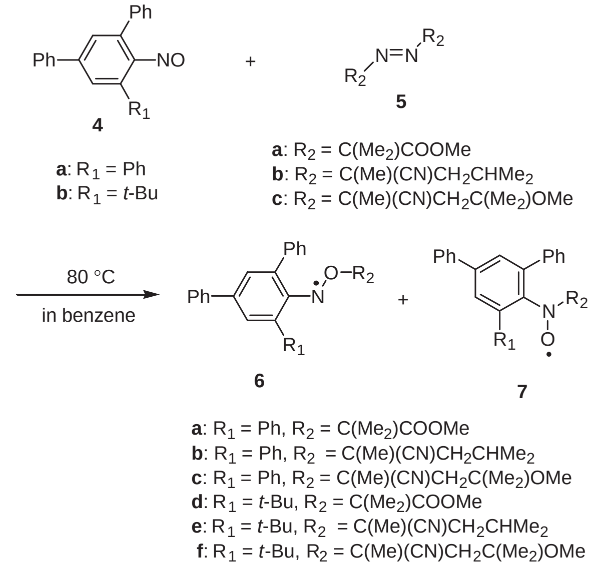


Chart 1.

N-tert-butoxyarylaminys **1**–**3** were prepared by the reaction of the lithium salts of 2,4,6-trisubstituted anilines with *tert*-butyl peroxybenzoate in THF at −78 °C. After column chromatography, they were isolated as red crystals in 17–25% yields. Interestingly, the isolated radicals were oxygen-insensitive and thermally very stable. The thermal stability was shown by the observation that although they were heated at 80 °C for 10 days in degassed benzene, 80% of the radical survived. A problem for this synthetic method is the use of butyllithium. This does not allow the introduction of functional groups into *N-tert*-alkoxyarylaminyls, and this limitation prevents the preparation of a wide vaiety of *N-tert*-alkoxyarylaminyls. Effort has been paid to overcome this problem, and we have now established a new convenient synthetic route to isolable *N-tert*-alkoxyarylaminyls. Herein we report the new synthetic method of *N-tert*-alkoxy-2,4-diphenyl-6-*tert*-butylphenylaminyls (**6**) by the reaction of 2,4-diphenyl-6-*tert*-butylnitrosobenzene[4] (**4b**) and azo compounds, **5**. This method is well known as the spin trapping technique which has been widely used to identify transient radicals in the fields of photochemistry and biochemistry.[9,10]

A general procedure for preparation of **6** is as follows: mixtures of 2,4,6-tri-substituted nitrosobenzenes **4** and azo compounds in benzene were heated to 80 °C for 0.5–4 h, and the resultant reaction mixtures were subjected to ESR measurements. When 2,4,6-triphenylnitrosobenzene[11] (**4a**) was used as the nitroso compound, the radicals detected were always *N-tert*-alkyl-2,4,6-triphenylphenylaminoxyls (**7a**–**7c**) alone, and the ESR signals due to the desired *N-tert*-alkoxy-2,4,6-triphenylphenylaminyls (**6a**–**6c**) were not detected. In contrast, **4b** was used, the reaction mixtures showed strong ESR signals due to *N-tert*-alkoxy-2,4-diphenyl-6-*tert*-butylphenylaminyls (**6d**–**6f**), and the ESR signals due to *N-tert*-alkyl-2,4-diphenyl-6-*tert*-butylphenylaminoxyls (**7d**–**7f**) were much weaker. This result prompted us to isolate **6d**–**6f**. Isolation of the radicals was quite easy: the reaction mixtures were concentrated under reduced pressure and the resultant residues were chromatographed to give **6d**–**6f** as red crystals in 18–49% yields (Scheme 1).[12] The results are summarized in Table 1.



Scheme 1.

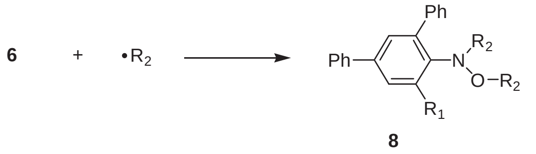
Table 1 shows that as the bulkiness of the *tert*-alkyl radicals generated by thermolysis of azo compounds increases, the yields of the corresponding **6** are increased. This is clearly shown by the results that the reactions of **4b** with **5b** or **4b** with **5c** give the corresponding **6** in higher yields than the reaction of **4b** with **5a**. This is further supported by the ESR measurements of the reaction mixtures. While the relative integrated ESR signal intensity ratios of **6d** to **7d** were ca. 5–6, those of **6e** to **7e** or **6f** to **7f** were ca. 10.

The yields of **6** also depended on the ratio of **5** to **4b**. A large excess of azo compounds reduced the yields of **6**. A typical example is shown by the reaction of **4b** with two equiv. of **5b**. The yield is only 18%, which is much lower than those for the reactions of **4b** with 0.65–1.0 equiv. of **5b** or **5c**. This can be readily accounted for in terms of the further coupling reaction between **6**

Table 1. Results for the preparation of **6** by the reaction of **4b** with **5** in benzene at 80 °C[a]

Azo Compound[b] (amount/mmol)	Ratio of **5** to **4b**	Time /h	Isolated radical[c] (yield[d]/%)
5a (0.515)	0.65	1.0	**6d** (20)
5a (0.515)	0.65	2.0	**6d** (32)
5a (0.515)	0.65	4.0	**6d** (37)
5a (0.793)	1.0	4.0	**6d** (38)
5b (0.515)	0.65	1.0	**6e** (27)
5b (0.793)	1.0	0.5	**6e** (49)
5b (1.59)	2.0	0.5	**6e** (18)
5c (0.515)	0.65	0.5	**6f** (33)
5c (0.793)	1.0	0.5	**6f** (49)

[a]**4b** 0.793 mmol, benzene 30 cm^3. [b]The $\tau_{1/2}$s of **5a** and **5b** in toluene at 80 °C are 80 and 10 min, respectively, and that of **5c** in toluene at 70 °C is $\approx$3.5 min. [c]All the radicals isolated gave satisfactory elemental analyses. [d]Isolated yield based on **4**.



Scheme 2.

and alkyl radicals giving **8**, shown in Scheme 2.

Although the elemental analyses for **6** gave satisfactory results,[12] we cannot unequivocally conclude that the isolated radicals are **6** only by their elemental analyses because the molecular formulas of **6** are the same as those of the corresponding **7**. The most convenient method to distinguish them is to compare their ESR parameters (a_N and g). ESR measurements were carried out using benzene as the solvent, and their a_N and g values were determined to be 0.988–0.998 mT and 2.0038–2.0039,[12] respectively. The ESR parameters for **6** obtained are very close to those for **1**–**3** ($a_N = 0.984$–1.05 mT, $g = 2.0041$–2.0043), but are quite different from those for aminoxyls **7** ($a_N = 1.27$ mT, $g = 2.0062$),[4] indicating that the isolated radicals are certainly *N-tert*-alkoxyphenylaminyls, **6**.

Fortunately, we succeeded in the X-ray crystallographic analysis of **6f**.[13] The ORTEP drawing is shown in Figure 1. The torsion angle of O1–N1–C1–C2 is −18.5(6)°, indicating that the π-conjugated system is somewhat twisted. The dihedral angles between the C1–C6 ring and the C7–C12 ring and between the C1–C6 ring and the C13–C18 ring are 69.7° and 38.7°, respectively, indicating that there is a serious steric congestion around the radical center.

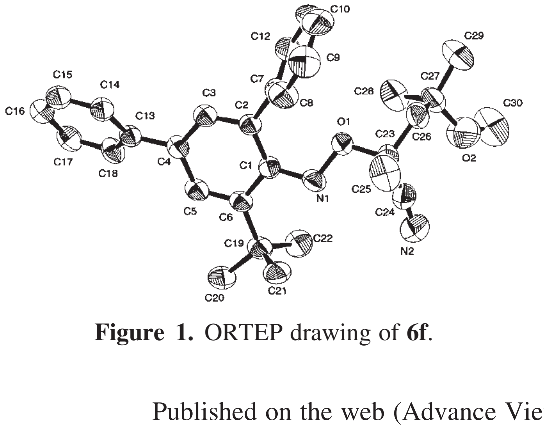


Figure 1. ORTEP drawing of **6f**.

References and Notes

1 a) W. C. Danen and F. A. Neugebauer, *Angew. Chem., Int. Ed. Engl.*, **14**, 783 (1975). b) W. C. Danen, C. T. West, and T. T. Kensler, *J. Am. Chem. Soc.*, **95**, 5716 (1973). c) R. A. Kaba and K. U. Ingold, *J. Am. Chem. Soc.*, **98**, 7375 (1976). d) H. Woynar and K. U. Ingold, *J. Am. Chem. Soc.*, **102**, 3813 (1980). e) W. Ahrens, K. Wieser, and A. Berndt, *Tetrahedron Lett.*, **1973**, 3141. f) A. T. Balaban, P. T. Frangopol, M. Frangopol, and N. Negoită, *Tetrahedron*, **23**, 4661 (1967). g) N. Negoita, R. Baican, and A. T. Balaban, *Tetrahedron Lett.*, **1973**, 1877. h) W. Ahrens and A. Berndt, *Tetrahedron Lett.*, **1973**, 4281. i) M. Negareche, M. Boyer, and P. Tordo, *Tetrahedron Lett.*, **22**, 2879 (1981).

2 Y. Miura and T. Tomimura, *J. Chem. Soc., Chem. Commun.*, **2001**, 627.

3 Y. Miura, T. Tomimura, N. Matsuba, R. Tanaka, M. Nakatsuji, and Y. Teki, *J. Org. Chem.*, **66**, 7456 (2001).

4 Y. Miura, N. Matsuba, R. Tanaka, Y. Teki, and T. Takui, *J. Org. Chem.*, **67**, 8764 (2002).

5 Y. Miura, T. Nishi, and Y. Teki, *J. Org. Chem.*, **68**, 10158 (2003).

6 a) "Magnetic Properties of Organic Materials," ed. by P. M. Lahti, Marcel Dekker, New York and Basel (1999). b) "Molecular Magnetism," ed. by K. Itoh and M. Kinoshita, Kodansha and Gordon and Breach, Tokyo and Amsterdam (2000).

7 C. J. Hawker, A. W. Bosman, and E. Harth, *Chem. Rev.*, **101**, 3661 (2001).

8 Y. Morita, J. Kawai, K. Fukui, S. Nakazawa, K. Sato, D. Shiomi, T. Takui, and K. Nakasuji, *Org. Lett.*, **3**, 3289 (2003), and references cited therein.

9 E. G. Janzen, *Acc. Chem. Res.*, **4**, 31 (1971).

10 S. Terabe and R. Konaka, *J. Chem. Soc., Perkin Trans. 2*, **1973**, 369.

11 S. Konaka, M. Kokaki, D. Shiomi, K. Sato, T. Takui, and K. Okada, *Synth. Met.*, **2001**, 1808.

12 A typical procedure for preparation of **6**. A solution of **4b** (250 mg, 0.793 mmol) and **5a** (185 mg, 0.79 mmol) in benzene (30 cm^3) was refluxed for 4 h. The mixture was evaporated under reduced pressure, and the residue was chromatographed on silica gel with 1:8 ethyl acetate–hexane to give **6d** in 38% yield. Mp 105–107 °C (MeOH); ESR data (benzene) $a_N = 0.993$ mT, $g = 2.0039$. Found: C, 77.77; H, 7.33; N, 3.40%. Calcd for $C_{27}H_{30}NO_3$: C, 77.85; H, 7.26; N, 3.36%. **6e**: mp 107–109 °C (MeOH); ESR data (benzene) $a_N = 0.988$ mT, $g = 2.0038$. Found: C, 81.69; H, 8.00; N, 6.49%. Calcd for $C_{29}H_{33}N_2O$: C, 81.84; H,7.82; N, 6.58%. **6f**: mp 114–117 °C (MeOH); ESR data (benzene) $a_N = 0.998$ mT, $g = 2.0038$. Found: C, 78.91; H, 7.78; N, 6.04%. Calcd for $C_{30}H_{35}N_2O_2$: C, 79.09; H, 7.74; N, 6.15%.

13 Crystal data for **6f**: $C_{30}H_{35}N_2O_2$, $M = 455.62$, monoclinic, $a = 10.470(2)$ Å, $b = 36.980(6)$ Å, $c = 6.8100(8)$ Å, $\beta = 97.120(7)°$, $V = 2616.4(7)$ Å^3, $T = -50$ °C, space group $P2_1/n$, (#14), $Z = 4$, μ(Mo Kα) $= 0.72$ cm^{-1}, 20344 reflections measured, 5929 unique ($R_{int} = 0.071$). No. of observations 2678 ($I > 2.30\sigma(I)$), No. of variable 317, $R_1 = 0.0996$, $R_w = 0.179$, GOF = 1.68. Crystal data reported in this manuscript have been deposited with Cambridge Crystallographic Data Centre as supplementary publication No. CCDC-261609. Copies of the data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html.

Published on the web (Advance View) February 26, 2005; DOI 10.1246/cl.2005.480