JOC Featured Article
pubs.acs.org/joc

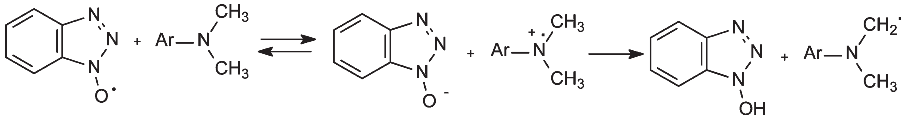
N-Demethylation of *N*,*N*-Dimethylanilines by the Benzotriazole *N*-Oxyl Radical: Evidence for a Two-Step Electron Transfer−Proton Transfer Mechanism

Enrico Baciocchi,[‡] Massimo Bietti,[§] Osvaldo Lanzalunga,*[,†,‡] Andrea Lapi,[†,‡] and Daniele Raponi[†]

[†]*Dipartimento di Chimica, Sapienza Università di Roma, and* [‡]*Istituto CNR di Metodologie Chimiche (IMC−CNR), Sezione Meccanismi di Reazione, c/o Dipartimento di Chimica, Sapienza Università di Roma, Piazzale A. Moro 5, I-00185 Rome, Italy, and* [§]*Dipartimento di Scienze e Tecnologie Chimiche, Università "Tor Vergata", Via della Ricerca Scientifica, I-00133 Rome, Italy*

osvaldo.lanzalunga@uniroma1.it

Received January 11, 2010



The reaction of the benzotriazole *N*-oxyl radical (BTNO) with a series of 4-X-*N*,*N*-dimethylanilines (X = CN, CF_3, $CO_2CH_2CH_3$, CH_3, OC_6H_5, OCH_3) has been investigated in CH_3CN. Product analysis shows that the radical, 4-X-$C_6H_4N(CH_3)CH_2^{\bullet}$, is first formed, which can lead to the *N*-demethylated product or the product of coupling with BTNO. Reaction rates were found to increase significantly by increasing the electron-donating power of the aryl substituents ($\rho^+ = -3.8$). With electron-donating substituents (X = CH_3, OC_6H_5, OCH_3), no intermolecular deuterium kinetic isotope effect (DKIE) and a substantial intramolecular DKIE are observed. With electron-withdrawing substituents (X = CN, CF_3, $CO_2CH_2CH_3$), substantial values of both intermolecular and intramolecular DKIEs are observed. These results can be interpreted on the basis of an electron-transfer mechanism from the *N*,*N*-dimethylanilines to the BTNO radical followed by deprotonation of the anilinium radical cation (ET−PT mechanism). By applying the Marcus equation to the kinetic data for X = CH_3, OC_6H_5, OCH_3 (rate-determining ET), a reorganization energy for the ET reaction was determined ($\lambda_{BTNO/DMA} = 32.1$ kcal mol^{-1}). From the self-exchange reorganization energy for the BTNO/BTNO$^-$ couple, a self-exchange reorganization energy value of 31.9 kcal mol^{-1} was calculated for the DMA$^{\bullet+}$/DMA couple.

Introduction

Short-lived *N*-oxyl radicals like phthalimide *N*-oxyl radical (PINO) and benzotriazole *N*-oxyl radical (BTNO) have received a great attention in recent years. The special interest for the two aminoxyl radicals is justified by the fact that the

---

(1) Ishii, Y.; Nakayama, K.; Takeno, M.; Sakaguchi, S.; Iwahama, T.; Nishiyama, Y. *J. Org. Chem.* **1995**, *60*, 3934–3935. Ishii, Y.; Iwahama, T.; Sakaguchi, S.; Nakayama, K.; Nishiyama, Y. *J. Org. Chem.* **1996**, *61*, 4520–4526. Yoshino, Y.; Hayashi, Y.; Iwahama, T.; Sakaguchi, S.; Ishii, Y. *J. Org. Chem.* **1997**, *62*, 6810–6813. Ishii, Y.; Sakaguchi, S.; Iwahama, T. *Adv. Synth. Catal.* **2001**, *343*, 393–427. Minisci, F.; Recupero, F.; Pedulli, G. F.; Lucarini, M. *J. Mol. Catal. A* **2003**, *204–205*, 63–90. Minisci, F.; Recupero, F.; Cecchetto, A.; Gambarotti, C.; Punta, C.; Paganelli, R. *Org. Process Res. Dev.* **2004**, *8*, 163–168. Sheldon, R. A.; Arends, I. W. C. E. *Adv. Synth. Catal.* **2004**, *346*, 1051–1071. Yang, G.; Ma, Y.; Xu, J. *J. Am. Chem. Soc.* **2004**, *126*, 10542. Yang, G.; Zhang, Q.; Miao, H.; Tong, X.; Xu, J. *Org. Lett.* **2005**, *7*, 263–266. Rajabi, F.; Clark, J. H.; Karimi, B.; Macquarrie, D. J. *Org. Biomol. Chem.* **2005**, *3*, 725–726. Aoki, Y.; Sakaguchi, S.; Ishii, Y. *Tetrahedron* **2006**, *62*, 2497–2500. Ishii, Y.; Sakaguchi, S. *Catal. Today* **2006**, *117*, 105–113. Sheldon, R. A.; Arends, I. W. C. E. *J. Mol. Catal. A* **2006**, *251*, 200–214. Recupero, F.; Punta, C. *Chem. Rev.* **2007**, *107*, 3800–3842.

(2) Call, H. P.; Mucke, I. *J. Biotechnol.* **1997**, *53*, 163–202. Li, K.; Xu, F.; Eriksson, K.-E. L. *Appl. Environ. Microbiol.* **1999**, *65*, 2654–2660. Sealey, B. J.; Ragauskas, A. J.; Elder, T. J. *Holzforschung* **1999**, *53*, 498–502. Srebotnik, E.; Hammel, K. E. *J. Biotechnol.* **2000**, *81*, 179–188. Balakshin, M.; Chen, C.-L.; Gratzl, J. S.; Kirkman, A. G.; Jakob, H. *J. Mol. Catal. B: Enzymatic* **2001**, *16*, 205–215. Potthast, A.; Rosenau, T.; Fischer, K. *Holzforschung* **2001**, *55*, 47–56. Fabbrini, M.; Galli, C.; Gentili, P. *J. Mol. Catal. B: Enzymatic* **2002**, *16*, 231–240. Geng, X.; Li, K.; Xu, F. *Appl. Microbiol. Biotechnol.* **2004**, *64*, 493–496. Annunziatini, C.; Baiocco, P.; Gerini, M. F.; Lanzalunga, O.; Sjögren, B. *J. Mol. Catal. B: Enzymatic* **2005**, *32*, 89–96. Xu, F.; Kulys, J. J.; Duke, K.; Li, K.; Krikstopaitis, K.; Deussen, H.-J. W.; Abbate, E.; Galinyte, V.; Schneider, P *Appl. Environ. Microbiol.* **2000**, *66*, 2052–2056. Xu, F.; Deuss, H.-J. W.; Lopez, B.; Lam, L.; Li, K. *Eur. J. Biochem.* **2001**, *268*, 4169–4176. D'Acunzo, F.; Baiocco, P.; Fabbrini, M.; Galli, C.; Gentili, P. *New J. Chem.* **2002**, *26*, 1791–1794. Baiocco, P.; Barreca, A. M.; Fabbrini, M.; Galli, C.; Gentili, P. *Org. Biomol. Chem.* **2003**, *1*, 191–197. Cantarella, G.; Galli, C.; Gentili, P. *New J. Chem.* **2004**, *28*, 366–372. Branchi, B.; Galli, C.; Gentili, P. *Org. Biomol. Chem.* **2005**, *3*, 2604–2614.

DOI: 10.1021/jo100040y

PINO radical is the active oxidant in several synthetically useful metal-catalyzed aerobic oxidations of organic compounds.[1] Moreover, PINO and BTNO play a key role in the oxidative degradation of lignin promoted by the laccase/O_2 system mediated by *N*-hydroxyphthalimide (HPI) and *N*-hydroxybenzotriazole (HBT),[2] a process which has a potential application in the pulp and paper industry.[3]

Thus, the reactivity of these short-lived aminoxyl radicals has been quite intensively investigated, but mainly in reactions where they behave as hydrogen atom abstractors from C−H[4] and O−H[5,6] bonds (HAT, Scheme 1, path a). Much less information is instead available about their involvement in electron transfer (ET) processes (Scheme 1, path b).[7]

Recently, however, we found evidence that PINO can *N*-dealkylate *N*,*N*-dimethylanilines by an ET mechanism[8] and that both *N*-oxyl radicals are very effective in the oxidation of ferrocenes to ferricinium cations.[9,10] From the latter study, it was also possible to determine that the intrinsic reactivity of BTNO in ET reactions is larger than that of PINO, which led to the prediction that in ET processes BTNO should be more reactive than PINO in spite of the lower (ca. 60 mV) reduction potential of the former radical.

In this context, it appeared of interest to investigate also the reaction of BTNO with *N*,*N*-dimethylanilines. On the basis of previous predictions and in consideration of the fact that the NO-H BDE in HBT is ca. 3 kcal/mol lower than that of HPI,[7] the ET mechanism should be favored in the possible competition with the hydrogen atom transfer (HAT) process and the reactivity of BTNO should be greater than that of PINO. The oxidative *N*-dealkylation of tertiary amines is attracting a continuous attention in recent years[11,12] for its great chemical and biological importance. This reaction has also the advantage that a number of reliable mechanistic criteria are available to assess the mechanistic dichotomy between HAT and ET mechanisms.[13,14]

In this paper, we report on a product and kinetic study of the reaction of BTNO with a number of 4-X-substituted *N*,*N*-dimethylanilines **1−6** (X = CN, CF_3, CO_2Et, Me, PhO, MeO) (Chart 1). Substituent effects on the reaction rates

SCHEME 1

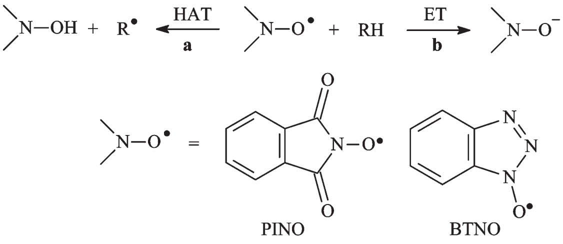
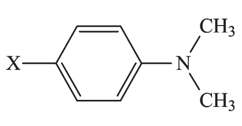


CHART 1



1 X = CN
2 X = CF_3
3 X = $CO_2C_2H_5$
4 X = CH_3
5 X = OC_6H_5
6 X = OCH_3

---

[3] Argyropoulos, D. S.; Menachem, S. B. *Biotechnology in the Pulp and Paper Industry*; Eriksson, K. E. L., Ed.; Springer-Verlag: Berlin, Heidelberg, 1997; pp 127−158.

[4] (a) Wentzel, B. B.; Donners, M. P. J.; Alsters, P. L.; Feiters, M. C.; Nolte, R. J. M. *Tetrahedron* **2000**, *56*, 7797–7803. (b) Minisci, F.; Punta, C.; Recupero, F.; Fontana, F.; Pedulli, G. F. *J. Org. Chem.* **2002**, *67*, 2671–2676. (c) Koshino, N.; Cai, Y.; Espenson, J. H. *J. Phys. Chem. A* **2003**, *107*, 4262–4267. (d) Koshino, N.; Saha, B.; Espenson, J. H. *J. Org. Chem.* **2003**, *68*, 9364–9370. (e) Minisci, F.; Recupero, F.; Cecchetto, A.; Gambarotti, C.; Punta, C.; Faletti, R.; Paganelli, R.; Pedulli, G. F. *Eur. J. Org. Chem.* **2004**, 109–119. (f) Annunziatini, C.; Gerini, M. F.; Lanzalunga, O.; Lucarini, M. *J. Org. Chem.* **2004**, *69*, 3431–3438. (g) Cai, Y.; Koshino, N.; Saha, B.; Espenson, J. H. *J. Org. Chem.* **2005**, *70*, 238–243. (h) Brandi, P.; Galli, C.; Gentili, P. *J. Org. Chem.* **2005**, *70*, 9521–9528. (i) Coniglio, A.; Galli, C.; Gentili, P.; Vadalà, R. *Org. Biomol. Chem.* **2009**, *7*, 155–160.

[5] Amorati, R.; Lucarini, M.; Mugnaini, V.; Pedulli, G. F.; Minisci, F.; Recupero, R.; Fontana, F.; Astolfi, P.; Greci, L. *J. Org. Chem.* **2003**, *68*, 1747–1754.

[6] Baciocchi, E.; Gerini, M. F.; Lanzalunga, O. *J. Org. Chem.* **2004**, *69*, 8863–8866.

[7] Galli, C.; Gentili, P.; Lanzalunga, O. *Angew. Chem., Int. Ed.* **2008**, *47*, 4790–4796.

[8] Baciocchi, E.; Bietti, M.; Gerini, M. F.; Lanzalunga, O. *J. Org. Chem.* **2005**, *70*, 5144–5149.

[9] Baciocchi, E.; Bietti, M.; Di Fusco, M.; Lanzalunga, O. *J. Org. Chem.* **2007**, *72*, 8748–8754.

[10] Baciocchi, E.; Bietti, M.; Di Fusco, M.; Lanzalunga, O.; Raponi, D. *J. Org. Chem.* **2009**, *74*, 5576–5583.

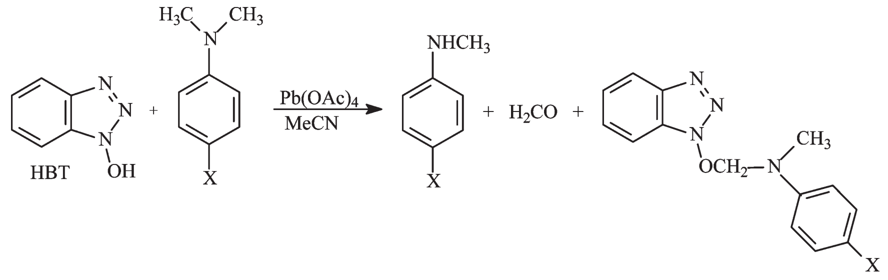
[11] (a) Ortiz de Montellano, P. R. *Cytochrome P450: Structure, Mechanism and Biochemistry*, 3rd ed.; Kluwer Academic/Plenum Publishers: New York, 2005. (b) Miwa, G. T.; Walsh, J. S.; Kedderis, G. L.; Hollenberg, P. F. *J. Biol. Chem.* **1983**, *258*, 14445–14449. (c) Heimbrook, D. C.; Murray, R. I.; Egeberg, K. D.; Sligar, S. G.; Nee, M. W.; Bruice, T. C. *J. Am. Chem. Soc.* **1984**, *106*, 1514–1515. Macdonald, T. L.; Gutheim, W. G.; Martin, R. B.; Guengerich, F. P. *Biochemistry* **1989**, *28*, 2071–2077. Sono, M.; Roach, M. P.; Coulter, E. D.; Dawson, J. H. *Chem. Rev.* **1996**, *96*, 2841. (d) Guengerich, F. P. *Chem. Res. Toxicol.* **2001**, *14*, 611. (e) Ortiz de Montellano, P. R.; De Voss, J. J. *Nat. Prod. Rep.* **2002**, *19*, 477. (f) Groves, J. T. *Proc. Natl. Acad. Sci. U.S.A.* **2003**, *100*, 3569. Meunier, B.; de Visser, S. P.; Shaik, S. *Chem. Rev.* **2004**, *104*, 3947. (g) Shaik, S.; Kumar, D.; de Visser, S. P.; Altun, A.; Thiel, W. *Chem. Rev.* **2005**, *105*, 2279. (h) Denisov, I. G.; Makris, T. M.; Sligar, S. G.; Schlichting, I. *Chem. Rev.* **2005**, *105*, 2253. (i) Groves, J. T. *J. Inorg. Biochem.* **2006**, *100*, 434.

[12] (a) Watanabe, Y. In *The Porphyrin Handbook*; Kadish, K. M., Smith, K. M., Guilard, R., Eds.; Academic Press: San Diego, 2000; Vol. 4, Chapter 30, p 97. (b) Meunier, B.; Robert, A.; Pratviel, G.; Bernardou, J. In *The Porphyrin Handbook*; Kadish, K. M., Smith, K. M., Guilard, R., Eds.; Academic Press: San Diego, 2000; Vol. 4, Chapter 31, p 119. (c) Montanari, F.; Casella, L. *Metalloporphyrins Catalyzed Oxidations*; Kluwer Academic Publishers: Dordrecht, The Netherlands, 1994. (d) Shannon, P.; Bruice, T. C. *J. Am. Chem. Soc.* **1981**, *103*, 4580–4582. (e) Fujii, H. *Coord. Chem. Rev.* **2002**, *226*, 51.

[13] (a) Miwa, G. T.; Walsh, J. S.; Kedderis, G. L.; Hollenberg, P. F. *J. Biol. Chem.* **1983**, *258*, 14445–14449. (b) Burka, L. T.; Guengerich, F. P.; Willard, R. J.; Macdonald, T. L. *J. Am. Chem. Soc.* **1985**, *107*, 2549–2551. (c) Dinnocenzo, J. P.; Karki, S. B.; Jones, J. P. *J. Am. Chem. Soc.* **1993**, *115*, 7111–7116. (d) Okazaki, O.; Guengerich, F. P. *J. Biol. Chem.* **1993**, *268*, 1546–1552. (e) Karki, S. B.; Dinnocenzo, J. P.; Jones, J. P.; Korzekwa, K. R. *J. Am. Chem. Soc.* **1995**, *117*, 3657–3664. (f) Guengerich, F. P.; Yun, C.-H.; Macdonald, T. L. *J. Biol. Chem.* **1996**, *271*, 27321–27329. (g) Manchester, J. L.; Dinnocenzo, J. P.; Higgins, L. A.; Jones, J. P. *J. Am. Chem. Soc.* **1997**, *119*, 5059–5070. (h) Chen, H.; de Groot, M. J.; Vermeulen, N. P. E.; Hanzlik, R. P.; Guengerich, F. P.; Yun, C.-H.; Macdonald, T. L. *J. Org. Chem.* **1997**, *62*, 8227–8230. (i) Goto, Y.; Watanabe, Y.; Fukuzumi, S.; Jones, J. P.; Dinnocenzo, J. P. *J. Am. Chem. Soc.* **1998**, *120*, 10762–10763. (j) Baciocchi, E.; Gerini, M. F.; Lanzalunga, O.; Lapi, A.; Mancinelli, S.; Mencarelli, P. *Chem. Commun.* **2000**, 393. (k) Shaffer, C. L.; Morton, M. D.; Hanzlik, R. P. *J. Am. Chem. Soc.* **2001**, *123*, 8502. (l) Bhakta, M. N.; Wimalasena, K. *J. Am. Chem. Soc.* **2002**, *124*, 1844. (m) Shaffer, C. L.; Harriman, S.; Koen, Y. M.; Hanzlik, R. P. *J. Am. Chem. Soc.* **2002**, *124*, 8268. (n) Bhakta, M. N.; Hollenberg, P. F.; Wimalasena, K. *Chem. Commun.* **2005**, 265. (o) Bhakta, M. N.; Hollenberg, P. F.; Wimalasena, K. *J. Am. Chem. Soc.* **2005**, *127*, 1376–1377. (p) Bhakta, M. N.; Wimalasena, K. *Eur. J. Org. Chem.* **2005**, 4801. (q) Cerny, M. A.; Hanzlik, R. P. *J. Am. Chem. Soc.* **2006**, *128*, 3346.

[14] (a) Lindsay Smith, J. R.; Mortimer, D. N. *J. Chem. Soc., Perkin Trans. 2* **1986**, 1743–1749. (b) Baciocchi, E.; Lanzalunga, O.; Lapi, A.; Manduchi, L. *J. Am. Chem. Soc.* **1998**, *120*, 5783–5787. (c) Baciocchi, E.; Gerini, M. F.; Lanzalunga, O.; Lapi, A.; Lo Piparo, M. G.; Mancinelli, S. *Eur. J. Org. Chem.* **2001**, 2305. (d) Fukuzumi, S.; Shimoosako, K.; Suenobu, T.; Watanabe, Y. *J. Am. Chem. Soc.* **2003**, *125*, 9074–9082. (e) Shearer, J.; Zhang, C. X.; Hatcher, L. Q.; Karlin, K. D. *J. Am. Chem. Soc.* **2003**, *125*, 12670–12671. (f) Wang, Y.; Lumar, D.; Yang, C.; Han, K.; Shaik, S. *J. Phys. Chem. B* **2007**, *111*, 7700–7710. (g) Nehru, K.; Seo, M. S.; Kim, J.; Nam, W. *Inorg. Chem.* **2007**, *46*, 293–298. (h) Chiavarino, B.; Cipollini, R.; Crestoni, M. E.; Fornarini, S.; Lanucara, F.; Lapi, A. *J. Am. Chem. Soc.* **2008**, *130*, 3208–3217.

SCHEME 2



have been determined together with the inter- and intramolecular deuterium kinetic isotope effects.

Results

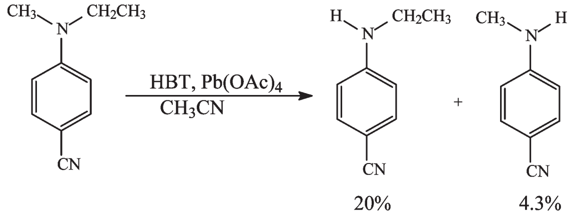
For product studies, the BTNO radical was generated in CH_3CN by reaction of HBT with $Pb(OAc)_4$, as previously described,[8] and was allowed to react with DMAs **1**−**6** (substrate/BTNO molar ratio ca. 3:1) at 25 °C for 10 min. At the end of the reaction, after workup, GC−MS and ^1H NMR analysis indicated that the corresponding *N*-methylanilines were formed as the major reaction products (yields ranging from 20% to 80% referred to BTNO equivalents). Formation of CH_2O was also detected by its conversion into its dimedone adduct. ^1H NMR analysis of the reaction mixture, performed before workup, indicated, however, the presence of two additional singlets at 5.1−5.3 ppm and 3.0−3.1 ppm (relative intensity = 2:3). These singlets were reasonably assigned (see the Experimental Section) to a cross-coupling product of BTNO and the α-aminomethyl radical formed by the BTNO-induced hydrogen abstraction from the *N*-Me group of the substrate. Evidently, this adduct is converted during workup into the *N*-demethylated product (vide infra), as the above signals were absent in the final mixture. Attempts were made to isolate this intermediate which, however, were unsuccessful because it was unstable during the chromatographic isolation procedure, always decomposing into *N*-methylaniline and HBT. Thus, the reaction of BTNO and *N*,*N*-dimethylaniline can be described as reported in Scheme 2.

Product analysis was also carried out using *N*-ethyl-*N*-methyl-4-cyanoaniline as substrate to establish the relative reactivity of the two *N*-alkyl groups. After workup and hydrolysis of the cross-coupling products, *N*-ethyl-4-cyanoaniline and *N*-methyl-4-cyanoaniline were identified as reaction products by GC−MS and ^1H NMR analysis, and the yields of these two products, determined by GC and ^1H NMR analysis and referred to the starting material, were 20% and 4.3%, respectively (Scheme 3).

Using *N*-methyl-*N*-trideuteriomethylanilines as substrates, product (intramolecular) deuterium isotope effects $(k_H/k_D)_{intra}$ were determined by measuring, by GC−MS analysis, the molar ratio between the dimedone adducts of CH_2O and CD_2O produced in the reaction with BTNO. In all cases, we observed substantial values of $(k_H/k_D)_{intra}$ that are listed in the last column of Table 1.

The kinetics of the reactions of DMAs **1**−**6** with BTNO were studied in CH_3CN at 25 °C. With the less reactive substrates **1**−**3**, BTNO was generated as in the products study, and its decay was followed spectrophotometrically at 480 nm (λ_{max}).[15] The spontaneous slow decay of BTNO was strongly accelerated in the presence of DMAs **1**−**3**, following clean pseudo-first-order kinetics in the presence of an excess of substrate. With the more reactive DMAs **4**−**6**, the kinetic studies have been carried out by laser flash photolysis (LFP) as described previously for the ET reactions from ferrocenes to the BTNO radical.[10] BTNO was produced by HAT from 1-hydroxybenzotriazole (HBT) to the cumyloxyl radical generated by 355 nm LFP of dicumyl peroxide (eqs 1−2 in Scheme 4).[16,17]

SCHEME 3



The BTNO signal is stable on the millisecond time scale. In the presence of an excess of DMAs **4**−**6**, a much faster decay of BTNO is observed[18] that follows first-order kinetics (see Figure 1 for the decay of BTNO in the absence and in the presence of 4-methoxy-*N*,*N*-dimethylaniline 0.22−1.08 mM).[19]

When the pseudo-first-order rate constants (k_{obs}) for the decay of the BTNO radical were plotted against the concentration of DMAs **1**−**6** excellent linear dependencies were observed (Figures S1−S6 in the Supporting Information), and the second-order rate constants (k_H) for the reactions of BTNO with DMAs were obtained from the slopes of these plots.

All the kinetic data are collected in Table 1. The redox potentials of the DMAs are also displayed in the same table.

---

[15] Galli, C.; Gentili, P.; Lanzalunga, O.; Lucarini, M.; Pedulli, G. F. *Chem. Commun.* **2004**, 2356–2357.

[16] Avila, D. V.; Lusztyk, J.; Ingold, K. U. *J. Am. Chem. Soc.* **1992**, *114*, 6576–6577. Avila, D. V.; Ingold, K. U.; Di Nardo, A. A.; Zerbetto, F.; Zgierski, M. Z.; Lusztyk, J. *J. Am. Chem. Soc.* **1995**, *117*, 2711–2718.

[17] The use of 355 nm laser irradiation of CH_3CN solutions of dicumyl peroxide has been preferred to that used in the previous work[8] for the kinetic analysis of the reactions of 4-phenoxy-*N*,*N*-dimethylaniline and 4-methoxy-*N*,*N*-dimethylaniline with the PINO radical where the latter species was produced by 266 nm laser irradiation of a CH_3CN solution of di-*tert*-butyl peroxide.

[18] The decay kinetics of the BTNO radical were followed at 380 nm since the residual absorption recorded at this wavelength is smaller than that observed at λ_{max} 480 nm, and the decay profiles are better defined.

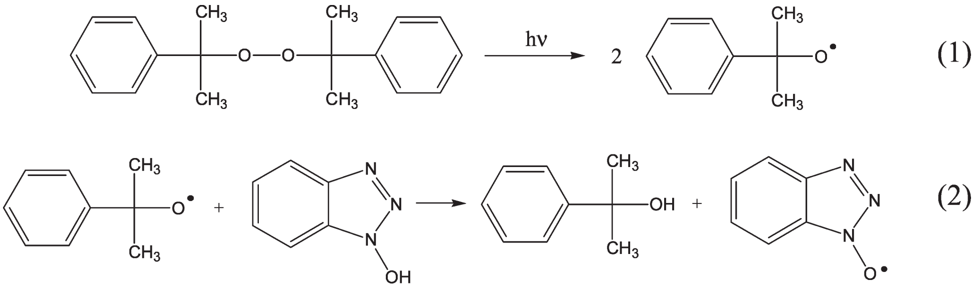
[19] *N*,*N*-Dimethylaniline exhibited a too low reactivity for the BTNO decay to be followed in the microsecond time-scale, and only an upper limit for the rate constant ($k_H < 10^5$ M^{-1} s^{-1}) could be given for the reaction of *N*,*N*-dimethylaniline with BTNO.

TABLE 1. Substrate Oxidation Potentials, Kinetic Data, and Inter- and Intramolecular Deuterium Isotope Effects for the Reaction of BTNO with 4-X-Substituted *N*,*N*-Dimethylanilines in CH_3CN at 25 °C

substrate (X =)	$E^{\circ a}$	k_H (M^{-1} s^{-1})^b	$k_D{}^{b,c}$ (M^{-1} s^{-1})	$(k_H/k_D)_{inter}{}^{b,d}$	$(k_H/k_D)_{intra}{}^{b,e}$
CN	1.05^f	$1.1(1) \times 10^{2\,h}$	$16(1)^h$	6.9(9)	7.8(5)
CF_3	1.04^f	$1.8(1) \times 10^{2\,h}$	$40(3)^h$	4.5(6)	6.4(3)
$CO_2C_2H_5$	0.97^f	$6.0(5) \times 10^{2\,h}$	$2.9(3) \times 10^{2\,h}$	2.1(4)	5.7(4)
CH_3	0.61^g	$9.5(2) \times 10^{5\,i}$	$8.0(5) \times 10^{5\,i}$	1.2(1)	2.6(1)
OC_6H_5	0.56^f	$1.4(2) \times 10^{6\,i}$	$1.5(2) \times 10^{6\,i}$	0.9(2)	2.4(2)
OCH_3	0.45^f	$2.2(2) \times 10^{7\,i}$	$2.2(1) \times 10^{7\,i}$	1.0(1)	2.3(3)

[a] V vs SCE in CH_3CN. [b] The number in parentheses represents the error (standard deviation) in the last digit. [c] Determined using 4-X-$C_6H_4N(CD_3)_2$ as substrates. [d] Determined kinetically by the ratio k_H/k_D. [e] Determined by product analysis of the oxidation of 4-X-$C_6H_4N(CH_3)(CD_3)$. [f] Reference 8. [g] Reference 20. [h] Determined spectrophotometrically. [i] Determined by LFP.

SCHEME 4



Intermolecular deuterium kinetic isotope effect $(k_H/k_D)_{inter}$ were also determined kinetically by measuring the rate constants for the deuterium abstraction reaction (k_D) from *N*,*N*-di(trideuteriomethyl)anilines 4-X-$C_6H_4N(CD_3)_2$ (see Figures S7−S12 in the Supporting Information) and comparing this value with the k_H values for the hydrogenated counterpart. All values of k_D and $(k_H/k_D)_{inter}$ are collected in Table 1.

Discussion

Product analysis of the reactions of *N*,*N*-dimethylanilines with BTNO clearly indicates the occurrence of a formal hydrogen transfer from the *N*-CH_3 group to BTNO with formation of an α-aminomethyl radical [4-$XC_6H_4N(CH_3)$-$CH_2^{\bullet}$], which is compatible with both a HAT mechanism (Scheme 5, path a) and an ET−PT mechanism (Scheme 5 paths b and c). The α-aminomethyl radical can be easily oxidized (e.g., E_{ox} is −0.85 V vs SCE for $C_6H_5N(CH_3)CH_2^{\bullet}$)[21] by $BTNO^{\bullet}$ (E_{red} = 0.63 V vs SCE)[10] to the corresponding carbocation that, by reaction with adventitious water, leads to the carbinolamine and then to *N*-methylaniline and CH_2O (Scheme 5, paths d and e), detected as its dimedone adduct.

The other possibility is that the α-amino carbon radical couples with BTNO to form an adduct (Scheme 5, path f). As already mentioned, this adduct can react with the small amount of H_2O present in the solvent to give the *N*-methylaniline, HBT, and formaldehyde (path g).[22]

A clear choice among the two reaction mechanisms (HAT and ET−PT) outlined above, leading to the key intermediate α-aminomethyl radical, was made possible by a careful examination of the kinetic data presented in Table 1, as described in the following.

A first observation is that the second-order rate constants k_H reported in Table 1 increase significantly by increasing the electron-donating power of the aniline ring substituent. A good linear correlation is obtained by plotting log k_H against the substituent σ^+ constants ($\rho^+ = -3.8$, $r^2 = 0.993$) as shown in Figure 2. Such a high and negative ρ value would be difficult to justify in a HAT mechanism, whereas it is fully consistent with a mechanism involving the formation of an intermediate radical cation, such as the ET−PT mechanism.

A further very strong support to the ET−PT mechanism comes from the results of the inter- and intramolecular deuterium kinetic isotope effect study. Accordingly, it can be noted that the reactions with the 4-X-*N*,*N*-dimethylanilines **4**−**6** substituted with electron-donating substituents (X = CH_3, OC_6H_5, OCH_3) do not exhibit a significant intermolecular deuterium kinetic isotope effect [$(k_H/k_D)_{inter} \approx 1$]. This crucial observation *excludes* the single-step HAT mechanism which *must* involve a partial C−H bond breaking in the transition state and therefore exhibit an intermolecular $k_H/k_D > 1$. At the same time, this observation clearly leads us to the reasonable conclusion that these substrates react by an ET−PT mechanism where the ET step is rate determining and the deprotonation of the radical cation occurs in a fast step. In line with this is also the observation (Table 1) that substrates **4**−**6** exhibit significant intramolecular deuterium isotope effects, $(k_H/k_D)_{intra}$. The latter values, determined by the product analysis (molar ratio between CH_2O and CD_2O) in the reaction of BTNO with *N*-methyl-*N*-trideuteriomethylanilines, clearly originate in the deprotonation step of the radical cation which is characterized by a primary deuterium kinetic isotope effect.

In contrast with that observed with *N*,*N*-dimethylanilines substituted by electron-donating groups, the substrates substituted by electron-withdrawing groups (**1**−**3**) exhibit a significant intermolecular deuterium kinetic isotope effect

---

(20) Baciocchi, E.; Calcagni, A.; Lanzalunga, O. *J. Org. Chem.* **2008**, *73*, 4110–4115.

(21) Wayner, D. D. M.; McPhee, D. J.; Griller, D. *J. Am. Chem. Soc.* **1988**, *110*, 132–137.

(22) A higher *N*-methylaniline/adduct molar ratio was observed in the oxidation of DMAs **4**−**6** containing electron-donating substituents. This result can be rationalized considering that when substituted with electron-donating groups the α-aminomethyl radicals are more easily oxidizable to the α-aminomethyl cation precursors of *N*-methylanilines.

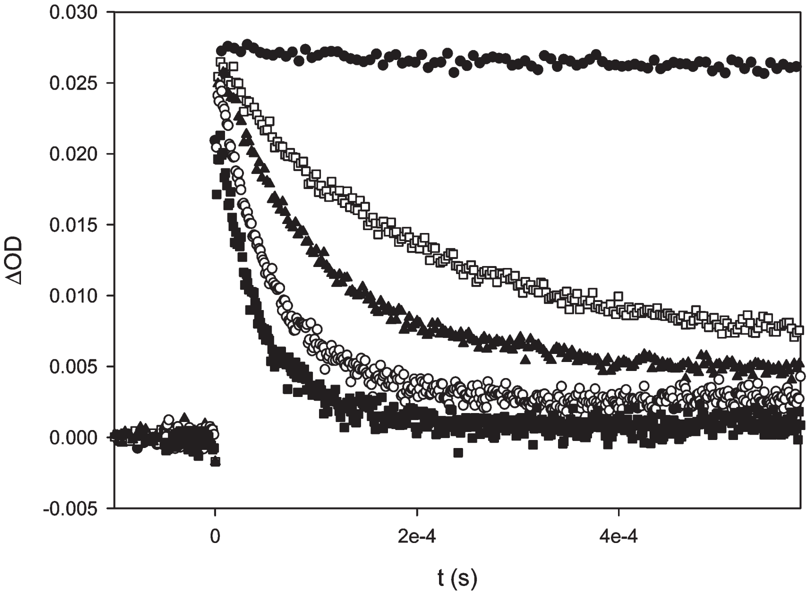
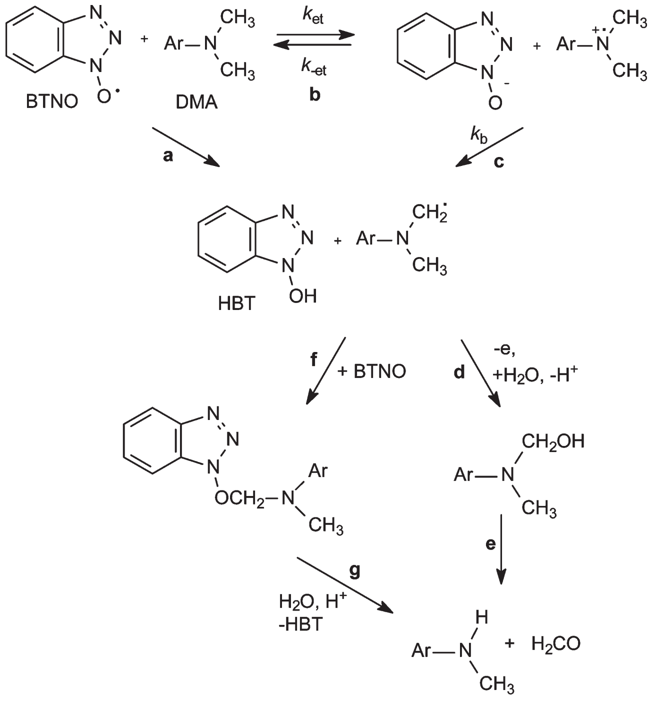


FIGURE 1. Time-resolved absorbance measured at 380 nm after laser excitation of a solution of dicumyl peroxide (1.0 M) and HBT (8 mM) in CH_3CN in the absence (filled circles) or in the presence of 4-CH_3O-$C_6H_4N(CH_3)_2$ 0.22 mM (empty squares), 0.43 mM (filled triangles), 0.86 mM (empty circles), and 1.08 mM (filled squares).

SCHEME 5



(Table 1). However, an ET−PT mechanism is again suggested for the reactions of these anilines on the basis of several grounds. For 4-CF_3-*N,N*-dimethylaniline (**2**) and

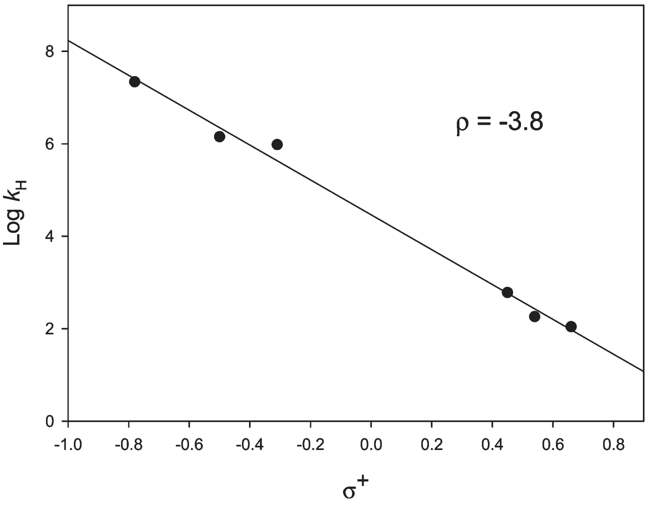


FIGURE 2. Dependence of the bimolecular rate constants for the reactions of BTNO with *N,N*-dimethylanilines **1**−**6** (k_H) upon the Brown−Okamoto σ^+ constants.

4-$CO_2C_2H_5$-*N,N*-dimethylaniline (**3**) clear evidence in this respect comes from the observation that the $(k_H/k_D)_{inter}$ values are different than the intramolecular deuterium kinetic isotope effects $(k_H/k_D)_{intra}$.[23] This finding is inconsistent with the single-step classical hydrogen abstraction (HAT) mechanism which predicts very close values of inter- and intramolecular deuterium kinetic isotope effects. It is instead fully in line with an ET−PT mechanism where the ET step is partially reversible so that the deprotonation step begins to contribute to the overall reaction rate.[8,13i]

It is reasonable that such a situation is observed with dimethylanilines substituted by electron withdrawing groups and not with those substituted by electron donating ones. In the latter case, the ET step is exergonic ($\Delta G°_{ET}$ ranging from -0.5 kcal mol^{-1} for X = CH_3 to -4.2 kcal mol^{-1} for

---

[23] We agree with one of the reviewers that different values of $(k_H/k_D)_{inter}$ and $(k_H/k_D)_{intra}$ and $(k_H/k_D)_{inter} > 1$ for *N,N*-dimethylanilines **1**−**3** might also be due to a competition between the ET−PT and HAT mechanism. We, however, believe that the process can be better described by the ET−PT mechanism with a reversible ET step on the basis of the fact that when X = CN and the HAT mechanism should compete more favorably with the ET−PT process, there is further evidence in favor of the ET−PT mechanism (*N*-demethylation much faster than *N*-deethylation in the reaction of *N*-ethyl-*N*-methyl-4-cyanoaniline with BTNO, vide infra).

X = OCH_3) and the rate of back electron transfer (k_{-ET} in Scheme 5) is expected to be low and much smaller than that of the deprotonation step (k_b in Scheme 5). Thus, the ET step is rate determining, as observed. With dimethylanilines substituted by strongly electron-withdrawing groups, like $CO_2C_2H_5$ and CF_3, the ET step is instead significantly endergonic (ΔG°_{ET} +7.8 kcal mol^{-1} for X = $CO_2C_2H_5$ and +8.8 kcal mol^{-1} for X = CF_3), the rate of back electron transfer increases and can therefore compete with the deprotonation step, becoming in part rate determining; an intermolecular deuterium kinetic isotope effect can therefore be observed. By applying the stationary state to the ET−PT mechanism, it can be easily shown that the $(k_H/k_D)_{inter}$ value depends upon the ratio of the rate constants of the back electron transfer (k_{-ET}) to that of the proton transfer (k_b) and should increase as the k_{-ET}/k_b ratio becomes larger.[13i]

When the k_{-ET}/k_b ratio becomes sufficiently large, a limit is reached where the first ET step is a preequilibrium, which is followed by the slow step (deprotonation of the radical cation). In this case, similar values of $(k_H/k_D)_{inter}$ and $(k_H/k_D)_{intra}$ should be observed. Such a limit situation probably holds with 4-CN-*N*,*N*-dimethylaniline, whose reaction with BTNO accordingly exhibits very close values of $(k_H/k_D)_{inter}$ and $(k_H/k_D)_{intra}$. However, as already mentioned, $(k_H/k_D)_{inter} \approx (k_H/k_D)_{intra}$ would be also the result expected if a HAT mechanism is taking over; thus, to make a choice in this case, an additional mechanistic criterion had to be used. This was provided by the study of the *N*-dealkylation of *N*-methyl-*N*-ethyl-4-cyanoaniline that resulted in *N*-demethylation ca. 3 times faster than *N*-deethylation (see the Results), a finding clearly suggesting that the ET−PT mechanism also holds with 4-CN-*N*,*N*-dimethylaniline. Accordingly, the preference for α-*N*-CH_3 deprotonation as compared to that of α-*N*-CH_2CH_3 is the expected outcome for a methyl(ethyl)aniline radical cation, which is justified by the higher acidity of the methyl protons as compared to the α-ethyl ones.[13d,f,14g] In the case of a HAT mechanism, the opposite result should hold, as actually found in the reaction of *tert*-butoxyl radical with tertiary amines, owing to the weaker C−H bond strength in the methylene group with respect to the methyl group.[24]

Summing up, the above discussion has provided substantial evidence that the ET−PT mechanism holds for the reaction of BTNO with all 4-X-*N*,*N*-dimethylanilines studied in this work. The rate is clearly determined in the ET step when the substituents (X = OCH_3, OC_6H_5, CH_3) are electron donating, whereas with electron-withdrawing groups (X = CO_2CH_3, CF_3) there is a contribution of the rate of the deprotonation step. With X = CN, the limit is reached where ET occurs in a preequilibrium and the deprotonation of the radical cation is the slow step.

The kinetic data for the dimethylanilines with electron-donating substituents where it has been shown that the experimental rate constant (k_H in Table 1) is actually the rate constant for the ET step ($k_H = k_{ET}$) are perfectly amenable to be treated in terms of the Marcus equation (eq 3),[25] where $\Delta G^\ddagger$ is the free energy of activation of the ET reaction, given by the Eyring equation (eq 4) with Z taken as 6×10^{11} M^{-1} s^{-1}.[26] $\Delta G^{\circ\prime}_{ET}$ is the free energy variation ΔG°_{ET} in the same reaction, corrected for the electrostatic contribution, and λ is the reorganization energy required for the electron transfer.

$$\Delta G^\ddagger = (\lambda/4)(1+\Delta G^{\circ\prime}_{ET}/\lambda)^2 \qquad (3)$$

$$\Delta G^\ddagger = RT \ln(Z/k_{ET}) \qquad (4)$$

TABLE 2. Activation Free Energies ($\Delta G^\ddagger$), Electron Transfer Free Energies Corrected for the Electrostatic Contribution ($\Delta G^{\circ\prime}_{ET}$) and Reorganization Energies for the Reaction of BTNO with *N*,*N*-Dimethylanilines 4−6 in CH_3CN at 25 °C

substrate	$\Delta G^{\ddagger a,b}$	$\Delta G^{\circ\prime}_{ET}{}^a$	λ^a
4, X = CH_3	8.0	−1.5	34.9
5, X = OC_6H_5	6.4	−2.6	30.6
6, X = OCH_3	5.3	−5.2	30.7

[a] In kcal mol^{-1}. [b] Calculated from the Eyring eq 4 using the k_H values reported in Table 1 and a collision frequency (Z) value of 6×10^{11} M^{-1} s^{-1}.

The values of $\Delta G^\ddagger$ and $\Delta G^{\circ\prime}_{ET}$ (kcal mol^{-1}) for the ET reaction of BTNO with *N*,*N*-dimethylanilines **4**−**6** are reported in Table 2. $\Delta G^\ddagger$ values are obtained by the rate constants in Table 1 via eq 4, and $\Delta G^{\circ\prime}_{ET}$ values are given by $F(E^\circ_{ox} - E^\circ_{red})$ (E°_{ox} is the BTNO reduction potential, 0.63 V vs SCE,[10] and E°_{red} are the oxidation potential of the *N*,*N*-dimethylanilines shown in Table 1) corrected for the electrostatic contribution arising from the charge variation in the reactants upon ET (see the Supporting Information for the calculation details). In the same table are also reported the λ values for the same reactions obtained from eq 5, which is derived from eqs 3 and 4.

$$\lambda = 2\Delta G^\ddagger - \Delta G^{\circ\prime}_{ET} + 2[(\Delta G^{\ddagger 2} - \Delta G^\ddagger \times \Delta G^{\circ\prime}_{ET})]^{1/2} \qquad (5)$$

Looking at the data in Table 2, it can be noted that the λ values obtained from the three reactions are quite similar, providing an average value of 32.1 (±1.9) kcal mol^{-1} that can be reasonable taken as the reorganization energy for the ET reaction of BTNO with *N*,*N*-dimethylanilines ($\lambda_{BTNO/DMA}$).

It is interesting to apply eq 5 to our previous kinetic data for the oxidation by PINO of the anilines **5** and **6** which should involve an ET rate-determining step. A reorganization energy of 41.2 kcal mol^{-1} is obtained,[27] which is significantly larger than that of the reaction with BTNO. This fully confirms the earlier conclusion that the intrinsic reactivity of BTNO in electron-transfer reactions is higher than that of PINO.[10] Thus, in line with the prediction that in ET reactions BTNO would be more reactive than PINO, we find that with 4-CH_3O-*N*,*N*-dimethyaniline, the reactivity of BTNO ($k_H = 2.2 \times 10^7$ M^{-1} s^{-1}) is significantly larger than that of PINO ($k_H = 3.7 \times 10^6$ M^{-1} s^{-1}).[8] A similar result is found comparing the reactivities of 4-C_6H_5O-*N*,*N*-dimethyaniline with the two *N*-oxyl radicals. Moreover, with BTNO, it was possible to measure the rate constant for the reaction with *N*,*N*-dimethyl-*p*-toluidine (**4**) while only a

---

(24) Griller, D.; Howard, J. A.; Marriott, P. R.; Scaiano, J. C. *J. Am. Chem. Soc.* **1981**, *103*, 619–623.

(25) Marcus, R. A. *Annu. Rev. Phys. Chem.* **1964**, *15*, 155.

(26) Eberson, L. *Electron Transfer Reactions in Organic Chemistry*; Springler Verlag: Berlin Heidelberg, 1986; Chapter 3.

(27) The somewhat lower λ value (37.1 kcal mol^{-1}) reported in ref 8 is probably due to the fact that it was obtained using also the kinetic data for the reactions with anilines substituted by electron-withdrawing substituents (endergonic electron transfer) which are somewhat influenced by the rate of the deprotonation of the radical cation.

lower limit ($<1 \times 10^5$ M^{-1} s^{-1}) could be given for the reaction of the same substrate with PINO.[8]

However, with *N,N*-dimethylanilines substituted by electron-withdrawing groups, the reverse situation is observed: rate constants for the reactions of BTNO with DMAs **1**, **2**, and **3** (k_H = 110 M^{-1} s^{-1}, 180 M^{-1} s^{-1} and 600 M^{-1} s^{-1}, respectively) are lower than those found with the PINO radical (k_H = 450 M^{-1} s^{-1}, 1.4×10^3 M^{-1} s^{-1} and 3.5×10^3 M^{-1} s^{-1}).[8] As discussed above, with these substrates, the proton transfer step significantly contributes to the overall rate of reaction. Thus, the reaction rate should also be influenced by the basicity of the species, $PINO^-$ or $BTNO^-$, abstracting the proton from the radical cation. As $PINO^-$ is a significantly stronger base than $BTNO^-$,[28] the larger reactivity of PINO than BTNO with *N,N*-dimethylanilines substituted by electron-withdrawing groups can be reasonably justified.

From the study of the reactions of BTNO and PINO with ferrocenes,[9,10] the reorganization energy for the self-exchange ET reactions in the $BTNO/BTNO^-$ and $PINO/PINO^-$ couples ($\lambda_{BTNO/BTNO^-}$ and $\lambda_{PINO/PINO^-}$) were determined as 32.3 and 49.1 kcal mol^{-1}, respectively, by application of the Marcus cross relation, which relates the reorganization energy (λ_{AB}) of an ET reaction ($A + B = A^{\bullet+} + B^{\bullet-}$) to the λ values of the self-exchange ET reactions of the reactants (eq 6).

$$\lambda_{AB} = (\lambda_{A^{\bullet+}/A} + \lambda_{B/B^{\bullet-}})/2 \qquad (6)$$

Now, if eq 6 is applied to the data for the reactions of BTNO and PINO with *N,N*-dimethylanilines, the value for the self-exchange ET in the $ArN(CH_3)_2^{+\bullet}/ArN(CH_3)_2$ couple ($\lambda_{DMA^{\bullet+}/DMA}$) can be calculated as 31.9 kcal mol^{-1} from the reactivity data for BTNO and 33.3 kcal mol^{-1} from the data for PINO.

A $\lambda_{DMA^{\bullet+}/DMA}$ value ≥ 30 kcal mol^{-1} is also suggested by the fact that the reorganization energies for the oxidation of ferrocenes by BTNO and PINO radicals (30[10,29] and 38.3[9] kcal mol^{-1}, respectively) are both smaller than those of the ET reactions of the two *N*-oxyl radicals with *N,N*-dimethylanilines (32.1 and 41.2 kcal mol^{-1} for BTNO and PINO, respectively). This indicates that the self-exchange barrier for the $ArN(CH_3)_2^{\bullet+}/ArN(CH_3)_2$ couple must be somewhat larger than that (27 kcal mol^{-1})[9] for the ferrocene/ferricinium couple. In agreement with this, it is found that the reactivity of BTNO with ethyl ferrocenecarboxylate (2.1×10^6 M^{-1} s^{-1})[10] is larger than that with 4-methyl-*N,N*-dimethylaniline (9.5×10^5 M^{-1} s^{-1}) in spite of the fact that the latter reaction is slightly exergonic ($\Delta G° = -0.5$ kcal mol^{-1}) and the former slightly endergonic ($\Delta G° = +0.5$ kcal mol^{-1}).

However, very intriguingly, the $\lambda_{DMA^{\bullet+}/DMA} \approx 32-33$ kcal mol^{-1} is significantly higher than that (ca. 15 kcal mol^{-1}) calculated from the experimentally determined rate constant for the ET self-exchange between *N,N*-dimethylaniline and its radical cation.[30]

Tentatively, we suggest that such a large difference might be related to the fact that eq 6 should hold only for strictly adiabatic reactions whereas it is generally considered that intermolecular ET reactions occur in a region between adiabatic and nonadiabatic behavior.[32] In a nonadiabatic reaction, the intermolecular electronic interaction (H_{ab}) in the ET transition state can become very important and influence the pre-exponential factor Z, whose value can change in the 10^9-10^{13} range[33] as well as the activation free energy, in a way which is different for the cross- and the self-exchange reactions. Clearly, in this situation a reliable interpretation of the above observation requires further studies, both theoretical and experimental. At the present we feel, however, that our λ values can be confidently used in a relative sense and in this respect they give reliable and useful information. Accordingly, there is little doubt in our conclusions that the intrinsic reactivity of BTNO in ET reactions is larger than that of PINO and that *N,N*-dimethylanilines, at least with *N*-oxyl radicals, exhibit a relatively low intrinsic ET reactivity, much lower than the one predicted on the basis of the $DMA^{+\bullet}/DMA$ self-exchange rate constant. The latter information may be important in view of the already mentioned great interest in the role of ET mechanisms in the oxidative *N*-dealkylation of *N,N*-dimethylanilines by enzymatic and biomimetic oxidants.

Experimental Section

Product Analysis. The substrate (0.1−0.2 mmol) in 1 mL of CH_3CN, $Pb(OAc)_4$ (0.02−0.03 mmol) in 3 mL of 1% CH_3COOH in CH_3CN, and HBT (0.1 mmol) in 3 mL of CH_3CN were separately degassed with argon for 20 min. By mixing the solutions of HBT and $Pb(OAc)_4$, the BTNO was generated and added to the solution of the substrate under argon. The reaction mixture was stirred at 25 °C for 10 min. The solvent was then removed under reduced pressure, and the residue was treated with dilute HCl and then neutralized with NaOH (2 N). The mixture was then extracted with CH_2Cl_2, and the collected organic extracts were dried over anhydrous Na_2SO_4 and analyzed by GC−MS and ^1H NMR. With all the substrates, the major product was the corresponding *N*-methylaniline (comparison with authentic specimens). The yields, however, were rather small (from 20% to 80% referred to the starting material) probably because part of BTNO is decomposed before the reaction with the substrate.[4h] ^1H NMR analysis of the reaction mixture carried out before the workup showed two additional singlets at 5.15 ppm and 3.0 ppm, with relative intensity = 2:3. These singlets can be reasonably assigned to the cross-coupling product of BTNO and the α-aminomethyl radical (shown in Scheme 2).[34] Attempts to isolate this adduct were unsuccessful because it was unstable during the

---

(28) Astolfi, P.; Brandi, P.; Galli, C.; Gentili, P.; Gerini, M. F.; Greci, L.; Lanzalunga, O. *New J. Chem.* **2005**, *29*, 1308.

(29) This value is the average of those obtained in the oxidation of ferrocenes by BTNO and in the oxidation of ferrocene by substituted BTNO radicals.

(30) $\lambda_{DMA^{+\bullet}/DMA} = 4\Delta G^{\circ\ddagger}$, where $\Delta G^{\circ\ddagger}$ is the activation free energy for the ET self-exchange between *N,N*-dimethylaniline and its radical cation. $\Delta G^{\circ\ddagger}$ is given by the Eyring equation $\Delta G^{\ddagger} = RT \ln(Z/k_{ex})$ with Z taken as 6×10^{11} M^{-1} s^{-1}, and k_{ex} is the experimentally determined ET self-exchange rate constant (ca. 10^9 M^{-1} s^1).[31]

(31) Goez, M. *Z. Phys. Chem.* **1990**, *169*, 123–132.

(32) Nelsen, S. F.; Trieber, D. A. II; Nagy, M. A.; Konradsson, A.; Halfen, D. T.; Splan, K. A.; Pladziewicz, J. R. *J. Am. Chem. Soc.* **2000**, *122*, 5940–5946.

(33) Nelsen, S. F.; Chen, L.-J.; Ramm, M. T.; Voy, G. T.; Powell, D. R.; Accola, M. A.; Seehafer, T. R.; Sabelko, J. J.; Pladziewicz, J. R. *J. Org. Chem.* **1996**, *61*, 1405–1412.

(34) In analogy with the adducts formed by PINO and α-aminomethyl radicals (see ref 8) the singlet at 5.2−5.3 ppm can be predicted for the methylene group of this adduct on the basis of the additive effect of the $C_6H_4N_2NO$ and $C_6H_5N(CH_3)$ substituents on the shielding constant. Moreover, the singlet at 3.1−3.2 ppm can be attributed to the *N*-methyl group of the adduct being slightly shielded with respect to the substrate *N*-methyl groups by the effect of the $CH_2ONN_2C_6H_4$ substituent.

chromatographic isolation procedure, always decomposing into the *N*-methylaniline and HBT. Formation of CH_2O was detected by its dimedone adduct. In this case, 0.5 mL of 0.2 M dimedone solution in 0.2 M NaOH was added, and the reaction was stirred for 30 min. Then dilute HCl was added dropwise until the mixture became acidic. The dimedone adduct was extracted with CH_2Cl_2 and analyzed by GC−MS (m/z = 292).

Reaction of *N*-ethyl-*N*-methyl-4-cyanoaniline with BTNO has been carried out under the same experimental conditions described above. After workup and hydrolysis, *N*-ethyl-4-cyanoaniline and *N*-methyl-4-cyanoaniline were identified as reaction products by GC−MS and ^{1}H NMR analysis by comparison with authentic specimens. The yields of the two products, determined by GC and ^{1}H NMR analysis, were 20% for *N*-ethyl-4-cyanoaniline and 4.3% for *N*-methyl-4-cyanoaniline.

The intramolecular $(k_H/k_D)_{intra}$ deuterium isotope effects were determined using the reaction procedure described above with *N*-methyl-*N*-trideuteriomethylanilines as substrates and measuring the ratio of the corrected signal intensities at m/z = 292 and 294 (corresponding to the dimedone adducts of CH_2O and CD_2O respectively). The results were confirmed in some cases by measuring the *N*-trideuteriomethylaniline/*N*-methylaniline ratio in the reaction mixtures.

Spectrophotometric Kinetic Studies. BTNO was generated by the oxidation of HBT (4 mM) with $Pb(OAc)_4$ (0.5 mM) in CH_3CN at 25 °C and under an argon atmosphere. A solution of the substrate (**1**−**3**) was added into the BTNO solution in the cuvette (substrate concentration in the range 0.7−4 mM), and the absorbance change was monitored at 380 nm. For all the substrates investigated each kinetic trace obeyed a first-order kinetic. Second-order rate constants were obtained by the plot of the observed rate constant k_{obs} vs the substrate concentration. It was verified that the self-decomposition of BTNO, generated by the oxidation of HBT (4 mM) with $Pb(OAc)_4$ (0.5 mM) in CH_3CN (at 25 °C under argon) was slow enough to allow the study of the reaction of BTNO with the *N*,*N*-dimethylanilines.

Laser Flash Photolysis Experiments. Laser flash photolysis experiments were carried out with an Applied Photophysics LK-60 laser kinetic spectrometer providing 8 ns pulses, using the third armonic (355 nm) of a Quantel Brilliant-B Q-switched Nd:YAG laser. The laser energy was adjusted to ≤10 mJ/pulse by the use of the appropriate filter. A 3 mL Suprasil quartz cell (10 mm × 10 mm) was used for all the experiments. N_2-saturated CH_3CN solutions of dicumyl peroxide (0.8 M), 1-hydroxybenzotriazole (8.2 mM), and dimethylanilines **4**−**6** (0.2−6.5 mM) were used. All the experiments were carried out at T = 25 ± 0.5 °C under magnetic stirring. Data were collected at individual wavelengths with an Agilent Infinium oscilloscope and analyzed with the kinetic package implemented in the instrument. Rate constants were obtained by monitoring the change of absorbance at the maximum absorption wavelength and by averaging 3−5 values. Each kinetic trace obeyed a first-order kinetic and second order rate constants were obtained from the slopes of the plots of the observed rate constants k_{obs} vs substrate concentration.

Acknowledgment. Financial support from the Ministero dell'Istruzione dell'Università e della Ricerca (MIUR) is gratefully acknowledged. We thank Prof. Lorenzo Stella for the use and assistance in the use of a LFP equipment.

Supporting Information Available: Instrumentation, materials, dependence of k_{obs} on the concentration of *N*,*N*-dimethylanilines and *N*,*N*-bis(trideuteriomethyl)anilines, and calculation of $\Delta G^{\circ\prime}$ values. This material is available free of charge via the Internet at http://pubs.acs.org.