

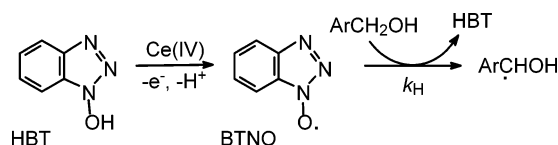
Kinetic Study of the Hydrogen Abstraction Reaction of the Benzotriazole-*N*-oxyl Radical (BTNO) with H-Donor Substrates

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The aminoxyl radical ($>\text{N}-\text{O}^\bullet$) BTNO (benzotriazole-*N*-oxyl) has been generated by the oxidation of 1-hydroxybenzotriazole (HBT; $>\text{N}-\text{OH}$) with a Ce^{IV} salt in MeCN. BTNO presents a broad absorption band with λ_{max} 474 nm and ϵ 1840 $\text{M}^{-1} \text{cm}^{-1}$, and spontaneously decays with a first-order rate constant of $6.3 \times 10^{-3} \text{ s}^{-1}$ in MeCN at 25 °C. Characterization of BTNO radical by EPR, laser flash photolysis, and cyclic voltammetry is provided. The spontaneous decay of BTNO is strongly accelerated in the presence of H-donor substrates such as alkylarenes, benzyl and allyl alcohols, and alkanols, and rate constants of H-abstraction by BTNO from a number of substrates have been spectroscopically investigated at 25 °C. The kinetic isotope effect confirms the H-abstraction step as rate-determining. Activation parameters have been measured in the 15–40 °C range with selected substrates. A correlation between E_a and $\text{BDE}(\text{C}-\text{H})$ (C–H bond dissociation energy) for a small series of H-donors has been obtained according to the Evans–Polanyi equation, giving $\alpha = 0.44$. From this plot, the experimentally unavailable $\text{BDE}(\text{C}-\text{H})$ of benzyl alcohol can be extrapolated, as ca. 79 kcal/mol. With respect to the H-abstraction step, peculiar differences in the ΔS^\ddagger parameter emerge between an alkylarene, $\text{ArC}(\text{H})\text{R}_2$, and a benzyl alcohol, $\text{ArC}(\text{H})(\text{OH})\text{R}$. The data acquired on the H-abstraction reactivity of BTNO are compared with those recently reported for the aminoxyl radical PINO (phthalimide-*N*-oxyl), generated from *N*-hydroxyphthalimide (HPI). The higher reactivity of radical PINO is explained on the basis of the higher energy of the $\text{NO}-\text{H}$ bond of HPI, as compared with that of HBT (88 vs ca. 85 kcal/mol, respectively), which is formed on H-abstraction from the RH substrate.

Transfer of hydrogen atom from C–H bonds to free radicals in general, and to oxygen-centered radicals in particular,¹ plays an important role in many processes, including the degradation of chemicals in the troposphere,² biochemical reactions,³ synthetic organic transformations,⁴ but also the pathogenesis of some diseases.⁵ Removal of hydrogen is instrumental to enable the reaction of a substrate with dioxygen.⁶ Aerobic oxidation of organic compounds operates in many important in-

dustrial processes through the involvement of radical active species from suitable catalysts.^{4,7} In this context, hydroxylamines ($>\text{N}-\text{OH}$) as precursors of nitroxyl radical ($>\text{N}-\text{O}^\bullet$) catalysts have recently gained considerable attention. For example, *N*-hydroxyphthalimide (HPI), in combination with dioxygen and metal salt cocatalysts such as $\text{Co}(\text{OAc})_2$ or $\text{Co}(\text{acac})_2$, provides a remarkable catalytic system for the oxidation of suitable organic compounds.^{4d,8,9} Alcohols, alkylarenes, amides, and even

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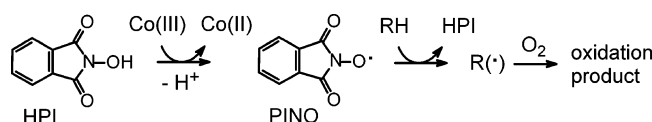
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SCHEME 1

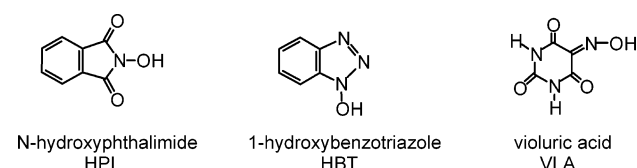


alkanes are accordingly oxidized under mild conditions. The key reactive intermediate in these procedures is the phthalimide-N-oxyl radical (PINO), formed in the preliminary interaction of HPI with O₂ and a Co(II) salt, as delineated in Scheme 1.^{8–10}

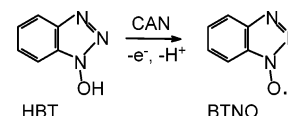
The synthetic value of the procedure has prompted studies on the reactivity features of PINO.¹⁰ In recent investigations, PINO was generated from HPI by the Pb(OAc)₄ oxidant and the resulting >N–O• species characterized by UV–vis spectrophotometry.¹¹ Kinetic studies of H-abstraction from suitable C–H- or O–H-containing substrates have provided fundamental information upon the reactivity of PINO toward organic compounds.^{11,12} Knowledge of the energy of the NO–H bond of HPI itself,⁹ as well as that of aryl-substituted HPI's, from EPR equilibration measurements, and of their redox potentials from cyclic voltammetry¹² has provided additional information upon the reactivity features of this remarkable oxidizing system.

Concerns about environmental pollution urge substitution of old synthetic procedures with “green” alternatives.^{4c,d} Catalytic systems enabling the activation of dioxygen for homogeneous oxidations represent one effort in this direction.⁴ A natural process of fundamental importance is the oxidative delignification of rotten wood carried out by white-rot fungi.¹³ A similar process would represent a dream for the paper-making industry that conventionally performs the delignification of wood pulp by utilizing chlorine-based polluting chemicals.¹⁴ Deligni-

CHART 1



SCHEME 2



fication with fungal enzymes might lead to novel, environment-respectful techniques.^{13a} Attempts in this direction have been reported,^{13,15} but the degradation of difficult to oxidize residues of lignin, for example, the benzylic alcohol groups, may require the widening of the substrate range of some enzymes by adding mediator compounds.^{13,15,16} Hydroxylamines, such as HPI or 1-hydroxybenzotriazole (HBT) or violuric acid (VLA) (Chart 1), have recently shown their proficiency in mediating the phenol oxidase laccase toward the aerobic oxidation of lignin models having the structure of benzyl alcohols.^{13c,15a–c,16}

Laccase, having a redox potential around 0.6–0.8 V vs NHE,^{16c} could never oxidize benzylic substrates endowed with redox potentials ≥ 1.4 V vs NHE by electron abstraction.¹⁷ In contrast, laccase/mediator systems have shown promises even in the degradative oxidation of wood pulp itself.¹⁸ The nitroxyl radical intermediate from these >N–OH mediators, generated by laccase, performs as the active species and promotes the radical cleavage of benzylic C–H bonds, thereby extending the (indirect) oxidation capability of laccase toward nonphenolic substrates.^{17a} This lead us back to the studies of the H-abstraction reactivity by >N–O• species. We have recently reported on the first generation of the aminoxyl radical from HBT (dubbed BTNO) by monoelectronic oxidation with cerium(IV) ammonium nitrate (i.e., CAN) in MeCN solution (Scheme 2).¹⁹

A full account of the generation and H-abstraction reactivity of this radical intermediate toward substrates containing C–H bonds of suitable energy is presented here. Because HBT is one of the most efficient mediators

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TABLE 1. Normalized Second-Order Rate Constant of H-Abstraction from H-Donor Substrates by BTNO at 25 °C^{a,b}

substrate, RH (no. of equivalent removable H atoms)	k_H (M ⁻¹ s ⁻¹) at 25 °C in MeCN ^{c,d}	BDE(C–H) of RH (kcal/mol) ^e	k_H (M ⁻¹ s ⁻¹) at 25 °C in AcOH with PINO radical ^f
C ₆ H ₅ CH ₂ OH (2)	0.94	83–85 ^g	–
C ₆ H ₅ CH ₂ OH (2)	0.57 ^h	83–85 ^g	5.7
4-MeO-C ₆ H ₄ CH ₂ OH (2)	3.1	82–84 ^g	–
4-MeO-C ₆ H ₄ CH ₂ OH (2)	3.4 ^h	82–84 ^g	22
4-MeO-C ₆ H ₄ CH ₂ OMe (2)	3.0	82–84 ^g	–
3,4-diMeO-C ₆ H ₃ CH ₂ OH (2)	11	82–84 ^g	–
decanol (2)	0.11	93	–
cyclohexanol (1)	0.33	92	–
4-MeO-toluene (3)	0.091	89–90	3.4
4-MeO-ethylbenzene (2)	0.35	85–87	–
4-MeO-isopropylbenzene (1)	0.55	83–85	–
1-(4-MeO-phenyl)ethanol (1)	5.9	82–84	–
PhCH=CHCH ₂ OH (2)	18	80–83	–
PhOH (1)	66	88 ^h	330 ⁱ
9-Ph-fluorene (1)	18	74	–
fluorene (2)	1.9	82	20
9,9-di-D-fluorene (2)	0.14 ^j	–	–
Ph ₃ CH (1)	2.3	81	59
9-OH-fluorene (1)	10	73 ^l	–
Ph ₂ CHOH (1)	3.2	79	58
Ph ₂ CH ₂ (2)	0.36	84	6.6
<i>p</i> -xylene (6)	ca. 0.02	89–90	0.99
<i>p</i> -An ₂ CHOH (1)	19	75	–
geraniol (2)	11	82	–
PhCH ₂ NEt ₂ (2)	too fast	85	–
PhCH ₂ COCH ₃ (2)	<0.001	82	–
PhCH ₂ CN	ca. 0.01	–	–
PhCHO (1)	ca. 0.8	87	11

^a The radical was generated from HBT with CAN in MeCN solution. Literature values of the normalized H-abstraction rate constants by PINO radical, generated from HPI with Pb(OAc)₄ in AcOH solution at 25 °C, are given. ^b Conditions: [BTNO], 0.5 mM; [RH], 5–25 mM in MeCN solution. Determinations in triplicate; typical error ±3%. ^c Monitored spectroscopically at 474 nm. ^d Normalized for the number of equivalent H-atoms in RH. ^e From ref 26. ^f Followed at 382 nm; from ref 11. ^g A range of values from different sources and techniques is reported in ref 26. ^h BDE(O–H). ⁱ Our determination. ^j As *k_D*. ^k In AcOH. ^l For 9-MeO-fluorene.

of laccase,¹⁷ our study may have relevance for the field of biodelignification as well.^{13,15}

Experimental Section

Materials. HBT (Aldrich) was used as received; all the substrates were obtained commercially and used without further purification. Cerium(IV) ammonium nitrate (CAN; Erba RPE) was oven-dried before use. Reagent grade glacial acetic acid and acetonitrile (Erba RPE) were used as solvents. Mono- α -deuterated benzyl and *p*-MeO-benzyl alcohols were already available in the laboratory from previous studies.^{16e} 9,9-Dideuterated fluorene was obtained from fluorene by means of hydrogen–deuterium exchange with *t*-BuOK in (CD₃)₂SO–D₂O, and its electron impact mass spectrum (*m/e* 168) was consistent with the replacement of two H-atoms with two D-atoms.

Instrumentation. The kinetic study was carried out with a Hi-Tech SFA-12 stopped flow instrument interfaced to a HP 8453 diode array spectrophotometer and having a thermostated cell holder. A conventional UV–vis spectrophotometer (Perkin-Elmer Lambda 18) was alternatively used. A thermocouple was employed for reading the temperature in the cuvette.

Kinetic Procedure. The BTNO species was generated in MeCN in a thermostated quartz cuvette, 1 cm optical path, by adding a 0.5 mM solution of CAN to a 0.5 mM solution of HBT. A broad absorption band developed almost immediately (15 ms) in the 350–600 nm region (λ_{max} at 474 nm, ϵ 1840 M⁻¹ cm⁻¹).¹⁹ The *A*₄₇₄ reading was not stable, but decayed with a half-life of 110 s. The rate of decay was unaffected by the use of deuterated MeCN. Rate constants of H-abstraction from H-donor substrates were determined at 25 °C in MeCN, by following the decrease of *A*₄₇₄ of BTNO. The initial concentra-

tion of the substrate was in the (0.5–2) × 10⁻² M range, to enable a pseudo-first-order treatment of the kinetic data. Plots of (*A_t* – *A_∞*) vs time were well-fitted by a first-order exponential over more than three half-lives, and the rate constant (*k'*) obtained. From a plot of three to five *k'* vs [subst]₀ data pairs, the second-order rate constant of H-abstraction (*k_H*) was obtained. Determination of H-abstraction rate constants was analogously carried out at different temperatures (three temperatures in the 13–43 °C range) with selected substrates and enabled calculation of the activation parameters from Arrhenius and Eyring plots.

Laser Flash Photolysis Experiment. Flash photolysis experiments were carried out with a laser spectrometer using the fourth harmonic (266 nm) of a Q-switched Nd:YAG laser. A 3 mL Suprasil quartz cell (10 mm × 10 mm) was used for all the experiments. Argon-saturated MeCN solutions containing di-*tert*-butyl peroxide (1.0 M) and HBT (10 mM) were used. The experiments were carried out at 25 °C under magnetic stirring.

Isotope Effect Determinations. As described previously,^{16e,19} α -monodeuterated benzyl alcohol, PhCH(D)OH, was oxidized with BTNO under the following experimental conditions: 60 mmol alcohol, 20 mmol HBT, and 20 mmol CAN, in 3 mL of MeCN at room temperature. After a 5 h reaction time and conventional workup with ethyl acetate, the relative amount of the PhCHO and PhCDO oxidation products was determined by GC–MS analyses in the SIM mode, enabling reckoning of the intramolecular *k_H*/*k_D* ratio. The intermolecular kinetic isotope effect for fluorene vs 9,9-dideuteriofluorene was calculated from the ratio of the *k_H* and *k_D* rate constants with BTNO (see Table 1).

Electrochemical Determinations. Cyclic voltammetry at the steady disk electrode (glassy carbon disk, 1.5 mm in diameter)^{16d} was carried out at 25 °C in MeCN containing 0.1

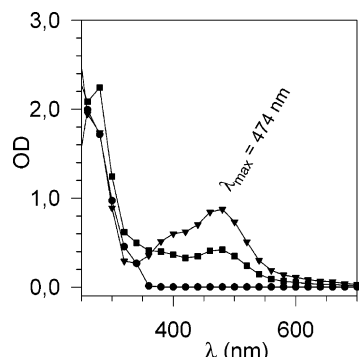


FIGURE 1. UV-vis spectrum of HBT (0.5 mM) in MeCN in the absence of CAN (●) and in the presence of CAN (0.5 mM) (▼) 15 ms after mixing and (■) 90 s after mixing.

M Bu_4NBF_4 . A three-electrode circuit was used with either an electrochemical computerized system (Amel System 5000, version 2.1) or a potentiostat with positive feedback ohmic-drop compensation and MPLI hardware (Vernier Software & Technology) controlled by a program written in C++ language for Windows 95/98. The auxiliary electrode was a platinum wire (surface 1 cm^2), and a saturated calomel electrode (SCE) was used as reference; the redox potential values are then referred to NHE. The sweep scan ranged from 10 mV/s to 10 V/s; the concentration of HBT was 1.7 mM, and a 2-fold excess of pyridine was used to deprotonate the $>\text{N}-\text{OH}$ mediator into the more easily oxidizable $>\text{N}-\text{O}^-$ form.

Results and Discussion

Characterization of the BTNO Radical. In keeping with the characterization of the PINO radical from HPI,¹¹ we provide here a full characterization of the aminoxyl radical from HBT. The absorption spectrum of a 0.5 mM solution of HBT in MeCN is reported in Figure 1 (trace ●).

Following the addition of a stoichiometric amount of the monoelectronic oxidant cerium(IV) ammonium nitrate (i.e., CAN) in MeCN at 25 °C, a new and broad absorption band in the 350–600 nm range develops (trace ▼), having λ_{max} at 474 nm and ϵ 1840 $\text{M}^{-1}\text{ cm}^{-1}$.¹⁹ Abstraction of an electron from HBT (E° 1.08 V vs NHE)^{16d} by CAN (E° 1.3 V vs NHE)²⁰ is exoergonic and occurs quantitatively. A practically superimposable UV-vis spectrum is obtained when using $\text{Pb}(\text{OAc})_4$ as the oxidant of HBT, in either AcOH or MeCN solutions.¹⁹ In comparison, PINO radical has λ_{max} at 382 nm with ϵ 1360 $\text{M}^{-1}\text{ cm}^{-1}$ in AcOH.¹¹

The spectrum of the oxidized species from HBT, both in MeCN and AcOH solution, is not stable (Figure 2), and the reading of the λ_{474} absorption decays according to an exponential curve that is almost clean first-order ($k_{\text{decay}} = 6.3 \times 10^{-3}\text{ s}^{-1}$ in MeCN at 25 °C) with a half-life of 110 s (20 s in AcOH solution). Espenson¹¹ and Masui²¹ had advanced hypotheses about the self-decomposition of PINO radical, which is second-order and has the first half-life of 7900 s at 25 °C, at $[\text{HPI}]_0 = 0.2\text{ mM}$ in AcOH. The nature of the self-decomposition of PINO is not precisely known yet, and we have not investigated the self-decomposition of the oxidized species from HBT any further.

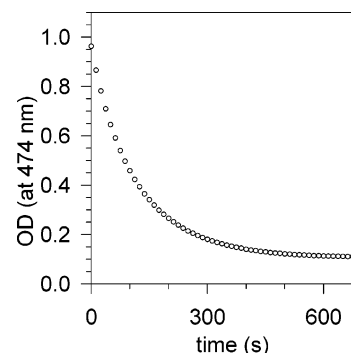
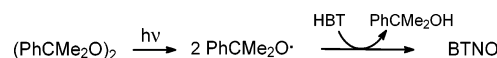


FIGURE 2. Self-decomposition of BTNO, generated from $[\text{HBT}] = [\text{CAN}] = 0.5\text{ mM}$ in MeCN. Readings were at A_{474} ; the half-life is 110 s.

Scheme 3



As a further characterization, laser flash photolysis of dicumyl peroxide at 355 nm in MeCN solution generates the cumyloxy radical,¹⁹ which abstracts a H-atom from HBT (Scheme 3), giving rise to the absorption spectrum of Figure 3:

An absorption profile with the same λ_{max} at 474 nm as that reported in Figure 1 can be recognized. In a new experiment, we generate the $t\text{-BuO}^\bullet$ radical by laser flash photolysis (LFP) of $(t\text{-BuO})_2$ at 266 nm in MeCN at 25 °C and, in the presence of HBT, an absorption spectrum perfectly consistent with that of Figure 3 is obtained. Therefore, the species resulting from H-abstraction from HBT (Figure 3) by either $\text{PhCMe}_2\text{O}^\bullet$ or $t\text{-BuO}^\bullet$ and that resulting from monoelectronic oxidation of HBT (Figure 1) with CAN do have the same spectral features, thus supporting the nature of an aminoxyl radical for both of them (Scheme 4). We have dubbed BTNO (i.e., benzotriazole nitroxyl radical) the radical species arising from HBT.¹⁹

The redox potential of HBT had been previously determined by cyclic voltammetry (CV) in buffered water (pH 5) as E° 1.08 V vs NHE.^{16d} In MeCN solution, a reversible monoelectronic peak is obtained at a sweep

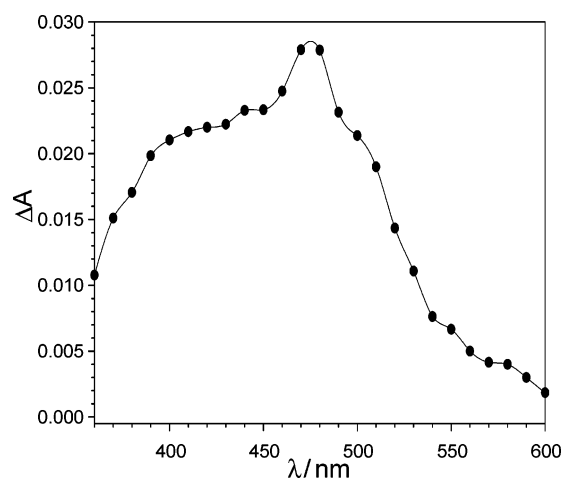


FIGURE 3. Absorption spectrum obtained after 355-nm laser flash photolysis of an Ar-saturated MeCN solution containing 1.0 M dicumyl peroxide and 0.03 M HBT, recorded 1.4 ms after the laser flash (from ref 19).

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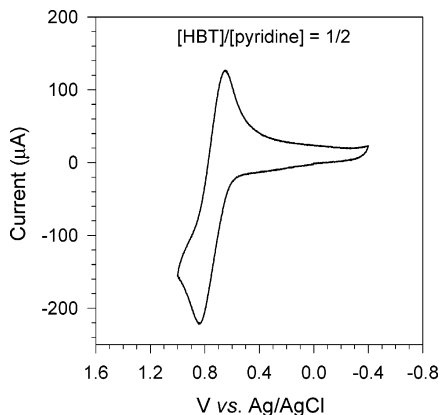


FIGURE 4. Cyclic voltammetry in MeCN solution; [HBT] = 1.65 mM, [Py] = 3.3 mM.

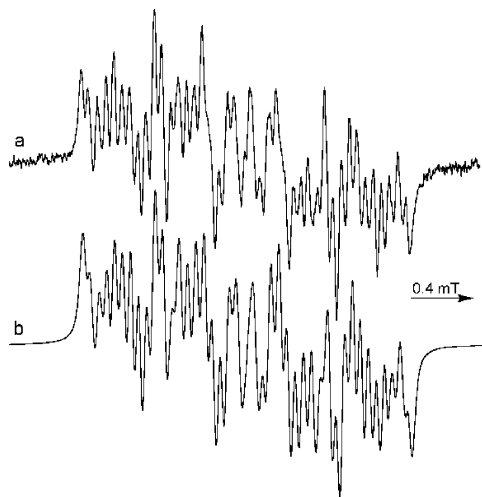
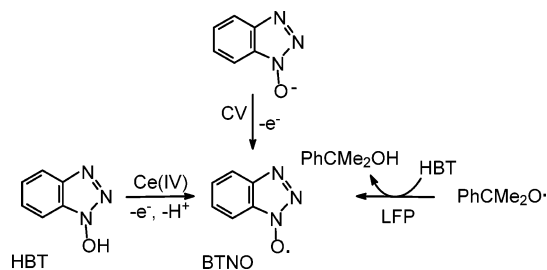


FIGURE 5. Experimental EPR spectrum of BTNO, obtained at room temperature by reaction of CAN (20 mM) with HBT (20 mM) in MeCN (a), and its computer simulation (b) (from ref 19).

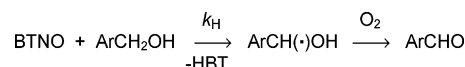
SCHEME 4



scan of 0.5 V/s (E° 0.97 V vs NHE; Figure 4) in the presence of a 2-fold molar amount of pyridine. This indicates one-electron oxidation of the conjugate base of HBT (pK_a 4.6)²² to BTNO (cf. Scheme 4).

Finally, an EPR spectrum of BTNO was obtained by mixing stoichiometric amounts of CAN and HBT in MeCN at 25 °C.¹⁹ This spectrum (Figure 5) was interpreted on the basis of the coupling of the unpaired electron with three different nitrogen nuclei (a_N = 0.056, 0.152, and 0.475 mT), and with three unequivalent

SCHEME 5



protons (a_H = 0.037, 0.203, and 0.458 mT), consistently with the structure of the BTNO radical, where two out of the four hydrogen atoms have almost the same hyperfine coupling constant.

Unfortunately, due to the short lifetime of BTNO, EPR equilibration experiments with species such as phenols having removable H-atoms and known bond dissociation energy BDE(O–H) values^{9b,23} was unfeasible. Determination of the BDE(NO–H) of HBT is thus lacking yet, whereas the corresponding value of BDE(NO–H) for HPI was acquired as 88.1 kcal/mol by EPR equilibration experiments.^{9b,12} Semiempirical calculations had previously provided values around 75–80 kcal/mol for the BDE(NO–H) of HBT,^{18b,24} whereas we have recently attained a higher value (i.e., 85 kcal/mol) from theoretical calculations (DFT) and also from a thermochemical cycle.²⁵

Hydrogen-Abstraction Reactivity of BTNO Radical. The spontaneous decay of BTNO, followed at λ_{474} , is strongly accelerated in the presence of H-donor substrates such as alkylarenes, benzyl or allyl alcohols, and alkanols, and the H-abstraction reactivity of BTNO from a number of substrates has been investigated here at 25 °C (Scheme 5)

BTNO was generated in the spectrophotometric cuvette at an initial 0.5 mM concentration in MeCN, by quickly mixing stoichiometric amounts of HBT and CAN solutions at 25 °C. The initial reading of A_{474} confirmed quantitative formation of BTNO. Fast addition by syringe of a solution of the C–H bearing substrate, at an initial concentration 10–50 times higher than that of BTNO, marked the beginning of the kinetic experiment. The progress of the reaction was monitored at 474 nm by stopped-flow or conventional spectrophotometers, the half-lives of the substrates ranging from 15 ms to tenths of seconds, respectively. Under these pseudo-first-order conditions, the H-abstraction rate was faster than the spontaneous decay of BTNO in all cases reported in Table 1, while product analysis had already confirmed the formation of the carbonyl derivative from selected precursors.^{17,19} No investigation was possible with more reactive H-donor substrates, as the reaction would be too fast to follow with our experimental technique, nor with less reactive substrates, whose “apparent” first-order rate constant matched the $k_{(\text{decay})}$ of BTNO.

(a) Rate Constants of H-Abstraction at 25 °C. The rate constants k' , determined at 25 °C under pseudo-first-order conditions (excess of substrate, at three or four different initial concentrations) from at least duplicated experiments, were converted into second-order H-abstraction rate constants (k_H) by determining the slope of a k' vs [subst]₀ plot, as shown in Figure 6 for 4-MeO-benzyl alcohol. The typical uncertainty of the kinetic determinations ranged from 2 to 5%.

Intercept values in these plots confirm the order of magnitude of the self-decay rate constant of BTNO. The k_H values reported in Table 1 for all the substrates

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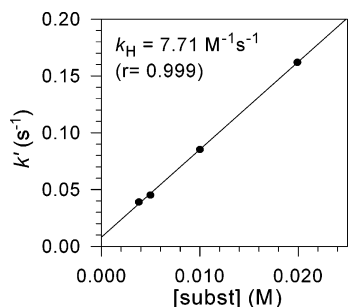


FIGURE 6. Pseudo-first-order (k') rate constants of H-abstraction from 4-MeO-benzyl alcohol by BTNO, in MeCN at 25 °C. The slope of the plot gives the k_H value.

investigated are normalized for the number of equivalent hydrogens.¹¹ Available values of the BDE(C–H) of the RH substrates are given.^{11,26} For a couple of substrates, the k_H rate constant was determined also in AcOH solution, CAN being the oxidant, to enable a better comparison with the reactivity data¹¹ of PINO presented in the table.

Some comments on the rate constants of Table 1 are possible. First of all, the matching value of k_H for 4-MeO-C₆H₄CH₂OH and 4-MeO-C₆H₄CH₂OMe confirms beyond any doubt that BTNO removes the H-atom from the benzylic C–H position and not from the O–H bond of the alcohol, in keeping with the much higher BDE (ca. 104 kcal/mol) of the latter.²⁶ Second, H-abstraction by BTNO becomes increasingly faster on going from an alkanol (decanol, 0.11 M⁻¹ s⁻¹) to benzyl alcohol (0.94 M⁻¹ s⁻¹) and further on to an allyl alcohol (geraniol, 11 M⁻¹ s⁻¹; cinnamyl alcohol, 18 M⁻¹ s⁻¹), thereby reflecting the BDE(C–H) of 93 kcal/mol, ca. 84 and ca. 82 M⁻¹ s⁻¹, respectively,²⁶ approximate as these values are. Analogously, increasing the number of Ph-substituents of the C–H group undertaking cleavage causes an increase of k_H value from ca. 0.02 M⁻¹ s⁻¹ in *p*-xylene (ArCH₃) to 0.33 M⁻¹ s⁻¹ in Ph₂CH₂ up to 2.2 M⁻¹ s⁻¹ in Ph₃CH; this reflects the trend of BDE(C–H) values of ca. 90, 84, and 81 kcal/mol, respectively.²⁶ Similarly, PhCH₂OH (one Ph) vs Ph₂CHOH (two Ph) gives k_H values (in M⁻¹ s⁻¹) of 0.94 vs 3.2, and fluorene vs 9-Ph-fluorene analogously gives 1.7 vs 18, in line with the corresponding BDE(C–H) data.²⁶ Although it is reasonable to expect that rate constants and thermochemical data do correlate in a radical process for structurally similar compounds, it is appropriate to point out that this comparison is dimensionally not homogeneous, because the reactivity data are free energies (ΔG^\ddagger), whereas the BDE(C–H) data are enthalpic values. A more homogeneous correlation has been sought, and found, through the determination of the activation parameters for the H-abstraction process of BTNO with selected substrates (vide infra). We simply observe at this stage that RH substrates endowed with BDE higher than 92–94 kcal/mol are almost unreactive with BTNO. Finally, the solvent (MeCN vs AcOH) does not affect the value of k_H substantially (Table 1), and this is conceivable for a radical process.

If we compare the different k_H 's obtained with BTNO and PINO, the substrate being equal, the rate values with the latter radical are always higher (Table 1). The higher reactivity of PINO ought to reflect the higher BDE of the NO–H bond in precursor HPI with respect to HBT (88 vs ca. 85 kcal/mol, respectively).^{9b,25} This difference is significant for a radical H-abstraction process by a >N–O• species: the stronger the O–H bond being formed, the faster the H-abstraction step. With other hydroxylamines, we plan to further investigate this comparison between H-abstraction reactivity of the >N–O• intermediate and the BDE(NO–H) value of the >N–OH species. Finally, in a literature report on the electrochemical generation of BTNO from HBT, the k_H of reaction with 3,4-diMeO-C₆H₃CH₂OH (i.e., veratryl alcohol) is given as 2.5 M⁻¹ s⁻¹ in buffered water solution.²⁷ This value, when compared with our own determination (i.e., 11 M⁻¹ s⁻¹, in Table 1) in MeCN, supports a similar reactivity of the BTNO species once generated by two independent methods in two different media. Future work on the comparison of reactivity between the electrochemical vs chemical (by CAN or other oxidants) method of generation of the >N–O• species is planned.

(b) Mechanistic Insight. Additional clues confirm the radical nature of the reaction of BTNO with the RH substrates of Table 1. The Hammett correlation for reaction of BTNO with *p*-substituted benzyl alcohols gave a ρ of –0.55 in MeCN,¹⁹ a value reasonably small for a radical process.²⁸ It compares with a ρ value of –0.41 for PINO vs the same substrates, when PINO was generated from HPI with Pb(OAc)₄ in AcOH solution.^{11a} Additional ρ values in the –0.5 to –0.7 range were obtained with the aminoxyl radicals generated from X-aryl-substituted HPIs according to the Ishii procedure (i.e., X-HPIs/Co(II)/MCBA/O₂)⁸ in MeCN.¹² In all these cases, better Hammett correlations were obtained vs σ^+ values, in agreement with the electrophilic character of the aminoxyl radicals.^{9a,10,28} Thus, a uniform pattern of selectivity among these structurally similar >N–O• species emerges. Lastly, firm evidence in favor of the intervention of a benzyl radical during the oxidation of benzyl alcohols with BTNO has been recently acquired through the interception of the radical intermediate by the use of a cyclizable probe substrate.²⁵

In the reaction of BTNO with *p*-MeOC₆H₄CH(D)OH in MeCN at room temperature, a k_H/k_D ratio (intramolecular) of 5.6 from product analysis was obtained.¹⁹ An additional experiment carried out here gives an intramolecular k_H/k_D value of 7 from product analysis for the reaction of BTNO with PhCH(D)OH. Moreover, an intermolecular k_H/k_D value of 13 from the ratio of the kinetic rate constants of fluorene vs 9,9-dideuteriofluorene with BTNO (Table 1) is consistent with a rate-determining H-abstraction step. The latter k_H/k_D value of 13 supports the contribution of tunnelling, as already commented on for the reactions of PINO with various H-donors (k_H/k_D values in the 11–27 range).^{11a,12,21} Finally, the relative reactivity of abstraction of a primary vs secondary vs tertiary benzylic hydrogen by BTNO, reckoned from comparing the rate constants of MeO–

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TABLE 2. Rate Constants and Activation Parameters for the H-Abstraction Reaction by BTNO from Selected RH Substrates at Various Temperatures^a

substrate (RH)	temp (°C) (±0.2)	k_H (M ⁻¹ s ⁻¹) ^b	E_a (kcal/mol) (±0.15) ^c	log A (M ⁻¹ s ⁻¹) (±0.5) ^c	ΔH^\ddagger (kcal/mol) (±0.15) ^d	ΔS^\ddagger (eu) (±1) ^d	BDE(C–H) of RH (kcal/mol) ^e
4-MeO-C ₆ H ₄ CH ₂ OH	18.5	2.48	6.8	13	6.2	–36	–
	29.8	3.36					
	40.8	5.75					
4-MeO-C ₆ H ₄ CH ₂ OH (in AcOH)	18.3	2.86	5.3	10	4.7	–40	
	29.7	3.78					
	41.5	5.66					
PhCH ₂ OH (in AcOH)	20.7	0.52	4.8	7.5	4.2	–46	
	30.1	0.64					
	41.3	0.88					
4-MeO-C ₆ H ₄ CH ₂ OMe	18.5	2.05	7.0	13	6.4	–35	
	30.0	3.24					
	41.2	4.93					
Ph ₂ CHOH	18.1	2.47	6.7	12	6.0	–36	79
	29.5	3.71					
	40.9	5.70					
9-OH-FL ^f	13.1	12.5	5.1	11	4.5	–38	ca. 73
	22.7	16.0					
	30.9	21.1					
Ph ₂ CH ₂	18.2	0.40	10.6	17	10.0	–26	84
	29.5	1.01					
	40.6	1.46					
Ph ₃ CH	18.8	1.63	8.8	16	8.2	–29	81
	29.3	2.52					
	40.3	4.75					
FL ^f	18.2	1.15	8.9	16	8.3	–29	82
	29.5	2.35					
	40.8	3.48					

^a Initial conditions as in Table 1. ^b Normalized values. Runs in triplicate; typical error ±3%. ^c From the Arrhenius equation. ^d From the Eyring equation. ^e From ref 26. ^f FL stands for fluorene.

C₆H₄CH₃ (taken as 1.0 M⁻¹ s⁻¹) vs MeO-C₆H₄CH₂Me (4.2 M⁻¹ s⁻¹) vs MeO-C₆H₄CHMe₂ (6.3 M⁻¹ s⁻¹) in Table 1, is in keeping with the BDE(C–H) values (88, 85, and 84 kcal/mol, respectively)²⁶ and perfectly in line with the relative rates (M⁻¹ s⁻¹) of 1:3.2:6.8 reported for the analogous reactions with *t*-BuO²⁹. The trend is confirmed by the relative rates (M⁻¹ s⁻¹) of 1:4.4:9.7 similarly obtained with the phenyl radical.²⁹ All this evidence supports a rate-determining H-abstraction process by BTNO toward H-donor substrates.

(c) Activation Parameters. Rate constants of H-abstraction from a few RH substrates by BTNO have been measured at various temperatures. The substrates were selected according to two requisites: (i) the BDE(C–H) of RH had to be known with reasonable accuracy, and (ii) the k_H at 25 °C had to be not so fast to let a too fast rate constant be foreseen at higher temperature(s) for our stopped flow device ($t_{1/2}$ not < 15 ms). The thermostated cell holder of the stopped flow allowed investigating the rate constants in the 10–50 °C range. At least three temperatures, spaced approximately 12–15 °C between them, were tested for each substrate. As explained before for the kinetic determinations at 25 °C (Table 1 and Figure 6), each second-order k_H value derives from averaging three or four pseudo-first-order rate constants determined at different initial concentrations of RH. The initial concentration of BTNO was 0.2–0.5 mM, and that of RH ranged between 5 and 20 mM. Once again BTNO was generated by quickly mixing HBT and CAN solutions in stoichiometric amounts, and the progress of the reaction was monitored at 474 nm.

The second-order rate constants (k_H), normalized for the number of equivalent hydrogen atoms in RH, are reported in Table 2 for each RH at the various temperatures investigated. From the Arrhenius equation ($\log k_H = \log A - E_a/RT$), the log A and E_a parameters were obtained, whereas from the Eyring equation ($\log k_H/T = \log k_B/h - \Delta H^\ddagger/RT + \Delta S^\ddagger/R$), the ΔH^\ddagger and ΔS^\ddagger were obtained.

A proper correlation between reactivity of H-abstraction and thermochemical data can now be attempted according to the Evans–Polanyi equation ($E_a = \alpha \text{BDE}(\text{C–H}) + \text{cost}$)³⁰ (Figure 7), because both the attained E_a parameters and the BDE(C–H) data of the RH substrates have the dimensions of enthalpy. Within the limited number of substrates that lend themselves to this analysis under our conditions, it can be quantitatively verified that the reactivity of H-abstraction follows the C–H bond energies linearly. The reaction of BTNO is increasingly slower (i.e., higher E_a value) toward increasingly stronger C–H bonds, and the slope of the correlation is $\alpha = 0.44$.

The α parameter indicates the selectivity of BTNO; a value of 0.44 suggests that the H-atom being removed is almost equally shared between the aminoxyl radical abstracting it and the C-atom that is losing it. The NO–H bond in formation and the C–H bond being cleaved must have therefore a comparable energy (vide infra). The α of PINO, reported by Espenson et al. as 0.38,^{11b} is slightly lower in value than that of BTNO; this is likely due to the fact that the BDE(NO–H) of HPI is higher (88 kcal/mol)^{9b,12} than that of HBT (85 kcal/mol),²⁵ thereby

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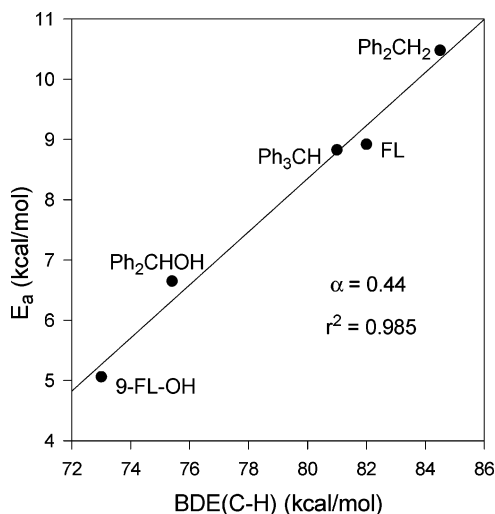


FIGURE 7. Evans–Polanyi plot for the H-abstraction reaction by BTNO with selected substrates (FL stands for fluorene).

endorsing a slightly earlier transition state of H-abstraction with PINO. In that investigation,^{11b} however, the Evans–Polanyi correlation was obtained starting from an Arrhenius treatment where it was *assumed* that the preexponential factor A was constant within the series of substrates investigated.^{11b} As our analysis shows, instead, this assumption is not warranted, with A ($\text{M}^{-1} \text{s}^{-1}$) values ranging from 8.9×10^4 (with 9-hydroxyfluorene) to 1.9×10^7 (with Ph_2CH_2). Analogously, the ΔS^\ddagger values range from -38 to -26 eu for the same two substrates, always being rather prominent in value as expected for a bimolecular H-abstraction step. Looking more closely at the entropic parameter for structurally similar compounds, we verify that replacement of one H atom with one OH group (e.g., Ph_2CH_2 vs Ph_2CHOH) geminal to the C–H bond undergoing cleavage causes a decrease of ΔS^\ddagger of 9 eu, i.e., from -27 to -36 eu, as if the transition state with the alcohol substrate would become more ordered. Consistently, ΔS^\ddagger decreases again 9 eu on passing from fluorene (-29 eu) to 9-hydroxyfluorene (-38 eu). Unfortunately, we cannot extend this C–H vs C–OH comparison any further, because of the lack of suitable substrates to test. For example, the rate constant of H-abstraction by BTNO from PhCH_3 (or from *p*-MeO-toluene), taken as a C–H substrate, is too slow for yielding reliable activation parameters to compare with that of PhCH_2OH (or of *p*-MeO-benzyl alcohol), as the corresponding C–OH substrate. More on this point, we wondered if the “spectator” OH group in either Ph_2CHOH or 9-hydroxyfluorene could be responsible for any peculiar H-bonding interaction with the approaching BTNO in the transition state, making up for the above-reported depression of ΔS^\ddagger with respect to the corresponding C–H substrates. A test of this hypothesis was done with the ether 4-MeO- $\text{C}_6\text{H}_4\text{CH}_2\text{OMe}$, where no H-bonding interaction toward BTNO would be structurally possible. Because the ΔS^\ddagger value comes out identical (-35 eu) within experimental errors to that of the corresponding alcohol 4-MeO- $\text{C}_6\text{H}_4\text{CH}_2\text{OH}$ (-36 eu), we conclude that no H-bonding interaction between BTNO and the R–OH

substrate is responsible for that depression of ΔS^\ddagger with respect to the RH counterpart. We plan to investigate this comparison of C–H vs C–OH reactivity with other $>\text{N}-\text{O}^\bullet$ species in the future.

From the linear Evans–Polanyi plot obtained (Figure 7), and from the experimental E_a value determined for 4-MeO- $\text{C}_6\text{H}_4\text{CH}_2\text{OH}$ (i.e., 6.8 kcal/mol), we extrapolate a BDE value of 77 ± 1 kcal/mol for the benzylic C–H bond of this specific substrate undergoing cleavage. This number, which is not experimentally available or reported with reasonable confidence for benzyl alcohols,²⁶ compares well with a BDE(C–H) of 81 ± 1 kcal/mol that we extrapolate for PhCH_2OH from the Evans–Polanyi plot of Espenson et al.^{11b} Because the BDE(C–H) of toluene is 88.5 kcal/mol,²⁶ our extrapolated values for ArCH_2OH (averaged as 79 ± 2 kcal/mol) point out to a significant weakening (of about 9 kcal/mol) of the benzylic C–H bond due to the presence of a geminal OH group. Finally, we have recently calculated a BDE of 85 kcal/mol for the NO–H bond of HBT,²⁵ by making use of a thermochemical cycle and theoretical calculations. This calculated BDE(NO–H) value is consistent with the present finding that BTNO abstracts H-atom efficiently from substrates endowed with C–H bonds in the 80–90 kcal/mol energy range (cf. Tables 1 and 2). In particular, it is consistent with the experimental finding of a value for the α of Evans–Polanyi close to 0.5. Lower values of BDE(NO–H)^{18b,24} for HBT would be inconsistent with the observed H-abstraction reactivity of BTNO.

Conclusions

The aminoxyl radical BTNO ($>\text{N}-\text{O}^\bullet$) has been generated from HBT by oxidation with a Ce^{IV} salt and characterized by spectrophotometry, EPR, cyclic voltammetry, and laser flash photolysis. Rate constants of H-abstraction (k_{H}) from a number of H-donor substrates by BTNO have been determined spectroscopically and range in value from 10^{-3} to $10^2 \text{ M}^{-1} \text{s}^{-1}$ at 25 °C in MeCN solution. The kinetic isotope effect confirms that the H-abstraction step is rate-determining. For selected substrates, the activation parameters have also been measured. Correlation of the energy of activation of H-abstraction by BTNO vs the energy of the C–H bond undergoing cleavage in the investigated substrates, by following the Evans–Polanyi equation, provides the selectivity ($\alpha = 0.44$) of this radical process. The unavailable BDE(C–H) of benzyl alcohol can be extrapolated as ca. 79 kcal/mol from the Evans–Polanyi plot. We compare the reactivity data of BTNO with similar H-abstraction results recently obtained with the aminoxyl radical PINO generated from HPI.¹¹ The higher reactivity of PINO is understandable on the basis of the higher energy of the NO–H bond of HPI that is formed on H-abstraction from the substrate, if compared with the corresponding NO–H bond energy of HBT (88 vs ca. 85 kcal/mol, respectively).

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