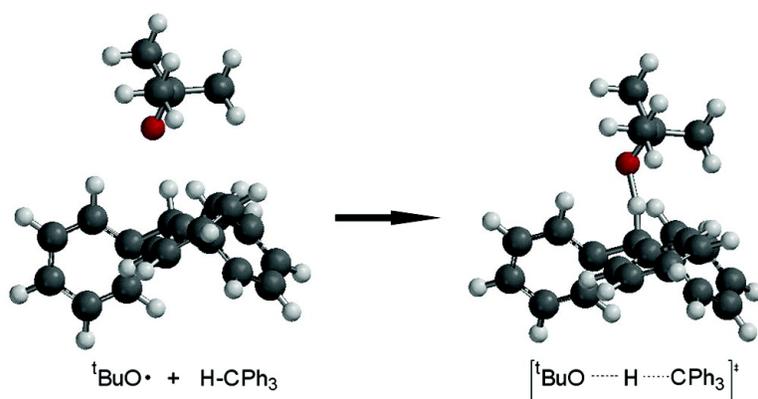


Chemistry of the *t*-Butoxyl Radical: Evidence that Most Hydrogen Abstractions from Carbon are Entropy-Controlled

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Chemistry of the *t*-Butoxyl Radical: Evidence that Most Hydrogen Abstractions from Carbon are Entropy-Controlled

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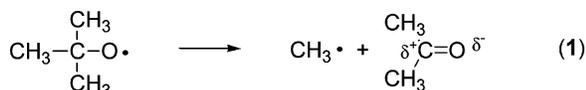
Abstract: Absolute rate constants and Arrhenius parameters for hydrogen abstractions (from carbon) by the *t*-butoxyl radical (${}^t\text{BuO}\cdot$) are reported for several hydrocarbons and tertiary amines in solution. Combined with data already in the literature, an analysis of all the available data reveals that most hydrogen abstractions (from carbon) by ${}^t\text{BuO}\cdot$ are entropy controlled (i.e., $T\Delta S^\ddagger > \Delta H^\ddagger$, in solution at room temperature). For substrates with C–H bond dissociation energies (BDEs) > 92 kcal/mol, the activation energy for hydrogen abstraction decreases with decreasing BDE in accord with the Evans–Polanyi equation, with $\alpha \approx 0.3$. For substrates with C–H BDEs in the range from 79 to 92 kcal/mol, the activation energy does not vary significantly with C–H BDE. The implications of these results in the context of the use of ${}^t\text{BuO}\cdot$ as a chemical model for reactive oxygen-centered radicals is discussed.

Introduction

In a series of papers starting in 1960,¹ Walling and co-workers reported the results of an intensive study of the mechanism and kinetics of free radical chlorinations of hydrocarbons by *tert*-butyl hypochlorite (${}^t\text{BuOCl}$) which laid the foundation of our current understanding of the chemistry of the *t*-butoxyl radical (${}^t\text{BuO}\cdot$). Initiated by common free radical initiators or light, the reaction of ${}^t\text{BuOCl}$ with hydrocarbons proceeds via a free radical chain process involving ${}^t\text{BuO}\cdot$ as the hydrogen abstractor (Scheme 1).

As a hydrogen abstractor, ${}^t\text{BuO}\cdot$ was found to exhibit modest selectivity. Competition studies revealed that for alkanes on a per-hydrogen basis, 3° (40) $>$ 2° (14) $>$ 1° (1). While selectivity crudely paralleled the strength of the C–H bond, there were some notable exceptions, e.g., aliphatic C–H bonds were comparable to benzylic C–H bonds in reactivity, despite an over 10 kcal/mol difference in bond strength.¹

It was also found that ${}^t\text{BuO}\cdot$ and other alkoxy radicals also undergo unimolecular decomposition (β -cleavage, eq 1). Well



before the term was coined, this β -cleavage reaction proved to be a suitable “free radical clock”² for measuring rates of competing bimolecular reactions involving ${}^t\text{BuO}\cdot$. In fact, one of the few examples of a significant solvent polarity effect on the rate of a radical reactions was discovered by Walling and Wagner who found that the relative rate of β -cleavage vs

Scheme 1



H-abstraction increased in more polar solvent.³ It was suggested that the rate of the β -cleavage process increased with solvent polarity (because of increased polarity in the transition state associated with the developing carbonyl moiety), but the rate of H-abstraction was solvent-independent, a hypothesis which was confirmed nearly three decades later by Luszyk et al.,⁴ Tsentelovich et al.,⁵ and Baciocchi et al.⁶

A number of studies also demonstrated that polar effects are important in hydrogen abstractions by ${}^t\text{BuO}\cdot$. For substituted toluenes, a ρ -value of -0.4 and a correlation to the σ^+ substituent constant was observed (suggesting a slight buildup of positive charge in the transition state).⁷ More recent work by Gleicher⁸ and Roberts⁹ provides additional evidence for the importance of polar effects.

In the intervening 40+ years, a large number of absolute rate constants and activation parameters for hydrogen abstractions by ${}^t\text{BuO}\cdot$ (and also the closely related cumyloxyl radical, $\text{C}_6\text{H}_5\text{C}(\text{CH}_3)_2\text{O}\cdot$) have been measured, mainly because of technological advances leading to the development of fast kinetic methods

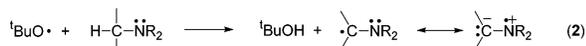
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such as kinetic EPR spectroscopy and laser flash photolysis.¹⁰ Indeed, the common belief that the chemistry of ^tBuO• was well-characterized has led to its use as the prototypical model for reactive oxygen-centered radicals in a variety of fields. For example, ^tBuO• chemistry has been used to test the efficiency and mechanism of action of antioxidants;^{11–14} a recent report points out some of the potential perils of applying this approach to determine antioxidant mechanism and activity.¹⁵ The chemistry of ^tBuO• has been used to study mechanisms of oxidative damage in living (e.g., oxidative damage to DNA,^{16–18} lipids,¹⁹ etc.) and nonliving (e.g., lubricants)²⁰ systems, and also to predict the oxidative sensitivity of pharmaceuticals.²¹ In atmospheric chemistry, ^tBuO• has been used to study mechanisms of degradation of volatile organic compounds (VOCs) in the stratosphere.²² Finally, ^tBuO• has been used in the context of biomimetic oxidations or chemical model studies to study mechanisms of enzyme-catalyzed oxidations (e.g., methane monooxygenase,²³ cytochrome P450,^{24,25} and monoamine oxidase).²⁶ In some model studies of monooxygenase chemistry using alkyl hydroperoxides and iron complexes, rather than generating high valent iron-oxo species, alkoxy radicals such as ^tBuO• are produced.^{27–30}

In a preliminary communication, we presented evidence suggesting that there are aspects of ^tBuO• chemistry that are not completely understood. Using laser flash photolysis (LFP), absolute rate constants and activation parameters were determined for hydrogen abstraction reactions (by ^tBuO•) from six tertiary amines (eq 2).³¹ (Absolute rate constants for hydrogen



abstraction by ^tBuO• from tertiary amines had been measured previously, though no activation parameters were reported.)^{32–34}

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Rate constants for hydrogen abstraction are generally expected to increase with decreasing bond strength. However, this trend was not observed for tertiary amines. For example, despite a higher C–H bond strength, triethylamine (α -C–H BDE = 91.7 kcal/mol)^{35,36} was found to be four times more reactive than triallylamine (α -C–H BDE = 82.6 kcal/mol).³⁵

An analysis of the activation parameters revealed that at room temperature, the free energy barrier (ΔG^\ddagger) for the reaction of ^tBuO• with tertiary amines was dominated more by entropic than enthalpic factors (i.e., the magnitude of $T\Delta S^\ddagger$ was greater than ΔH^\ddagger). This means that rate constants and selectivities measured at ambient temperature provide a distorted view of the intrinsic reactivities of amines in radical reactions and suggests that (in some cases at least) the chemistry of ^tBuO• is not sufficiently understood for use as a general chemical model to mimic the behavior of oxygen-centered radicals.³¹

The scope of the study has been significantly expanded and activation parameters for twelve new substrates are reported. These results, taken in conjunction with literature values for other substrates span C–H bond strengths ranging from 79 to 101 kcal/mol, and provide a comprehensive view of hydrogen abstractions from carbon by ^tBuO•.

Experimental Section

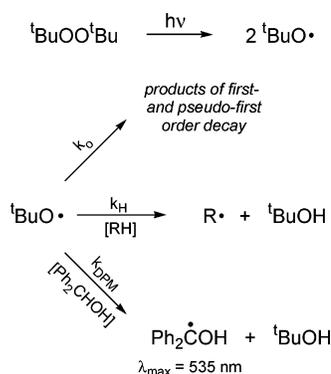
Materials. All of the solvents and fine chemicals used in this study were obtained from Aldrich and used as received (except as noted). The liquid amines and hydrocarbons were vacuum distilled immediately before use. Diphenylmethanol was sublimed under vacuum immediately before use. Di-*tert*-butyl peroxide was purified by passing through a column of activated alumina.

Apparatus. Steady-state UV–vis spectra were recorded on a Hewlett-Packard diode array UV–vis spectrophotometer (HP 8452A). Laser flash photolysis (LFP) experiments were conducted using an Applied Photophysics LKS.60 spectrometer using the third harmonic of a Continuum Surelite I-10 Nd:YAG laser (4–6 ns pulse, 355 nm). Transient signals were monitored by a Hewlett-Packard Infinium digital oscilloscope and analyzed with the Applied Photophysics SpectraKinetic Workstation software package (v. 4.59). Variable temperature experiments were performed with a jacketed cell holder connected to a VWR Scientific Products (PolyScience) variable temperature circulating bath (model 1150-A). The cell holder was equipped with a thermocouple to measure the temperature directly adjacent to the cuvette. Samples were thermally equilibrated prior to photolysis by placing the cuvettes in a tray in the circulating bath for at least 10 min. Afterward, the samples were placed in the spectrometer and equilibrated for an additional 10 min. (This protocol was checked by placing a thermometer directly into representative samples and verifying that the internal temperature was identical to that measured by the thermocouple over the temperature range of these studies). Concentrations were corrected for the thermal expansion of the solvent over the temperature range.

Laser Flash Photolysis (LFP). Substrates were prepared in a 2:1 solution of di-*t*-butyl peroxide:benzene and deoxygenated prior to photolysis. (Steady-state UV–vis spectra were recorded to verify that

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Scheme 2



di-*tert*-butyl peroxide was the only species absorbing at the excitation wavelength). In most LFP experiments, a fixed concentration of diphenylmethanol (0.100 M) was utilized as a spectroscopic probe, monitoring the signal buildup at 535 nm (vide infra). Low laser power (ca. 10–20 mJ) was used in all experiments to eliminate any laser power dependency to the observed rate constants thereby minimizing the contributions of radical–radical reactions to the observed rate constant. Substrate concentrations were varied over a factor of 10 over five separate experiments (vide infra).

Viscosity Studies. In lieu of a diphenylmethanol probe, only substrates whose corresponding radicals exhibited a significant UV–vis absorbance were used and the kinetics followed by monitoring the buildup of this absorbance. The amount of di-*tert*-butyl peroxide in solution was decreased to 7.5% to minimize its contribution to the bulk viscosity of the solution. Substrate concentrations were varied by over an order of magnitude. Viscosity measurements were performed on each solution using a Oswald viscometer at room temperature. The apparatus constant for the viscometer was measured using water at 25 °C.

Calculations. Density functional theory calculations were performed using the Titan molecular modeling software (Wavefunction, Inc., Irvine, CA 92612 and Schrodinger, Inc., Portland, Oregon, 1998).

Results

Rate Constants and Arrhenius Parameters. $\text{tBuO}\cdot$ was generated by flash photolysis of di-*tert*-butylperoxide (Scheme 2), following the protocol developed by Scaiano et al.^{37,38} $\text{tBuO}\cdot$ is spectroscopically invisible at wavelengths > 300 nm, so the kinetics were followed by monitoring the absorbance of the products. In most cases, however, the substrates (RH) do not yield radicals ($\text{R}\cdot$) which absorb strongly (or at all) at wavelengths > 300 nm, and a fixed concentration of a spectroscopic “probe” was added (typically diphenylmethanol, which after hydrogen abstraction, yields the diphenylhydroxymethyl radical which absorbs at 535 nm).³⁷

Upon the basis of Scheme 2 and eq 3

$$k_{\text{obs}} = k_o + k_{\text{DPM}}[\text{Ph}_2\text{CHOH}] + k_{\text{H}}[\text{RH}] \quad (3)$$

for parallel (pseudo) first-order kinetics, the second-order rate constant for hydrogen abstraction from the substrate (k_{H}) was obtained from the slope of a plot of the observed rate constant (k_{obs}) vs [RH] at each temperature. In all cases, at least five different solutions with RH concentrations varying by at least 1 order of magnitude were studied (at each temperature).

Table 1. Rate Constants and Arrhenius Parameters for Hydrogen Abstraction by $\text{tBuO}\cdot$ from a Variety of Substrates (Uncertainties in the last reported digits are in parentheses)

substrate	T range (°C)	log(k_{H}) at 25 °C ^a	E_{a} (kcal/mol)	log A (A in units of M ⁻¹ s ⁻¹)	C–H BDE (kcal/mol)
amines^b					
tribenzylamine (3)	5 → 80	7.62	1.34(16)	8.60(10)	89.1(6) ^c
<i>N,N</i> -dibenzylaniline (2)	10 → 80	7.27	2.02(18)	8.75(15)	85(2) ^c
DABCO (2)	10 → 70	7.06	2.15(18)	8.63(11)	94(2) ^d
triethylamine (2)	10 → 80	7.95	2.20(21)	9.56(12)	82.6(8) ^c
triethylamine (3)	10 → 70	7.99	2.38(49)	9.73(25)	90.7(4) ^{c,e}
quinuclidine (2)	10 → 70	7.02	2.41(66)	8.78(31)	96(2) ^d
<i>N</i> -methylpyrrole (1)	10 → 80	6.86	2.42(70)	8.62(32)	91(2) ^f
<i>N,N</i> -dimethylaniline (2)	10 → 80	8.01	2.54(61)	9.87(29)	92(1) ^c
hydrocarbons					
triphenylmethane (1)	10 → 70	6.31	1.86(36)	7.67(19)	81(1) ^g
diphenylmethane (2)	10 → 70	6.53	2.42(53)	8.30(26)	84(1) ^g
allylbenzene (1)	10 → 80	6.51	2.48(31)	8.15(18)	82(2) ^f
cyclohexane (4)	10 → 70	5.91	4.42(78)	9.15(35)	98.7(5) ^h
		5.92 ⁱ	3.11(24) ⁱ	8.2(20) ⁱ	98.7(5) ^h
toluene (3)	10 → 80	5.28	3.46(49)	7.81(24)	90(1) ^h
cyclopentane	−20 → 25	5.93 ⁱ	3.47(59) ⁱ	8.47(45) ⁱ	97(2) ^f
<i>t</i> -butylbenzene	−26 → 10	4.60 ⁱ	6.14(60) ⁱ	9.1(8) ^j	101(2) ^f
alcohols					
diphenylmethanol (1)	10 → 70	6.84	2.03(28)	8.33(16)	79(2) ^f
	−35 → 70	6.91 ^j	1.99(35) ^j	8.37(28) ^j	79(2) ^f
methanol	−20 → 30	4.72 ^k	5.30(30) ^k	8.6(2) ^k	98(1) ^h
ethers					
1,3-dioxolane	−35 → 70	6.90 ^j	3.00(80) ^j	9.1(7) ^j	93(2) ^f
2-methyl-1,3-dioxolane	−35 → 70	7.10 ^j	2.09(32) ^j	8.63(26) ^j	93(2) ^f
THF	−35 → 70	6.87 ^j	2.5(10) ^j	8.7(8) ^j	94(2) ^f
<i>t</i> -butyl methyl ether	−20 → 30	4.99 ^k	5.2(3) ^k	8.8(2) ^k	96(2) ^f
anisole	−42 → 20	4.98 ⁱ	5.21(19) ⁱ	8.8(2) ⁱ	98(2) ^f
	−20 → 30	4.48 ^k	5.9(3) ^k	8.8(0.2) ^k	

^a Calculated from Arrhenius parameters. ^b Value in parentheses indicates number of times study was performed. ^c Ref 35. ^d Ref 40. ^e Ref 36. ^f Calculated (B3LYP/6-31G*/CC–PVTZ(−F)) as described herein. ^g Ref 41. ^h Ref 42. ⁱ Ref 43. ^j Ref 44. ^k Ref 45.

Arrhenius parameters for hydrogen abstraction were determined via nonlinear regression analysis in accordance with the Arrhenius equation (eq 4):³⁹

$$k = A \exp\left(\frac{-E_{\text{a}}}{RT}\right) \quad (4)$$

reported errors are based upon 95% confidence limits of the parameters. To verify reproducibility, several of the experiments were repeated over the course of the study; the details are reported in the Supporting Information. Averaged results are summarized in Table 1.

In addition to expanding the scope of our earlier study,³¹ some of the activation parameters have been revised and are considered more accurate than the previously reported values. Meticulous purification of the reactants and an extended temperature range for the Arrhenius studies have led to more reliable and reproducible values.

Solvent Viscosity Effects on k_{H} . To probe for possible solvent viscosity effects, the rate constant for hydrogen abstraction from three tertiary amines (*N,N*-dimethylaniline, *N,N*-dibenzylaniline, and tribenzylamine) were measured in several *n*-hydrocarbon solvents and benzene. The results are summarized in Tables 2 and 3.

Estimates of C–H Bond Dissociation Energies. When no experimental values of C–H bond dissociation energies for the

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Table 2. Effect of Solvent Viscosity on the Rate Constant for Hydrogen Abstraction from *N,N*-Dimethylaniline by ${}^t\text{BuO}\cdot$ at 25 °C

solvent	η (cP)	k_{H} ($\text{M}^{-1}\text{s}^{-1}$)
<i>n</i> -C ₅ H ₁₂	0.225	1.2×10^8
<i>n</i> -C ₆ H ₁₄	0.293	1.1×10^8
<i>n</i> -C ₈ H ₁₈	0.518	1.1×10^8
C ₆ H ₆	0.831	1.1×10^8
<i>n</i> -C ₁₄ H ₃₀	1.92	9.7×10^7
<i>n</i> -C ₁₆ H ₃₄	2.9	7.8×10^7

Table 3. Effect of Solvent Viscosity on the Rate Constant for Hydrogen Abstraction from *N,N*-Dibenzylaniline and Tribenzylamine by ${}^t\text{BuO}\cdot$ at 25 °C

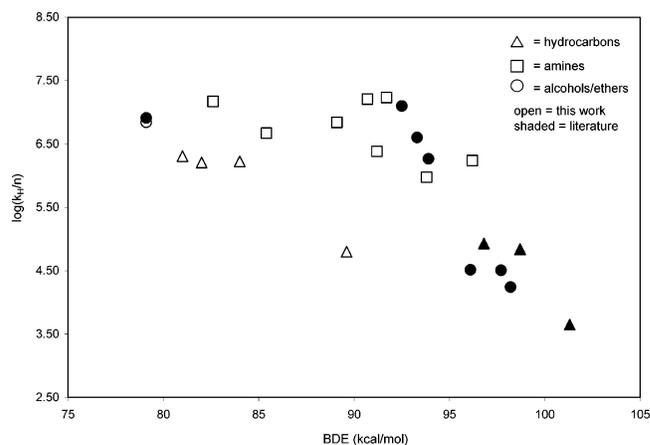
substrate	k_{H} ($\text{M}^{-1}\text{s}^{-1}$)	k_{H} ($\text{M}^{-1}\text{s}^{-1}$)	k_{H} ($\text{M}^{-1}\text{s}^{-1}$)
	in pentane ($\eta = 0.2$ cP)	in benzene ($\eta = 0.8$ cP)	in hexadecane ($\eta = 3$ cP)
<i>N,N</i> -dibenzylaniline	5.5×10^7	4.8×10^7	5.6×10^7
tribenzylamine	2.2×10^7	1.9×10^7	1.9×10^7

substrates pertinent to this study were available, they were estimated using density functional theory^{46,47} as follows: Geometry optimizations at the B3LYP/6-31G* level followed by single point energy calculations (B3LYP/CC-PVTZ(-F)), were performed on the substrate and its corresponding free radical to obtain the difference in their energy (ΔE). Using 17 compounds with known C–H BDEs (ranging from 81 to 132 kcal/mol), a plot of BDE vs ΔE was constructed and analyzed by linear least squares regression analysis. Unknown C–H BDEs were estimated by calculating ΔE using DFT as described above, and using the results of the regression analysis (see Supporting Information). Literature and calculated values of pertinent C–H BDEs are also summarized in Table 1.

Discussion

Rate constants for hydrogen abstraction are expected to increase with decreasing bond strength. The classic method for conceptualizing this is based upon the Evans–Polanyi relationship which predicts a linear relationship between the log of the rate constant for hydrogen abstraction and the enthalpy of the reaction: $\log(k_{\text{H}}) = \alpha\Delta H^\circ + \text{constant}$. ΔH° is directly related to the strength of the breaking bond; for H-abstractions by ${}^t\text{BuO}\cdot$, $\Delta H^\circ = \text{BDE}(\text{C–H}) - \text{BDE}(\text{OH})$. The proportionality constant α is believed to be a measure of transition state location: A value of $\alpha < 0.5$ implies an early, more reactant-like transition state, whereas $\alpha > 0.5$ implies a late, more product-like transition state.⁷

Using values for k_{H} at 25 °C (Table 1), a plot of $\log(k_{\text{H}}/n)$ vs BDE (where n is the number of abstractable hydrogens) is presented in Figure 1. Upon the basis of the observed scatter, no simple relationship between $\log(k_{\text{H}}/n)$ and C–H BDE in the context of the Evans–Polanyi relationship is evident. Through the scatter, however, there appears to be curvature in the plot, with two distinct regions discernible: For substrates with C–H

**Figure 1.** Absolute rate constants for hydrogen abstraction by ${}^t\text{BuO}\cdot$ ($\log(k_{\text{H}}/n)$, where n is the number of abstractable hydrogens) from a variety of substrates as a function of C–H bond dissociation energy.

BDEs greater than 92 kcal/mol, $\log(k_{\text{H}}/n)$ decreases with increasing bond strength as expected on the basis of the Evans–Polanyi equation. However, for substrates with C–H BDEs less than 92 kcal/mol, $\log(k_{\text{H}}/n)$ seems to level off at a value of about 6.6, independent of C–H BDE.

At first glance, these results might be explained on the basis of the reactivity-selectivity principle. The strength of the O–H bond in ${}^t\text{BuOH}$ is 105 kcal/mol,⁴² which means that all of these reactions are exothermic by 3–25 kcal/mol, and because of its high reactivity, ${}^t\text{BuO}\cdot$ is expected to exhibit low selectivity. In the context of the Evans–Polanyi relationship, a low value of α is expected, consistent with an early, reactant-like transition state. On this basis, despite having C–H bond which is weaker by 8 kcal/mol, triallylamine and triethylamine react at nearly the same rate with ${}^t\text{BuO}\cdot$. Similarly, on a per hydrogen basis, the rate constant for reaction of cyclohexane and toluene are the same, despite the fact that the C–H bond in toluene is 10 kcal/mol weaker. At the extreme, the high reactivity/low selectivity argument would suggest that every encounter of ${}^t\text{BuO}\cdot$ would lead to reaction (i.e., the onset of diffusion control), and this might explain why $\log(k_{\text{H}}/n)$ does not vary significantly with structure for substrates with low C–H BDEs. However, the observed bimolecular rate constants are lower than values typically associated with a diffusion-controlled reactions in solution (10^9 – 10^{10} $\text{M}^{-1}\text{s}^{-1}$).⁴⁸

To understand the reason for this apparent breakdown in normal activation/driving force relationships, it is critical to go beyond the rate constants and examine the activation parameters for hydrogen abstraction by ${}^t\text{BuO}\cdot$. Recalling the relationships between $\log(A)$ and E_a of the Arrhenius equation and the enthalpy and entropy of activation of activated complex theory (eqs 5 and 6),³⁹

$$\Delta H^\ddagger = E_a - RT \quad (5)$$

$$\Delta S^\ddagger = R \left(\ln \left(\frac{h}{k_{\text{B}}T} \right) + 2.303 \log A - 1 \right) \quad (6)$$

in Figure 2 a plot of $-T\Delta S^\ddagger$ vs ΔH^\ddagger is presented, constructed from these results and data already reported in the literature;

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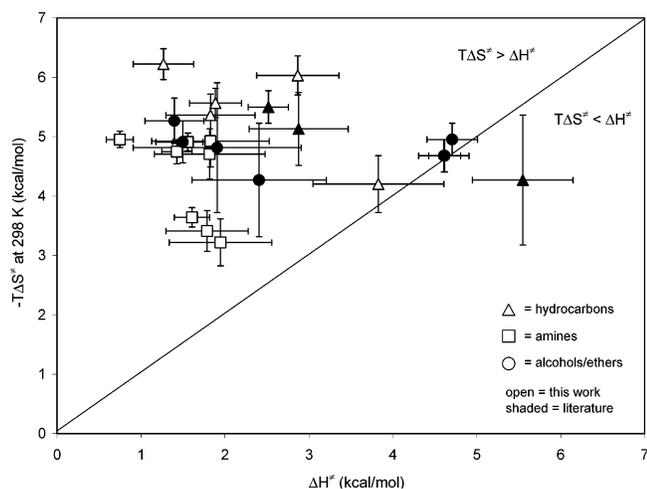


Figure 2. Plot of $-T\Delta S^\ddagger$ vs ΔH^\ddagger for hydrogen abstractions by $t\text{BuO}^\bullet$ at room temperature.

the diagonal line corresponds to $-T\Delta S^\ddagger = \Delta H^\ddagger$ (at 298 K). It should be noted that the derived ΔH^\ddagger and ΔS^\ddagger refer to a reference state where one mole of reactants, each at 1 M concentration, are converted to one mole of the transition state, also at 1 M concentration.

A critical feature about $t\text{BuO}^\bullet$ chemistry emerges from this analysis: **At room temperature, most hydrogen abstractions by $t\text{BuO}^\bullet$ in solution are entropy-controlled.** What this means is that the free energy barrier ($\Delta G^\ddagger = \Delta H^\ddagger - T\Delta S^\ddagger$) for hydrogen abstraction is governed more by the entropy rather than the enthalpy of activation. This point is illustrated graphically in Figure 2, which clearly shows for most substrates at room temperature, $-T\Delta S^\ddagger > \Delta H^\ddagger$ (i.e., most of the points in Figure 2 fall above the line corresponding to $-T\Delta S^\ddagger = \Delta H^\ddagger$). This means alkoxy radicals are so reactive that rates of hydrogen abstractions are governed more by issues of orientation, trajectory, accessibility, etc., than by the strength of the C–H bond. Entropy-controlled reactions are not common in organic chemistry and do not follow “normal” structure/reactivity and/or linear free energy relationships. Examples of reported entropy-controlled reactions include additions of carbenes to multiple bonds^{49,50} and radical–radical recombination reactions.⁵¹ Some of these reactions are characterized by very low activation energies, or in some cases, even negative activation energies and/or curved Arrhenius plots, low A-factors, and rate constants below the diffusion-controlled limit. For all substrates examined in this study, “normal” Arrhenius behavior was observed.

Does the activation energy (or ΔH^\ddagger) vary sensibly with the strength of the C–H bond? A plot of activation energies vs BDE (Figure 3) reveals two distinct regions: For substrates with C–H BDEs greater than about 92 kcal/mol, the activation energy decreases as the C–H bond becomes weaker (as is normally observed for hydrogen abstraction processes). From this region of the plot, an α value of about 0.3 is obtained, suggesting an early transition state reminiscent of other high reactivity/low selectivity radicals such as Cl^\bullet .⁷ (However, unlike

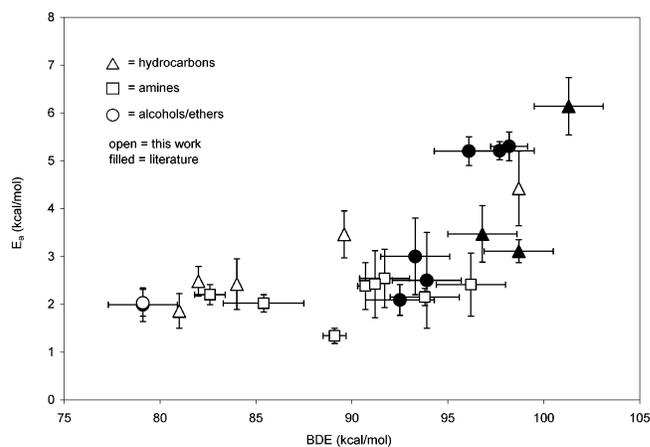


Figure 3. Activation energy for hydrogen abstraction by $t\text{BuO}^\bullet$ vs C–H BDE.

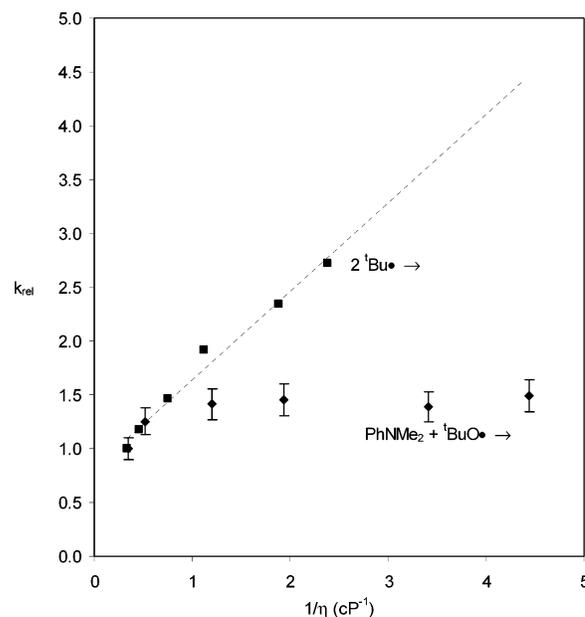


Figure 4. Solvent viscosity effect—hydrogen abstraction from *N,N*-dimethylaniline by $t\text{BuO}^\bullet$ compared to a bona fide diffusion controlled reaction (data from Table 2 and ref 53).

Cl^\bullet ,⁵² the rate constants are well below the diffusion-controlled limit). For substrates with C–H BDEs less than 92 kcal/mol, the activation energy levels off to a value of about $2 (\pm 1/2)$ kcal/mol and does not vary significantly with C–H BDE ($\alpha = 0$).

An activation energy of ca. 2 kcal/mol is very close to the activation energy for viscous flow for relatively low viscosity solvents such as benzene, and the possibility that the level region of Figure 3 might be attributable to the onset of diffusion control was addressed. This was accomplished by examining the effect of solvent viscosity on k_H for substrates with BDEs less than 92 kcal/mol and with low E_a 's. Upon the basis of the Stokes–Einstein and von Smoluchowski equations, it is expected that the diffusion controlled rate constant (k_{diff}) will vary linearly with the inverse of solvent viscosity (at constant temperature).⁴⁸ In Figure 4, the effect of solvent viscosity for the reaction of $t\text{BuO}^\bullet$ with *N,N*-dimethylaniline (C–H BDE = 91.7 kcal/mol;

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$E_a = 2.54$ kcal/mol) is compared to the effect of solvent viscosity on a bona fide diffusion controlled reaction—combination/disproportionation of the *tert*-butyl radical (using data of Schuh and Fischer).⁵³ This figure clearly demonstrates that there is no significant effect of solvent viscosity on the rate constant for hydrogen abstraction from *N,N*-dimethylaniline by ${}^t\text{BuO}\cdot$. For other substrates in the “level” region of the E_a vs C–H BDE plot such as *N,N*-dibenzylaniline (C–H BDE = 89.1 kcal/mol; $E_a = 2.01$ kcal/mol) and tribenzylamine (C–H BDE = 85.4 kcal/mol; $E_a = 1.34$ kcal/mol), a 1 order of magnitude variation in solvent viscosity had no discernible effect on k_H (Table 3). Consequently, it appears that the leveling off observed in the E_a vs C–H BDE plot cannot be attributed to the onset of diffusion control.

There are several possible explanations for the observation that the activation energies are independent of BDE (for substrates with C–H BDE < 92 kcal/mol), including the possibility that this is an experimental artifact. There are errors associated with the measurement of both E_a and the C–H BDE, and a fair amount of scatter in the data. Could these errors obscure what is actually a linear relation between these two quantities?

With regard to errors in the reported activation energies, there has been some discussion in the literature regarding what is often referred to as a compensation effect in regression analysis (i.e., within limits of uncertainty, the data can be fit equally well with a lower $E_a/\log(A)$ or higher $E_a/\log(A)$).⁵⁴ At the present time, there appears to be no clear consensus as to how to report the error in E_a or $\log(A)$ to account for this compensation effect; standard practice is to report standard errors or 95% confidence limits derived from the regression analysis. Also, there has been discussion of the use of the linearized vs nonlinearized forms of the Arrhenius equation, and the issue of proper weighting of the data.^{54–56}

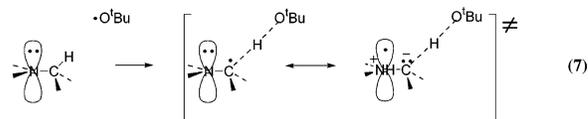
In these experiments, a temperature range of ca. 10–80 °C was used to avoid freezing of the solution, or thermal decomposition of the ${}^t\text{BuO}\cdot$ precursor, di-*tert*-butyl peroxide). For our data in Table 1, 95% confidence limits are provided for E_a and $\log(A)$ based upon the regression statistics. Under the assumption that the error in k was independent of temperature, these values are derived from fitting of the nonlinear equation. However, it should be noted that within reported error limits, the results are identical using the linearized form of the Arrhenius equation. Finally, in addition to spot-checking our technique by repeating Arrhenius studies previously reported in the literature, several of the new experiments were performed and repeated several times in their entirety over the course of this study. Accordingly, we are confident that the values of the Arrhenius parameters reported in this investigation and in the literature are accurate and reproducible.

In terms of a “chemical” explanation for these results, we offer the following hypotheses:

1. In some instances, steric interactions attributable to the bulky ${}^t\text{BuO}\cdot$ may force other, radical stabilizing substituents on the substrate out of conjugation with the developing radical center. For example, in the calculated (B3LYP/6-31G**) transition state for the reaction of ${}^t\text{BuO}\cdot$ and Ph_2CH , only one

of the two phenyl groups is oriented properly to stabilize the developing radical center; the other is twisted out of conjugation. Similarly for $\text{Ph}_3\text{CH} + {}^t\text{BuO}\cdot$, only one of three phenyl groups is oriented properly. Hence, the fact that the activation energies for PhCH_3 , Ph_2CH_2 , and Ph_3CH are so similar may be attributable that only one phenyl group is available for stabilizing the transition state in each instance.

2. For the reaction ${}^t\text{BuO}\cdot +$ tertiary amines, stereoelectronic considerations are important³² and interaction between the developing radical center and nitrogen lone pair in the transition state may be more important than interactions with other, radical stabilizing substituents (eq 7). However, it should be noted that



for quinuclidine and DABCO, the nitrogen lone pair cannot provide this stabilization, yet the activation energies are only slightly greater than that of the other amines which do not possess this geometric constraint.

3. These hydrogen abstractions may be so exothermic that there is not a significant barrier associated with the bond making/bond breaking process. The nominal activation energies may result from residual steric interactions between the bulky *tert*-butyl group and the substrate.

4. Somewhat related to #3, Houk has examined the flexibility of the transition state for the reaction of hydroxyl radical and methane (HF/3-21G and MP2/6-31G**) and found that lengthening the C–O bond in the transition state by 0.1 Å over the optimum length increases the activation energy by 1.2 kcal/mol.⁵⁷ For substrates with weak C–H bonds, although one would expect that the E_a would decrease with increasing bond strength, this trend may be interrupted because ${}^t\text{BuO}\cdot$ cannot get close enough to the substrate in the transition state to attain the optimal bond length.

The experimental results do not allow us to determine which (if any) of the possibilities is most likely and in future work, this will be addressed by current theories pertaining to hydrogen abstractions reactions (e.g., the Zavitsas nonparametric model for calculating activation energies of hydrogen abstraction reactions,^{58,59} Roberts’ extended Evans–Polanyi relationship,⁶⁰ and recent approaches offered by Mayer).^{61,62} Ab initio calculations of transition state structures and energetics will also be performed.

The final issue to consider pertaining to activation parameters for hydrogen abstraction by ${}^t\text{BuO}\cdot$ is the magnitude of $\log(A)$, which via eq 6, is directly related to the entropy of activation. The statement that most hydrogen abstractions (from carbon) by ${}^t\text{BuO}\cdot$ are entropy-controlled does not necessarily mean that the entropy requirements in the transition states for these reactions are unusually stringent. For the substrates listed in

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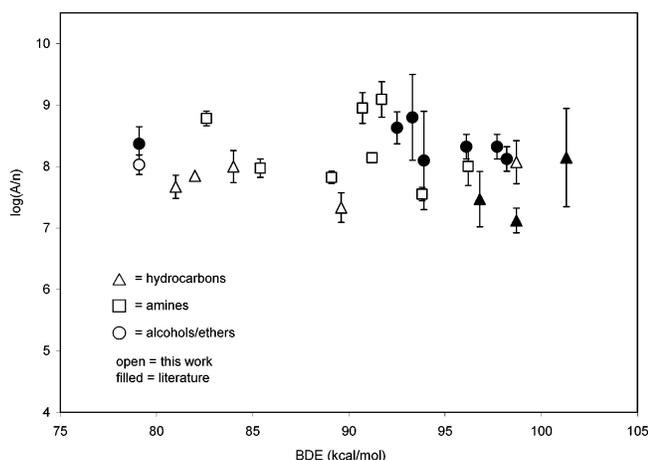


Figure 5. Variation of $\log(A/n)$ for hydrogen abstractions by $t\text{BuO}\cdot$ as a function of C–H BDE (n is the number of abstractable hydrogens).

Table 1, ΔS^\ddagger ranges from -8 to -19 eu. These values are smaller than bimolecular reactions with a high degree of order in the transition state such as the Diels–Alder reaction. For example, for the dimerization of cyclopentadiene⁶³ and reaction of maleic anhydride with 9,10-dimethylantracene,⁶⁴ ΔS^\ddagger 's are -29 and -39 eu, respectively.

At this time, it is not clear whether $\log(A)$ varies in any sort of systematic way with structure. A plot of $\log(A/n)$ vs C–H BDE (Figure 5, where n is the number of abstractable hydrogens) shows that for most substrates, $\log(A/n)$ hovers around 8.0, and it appears that tertiary amines consistently have a slightly higher $\log(A/n)$ than aromatic hydrocarbons. Considered in light of the experimental error associated with these values and scatter in Figure 5, it is inappropriate to draw any meaningful conclusions at this time. (We plan on addressing this matter in the future via the ab initio calculations mentioned earlier).

Conclusions

Although the results presented in this paper raise many new questions regarding the chemistry of alkoxy radicals that can only be addressed by additional work (theory and experiment), there are a number of significant conclusions that can be

stated: (1) At room temperature, most hydrogen abstractions (from carbon) by $t\text{BuO}\cdot$ in solution are entropy-controlled; the free energy barrier is governed more by $T\Delta S^\ddagger$ than by ΔH^\ddagger . (2) For substrates with C–H BDE > 92 kcal/mol, normal reactivity trends are observed—the activation energy decreases with decreasing C–H bond strength. (3) For substrates with C–H BDE < 92 kcal/mol, the activation energy levels off to a value of approximately 2 kcal/mol. Solvent viscosity studies demonstrate that this leveling is not attributable to the onset of diffusion control.

As noted in the Introduction, the chemistry of $t\text{BuO}\cdot$ has frequently been used as a chemical model for reactive oxygen-centered radicals in a variety of contexts, and some comments regarding the viability of this approach are appropriate. For reactive substrates, hydrogen abstractions by $t\text{BuO}\cdot$ are dominated by entropy considerations. This means that any intrinsic reactivity trends associate with a substrate, or class of substrates, are masked. It appears that much of the behavior associated with $t\text{BuO}\cdot$ is unique, likely arising from numerous issues pertaining to steric bulk. Hence, $t\text{BuO}\cdot$ may not be representative of other (smaller) alkoxy radical, and other reactive oxygen-centered species in general.

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Supporting Information Available: Tables summarizing absolute rate constants as a function of temperature and pertinent Arrhenius plots for all substrates used in this study, a summary of Arrhenius parameters obtained in individual trials, results of B3LYP calculations to estimate unknown C–H bond dissociation energies of several substrates, and calculated transition states for the reaction of $t\text{BuO}\cdot$ with toluene and triphenylmethane. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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