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Kinetic Solvent Effects on Hydrogen Abstraction Reactions

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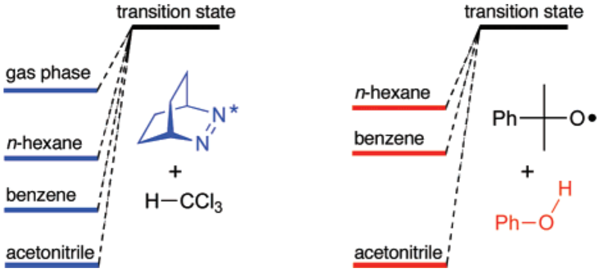
ABSTRACT



Kinetic solvent effects on hydrogen abstractions, namely, acceleration in nonpolar solvents, have been presumed to be restricted to O–H hydrogen donors. We demonstrate that also abstractions from C–H and even Sn–H bonds by cumyloxyl radicals and n,π*-excited 2,3-diazabicyclo-[2.2.2]oct-2-ene are fastest in the gas phase and nonpolar solvents but slowest in acetonitrile. Accordingly, solvent effects on hydrogen abstractions are more general, presumably due to stabilization of the reactive oxygen or nitrogen species in polar solvents.

In contrast to ionic reactions, radical reactions display generally small and frequently negligible kinetic solvent effects.[1] Hydrogen abstraction reactions of alkoxyl radicals from phenols are a notable exception because they proceed with substantially lower rate constants in polar and especially hydrogen-bond-donating solvents.[2−9] This has been attributed to the involvement of the reactive O−H in a hydrogen-bond network, which offers protection toward the attack of the reactive alkoxyl radical. In line with this argument, conceptually advanced by Ingold and co-workers,[9] hydrogen donors with C−H bonds displayed no detectable kinetic solvent effects in their reaction with cumyloxyl,[10] peroxyl,[11] and 1,1-diphenyl-2-picrylhyrazyl (DPPH) radicals.[12] The current understanding in radical chemistry is therefore that only hydrogen abstractions from O−H bonds, but not those from C−H bonds, are expected to be slowed in polar solvents.[9] This "solvent effects only for O−H abstractions" rule has in fact been so well-established that it has occasionally been applied to mechanistically discriminate between hydrogen abstraction from C−H and O−H bonds.[13] The present results, which are based on a comprehensive set of kinetic data, show

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that such an assignment to the type of hydrogen-donating group (O−H vs C−H), solely on the basis of a kinetic solvent effect, may not be compulsory. In particular, we observed sizable solvent effects also in hydrogen abstractions from C−H and even Sn−H bonds, which calls for a generalization.

Accurate measurements of rate constants for hydrogen abstraction, as required for the investigation of solvent effects, depend critically on the direct spectroscopic and time-resolved monitoring of the abstracting species.[14] In our experimental studies (cf. Supporting Information), we employed two types of reactive species, which fulfill the prerequiste of direct monitoring and which additionally exhibit a clear-cut radical-like reactivity and high hydrogen abstracting propensity (Figure 1). The first species, the cumyloxyl radical (CumO$^\bullet$), shows, as first observed by Lusztyk and co-workers,[15] a characteristic transient absorption in the visible range, which can be conveniently generated by 308 nm laser-flash photolysis of dicumylperoxide. The second species studied is the n,π* singlet-excited state of 2,3-diazabicyclo[2.2.2]oct-2-ene (DBO). Although the hydrogen abstractions of singlet-excited DBO (as well as singlet-excited ketones) proceed with low quantum yields,[16−21] owing to the intervention of a conical intersection on the excited-state hypersurface,[20−26] the mechanism of this photoreaction, which involves a transition state for hydrogen atom abstraction, has been established in detail through comprehensive computational[21−24] and experimental[19,21,24,26−31] investigations. In particular, DBO is known to undergo pure hydrogen abstraction reactions without notable complications due to competitive charge-transfer.[31] The latter mechanism is commonly encountered for alternative excited-state radical models, e.g., n,π* triplet-excited benzophenone.[20,31,32] In addition, hydrogen abstractions by singlet-excited DBO can be monitored with very high precision by time-resolved fluorescence. The choice of the reactive states (electrophilic for cumyloxyl vs nucleophilic for DBO)[30] as well as the broad range of hydrogen donors (electrophilic C−H in chloroform and O−H in alcohols vs nucleophilic C−H in alcohols, ethers, and alkanes, or Sn−H in tin hydrides) were meant to allow further generalizations.[16,19−21,24,29]

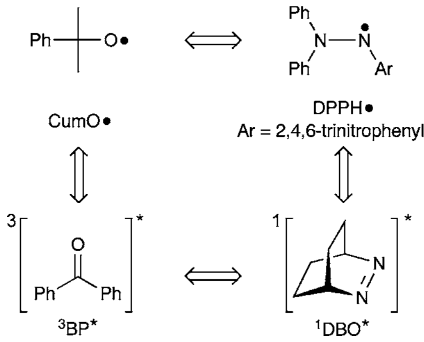

Figure 1. Conceptual relationship between reactive species and spectroscopic probes with high hydrogen abstraction propensity: oxygen centered (left), nitrogen centered (right), ground-state radicals (top), and n,π*-excited states (bottom).

In analogy to previous studies,[3,29] the rate constants for hydrogen abstraction (k_H) were taken as the scavenging rate constants for cumyloxyl radicals (Table 1, Figure 2) and as the fluorescence quenching rate constants for singlet-excited DBO (Table 2, Figure 3). The data were determined in the gas phase, *n*-hexane, benzene, and acetonitrile. Selected measurements in the more viscous cyclohexane (values in square brackets) showed that viscosity effects on the rate

Table 1. Scavenging Rate Constants for Cumyloxyl Radicals

	$k_H/(10^7\ M^{-1}\ s^{-1})$[a]		
scavenger	*n*-hexane	benzene	acetonitrile
phenol	90 [72][b]	28	0.58
tri-*n*-butyltin hydride	37	26	40
1,3-cyclohexadiene	8.9 [7.5][b]	6.5	5.3
1,4-cyclohexadiene	6.7	5.4	5.9
hexamethylbenzene	1.6	1.4	0.73
diphenylmethanol[c]	1.0[d]	0.62	0.28
tetrahydrofuran	0.83	0.72	0.47

[a] 10% estimated error. [b] Value in cyclohexane. [c] Data measured for *tert*-butoxyl radicals. [d] Measured in *n*-hexane/benzene (2:1).

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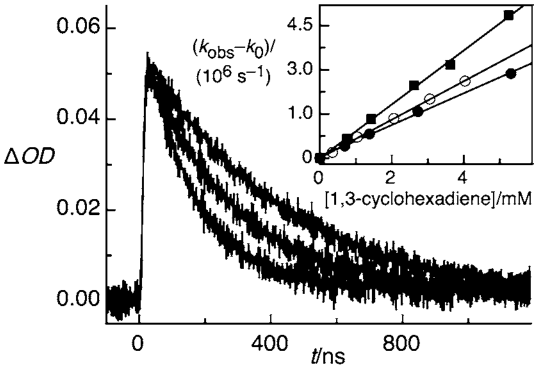

Figure 2. Transient decay traces of cumyloxyl radicals in air-equilibrated benzene with varying amounts of tetrahydrofuran (0.20, 0.40, and 0.77 M, from top to bottom). The inset shows the kinetic plots for radical scavenging by 1,3-cyclohexadiene in acetonitrile (●), benzene (○), and *n*-hexane (■).

constants were smaller than their variations with solvent polarity.

Cumyloxyl radicals were generated in aerated solution and monitored at 485 nm. The transient decays (Figure 2) were fitted according to monoexponential functions at different hydrogen donor concentrations, [HD]. The observed rate constants (k_{obs}) were plotted according to $k_{obs} = k_0 + k_H[HD]$ to afford the k_H values from the slope (cf. inset in Figure 2).[33] The extrapolated lifetimes of cumyloxyl radicals in the absence of a quencher ($1/k_0$; 1.3 μs in acetonitrile, 2.1 μs in benzene, 250 ns in *n*-hexane, and 90 ns in cyclohexane) were in excellent agreement with reported values (1.33 μs in acetonitrile and 2.06 μs in benzene).[15]

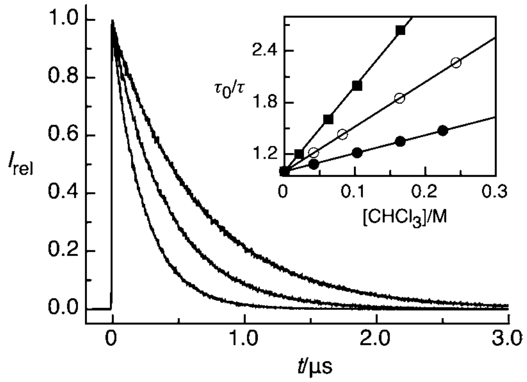

Figure 3. Fluorescence decay traces of DBO in degassed acetonitrile with varying amounts of tri-*n*-butyltin hydride (0, 13, and 37 mM, from top to bottom). The inset shows the kinetic Stern−Volmer plots for the quenching by chloroform in degassed acetonitrile (●), benzene (○), and *n*-hexane (■).

The fluorescence of singlet-excited DBO ($\lambda_{exc} = 373$ nm) in deaerated solution was monitored at 450 nm by time-correlated single-photon counting. Fluorescence lifetimes in the gas phase (vacuum)[28] were measured with a laser-flash photolysis system ($\lambda_{exc} = 355$ nm, $\lambda_{obs} = 450$ nm). The monoexponential decays (Figure 3) afforded the fluorescence lifetimes in the absence (τ_0) and presence (τ) of a hydrogen donor. They were plotted according to $\tau_0/\tau = 1 + k_H\tau_0[HD]$ to yield the k_H values from the slope (cf. inset in Figure 3). The data set for singlet-excited DBO is more extensive (Table 2) because of its higher reactivity with certain solvents (methanol, chloroform) and the high specificity of fluorescence monitoring.[33]

Table 2. Fluorescence Quenching Rate Constants for DBO

	$k_H/(10^7\ M^{-1}\ s^{-1})^a$			
quencher	gas phase	*n*-hexane	benzene	acetonitrile
phenol	40000	2100 [1000]^b	740	95^{c,d}
diphenylmethanol		91	19	2.2
diphenylmethane		46	23	24
tri-*n*-butyltin hydride		37	13.1	7.1
1,3-cyclohexadiene	33	17	8.4	3.8
hexamethylbenzene		8.1	2.4	1.6^c
methanol	11^e	7.4	4.9	4.5^f
triphenylmethane		7.1	1.7	1.3
1,4-cyclohexadiene	17	4.3	3.9	2.0
chloroform	17^e	3.4	1.1	0.31
tetrahydrofuran	2.6^e	0.25	0.13	0.075

[a] 10% estimated error in solution, 20% in the gas phase. [b] Value in cyclohexane. [c] From ref 31. [d] Value in water: 4.9×10^8 M^{-1} s^{-1}. [e] Value from ref 28. [f] Value in water: 1.6×10^6 M^{-1} s^{-1}.

The combined kinetic data demonstrate, with one evident exception (tri-*n*-butyltin hydride in acetonitrile in Table 1), that the hydrogen abstraction reactions are subject to significant kinetic solvent effects regardless of the nature of abstractable hydrogen (O−H, C−H, or Sn−H) and regardless of the electrophilicity of the hydrogen donors or abstracting species. Hydrogen abstractions proceed generally faster in the nonpolar solvent *n*-hexane and slowest in acetonitrile. For DBO, even the absolute rate constants in the gas phase (as the "most nonpolar" medium, cf. Table 2)[28] fit perfectly into this trend, whereas in water the lowest rate constants were determined (only for phenol and methanol as O−H donors, cf. footnotes d and f in Table 2). The kinetic solvent effect is most pronounced for phenol, and we interpret the corresponding gas-phase and *n*-hexane values for DBO as being collision- and diffusion-controlled,[34] respectively. However, the solvent effects are also very large for the hydrogen abstraction of singlet-excited DBO from diphenylmethanol, tri-*n*-butyltin hydride, and chloroform which act as C−H or Sn−H hydrogen donors (Table 2). Important to note, the kinetic solvent effect for chloroform, where C−H

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(33) The transient absorption-based measurements with cumyloxyl radicals, which required 308 nm excitation, could not be performed in the cases of di- and triphenylmethane; a residual absorbance of these specific samples and an associated strong transient signal interfered. For diphenylmethanol, where the absorbance of the formed ketyl radical prevented also the direct monitoring of cumyloxyl radicals, *tert*-butoxyl radicals were used instead. They were generated from di-*tert*-butylperoxide by 308 nm excitation and indirectly followed by observing the rise kinetics of the diphenylhydroxymethyl radical at 335 nm. Cf.: Griller, D.; Howard, J. A.; Marriott, P. R.; Scaiano, J. C. *J. Am. Chem. Soc.* **1981**, *103*, 619−623.

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bonds are being abstracted, is much larger than that for methanol, where O−H bonds are involved[20,21,26,29] (note that the high absolute reactivity of singlet-excited DBO toward O−H bonds is related to its nucleophilic character);[30] the latter comparison is particularly meaningful because deuterium isotope effects are fully manifested for both chloroform and methanol (ca. 10),[21,26,28,29] such that a pure excited-state hydrogen abstraction affirmatively applies.

Consequently, kinetic solvent effects on hydrogen abstractions are more general than previously presumed. In particular, solvent effects in favor of a lower reactivity in polar media are not limited to abstractions from O−H bonds. They are also found for abstractions from C−H bonds (factors up to 10 for *n*-hexane vs acetonitrile), and their magnitude depends strongly on the particular acceptor−donor combination (Tables 1 and 2).

Kinetic solvent effects are commonly explained in terms of a differential stabilization of the reactants and the transition state.[1] For example, phenols as hydrogen donors are thought to be stabilized by the interaction of polar (hydrogen-bond-accepting) solvents with the hydroxyl group.[2−9] This solvation of the reactive group must be sacrificed in the transition state for hydrogen transfer, thereby accounting for the lower observed reactivity.

Our present data reveal that a lower reactivity in polar solvents is also observed for abstractions of *nonprotic* hydrogens (C−H, Sn−H), including *nonpolar* hydrogen donors such as cyclohexadienes. In these cases, the lower reactivity is likely due to a stabilization of the polar reactive species itself. In particular, the electronegative atoms (O, N) of the abstracting species must experience a desolvation in the course of the hydrogen atom transfer similar to that postulated for the hydroxyl group in phenols as hydrogen donors. In line with the dipolar solvent stabilization of the abstracting species, the kinetic solvent effects are much more pronounced for the highly polar, singlet-excited state of DBO (μ ca. 3.5 D)[35,36] than for the less polar cumyloxyl radical (μ= 1.6 D).[37] Accordingly, solvent effects on hydrogen abstractions show a sizable dependence on the nature of the abstracting species. This contrasts the conclusion reached for phenols as hydrogen donors,[3,11] for which apparently the most pronounced solvent stabilization of the particular donors overwrites the smaller solvent stabilization of the acceptor.

Accordingly, the lower reactivity in polar solvents should be general for polar, i.e., heteroatom-centered, hydrogen abstracting species (alkoxyl radicals, peroxyl radicals, hydrazyl radicals, nitroxyl radicals, n,π*-excited azoalkanes, and ketones), and it only becomes most pronounced for hydrogen abstractions from protic bonds (phenols). Solely hydrogen abstractions between nonpolar radicals and nonpolar hydrogen donors should be insensitive to kinetic solvent effects, as neither polar effects in the transition state[28,30,31,38] nor the described dipolar solvation of the reactants apply. Unfortunately, this conjecture is difficult to test because the corresponding prototypal reactions, e.g., of carbon-centered radicals with alkanes, display intrinsically high activation barriers,[39] such that most experimental rate data are restricted to the gas phase at elevated temperature.[40]

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Supporting Information Available: Experimental methods. This material is available free of charge via the Internet at http://pubs.acs.org.

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