ORGANIC LETTERS

2010
Vol. 12, No. 16
3654−3657

Kinetic Solvent Effects on Hydrogen Abstraction Reactions from Carbon by the Cumyloxyl Radical. The Role of Hydrogen Bonding

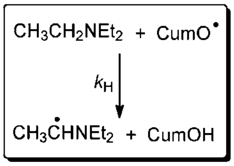
Massimo Bietti* and Michela Salamone

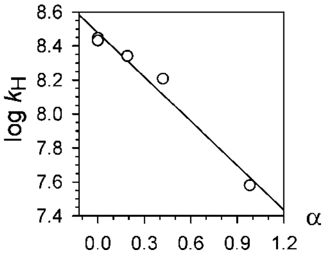
Dipartimento di Scienze e Tecnologie Chimiche, Università "Tor Vergata", Via della Ricerca Scientifica, 1 I-00133 Rome, Italy

bietti@uniroma2.it

Received June 24, 2010

ABSTRACT





A kinetic study of the H-atom abstraction reactions from 1,4-cyclohexadiene and triethylamine by the cumyloxyl radical has been carried out in different solvents. Negligible effects are observed with 1,4-cyclohexadiene, whereas with triethylamine a significant decrease in rate constant (k_H) is observed on going from benzene to MeOH. A good correlation between log k_H and the solvent hydrogen bond donor parameter α is observed, indicative of an H-bonding interaction between the amine lone pair and the solvent.

Hydrogen atom abstraction reactions from a variety of substrates by alkoxyl radicals have attracted considerable interest.[1−12] Among these studies, particular attention has been devoted to the study of solvent effects on these processes.[13−17] In a 1993 paper,[18] Ingold and Lusztyk clearly showed the absence of any significant kinetic solvent effect (KSE) for the H-atom abstraction reaction from cyclohexane

---

(1) Kawashima, T.; Ohkubo, K.; Fukuzumi, S. *J. Phys. Chem. B* **2010**, *114*, 675–680.

(2) Cosa, G.; Scaiano, J. C. *Org. Biomol. Chem.* **2008**, *6*, 4609–4614.

(3) (a) Lundgren, C. V.; Koner, A. L.; Tinkl, M.; Pischel, U.; Nau, W. M. *J. Org. Chem.* **2006**, *71*, 1977–1983. (b) Pischel, U.; Nau, W. M. *J. Am. Chem. Soc.* **2001**, *123*, 9727–9737.

(4) (a) Finn, M.; Friedline, R.; Suleman, N. K.; Wohl, C. J.; Tanko, J. M. *J. Am. Chem. Soc.* **2004**, *126*, 7578–7584. (b) Tanko, J. M.; Friedline, R.; Suleman, N. K.; Castagnoli, N., Jr. *J. Am. Chem. Soc.* **2001**, *123*, 5808–5809.

(5) Correia, C. F.; Borges dos Santos, R. M.; Estácio, S. G.; Telo, J. P.; Costa Cabral, B. J.; Martinho Simões, J. A. *ChemPhysChem* **2004**, *5*, 1217–1221.

(6) (a) Font-Sanchis, E.; Aliaga, C.; Bejan, E. V.; Cornejo, R.; Scaiano, J. C. *J. Org. Chem.* **2003**, *68*, 3199–3204. (b) Font-Sanchis, E.; Aliaga, C.; Cornejo, R.; Scaiano, J. C. *Org. Lett.* **2003**, *5*, 1515–1518. (c) Bejan, E. V.; Font-Sanchis, E.; Scaiano, J. C. *Org. Lett.* **2001**, *3*, 4059–4062.

(7) Lindsay Smith, J. R.; Nagatomi, E.; Stead, A.; Waddington, D. J.; Bévière, S. D. *J. Chem. Soc., Perkin Trans. 2* **2000**, 1193–1198.

(8) Lucarini, M.; Pedrielli, P.; Pedulli, G. F.; Valgimigli, L.; Gigmes, D.; Tordo, P. *J. Am. Chem. Soc.* **1999**, *121*, 11546–11553.

(9) Weber, M.; Fischer, H. *J. Am. Chem. Soc.* **1999**, *121*, 7381–7388.

(10) Erben-Russ, M.; Michel, C.; Bors, W.; Saran, M. *J. Phys. Chem.* **1987**, *91*, 2362–2365.

(11) Baignée, A.; Howard, J. A.; Scaiano, J. C.; Stewart, L. C. *J. Am. Chem. Soc.* **1983**, *105*, 6120–6123.

(12) Paul, H.; Small, R. D., Jr.; Scaiano, J. C. *J. Am. Chem. Soc.* **1978**, *100*, 4520–4527.

(13) Litwinienko, G.; Ingold, K. U. *Acc. Chem. Res.* **2007**, *40*, 222–230.

(14) Aliaga, C.; Stuart, D. R.; Aspée, A.; Scaiano, J. C. *Org. Lett.* **2005**, *7*, 3665–3668.

(15) Kim, S. S.; Kim, S. Y.; Ryou, S. S.; Lee, C. S.; Yoo, K. H. *J. Org. Chem.* **1993**, *58*, 192–196.

(16) Das, P. K.; Encinas, M. V.; Steenken, S.; Scaiano, J. C. *J. Am. Chem. Soc.* **1981**, *103*, 4162–4166.

(17) Walling, C. *Pure Appl. Chem.* **1967**, *15*, 69–80.

(18) Avila, D. V.; Brown, C. E.; Ingold, K. U.; Lusztyk, J. *J. Am. Chem. Soc.* **1993**, *115*, 466–470.

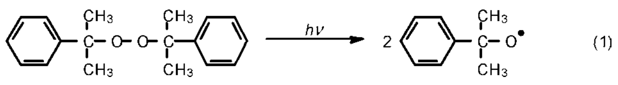
10.1021/ol101448e

by the cumyloxyl radical (CumO$^\bullet$), and the general statement was made that "For alkoxyl radical hydrogen atom abstraction from alkanes (and from other substrates which are not, themselves, solvated to a significantly greater extent in polar relative to nonpolar solvents) we expect the abstraction rate constants to be essentially solvent independent. Of course, this rule will not hold if the substrate itself is strongly solvated by certain solvents...". Later, this expectation was verified for the H-atom abstraction reaction from 1,4-cyclohexadiene by the *tert*-butoxyl radical (*t*-BuO$^\bullet$),[19] where again no significant kinetic solvent effect (KSE) was observed, and, in turn, for the H-atom abstraction reactions from phenolic substrates,[13,20−23] hydroperoxides,[23] and aniline,[21] where significant KSEs were instead reported. With the latter substrates, the rate constants for H-atom abstraction from the OH or NH_2 group by alkoxyl radicals (k_H) were observed to decrease with an increase in the solvent hydrogen bond acceptor (HBA) ability. On the basis of the absence of any relevant KSE in the H-atom abstraction reactions from carbon described above,[18,19] solvent effects on the H-abstracting reactivity of the alkoxyl radical could be ruled out, and accordingly, this behavior was explained in terms of the modulation of the reactivity of these substrates via hydrogen-bonding interactions between the substrate OH or NH_2 group and the solvent. Good correlations were observed between log k_H and the relative hydrogen bond acceptor (HBA) properties of the solvents expressed by the β_2^H constant.[13,20,21]

Very recently, however, Pischel and Nau reported on the observation of sizable solvent effects on H-abstraction reactions from carbon by CumO$^\bullet$ for a variety of substrates,[24] showing that k_H values generally decrease with increasing solvent polarity, and suggesting, in contrast with previous findings, that "the lower reactivity is likely due to a stabilization of the polar reactive species itself. In particular, the electronegative atoms 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".

On the basis of these observations, it seemed particularly interesting to obtain additional information on the role of solvent effects on H-abstraction reactions from carbon, and for this purpose we have carried out a detailed time-resolved kinetic study in five different solvents (benzene, chlorobenzene, acetonitrile, 2-methyl-2-propanol, and methanol) on the reactions of CumO$^\bullet$ with two selected H-atom donors: 1,4-cyclohexadiene (CHD) and triethylamine (Et_3N).

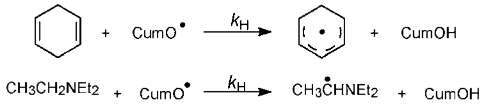
CumO$^\bullet$ has been generated by 266 or 355 nm laser flash photolysis (LFP) of nitrogen-saturated solutions ($T = 25$ °C) containing dicumyl peroxide (eq 1).



(1)

As described previously, CumO$^\bullet$ is characterized by a broad absorption band in the visible region of the spectrum centered at 485 nm,[25,26] whose position is slightly red-shifted in MeOH.[27] Under these conditions, CumO$^\bullet$ decays mainly by C−CH_3 β-scission,[18,25] with the exception of the experiments carried out in MeOH solution where H-atom abstraction from the solvent is instead the predominant reaction.[29]

The reactions of CumO$^\bullet$ with CHD and Et_3N have been studied by LFP. It is well established that these reactions proceed by C−H abstraction from the CH_2 positions of both substrates,[30] as described in eqs 2 and 3.



(2)

(3)

A number of rate constants for the reactions of both CHD and Et_3N with *t*-BuO$^\bullet$ and CumO$^\bullet$, measured under different experimental conditions, are available in the literature.[31,32]

The time-resolved spectra observed after reaction of CumO$^\bullet$ with CHD and Et_3N in MeCN solution are reported in the Supporting Information (Figures S1 and S2).

Kinetic studies have been carried out by LFP following the decay of the CumO$^\bullet$ visible absorption band at 490 nm as a function of the CHD or Et_3N concentration. When the

---

[19] Wayner, D. D. M.; Lusztyk, J.; Pagé, D.; Ingold, K. U.; Mulder, P.; Laarhoven, L. J. J.; Aldrich, H. S. *J. Am. Chem. Soc.* **1995**, *117*, 8131–8144.

[20] Snelgrove, D. W.; Lusztyk, J.; Banks, J. T.; Mulder, P.; Ingold, K. U. *J. Am. Chem. Soc.* **2001**, *123*, 469–477.

[21] MacFaul, P. A.; Ingold, K. U.; Lusztyk, J. *J. Org. Chem.* **1996**, *61*, 1316–1321.

[22] Valgimigli, L.; Banks, J. T.; Ingold, K. U.; Lusztyk, J. *J. Am. Chem. Soc.* **1995**, *117*, 9966–9971.

[23] Avila, D. V.; Ingold, K. U.; Lusztyk, J.; Green, W. H.; Procopio, D. R. *J. Am. Chem. Soc.* **1995**, *117*, 2929–2930.

[24] Koner, A. L.; Pischel, U.; Nau, W. M. *Org. Lett.* **2007**, *9*, 2899–2902.

[25] Baciocchi, E.; Bietti, M.; Salamone, M.; Steenken, S. *J. Org. Chem.* **2002**, *67*, 2266–2270.

[26] (a) 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. (b) Avila, D. V.; Lusztyk, J.; Ingold, K. U. *J. Am. Chem. Soc.* **1992**, *114*, 6576–6577.

[27] In MeOH, the CumO$^\bullet$ visible absorption band is centered around 500 nm. As a matter of comparison, a 30 nm red-shift in the position of this band ($\lambda_{max} = 515$ nm) is observed in 2,2,2-trifluoroethanol (see ref 28).

[28] Bietti, M.; Gente, G.; Salamone, M. *J. Org. Chem.* **2005**, *70*, 6820–6826.

[29] Banks, J. T.; Scaiano, J. C. *J. Am. Chem. Soc.* **1993**, *115*, 6409–6413.

[30] For reaction (2), see ref 24. For reaction (3), see ref 3b.

[31] For CHD . (a) CumO$^\bullet$ + CHD. 308 nm LFP, rt, in hexane, benzene, and MeCN, following the decay of CumO$^\bullet$; $k_H = 6.7$, 5.4, and 5.9×10^7 M^{-1} s^{-1}, respectively (ref 24). (b) *t*BuO$^\bullet$ + CHD. LFP, $T = 20$ °C, in isooctane, CCl_4, benzene, and MeCN; $k_H = 3.0 \pm 0.4 \times 10^7$ $M^{-1}s^{-1}$ (ref 19). (c) *t*-BuO$^\bullet$ + CHD. 337.1 nm LFP, $T = 22$ °C, in (t-BuO)$_2$/benzene 2:1, PhCH(OH)Ph probe; $k_H = 5.3 \times 10^7$ M^{-1} s^{-1} (ref 33). (d) *t*-BuO$^\bullet$ + CHD. 347.1 nm LFP, rt, in (t-BuO)$_2$/benzene 2:1, PhCH(OH)Ph probe; $k_H = 5.4 \times 10^7$ M^{-1} s^{-1} (ref 12).

[32] For Et_3N. (a) CumO$^\bullet$ + Et_3N. 308 nm LFP, rt, in MeCN, following the decay of CumO$^\bullet$; $k_H = 1.6 \times 10^8$ M^{-1} s^{-1} (ref 3b). (b) *t*-BuO$^\bullet$ + Et_3N. 355 nm LFP, rt, in (t-BuO)$_2$, following the buildup of the α-aminoalkyl radical; $k_H = 1.1 \times 10^8$ M^{-1} s^{-1} (ref 34)). (c) *t*BuO$^\bullet$ + Et_3N. 355 nm LFP, $T = 22$ °C, (t-BuO)$_2$/benzene 2:1, PhCH(OH)Ph probe; $k_H = 1.59 \times 10^8$ $M^{-1}s^{-1}$ (ref 4b). (d) *t*-BuO$^\bullet$ + Et_3N. 337.1 nm LFP, $T = 22$ °C, (t-BuO)$_2$/benzene 2:1, PhCH(OH)Ph probe; $k_H = 1.8 \times 10^8$ M^{-1} s^{-1} (ref 35).

[33] Effio, A.; Griller, D.; Ingold, K. U.; Scaiano, J. C.; Sheng, S. J. *J. Am. Chem. Soc.* **1980**, *102*, 6063–6068.

observed rate constants (k_{obs}) have been plotted against substrate concentration, excellent linear dependencies have been observed, and the second-order rate constants for H-atom abstraction from CHD and Et_3N by $CumO^•$ (k_H) have been obtained from the slopes of these plots. As an example, the plots of k_{obs} vs [Et_3N] and of k_{obs} vs [CHD] for the reactions between $CumO^•$ and both Et_3N (filled circles) and CHD (empty circles) carried out in benzene and MeOH solution are shown in Figure 1.

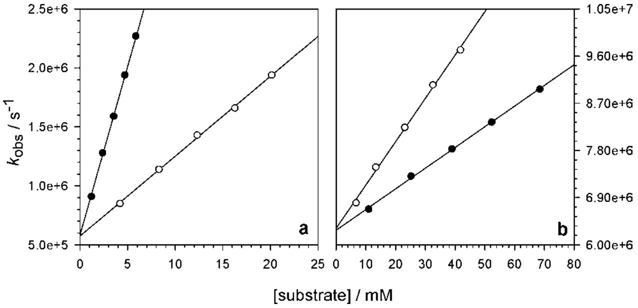


Figure 1. Plots of the observed rate constant (k_{obs}) against [substrate] for the reactions of the cumyloxyl radical ($CumO^•$) with triethylamine (filled circles) and 1,4-cyclohexadiene (empty circles), measured in nitrogen-saturated benzene (a) or MeOH (b) solutions at $T = 25$ °C, following the decay of $CumO^•$ at 490 nm. From the linear regression analysis: (a) $CumO^• + Et_3N$: intercept $= 5.86 \times 10^5$ s^{-1}, $k_H = 2.85 \times 10^8$ M^{-1} s^{-1}, $r^2 = 0.9994$; $CumO^•$ + 1,4-CHD: intercept $= 5.75 \times 10^5$ s^{-1}, $k_H = 6.77 \times 10^7$ M^{-1} s^{-1}, $r^2 = 0.9989$. (b) $CumO^• + Et_3N$: intercept $= 6.28 \times 10^6$ s^{-1}, $k_H = 3.94 \times 10^7$ M^{-1} s^{-1}, $r^2 = 0.9991$; $CumO^•$ + 1,4-CHD: intercept $= 6.32 \times 10^6$ s^{-1}, $k_H = 8.26 \times 10^7$ M^{-1} s^{-1}, $r^2 = 0.9974$.

Additional plots for the same reactions, carried out in chlorobenzene, MeCN, and *t*-BuOH are reported in the Supporting Information (Figures S3−S12). All the kinetic data thus obtained are collected in Table 1.

Table 1. Second-Order Rate Constants (k_H) for the Reactions of the Cumyloxyl Radical ($CumO^•$) with Triethylamine (Et_3N) and 1,4-Cyclohexadiene (CHD), Measured in Different Solvents at $t = 25$ °C[a]

solvent	α^b	$\lambda_{ex}{}^c$ (nm)	k_H $(Et_3N)^d/s^{-1}$	k_H $(CHD)^d/s^{-1}$
MeCN	0.19	266	$2.0 \pm 0.1 \times 10^8$	$6.65 \pm 0.02 \times 10^7$
			$1.47 \pm 0.03 \times 10^{8\,e}$	
			$9.2 \pm 0.1 \times 10^{7\,f}$	
		355	$2.19 \pm 0.05 \times 10^8$	$6.56 \pm 0.03 \times 10^7$
benzene	0.00	355	$2.8 \pm 0.1 \times 10^8$	$6.79 \pm 0.04 \times 10^7$
PhCl	0.00	355	$2.7 \pm 0.1 \times 10^8$	$6.90 \pm 0.05 \times 10^7$
*t*BuOH	0.42	355	$1.61 \pm 0.03 \times 10^8$	$8.3 \pm 0.1 \times 10^7$
MeOH	0.98	355	$3.8 \pm 0.1 \times 10^7$	$8.25 \pm 0.03 \times 10^7$

[a] 266 nm LFP, N_2-saturated, [dicumyl peroxide] = 10 mM. 355 nm LFP, N_2-saturated, [dicumyl peroxide] = 0.7−1.0 M. [b] Solvent hydrogen bond donor (HBD) parameter (see ref 37). [c] Excitation wavelength. [d] Determined from the slope of the k_{obs} vs [substrate] plots, where in turn k_{obs} values have been measured following the decay of the $CumO^•$ visible absorption band at 490 nm. Average of at least two determinations. [e] In the presence of 1 M H_2O. [f] In the presence of 4.7 M H_2O.

The reactions have been initially studied in MeCN solution employing 266 nm laser light for the generation of $CumO^•$. The k_H values measured for H-atom abstraction from both Et_3N and CHD displayed in Table 1 are in reasonable agreement with those measured previously by other groups.[31,32] Very interestingly, a substantial decrease in rate constant has been observed for the reaction between $CumO^•$ and Et_3N when relatively small amounts of H_2O have been added to the solution. This decrease in k_H indicates that water exerts an important role on the H-atom abstraction process, and accordingly, in order to obtain quantitative information on the role of solvent effects on these processes we have moved to 355 nm LFP. As compared to 266 nm LFP experiments, under these conditions a larger variety of solvents can be employed (in particular, benzene and chlorobenzene, which absorb at 266 nm), and moreover, significantly higher Et_3N concentrations can be used.

With both substrates, no significant difference in reactivity has been observed in MeCN solution when employing 266 or 355 nm LFP. The results displayed in Table 1 clearly show that in benzene solution (Figure 1a) Et_3N undergoes α-C-H abstraction with a rate constant that is about three times higher than that measured for CHD, whereas in MeOH solution (Figure 1b) the opposite situation is observed with k_H that increases by a factor 2 on going from Et_3N to CHD.

Very interestingly, with Et_3N a 7-fold decrease in reactivity has been observed on going from benzene or chlorobenzene to MeOH. To our knowledge, this represents the largest KSE observed for H-atom abstraction from carbon by an alkoxyl radical.[36] A reasonably good correlation ($r^2 = 0.9714$) has been observed between log k_H and the solvent hydrogen bond donor (HBD) parameter α,[37] as shown in Figure 2.

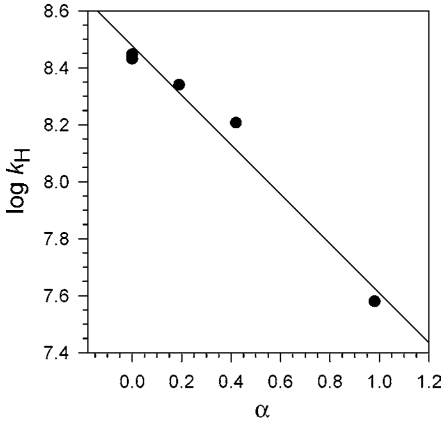


Figure 2. Plot of log k_H against the solvent hydrogen bond donor parameter α for the reactions of the cumyloxyl radical with Et_3N in different solvents at $t = 25$ °C. From the regression analysis: intercept = 8.48; slope = −0.869; $r^2 = 0.9714$.

Griller and Scaiano have clearly shown that in the reactions between tertiary amines and *t*-$BuO^•$ H-atom abstraction is

---

(34) Lalevée, J.; Graff, B.; Allonas, X.; Fouassier, J. P. *J. Phys. Chem. A* **2007**, *111*, 6991–6998.

most rapid when the α-C−H bond being broken can be eclipsed with the nitrogen lone pair.[35] Accordingly, 1,4-diazabicyclo[2,2,2]octane (DABCO), where this overlap is not possible, undergoes α-C−H abstraction by t-BuO$^•$ and CumO$^•$ with rate constants that are between 6 and 16 times lower than those measured in their reactions with Et_3N.[3b,34,35] Along this line, and following the correlation shown in Figure 2, the KSE observed for the CumO$^•$ + Et_3N reaction can be reasonably explained in terms of a hydrogen-bonding interaction between the nitrogen lone pair and the solvent. This interaction decreases the degree of overlap between the α-C−H bond and the nitrogen lone pair in the transition state for H-atom abstraction, thus lowering the reactivity. This is in line with Ingold and Lusztyk's prediction[18] where, however, in the present case, in contrast to the H-atom abstraction reactions from phenols, hydroperoxides, and aniline, the interaction with the solvent does not directly involve the abstractable H atom. In particular, steric effects due to the solvent on the H-atom abstraction reaction from Et_3N by CumO$^•$ can be reasonably ruled out on the basis of the observation that k_H decreases on going from t-BuOH to MeOH.

With CHD, no significant difference in rate constant has been observed when the reaction has been studied in MeCN, benzene, or chlorobenzene, whereas a slight (and reproducible) increase in k_H has been observed in MeOH and t-BuOH. The former results are essentially in line with the previous observation that this reaction shows no KSE,[19] where, however, the study has been limited to isooctane, CCl_4, benzene, and MeCN, suggesting moreover that the differences in k_H observed, for the same reaction, by Pischel and Nau between hexane, benzene, and MeCN are likely due to experimental errors.[24,31a] In addition, the observation that k_H increases on going from benzene, chlorobenzene and MeCN to alcoholic solvents is also in contrast with the previous observation of a decrease in reactivity with increasing solvent polarity,[24] ruling out the hypothesis that in these processes the reactivity is governed by a solvent-dependent stabilization of CumO$^•$. The observed solvent effects on the reaction between CumO$^•$ and CHD can be reasonably rationalized in terms of an increase in differential solvation between reactants and transition state on going from aprotic to protic solvents. Additional experiments on CHD and on different C−H hydrogen atom donors may allow a better understanding of this peculiar effect.

In conclusion, by means of a detailed time-resolved kinetic study, we have clearly shown that the H-atom abstraction reaction from Et_3N by CumO$^•$ shows a significant KSE that, on the basis of the correlation between log k_H and the solvent HBD parameter α, has been interpreted in terms of a hydrogen-bonding interaction between the nitrogen lone pair and the solvent. This represents the largest KSE observed for H-atom abstraction from carbon by an alkoxyl radical. Negligible solvent effects have been instead observed for the corresponding reaction of 1,4-cyclohexadiene.

Acknowledgment. Financial support from the Ministero dell'Istruzione dell'Università e della Ricerca (MIUR) is gratefully acknowledged. We thank Gino A. DiLabio (National Institute for Nanotechnology, Edmonton, Canada) for helpful discussions and Lorenzo Stella (Università "Tor Vergata", Rome, Italy) for the use of LFP equipment.

Supporting Information Available: Time-resolved absorption spectra observed after reaction of CumO$^•$ with CHD and Et_3N. Plots of k_{obs} vs [substrate] for the reactions of the cumyloxyl radical with CHD and Et_3N. This material is available free of charge via the Internet at http://pubs.acs.org.

OL101448E

---

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

(36) Recently, Scaiano reported a 12-fold decrease in reactivity on going from hexane to MeCN for the formal C−H abstraction reaction from the lactone antioxidant HP-136 by t-BuO$^•$ (see ref 14). This KSE has been explained, however, in terms of an H-atom abstraction reaction from the OH group of the enol form in equilibrium with the lactone.

(37) Reichardt, C. *Solvents and Solvent Effects in Organic Chemistry*, 3rd ed.; Wiley-VCH: Weinheim, 2003.