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Kinetics of Nitroxide Radical Trapping. 1. Solvent Effects[1]

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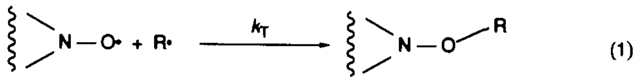
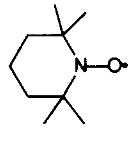
Abstract: Solvent effects on the kinetics of the nitroxide radical trapping (NRT) of various carbon-centered radicals have been probed both by using the radical "clock" method and by the laser flash photolysis (LFP) technique. Although the rate constants for NRT, k_T, are lower than the diffusion-controlled limit they are, nevertheless, influenced by solvent viscosity. Rate constants are even more strongly influenced by the ability of the solvent to solvate the nitroxide. Thus, using the 2,2-dimethyl- to 1,1-dimethyl-3-butenyl radical clock rearrangement, $1^\bullet \xrightarrow{k_C} 2^\bullet$, at 80 °C ($k_C = 2.4 \times 10^7$ s^{-1}) with 1,1,3,3-tetramethylisoindole-2-oxyl (TMIO) as the trap, in 32 solvents ranging from alkanes to aqueous methanol, it was found that log (k_T/k_C)/M^{-1}) was strongly correlated with the nitroxide's solvation, as gauged by the solvent's effect on the nitrogen hyperfine splitting of a structurally analogous nitroxide ($\langle r \rangle = 0.961$ for 26 nonhydroxylic solvents, the hydroxylic solvents forming a separate group). Similar results were obtained at 80 °C with five other radical clocks using smaller solvent sets. Comparison of these radical clock data with the kinetic results obtained by LFP at 18 °C for the NRT of benzyl (22 solvents), *n*-nonyl (4), and neopentyl (6) radicals by Tempo provides the first unequivocal proof that the kinetics of commonly used alkyl radical clock rearrangements are essentially uninfluenced by solvent properties. Although NRT is primarily an activation-controlled reaction, the magnitude of k_T is decreased by an increase in solvent viscosity as is clearly indicated by LFP data for the trapping of benzyl radicals by the sterically unencumbered, Bredt's rule protected nitroxide, 9-azabicyclo[3.3.1]nonane-*N*-oxyl (ABNO) in saturated hydrocarbons ($\eta = 0.3$–16 cP). Using a model for a partially diffusion-controlled reaction, we obtained a theoretical diffusion-controlled limiting rate constant, $k_s \approx 3.5 \times 10^9$ M^{-1} s^{-1}, for ABNO/benzyl coupling in a solvent of viscosity $\eta = 1$ versus an extrapolated zero viscosity or "activation" limit, $k_\infty = 1.4 \times 10^9$ M^{-1} s^{-1}. The Tempo/benzyl coupling in saturated hydrocarbons is less curtailed by diffusion since the diffusion/activation ratio is higher, viz., $k_s/k_\infty \approx 3.0 \times 10^9/0.48 \times 10^9$ (for $\eta = 1$).

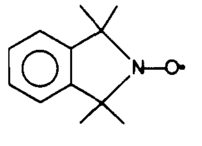
By analogy with many other radical–radical reactions, and in the absence of strong experimental evidence to the contrary, there has been a general expectation[3,4] that the coupling of nitroxides with carbon-centered radicals (reaction 1) in organic solvents will be a diffusion-controlled process.[5] However, recent time-resolved measurements using laser flash photolysis[6] (LFP) and an application[7] of the "radical-clock"[8] methodology have established that stable nitroxides such as 2,2,6,6-tetramethylpiperidin-1-oxyl (Tempo) and 1,1,3,3-tetramethylisoindoline-2-oxyl (TMIO) trap alkyl radicals with rate constants which are about an order of magnitude slower than the rate constants for the bimolecular self-reactions of the alkyl radicals. For example,[6] nitroxide radical trapping (NRT) rate constants, k_T,[9] for Tempo[10] in isooctane at room temperature are 1.2×10^9, 7.6×10^8, and 4.9×10^8 M^{-1} s^{-1} for *n*-nonyl, *tert*-butyl, and benzyl radicals, respectively. For comparison,[12] the room temperature rate constants for the alkyl radical bimolecular self-reactions in comparable solvents are 2.4×10^{10} M^{-1} s^{-1} for *n*-pentyl,[13] 7×10^9 M^{-1} s^{-1} for *tert*-butyl,[14] and 5×10^9 M^{-1} s^{-1} for benzyl.[15]



(1)



Tempo

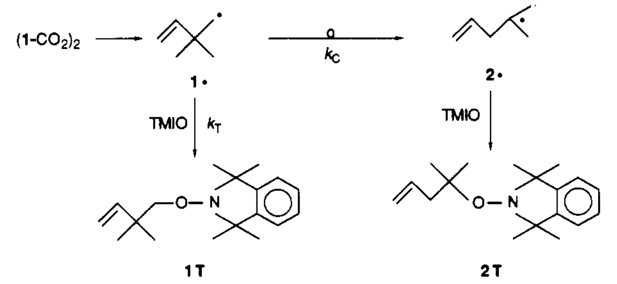


TMIO

The departure of NRT kinetics from diffusion-controlled values is also evident in their temperature dependence. Thus, the Arrhenius parameters for NRT, viz., log (A_T/M^{-1} s^{-1}) = 9.5–10.5 and E_T = 0.3–1.7 kcal/mol,[6,7] are significantly lower than the parameters for diffusion-limited reactions which, typically, are[12] log (A/M^{-1} s^{-1}) ~ 11.5 and E ~ 3.0 kcal/mol.

The application of NRT as an accurate kinetic probe in free radical reactions requires reliable k_T values in a variety of solvents.

Scheme I



Earlier investigations[16] revealed that the reactivity of TMIO is markedly affected by the polarity of the solvent. Furthermore,

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(3) Robbins, W. K.; Eastman, R. H. *J. Am. Chem. Soc.* **1970**, *92*, 6077–6079.

(4) Mathew, L.; Warkentin, J. *J. Am. Chem. Soc.* **1986**, *108*, 7981–7984.

(5) However, spin statistical factors cause the rate constants for diffusion-controlled radical–radical reactions to be $\approx 0.25 k_{diff}$ (vide infra).

(6) Chateauneuf, J.; Lusztyk, J.; Ingold, K. U. *J. Org. Chem.* **1988**, *53*, 1629–1632.

(7) Beckwith, A. L. J.; Bowry, V. W.; Moad, G. *J. Org. Chem.* **1988**, *53*, 1632–1641.

(8) Griller, D.; Ingold, K. U. *Acc. Chem. Res.* **1980**, *13*, 317–323.

(9) For simplicity, the nitroxides used in this work are generally denoted by T$^\bullet$, their radical-trapping rate constants by k_T, and the radical-trapping reactions by $U^\bullet + T^\bullet \rightarrow UT$ for the unrearranged radical and $R^\bullet + T^\bullet \rightarrow RT$ for the rearranged radical.

(10) Values of k_T for Tempo and TMIO are very similar.[6,7] For example,[7] for the ethyl radical in cyclohexane at 80 °C k_T(TMIO) = (1.05 ± 0.05)k_T(Tempo). This similarity does not extend to much less hindered nitroxides (vide infra and ref 11).

(11) Bowry, V. W.; Ingold, K. U. *J. Am. Chem. Soc.*, following paper in this issue.

(12) For reviews and data compilations see (a) Ingold, K. U. In *Free Radicals*; Kochi, J. K., Ed.; Wiley: New York, NY, 1973; Vol. 1, pp 37–112. (b) Koenig, T.; Fischer, H. In *Free Radicals*; Kochi, J. K., Ed.; Wiley: New York, NY, 1973; Vol. 1, pp 157–189. (c) Fischer, H.; Paul, H. *Acc. Chem. Res.* **1987**, *20*, 200–206. (d) Griller, D. In *Landolt-Börnstein, New Series, Radical Reaction Rates in Liquids*; Fischer, H., Ed.; Springer-Verlag: Berlin, 1984; Vol. 13a, pp 5–134.

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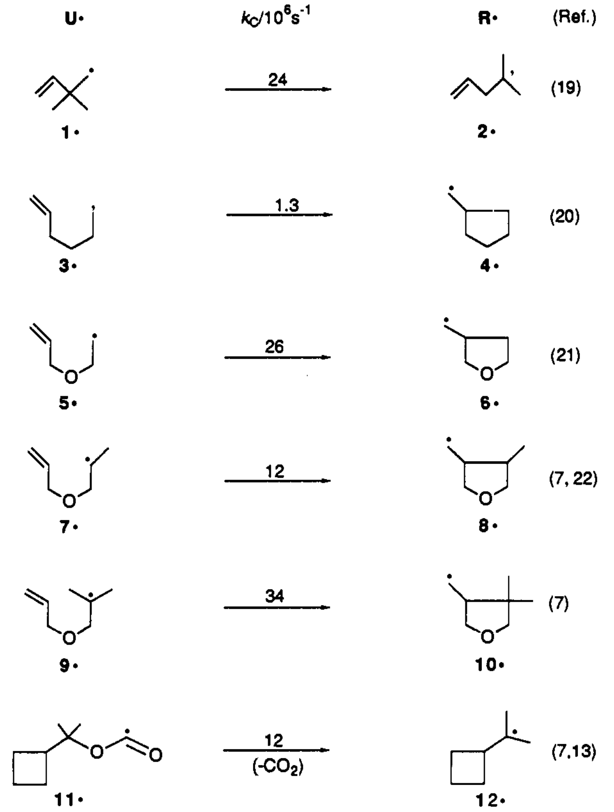
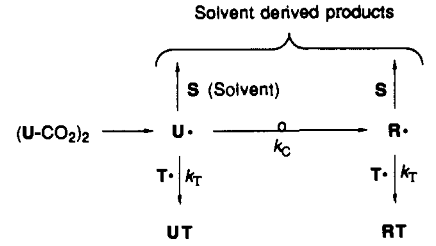
Chart I. Radical Clock Reactions ($U^\bullet \rightarrow R^\bullet$) and Rate Constants at 80 °C



pulse radiolytic data for NRT in water[17] indicates that k_T values in this solvent are significantly lower than in hydrocarbon solvents.[6] To define the nature of this solvent dependence, we have employed the radical-clock[8] approach in which NRT of a carbon-centered radical competes with a unimolecular rearrangement or scission of the carbon-centered radical, the latter reaction occurring with a known rate constant, $k_{Clock} = k_C$ (see, e.g., Scheme I). Since this procedure yields only the rate constant ratio, k_T/k_C, there is some ambiguity as to whether the solvent dependence derives from the radical-trapping reaction or from the clocking reaction. The former is the more likely since what little evidence is available[18] suggests that there are no significant solvent effects on the rearrangement of the 5-hexenyl radical, **3**$^\bullet$, to the cyclopentylmethyl radical, **4**$^\bullet$ (see Chart I). Nevertheless, we also made a large number of absolute measurements of k_T in selected solvents by LFP.[6] These have confirmed that the observed solvent effects in the radical-clock experiments are due primarily to the NRT reactions.

Results

Scheme II



Radical Clock Measurements. The method has been described in an earlier paper.[7] In brief, unrearranged clock radicals, $U^\bullet$ were thermally generated at 80 °C in the presence of a large excess of the nitroxide. Kinetic competition between the unimolecular clock reaction of this radical to form the rearranged radical $R^\bullet$ ($U^\bullet \rightarrow R^\bullet$, rate constant k_C, see Chart I[7,13,19-22]) and radical trapping by the nitroxide (reaction 1) produces mixtures of trialkylhydroxylamines (i.e., unrearranged UT and rearranged RT, see Scheme I)[9] the compositions of which are governed by the pseudo-first-order equation

$$[UT]/[RT] = [T^\bullet](k_T/k_C) \tag{I}$$

With TMIO as the nitroxide trap the [UT]/[RT] ratios were readily determined by HPLC with UV detection and quantitation of the trialkylhydroxylamine products.

The isomerization of the 2,2-dimethyl-3-butenyl radical, **1**$^\bullet$ (see Scheme I), was used as the "standard" clock reaction in this study for both practical and theoretical reasons, including the following: (i) The products, **1T** and **2T**, are stable,[23] chromatographically well separated, and have high retention on reversed-phase HPLC, and thus they are not likely to be confused with byproducts arising from NRT of solvent-derived radicals or from direct nitroxide/peroxide[24,25] reactions. (ii) The relatively fast rearrangement of this clock (see Chart I) allows HPLC analyses of "neat" reaction mixtures, whereas reaction mixtures from slower clocks, such as the 5-hexenyl radical, **3**$^\bullet$, have to be concentrated prior to analysis. (iii) Radical **1**$^\bullet$ is neopentylic, nonpolar, and relatively compact—factors which would be expected to minimize solvent effects on the clocking reaction, i.e., on k_C.

The solvents chosen for this study include those most commonly employed during organic syntheses via free radicals and for kinetic studies on radical reactions. They display a wide range of solvent polarities, ranging from aliphatic hydrocarbons to mixtures of methanol and water. Diethyl malonate and methyl acrylate were included because of indications[26,27] that they display especially strong binding with nitroxides or other radicals. It is worth noting that NRT experiments can be carried out even in solvents, such as CCl_4, which cannot be used for tin hydride-promoted radical-chain reactions.

The unrearranged radical, $U^\bullet$, and the rearranged radical, $R^\bullet$, may both react with the solvent (see Scheme II). The former reaction will not affect the [UT]/[RT] ratio but the latter reaction will increase this ratio. If it is significant it may be detected by a positive intercept at $[T^\bullet] = 0$ in a plot of [UT]/[RT] vs $[T^\bullet]$ (cf. eqs I and II[28]).

$$[UT]/[RT] = (k_S/k_C)[S] + (k_T/k_C)[T^\bullet] \tag{II}$$

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(23) The trapped tertiary alkyl radical, **2T**, is the most heat-sensitive trialkylhydroxylamine, but even so, it had a life-time at 126 °C of 19 h in cyclohexane and 3 h in ethanol.

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(28) Scheme II and eq II assume, for simplicity, equal trapping rates for $U^\bullet$ and $R^\bullet$. If this is not the case, i.e., if $k_T{}^U = \alpha k_T{}^R$, ($\alpha \neq 1$) eq II becomes $[UT]/[RT] = \alpha(k_S/k_C)[S] + (k_T{}^U/k_C)[T^\bullet]$. This extrapolation procedure is the only reliable guide to the occurrence of $R^\bullet + S$ reactions because solvent-derived trialkylhydroxylamines, ST, can also be formed via the $U^\bullet + S$ reaction. Furthermore, some ST are unstable, e.g., Cl_3C–T (formed when S = CCl_4) partially decomposes during an HPLC analysis. Moreover, if S yields a polar radical the ST may be difficult to distinguish by HPLC from $T^\bullet$ and from $T^\bullet$-induced peroxide decay products,[7,24,25] e.g., in acrylonitrile some ST co-eluted with the TMIO under the conditions used to analyze UT and RT.[29]

(29) Bowry, V. W. Unpublished results.

Table I. Effects of Solvents on k_T/k_C at 80 °C Using $1^\bullet \rightarrow 2^\bullet$ as the Radical Clock and TMIO as the Nitroxide Trap

no.	solvent	$[T^\bullet]/10^{-3}$ M[a]	[**1**T]/[**2**T][b]	$(k_T/k_C)/M^{-1}$ [c]	a^N/G[d]	c/(cal cm^{-3})
1	isooctane	19.7, 39.1	0.62, 1.29	32.2 (4)	15.22[f]	48
2	*n*-pentane	18.6, 37.4	0.56, 1.08	33.1 (3)	15.22[f,g]	49
3	*n*-hexane	19.2, 39.4	0.61, 1.23	31.8 (2)	15.22	53
6	*n*-dodecane	19.9, 39.9	0.64, 1.24	27.1 (8)	15.22[f]	63
9	cyclopentane	19.6, 38.7	0.57, 1.13	29.2 (2)	15.24[g]	76
10	cyclohexane	17.9, 35.6	0.50, 1.03	28.5 (4)	15.25[g]	68
11	cyclooctane	17.4, 35.8	0.45, 0.93	26.0 (2)		
13	benzene	17.9, 35.7	0.28, 0.56	16.0 (2)	15.53	85
14	chlorobenzene	18.9, 37.7	0.27, 0.54	14.4 (1)	15.56	90
15	perfluorobenzene	40.9	0.61	14.9	15.55[g]	66
16	diethyl ether	15.5, 43.0	0.29, 0.80	18.6 (4)	15.42	55
17	1,2-dimethoxyethane	32.9, 66.4	0.52, 1.05	15.8 (0)	15.53	74
18	tetrahydrofuran	35.6, 70.7	0.52, 1.07	15.1 (4)	15.47	83
19	1,4-dioxan	33.8, 67.4	0.51, 1.01	15.0 (6)	15.54	100
20	CCl_4	4.9, 15.6, 40.0, 77.0	0.16_5, 0.37, 0.76, 1.44	17.5[h]	15.40	74
21	$CHCl_3$	24.3, 48.1	0.20, 0.44	8.2 (4)	15.78	86
22	CH_2Cl_2	16.6, 85.7	0.13, 0.66	7.7 (2)	15.78	94
23	acetone	35.8, 87.7	0.51, 1.26	14.5 (2)	15.62	98
24	acetonitrile	79.1	0.64	8.1	15.76	141
25	ethyl acetate	44.4	0.67	15.8	15.52[g]	83
26	diethyl malonate	17.9, 35.7, 71.2	0.26, 0.54, 1.02	14.8 (2)	15.52[i]	106
27	methyl acrylate	22.0, 50.0, 96.0	0.89, 1.08, 1.68	10.9[j]	15.59[i]	79
28	3 + 27 (1:1, v/v)	21.0, 52.0, 95.0	0.59, 1.23, 1.78	15.9[k]		
29	dimethyl sulfoxide	36.5, 72.1	0.40, 0.82	11.2 (2)	15.77	144
30	*N,N*-dimethylformamide	33.6, 66.4	0.44, 0.89	13.2 (2)	15.67	147
31	propylene carbonate	79.0	0.84_5	10.7	15.83[g]	177
32	*tert*-butyl alcohol	29.5	0.37	12.7	15.91	113
33	isopropyl alcohol	16.9, 67.1	0.20, 0.79	11.7 (3)	16.04	132
34	ethanol	35.4, 71.4	0.39, 0.82	11.3 (2)	16.08	162
35	methanol	35.8, 89.3	0.37, 0.91	10.2 (3)	16.20	209
36	H_2O + 35 (1:3, v/v)	67.7	0.87	12.8		
38	ethylene glycol	14.2, 28.8	0.44, 0.88	30.6 (1)	16.30	214

[a] Corrected for thermal expansion of the solvent and for consumption of the TMIO. [b] Respective values averaged from at least two analyses for each $[T^\bullet]$. [c] Mean value calculated using eq I unless otherwise noted. Standard deviations (in parentheses) are in units of the last significant figure. [d] Values are from ref 53 unless otherwise noted. [e] Cohesive pressure c ($=\delta^2$, where δ is the Hildebrand solubility parameter) at 25 °C. Values of δ at 25 °C were taken from: Barton, A. F. M. *Handbook of Solubility Parameters and Other Cohesion Parameters*; CRC Press: Boca Raton, FL, 1983. (Note, 1.0 cal cm^{-3} = 41.3 atm). [f] Assumed to be the same as for *n*-hexane. [g] Interpolated using data for di-*tert*-butyl nitroxide taken from ref 54. [h] According to eq II, these data yield: $[\mathbf{1}T]/[\mathbf{2}T] = 0.081 + 17.5\,([T^\bullet]/M)$, correlation coefficient, $\langle r \rangle = 0.999$. [i] Measured for this work with Tempo and corrected by −0.09 G to make the value measured for Tempo in isooctane (viz., 15.31 G) coincide with the value reported in ref 53 in isooctane. [j] According to eq II, these data yield: $[\mathbf{1}T]/[\mathbf{2}T] = 0.606 + 10.9\,([T^\bullet]/M)$, $\langle r \rangle = 0.989$. [k] According to eq II, these data yield: $[\mathbf{1}T]/[\mathbf{2}T] = 0.311 + 15.9\,([T^\bullet]/M)$, $\langle r \rangle = 0.991$.

Data obtained from NRT reactions at 80 °C in 32 solvents using **1** → **2** as the radical clock and TMIO as the trap are summarized in Table I. In each solvent the product data were consistent with kinetic equation I except for carbon tetrachloride (solvent 20) and methyl acrylate (27 and 28) where the data were consistent with kinetic equation II (see footnotes *h*, *j*, and *k* in Table I).[30]

The effect of certain representative solvents on k_T/k_C values was assessed in the same way for the five other clock radicals shown in Chart I. Radicals **3** and **5** were generated from the corresponding diacyl peroxides, $(U\text{-}CO_2)_2$, and thus afforded simple product mixtures similar to those from $(\mathbf{1}\text{-}CO_2)_2$.[7] Radicals **7**, **9**, and **11**, on the other hand, were generated from *tert*-butyl peroxyesters (reaction 2) and afforded more complex product mixtures arising from concomitant reactions of the *tert*-butoxyl radicals (reactions 3 and 4).

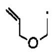
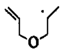
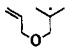
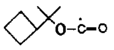
$$U\text{-}C(O)OOCMe_3 \rightarrow U^\bullet + CO_2 + Me_3CO^\bullet \qquad (2)$$

$$Me_3CO^\bullet + S \rightarrow Me_3COH + S^\bullet \xrightarrow{T^\bullet} ST \qquad (3)$$

$$Me_3CO^\bullet \rightarrow Me_2CO + Me^\bullet \xrightarrow{T^\bullet} MeT \qquad (4)$$

Values of k_T/k_C for the selected clock/solvent combinations have been expressed in Table II relative to the k_T/k_C values found for each clock in cyclohexane. It can be seen that the solvent effects on k_T/k_C values are very similar for all six clocks—a fact which certainly suggests that the solvents influence k_T to a much greater extent than k_C. Indeed, the differences in relative k_T/k_C values between some of the clocks which can be seen in benzene, methylene chloride, and ethanol are so small that they are more likely to reflect experimental errors than some specific solvent effect on one or more of the clocking reactions.

Table II. Effects of Selected Solvents on Relative (k_T/k_C)/M Values at 80 °C for Various Radical Clocks Reacting with TMIO[a]

no.	solvent	 **1**·	 **3**·	 **5**·	 **7**·	 **9**·	 **11**·
10	cyclohexane	(1)[b]	(1)[b]	(1)[b]	(1)[b]	(1)[b]	(1)[b]
3	*n*-hexane	1.1	1.2	1.1	1.1	1.1	1.2
13	benzene	0.56	0.76	0.62	0.72	0.55	0.85
22	CH_2Cl_2	0.27	0.34	0.20	0.24	0.23	0.20
34	ethanol	0.40	0.40			0.34	
10	cyclohexane	28.5[c]	1030[c]	77[c]	28[c]	53[c]	169[c]

[a] Values given are the mean of data from two nitroxide concentrations (cf. Table I). [b] Assumed. [c] Absolute values of $(k_T/k_C)/M^{-1}$ in cyclohexane.

The effect of temperature on k_T/k_C ratios was also examined from 60 to 120 °C using three of the clocks and the same selected solvents as in Table II. Relative Arrhenius parameters are given in Table III, with cyclohexane again chosen as the reference solvent. Unfortunately, the experimental uncertainties (see footnotes *b* and *c* in Table III) are comparable in magnitude to the observed solvent variation in the Arrhenius parameters, although in ethanol the limited data available does suggest that both log $(A_T/A_C/M^{-1})$ and $E_T - E_C$ may be slightly larger than in the other four solvents. Since the kinetic solvent effect arises from

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[30] If we take k_C for **1** → **2** to be 2.4×10^7 s^{-1} at 80 °C[19] and α (see footnote 28) = 1.4,[6] the magnitude of the intercepts reported in footnotes *h* and *j* yield bimolecular rate constants, k_S, of 1.6×10^5 M^{-1} s^{-1} and 9×10^5 M^{-1} s^{-1}, for the reactions of the tertiary radical **2** with CCl_4 and methyl acrylate, respectively, at this temperature.

Table III. Effects of Selected Solvents on Relative Arrhenius Parameters for Various Radical Clocks Reacting with TMIO[a]

		$1^\bullet \to 2^\bullet$		$3^\bullet \to 4^\bullet$		$9^\bullet \to 10^\bullet$	
no.	solvent	Δ log $A_{T/C}$[b]	$\Delta E_{T/C}$[c]	Δ log $A_{T/C}$[b]	$\Delta E_{T/C}$[c]	Δ log $A_{T/C}$[b]	$\Delta E_{T/C}$[c]
10	cyclohexane	(0)[d]	(0)[d]	(0)[d]	(0)[d]	(0)[d]	(0)[d]
3	*n*-hexane	0.2	0.3	0.1_5	0.1	-0.2_5	−0.4
13	benzene	0.0	0.4	−0.4	-0.4_5	−0.1	0.0
22	CH_2Cl_2	−0.1	0.9	0.2	1.0	−0.8	−3.3
34	ethanol	0.8	1.9	1.3	2.7		
10	cyclohexane	−2.0[e]	−5.6[f]	−1.0[e]	−6.4[f]	−0.6[e]	-3.8_5[f]

[a] Reaction temperatures: 60, 80, 100, and 125 °C (±0.3 °C). [b] $\Delta \log A_{T/C} = \log ((A_{NRT}/A_{clock})/M^{-1})_{cyclohexane} - \log ((A_{NRT}/A_{clock})/M^{-1})_{solvent}$; median 95% confidence limits (2σ) based on random scatter are ±0.9 log unit. [c] $\Delta E_{T/C} = (E_{NRT} - E_{clock})_{cyclohexane} - (E_{NRT} - E_{clock})_{solvent}$ (kcal/mol); median 95% confidence limits (2σ) based on random scatter are ±0.5 kcal/mol. [d] Assumed. [e] Absolute value of log $((A_T/A_C)/M^{-1})$ in cyclohexane. [f] Absolute value of E_T/E_C (kcal/mol) in cyclohexane.

the trapping reaction (vide infra), this could imply that in ethanol A_T is enhanced by a factor of ca. 10 and E_T by ca. 2 kcal/mol.

Laser Flash Photolysis Measurements. The experimental procedures[6] and instrumentation[31] have been described in detail elsewhere. In brief, LFP (308 nm) of dibenzyl ketone afforded benzyl radicals "instantaneously" and their decay was monitored via their 317-nm absorption. In the absence of radical quenchers the decay was second order but the addition of a nitroxide (typically [$T^\bullet$] was increased from zero to ca. 10^{-2} M in five to seven increments of 2×10^{-3} M)[32] produced more rapid decay of the benzyl radicals which now followed pseudo-first-order kinetics. Variation of the experimental first-order rate constant, k_{exptl}, with [$T^\bullet$] was linear and afforded the NRT rate constants (k_T, see Table IV) by least-squares fitting of the data to eq III. In the case of

$$k_{exptl} = k_0 + k_T[T^\bullet] \tag{III}$$

the *n*-nonyl and neopentyl radicals, generation was by 308 nm LFP of the parent diacyl peroxides (reaction 5). Since these two radicals do not have an absorption in the near-UV region the reaction was carried out in the presence of 1,1-diphenylethylene as a "probe".[6,31,36] The alkyl radicals add to the probe to form 1,1-diphenylcarbinyl radicals (reaction 6) and the growth of the absorption due to these latter radicals was monitored at 327 or 329 nm.[6,37,38] The pseudo-first-order grow-in rate constant, k_{exptl}, for this absorption affords k_T (see Table IV) by least-squares fitting of the data to eq IV.[39]

$$(U\text{–}CO_2)_2 \xrightarrow[308\ \text{nm}]{h\nu} 2U^\bullet + 2CO_2 \tag{5}$$

$$U^\bullet + H_2C{=}C(C_6H_5)_2 \to UCH_2\dot{C}(C_6H_5)_2 \tag{6}$$

$$k_{exptl} = k_0 + k_6[H_2C{=}C(C_6H_5)_2] + k_T[T^\bullet] \tag{IV}$$

Table IV. Effects of Solvents on the Absolute Rate Constants for Tempo Trapping of Benzyl, *n*-Nonyl, and Neopentyl Radicals As Measured by LFP at 18 ± 2 °C

		benzyl radicals[a]		
no.	solvent	$k_T/(10^7\ M^{-1}\ s^{-1})$[b]	η/cP[c]	a^N/G[d]
1	isooctane	48 ± 3	0.53	15.22[e]
2	*n*-pentane	50 ± 15	0.236	15.22[e,f]
3	*n*-hexane	48 ± 4	0.324	15.22
4	*n*-heptane	46 ± 3	0.418	15.22[e]
5	*n*-octane	44 ± 2	0.555	15.22[e]
7	*n*-hexadecane	31 ± 4	3.55	15.22[e]
8	7 + paraffin oil	13 ± 2	17[g]	15.22[e]
9	cyclopentane	39 ± 2	0.447	15.24[f]
10	cyclohexane	41 ± 2	1.01	15.25[f]
12	$(H_3C)_2\overline{CCH_2C}(CH_3)_2$	43 ± 5		
13	benzene	18 ± 1	0.675	15.53
14	chlorobenzene	17 ± 2	0.83	15.56
16	diethyl ether	26 ± 2	0.239	15.42
18	tetrahydrofuran	23 ± 3	0.499	15.47
19	1,4-dioxan	16 ± 2	1.37	15.54
22	CH_2Cl_2	5.6 ± 0.4	0.444	15.78
24	acetonitrile	9.5 ± 0.7	0.390	15.76
25	ethyl acetate	17 ± 2	0.461	15.52[f]
34	ethanol	15 ± 1	1.23	16.08
35	methanol	13 ± 1	0.607	16.20
37	H_2O + 35 (1.8:1, v/v)	12 ± 1[g]		(16.99)[h]
38	ethylene glycol	7.9 ± 0.2	22	16.30

no.	solvent	*n*-nonyl radicals[i] $k_T/(10^7\ M^{-1}\ s^{-1})$	neopentyl radicals[i] $k_T/(10^7\ M^{-1}\ s^{-1})$
1	isooctane	95 ± 6	64 ± 12
3	*n*-hexane		61 ± 9
10	cyclohexane	85 ± 18	52 ± 8
13	benzene	67 ± 16	42 ± 1
24	acetonitrile	15 ± 3	15 ± 3
35	methanol		17 ± 3

[a] Generated by 308 nm LFP of 3×10^{-3} M dibenzyl ketone and monitored by their own 317 nm absorption. [b] ±2σ (95% confidence limits). [c] All at 18 °C. Values have been taken (unless otherwise noted) from: Viswanath, D. S.; Natarajan, G. *Data Book on the Viscosity of Liquids*; Hemisphere Publishing Co.: New York, 1989; and from: Andrussow, L. In *Landolt–Börnstein*; Springer-Verlag: Berlin, 1969; Vol. II, Part 5, pp 148–265. [d] Values are from ref 53 unless otherwise noted. [e] Assumed to be the same as for *n*-hexane. [f] Interpolated using data for di-*tert*-butyl nitroxide taken from ref 54. [g] Measured for 3×10^{-3} M dibenzyl ketone in the mixed solvent actually employed. [h] Value for pure water. [i] Generated by 308 nm LFP of 1.5×10^{-3} M solutions of the parent diacyl peroxides and monitored at 329 nm via their addition to 0.10 M 1,1-diphenylethylene.

Table V. Effects of Solvents on the Absolute Rate Constants for ABNO Trapping of Benzyl Radicals[a] As Measured by LFP at 18 ± 2 °C

no.	solvent	$k_T/(10^7\ M^{-1}\ s^{-1})$	η/cP[c]
1	isooctane	120 ± 9	0.53
3	*n*-hexane	131 ± 11	0.324
6	*n*-dodecane	103 ± 4	1.58
7	*n*-hexadecane	58 ± 4	3.55
8′	7 + paraffin oil	19 ± 2	16[d]
9	cyclopentane	100 ± 15	0.447
10	cyclohexane	86 ± 9	1.01
13	benzene	42 ± 1	0.675
24	acetonitrile	19 ± 2	0.390

[a] Generated by 308 nm LFP of 3×10^{-3} M dibenzyl ketone and monitored by their own 317 nm absorption. [b] ±2σ (95% confidence limits). [c] All at 18 °C. Values have been taken (unless otherwise noted) from Viswanath, D. S.; Natarajan, G. *Data Book on the Viscosity of Liquids*; Hemisphere Publishing Co.: New York, 1989; and from Andrussow, L. In *Landolt–Börnstein*; Springer-Verlag: Berlin, 1969; Vol. II, Part 5, pp 148–265. [d] Measured for 3×10^{-3} M dibenzyl ketone in the mixed solvent actually employed.

In nonviscous solvents the trapping of benzyl and alkyl radicals by Tempo and TMIO occurs at rates which are significantly below the diffusion-controlled limit. To explore the possibility that this is due, in whole or in part, to a steric retardation of trapping by

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[31] Scaiano, J. C. *J. Am. Chem. Soc.* **1980**, *102*, 7747–7753. Scaiano, J. C.; Tanner, M.; Weir, D. *J. Am. Chem. Soc.* **1985**, *107*, 4396–4403.

[32] Because carbon-centered radicals react rapidly with nitroxides the quenching plots made according to eq V could be obtained at [$T^\bullet$] < 2×10^{-2} M. Such low maximum $T^\bullet$ concentrations reduced the significance of photochemical $T^\bullet$/solvent reactions such as halogen atom transfer from CH_2Cl_2[33,34] and hydrogen atom transfer from CH_3CN.[35]

[33] Chateauneuf, J.; Lusztyk, J.; Ingold, K. U. *J. Org. Chem.* **1990**, *55*, 1061–1065.

[34] Unfortunately, the halogen atom transfer reaction precluded all LFP measurements of k_T in CCl_4, $CHCl_3$, and Freons. In CH_2Cl_2 this reaction is less important which allowed k_T to be measured for the benzyl radical but not for the *n*-nonyl and neopentyl radicals.

[35] Johnston, L. J.; Tencer, M.; Scaiano, J. C. *J. Org. Chem.* **1986**, *51*, 2806–2808.

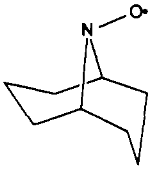
[36] Paul, H.; Small, R. D., Jr.; Scaiano, J. C. *J. Am. Chem. Soc.* **1978**, *100*, 4520–4527.

[37] Bowry, V. W.; Lusztyk, J.; Ingold, K. U. *J. Am. Chem. Soc.* **1991**, *113*, 5687–5698.

[38] The 327–329 nm absorption due to the $UCH_2\dot{C}(C_6H_5)_2$ radicals grows to a "plateau" (see figure in ref 6) because these radicals are about an order of magnitude less reactive than nonresonance stabilized $U^\bullet$ radicals toward the sterically hindered nitroxides, Tempo and TMIO.

[39] Values of k_T obtained by the probe technique are somewhat less precise than the more directly measured k_T values for the benzyl radical (cf. confidence limits in Table IV).

the four methyl groups adjacent to the >N–O• moieties in these two nitroxides, we synthesized the sterically unencumbered, Bredt's rule protected nitroxide, 9-azabicyclo[3.3.1]nonane-*N*-oxyl (ABNO).[40–44] Rate constants for benzyl radical trapping by ABNO in various solvents were measured by LFP as described above. They are given in Table V. Unfortunately, rate constants for the ABNO trapping of *n*-nonyl and neopentyl radicals could not be determined by LFP using 1,1-diphenylethylene as a probe. This is because ABNO shows little tendency to discriminate between sterically crowded, resonance-stabilized radicals such as $UCH_2\dot{C}(C_6H_5)_2$ and sterically undemanding nonstabilized radicals.[11]



ABNO

Discussion

"Slow" Radical–Radical Reactions. General Comments. Several classes of radicals are known to undergo their bimolecular self-reactions at rates which are significantly slower than the diffusion-controlled limits. The effect of solvents on such "slow" bimolecular radical self-reactions has, for example, been examined for transient nitroxides,[17,40,45] for sterically-hindered phenoxyl radicals,[46] and for *tert*-butylperoxyl radicals,[47] with the magnitudes of the observed solvent effects varying from dramatic for the nitroxides to moderate for the phenoxyls to negligible for the peroxyl radical. It appears to be generally agreed[45–47] that all "slow" bimolecular self-reactions of radicals, X•, involve the reversible formation of an intermediate, (2X), which may lie on (reaction 7) or off (reaction 8) the overall reaction pathway from

$$X^\bullet + X^\bullet \rightleftarrows (2X) \rightleftarrows \text{products} \qquad (7)$$

$$(2X) \rightleftarrows X^\bullet + X^\bullet \rightleftarrows \text{products} \qquad (8)$$

the radicals to the final products. Considering what is probably the more common situation which is represented by reaction 7, the radicals react in the first, diffusion-controlled step to form a short lived "intermediate", which may be just a caged radical pair or may be some kind of complex stabilized, for example, by dipole–dipole interactions, or may even be an identifiable but short-lived σ-bonded molecule.[48] This intermediate can then decay back to the starting radicals or forward to the products with both of these reactions involving activated transition states. These reactions are therefore slower than diffusion-control, and the solvent effects arise because of differences in the free energies of solvation of X•, (2X), and the activated transition states.

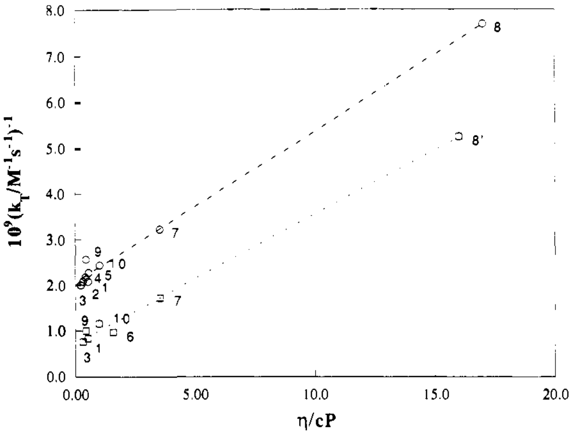


Figure 1. Plot of the reciprocal of the LFP measured rate constant for benzyl radical trapping at 18 °C by Tempo, ○, and by ABNO, □, versus viscosity in saturated alkane solvents. Data have been taken from Tables IV and V.

Activation vs Diffusion Control in NRT. We are not aware of any previous study of solvent effects on a "slow" radical–radical reaction which involves different radicals. The effects we have observed are rather modest. For example, comparing the "fastest" solvent, pentane (2), with the "slowest" solvent, methylene chloride (22), we find for the TMIO trapping of **1** at 80 °C that k_T/k_C decreases by a factor of 4.3 (from 33.1 to 7.7 M^{-1}, see Table I), while for the Tempo trapping of the benzyl radical at 18 °C k_T decreases by a factor of 9 (from 5.0×10^8 to 5.6×10^7 M^{-1} s^{-1}, see Table IV).

The solvent effects on NRT presumably arise for the reason outlined above for the "slow" bimolecular reactions of identical radicals. That is, considering only the simple case analogous to that shown in reaction 7, a carbon-centered radical, U•, and a nitroxide, T•, react reversibly to form an intermediate complex, C, which can rearrange via an activated transition state to the trialkylhydroxylamine product, UT, reaction 9.

$$U^\bullet + T^\bullet \underset{k_d}{\overset{k_s}{\rightleftarrows}} C \xrightarrow{k_p} UT \qquad (9)$$

The experimental rate constant for trapping, k_T, is given by

$$k_T = k_s k_p/(k_d + k_p) \qquad (V)$$

where k_s corresponds to the diffusion-controlled encounters of radical pairs in the singlet state. This is $^1/_4$ of the total diffusion-controlled encounter rate since the spin statistical factor of $^1/_4$ must be introduced to account for the nonreactive encounters of radical pairs in triplet states.[5,12a,12c] The customary combination[12a,12c] of the von Smoluchowski equation for a diffusion-controlled reaction with the Stokes–Einstein relation, modified to a molecular scale,[49] yields

$$k_s \approx (R/\text{erg K}^{-1}\ \text{mol}^{-1})(T/\text{K})/10(\eta/\text{cP})\ M^{-1}\ s^{-1} \qquad (VI)$$

(corresponding to $k_s \approx 2.4 \times 10^9$ M^{-1} s^{-1} at 18 °C in a solvent $\eta = 1.0$ cP).

Equation V can be rearranged to

$$k_T^{-1} = k_\infty^{-1} + k_s^{-1} \qquad (VII)$$

where $k_\infty = k_p(k_s/k_d)$ is the limiting bimolecular rate constant

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[40] Mendenhall, G. D.; Ingold, K. U. *J. Am. Chem. Soc.* **1973**, *95*, 6395–6400.

[41] ABNO was chosen because it is more persistent in solution than nortropane-*N*-oxyl[40] and because it lacks the potentially photolabile carbonyl group which is present in 9-azabicyclo[3.3.1]nonan-3-one *N*-oxyl which was the first Bredt's rule protected nitroxide to be synthesized.[42]

[42] Dupeyre, R.-M.; Rassat, A. *J. Am. Chem. Soc.* **1966**, *88*, 3180–3181.

[43] The X-ray structure of 9-azabicyclo[3.3.1]nonan-3-one *N*-oxyl indicates a twin-chair conformation[44] but space-filling molecular models suggest that for ABNO this conformation would be less stable than a boat–chair conformation.

[44] Capiomont, A.; Chion, B.; Lajzerowicz, J. *Acta Crystallogr.* **1971**, *B27*, 322–326.

[45] Adamic, K.; Bowman, D. F.; Gillan, T.; Ingold, K. U. *J. Am. Chem. Soc.* **1971**, *93*, 902–908. Bowman, D. F.; Brokenshire, J. L.; Gillan, T.; Ingold, K. U. *J. Am. Chem. Soc.* **1971**, *93*, 6551–6555. Bowman, D. F.; Gillan, T.; Ingold, K. U. *J. Am. Chem. Soc.* **1971**, *93*, 6555–6561. Mendenhall, G. D.; Ingold, K. U. *J. Am. Chem. Soc.* **1973**, *95*, 6390–6394. Griller, D.; Perkins, M. J. *J. Am. Chem. Soc.* **1980**, *102*, 1354–1357. Marriott, P. R.; Ingold, K. U. *J. Phys. Chem.* **1980**, *84*, 937–938. Castelhano, A. L.; Griller, D.; Ingold, K. U. *Can. J. Chem.* **1982**, *60*, 1501–1503.

[46] Rüegge, D.; Fischer, H. *J. Chem. Soc., Faraday Trans. 1* **1988**, *84*, 3187–3205 and references cited.

[47] Bennett, J. E. *J. Chem. Soc., Faraday Trans.* **1990**, *86*, 3247–3252, and references cited.

[48] E.g., di-*tert*-butyl tetroxide.

[49] The diffusion coefficient of large species, A, in a fluid of viscosity, η, is given by the usual Stokes–Einstein relation: $D_A = kT/6\pi\eta r_A$, where r_A is the molecular radius of A. However, for a molecular-sized A the numerical coefficient should be reduced from 6 to about 4 or, for small molecules, even to a number less than 4, i.e., $D_A \gtrsim kT/4\pi\eta r_A$. See Edward, J. T. *J. Chem. Educ.* **1970**, *47*, 261–270.

in a solvent having no viscosity. For NRT that is "slow" relative to the encounter of singlet radical pairs $k_\infty \ll k_s$, and hence $k_T = k_\infty$. Thus, the reaction rate is determined solely by the difference in the free energy of the (solvated) transition state for the C $\rightarrow$ UT reaction and the free energies of the (solvated) radicals U$^\bullet$ and T$^\bullet$; i.e., the reaction is activation-controlled. For NRT that is "fast" relative to the encounter of singlet radical pairs $k_p \gg k_d$, i.e., $k_\infty \gg k_s$, and hence $k_T = k_s$. In this case, the reaction rate is determined by the transport properties of the solvent/reactant system.

LFP Study of Viscosity Effects on NRT in Saturated Hydrocarbon Solvents. Between the extremes of activation and diffusion control the reaction kinetics may be analyzed in terms of viscosity-dependent and viscosity-independent components. That is, since $k_s \propto \eta^{-1}$ (eq VI) and k_∞ is *defined* to be independent of viscosity, eq VII may be rewritten as

$$k_T^{-1} = k_\infty^{-1} + \eta(k_s\eta)^{-1} \qquad \text{(VIII)}$$

A plot of k_T^{-1} vs η should therefore yield a straight line with an intercept = k_∞^{-1} and a slope = $(k_s\eta)^{-1}$, *provided* there are no significant differences in the free energies of solvation between the reactants and the transition state. Thus, for a series of solvents, similar except for η, the diffusion-controlled limit for NRT is given by $k_s = (\eta \text{ slope})^{-1}$, i.e., for a solvent with $\eta = 1$, $k_s = \text{slope}^{-1}$.

Differences in the solvation free energies of the reactants and transition state are expected to be both minimal and constant for saturated hydrocarbon solvents. Plots of the LFP measured values of k_T^{-1} at 18 °C vs η at 18 °C are shown in Figure 1 for saturated hydrocarbon solvents and the benzyl radical/Tempo pair (data from Table IV) and benzyl radical/ABNO pair (Table V). For benzyl/Tempo, $k_\infty = 4.8 \times 10^8$ M^{-1} s^{-1} and $k_s\eta = 3.0 \times 10^9$ M^{-1} s^{-1} cP, $\langle r \rangle = 0.997$; while for benzyl/ABNO, $k_\infty = 1.4 \times 10^9$ M^{-1} s^{-1} and $k_s\eta = 3.5 \times 10^9$ M^{-1} s^{-1} cP, $\langle r \rangle = 0.997$.

The two calculated $k_s\eta$ values are in very satisfactory agreement with the value of ca. 2.4×10^9 M^{-1} s^{-1} cP predicted from a simple, diffusion-controlled model based on the von Smoluchowski and Stokes–Einstein equations and modified to a molecular scale[49] (vide supra).

The activation-controlled (i.e., limiting) rate constant, k_∞, for benzyl + Tempo in saturated hydrocarbon solvents has $^1/_3$ the magnitude of k_∞ for benzyl + ABNO in such solvents. This suggests that steric factors retard NRT by Tempo though, for this pair of nitroxides, there may also be some contribution from enthalpic effects since NRT by ABNO is expected to be ca. 6 kcal/mol more exothermic than NRT by Tempo.[50] However, the importance of steric factors in retarding NRT by Tempo is essentially confirmed by the k_∞ values that can be estimated from the Tempo NRT data for the nonyl and neopentyl radicals in the low viscosity saturated hydrocarbon solvents (see Table IV); i.e., $k_\infty \sim 1 \times 10^9$ M^{-1} s^{-1} for the nonyl radical and $k_\infty \sim 6.7 \times 10^8$ M^{-1} s^{-1} for the sterically more crowded neopentyl radical.

LFP Study of the Effects of Polar Solvents on NRT. If the NRT data for benzyl + Tempo or for benzyl + ABNO in any of the nonsaturated hydrocarbon solvents are plotted according to eq VIII all of the points are found to lie well above the corresponding lines (shown in Figure 1) for the saturated hydrocarbon solvents. This means that all these reactions are slower than would be predicted from the solvents' viscosities (as can also be seen by inspection of Tables IV and V). For all these solvents there must therefore be a difference between the free energies of solvation of the reactants and transition state, with the reactant radicals being more strongly solvated than the transition state. The carbon-centered radicals, U$^\bullet$, are not expected to be solvated to any significantly different extents from the corresponding U moieties in the product hydroxylamines, UT. However, there is abundant evidence to show that nitroxides are rather strongly solvated in polar, polarizable, and hydrogen-bonding solvents,[52-56] and they would be expected to be more strongly solvated than the T moiety of UT. We therefore attribute "reduced" k_T values in nonsaturated hydrocarbon solvents to preferential solvation of the nitroxide.

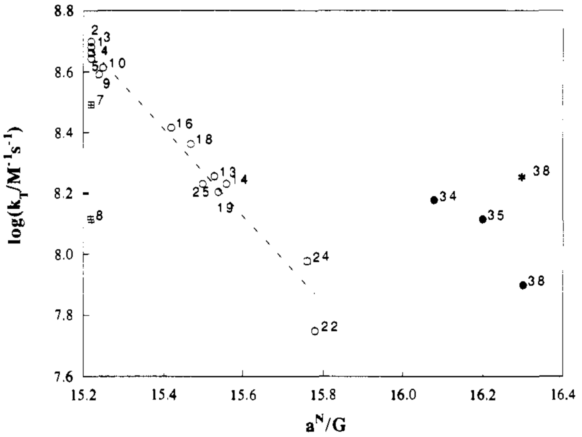
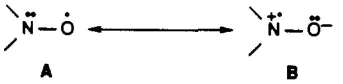


Figure 2. Plot of the logarithm of the LFP measured rate constant for benzyl radical trapping at 18 °C by Tempo versus the nitrogen hyperfine splitting for 4-amino-Tempo[53] in various solvents. Data have been taken from Table IV. The hydroxylic solvents are shown as filled circles. The asterisk for solvent 38 has been plotted at the estimated k_T for a solvent having all the properties of ethylene glycol except its high viscosity and on the assumption that a^N would be unchanged in such a hypothetical solvent (see text). The correlation line which has been drawn through the data for the nonhydroxylic solvents has been calculated without including the very viscous solvents, 7 and 8, which are shown as boxes.

It is not surprising that nitroxides should be rather strongly solvated by solvents other than saturated hydrocarbons, because in a valence bond representation of the nitroxide's three-electron bond, i.e.,



the two canonical forms, A and B, make about equal contributions to the overall electron distribution. Nitroxides therefore have substantial dipole moments.[57] Polar, polarizable, and hydrogen-bonding solvents stabilize the dipolar form, B, thereby increasing the spin density on nitrogen. This phenomenon can readily be quantified by measuring the ^{14}N hyperfine splitting, a^N, of a nitroxide in a variety of solvents,[53-55] since this quantity measures directly perturbations of the ground-state wave function of the solute radicals with good precision and with little interference from other species.[54]

In any analysis of solvent effects on chemical reactions it is customary to seek a linear relation between a solvent parameter and the logarithm of the rate constants for reaction, i.e., a "linear free energy" relationship.[56,59] For alkyl radical trapping by nitroxides we expected that the nitroxide's a^N values would provide a better correlation with log k_T than any of the other commonly used solvent parameters[46,56] because a^N values probe solvent/

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(50) The hydroxylamines obtained by reduction of ABNO and Tempo have O–H bond strengths of 76.2 and 69.6 kcal/mol, respectively.[51]

(51) Mahoney, L. R.; Mendenhall, G. D.; Ingold, K. U. *J. Am. Chem. Soc.* **1973**, *95*, 8610–8614.

(52) See ref 45 and references cited.

(53) Knauer, B. R.; Napier, J. J. *J. Am. Chem. Soc.* **1976**, *98*, 4395–4400.

(54) Reddoch, A. H.; Konishi, S. *J. Chem. Phys.* **1979**, *70*, 2121–2130.

(55) Kecki, Z.; Lyczkowski, B.; Kolodziejski, W. *J. Solution Chem.* **1986**, *15*, 413–422.

(56) Reichardt, C. *Solvents and Solvent Effects in Organic Chemistry*; VCH: New York, 1988.

(57) E.g., Tempo has a bulk dipole moment, $\mu = 3.1$ D.[58]

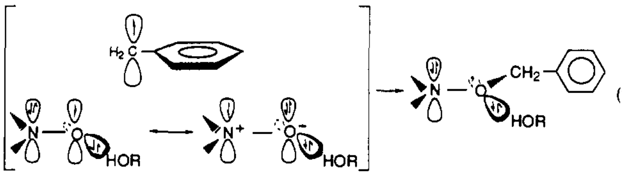
(58) Rosantzev, E. G.; Guv'yanova, E. N. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1966**, 979–983.

(59) See also, e.g., Abraham, M. H. *Progress in Physical Organic Chemistry*; Interscience: New York, 1974; Vol. 11, pp 1–87. Sjöström, M.; Wold, S. *Acta Chem. Scand.* **1981**, *B35*, 537–554; **1986**, *B40*, 270–277. Kamlet, M. J.; Taft, R. W. *Acta Chem. Scand.* **1985**, *B39*, 611–628; **1986**, *B40*, 619–624. Kamlet, M. J.; Doherty, R. M.; Famini, G. R.; Taft, R. W. *Acta Chem. Scand.* **1987**, *B41*, 589–598.

nitroxide interactions *at the molecular level in that region of the nitroxide which becomes involved in the chemical reaction.* This expectation was borne out in practice.[60]

In Figure 2 values of log (k_T/M^{-1} s^{-1}) for the benzyl radical/Tempo reaction have been plotted against the a^N values (in gauss) measured by Knauer and Napier[53] for the 4-amino-Tempo radical[61] using the data from Table IV. With the exception of the hydroxylic solvents and the two viscous solvents, 7 and 8, there is a fairly good linear correlation between log k_T and a^N, $\langle r \rangle$ = 0.986. This implies that the more strongly the solvent molecules interact with the nitroxide, i.e., the more they stabilize canonical structure B and increase a^N, the more difficult it becomes for an attacking benzyl radical to displace the solvent molecules from the nitroxide and reach the transition state on the pathway to products.[62]

For the alcoholic solvents the k_T values are very much greater than would be expected from the a^N values in these solvents. Pulse radiolytic measurements[17] indicate that water also does not retard the rate of NRT to quite the extent which might be expected from its polarity.[64] We attribute "anomalous" NRT in hydroxylic solvents to the specific formation of a hydrogen bond between the alcohol and nitroxide. Such a specific hydrogen bond would stabilize canonical structure B and thereby enhance a^N to a greater extent than the more undirected associative interactions of polar but nonhydroxylic solvents. However, such a hydrogen bond would deactivate the nitroxide as a radical trap to a relatively lesser extent than the undirected associative interactions of polar, nonhydroxylic solvents. Thus, the correlation between log (k_T/(M^{-1} s^{-1})) and a^N which holds for nonhydroxylic solvents breaks down when the solvent can hydrogen bond to the nitroxide. Indeed, it may not even be necessary to break the hydrogen bond to the nitroxide in order to reach the transition state for radical trapping since the relevant alcohol molecule(s) is (are) presumably bonded to the relatively exposed lone pair(s) of the nitroxide's oxygen atom and these are perpendicular to the radical's π orbital. The alcohol may not, therefore, interfere with the approaching benzyl radical and may remain hydrogen bonded to the hydroxylamine product (cf. reaction 10). On the other hand, if the hydrogen bond is broken during reaction then NRT in hydroxylic solvents would be expected to have enhanced activation enthalpies compared with the enthalpies in non-hydrogen-bonding solvents. The rate reducing effect of the enhanced activation enthalpy would, however, be partly, or completely, compensated by an enhanced activation entropy due to the release of the hydrogen-bonded alcohol into the bulk solvent. That some such compensation effect may be operative is suggested if the activation parameters measured for NRT by TMIO of **1**• and **3**• (relative to their respective rearrangements) in ethanol are compared with the parameters measured in the other four, nonhydroxylic solvents (including the very "slow" solvent, methylene chloride; see Table III).



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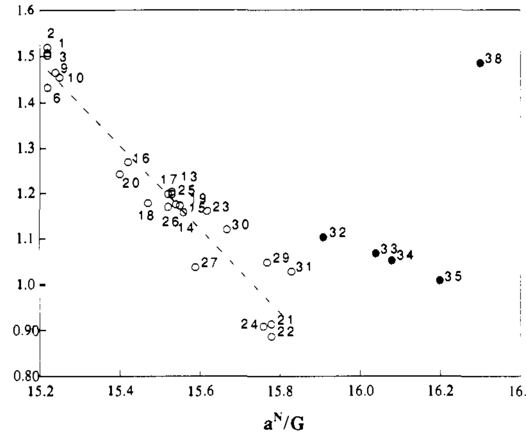

Figure 3. Plot of log ((k_T/k_C)/M^{-1}) at 80 °C using the **1**• → **2**• rearrangement as the radical clock and TMIO as the nitroxide trap versus the nitrogen hyperfine splitting for 4-amino-Tempo[53] in various solvents. Data have been taken from Table I. The hydroxylic solvents are shown as the filled circles.

Viscosity effects on the Tempo NRT of benzyl are negligible in the polar solvents except in the case of ethylene glycol (η = 22 cP at 18 °C). In a saturated hydrocarbon having the same viscosity k_T can be predicted from the appropriate correlation shown in Figure 1 to have a value of 1.06 × 10^8 M^{-1} s^{-1}, which is not much greater than the measured value of 7.9 × 10^7 M^{-1} s^{-1}. The measured NRT rate constant in ethylene glycol can be "corrected" so as to allow for the viscosity-induced reduction in the rate of reaction. We estimate that the value of k_T would be ca. 1.8 × 10^8 M^{-1} s^{-1} in a solvent which has all the properties of ethylene glycol *excepting* only a "normal" viscosity of ca. 0.5–1.0 cP. This "corrected" data point is shown as an asterisk in Figure 2.

Although the range of solvent types examined during the LFP measurements of k_T for the trapping of benzyl radicals by ABNO (Table V) and of the *n*-nonyl and neopentyl radicals by Tempo (Table IV) was much more limited than for the benzyl/Tempo reaction, the same trends in k_T are apparent. For example, if we compare the k_T values measured in isooctane (a "fast" solvent) with those measured in acetonitrile (a very "slow" solvent), the ratios of these rate constants are 5.1 (benzyl/Tempo), 6.3 (benzyl/ABNO), 6.3 (nonyl/Tempo), and 4.3 (neopentyl/Tempo). We conclude, therefore, that while the absolute magnitudes of k_T in a particular solvent can vary by a factor of 2 or 3 at 18 °C depending on whether a benzyl or an alkyl radical is trapped and on whether the trap is a hindered or nonhindered nitroxide, the *relative* effects of different solvents on trapping rate constants are essentially identical for the four systems examined. At this time, neither a more detailed analysis of the current LFP data nor the gathering of a more extensive data base would appear to be justified.

Clock Studies of Solvent Effects on NRT. The 80 °C kinetic data showing the effect of a wide range of solvents on the trapping of radical **1**• by TMIO relative to its rearrangement to radical **2**• (see Table I) can be analyzed in the manner described above for the benzyl/Tempo system. Thus, the limiting, *activation-controlled* value for k_T/k_C in noncomplexing, saturated hydrocarbon solvents must be ca. 32–33 M^{-1} which, when combined with k_C = 2.4 × 10^7 s^{-1} at 80 °C,[19] yields k_T = k_∞ = 7.8 × 10^8 M^{-1} s^{-1}. The k_∞ value estimated for trapping of **1**• by TMIO at 80 °C is not significantly different from the estimated k_∞ value for trapping of the structurally related neopentyl radical by Tempo at 18 °C, viz., ca. 6.7 × 10^8 M^{-1} s^{-1} (vide supra). Since Tempo

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[60] Because a^N values correlate rather well with a number of other solvent polarity parameters which probe the solvent at the molecular level,[53,56] relatively good correlations of log k_T could also be obtained with these parameters. However, in no case was the correlation quite as good as with a^N.

[61] This particular solvent polarity scale should be generally applicable to reactions involving hindered nitroxides since it has been shown[53] that a^N values for 4-amino-Tempo (4-amino-2,2,6,6-tetramethylpiperidin-*N*-oxyl) correlate linearly with a^N values for other hindered nitroxides (including Tempo[55] and di-*tert*-butyl nitroxide[53,54]). The effects of solvents on the *relative* magnitude of a^N for the nonhindered nitroxide, ABNO, are also similar to their effects on a^N for the hindered nitroxides. Thus, for ABNO in isooctane, benzene, and acetonitrile, a^N = 18.18, 18.31, and 18.51 G, respectively, ratios: 1.0:1.007:1.018, while for 4-amino-Tempo the corresponding ratios are 1.0:1.020:1.035.

[62] Note that increased solvent polarity has only a minor effect on the spin distribution in nitroxides and that the effect of polar solvents on k_T cannot, therefore, be attributed to a reduction of the spin density at oxygen, ρ^O. Thus, calculations[63] show that for Tempo ρ^O is only slightly lower in methanol (0.51) than in cyclohexane (0.54).

[63] Aurich, H.-G.; Hahn, K.; Stork, K.; Weiss, W. *Tetrahedron* **1977**, *33*, 969–975.

[64] For example,[65] Tempone trapping of the cyclopentyl radical in water at room temperature has k_T = (4.0 ± 0.4) × 10^8 M^{-1} s^{-1}.

[65] Asmus, K. D.; Nigam, S.; Willson, R. L. *Int. J. Radiat. Biol.* **1976**, *29*, 211–219.

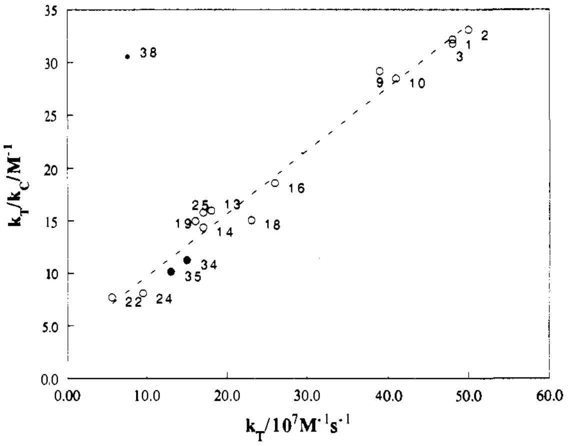

Figure 4. Plot of $(k_T/k_C)/M^{-1}$ for the **1**$^\bullet$/TMIO system at 80 °C versus $k_T/(M^{-1}\ s^{-1})$ for the benzyl/Tempo system at 18 °C. Data have been taken from Tables I and IV. The "well-behaved" hydroxylic solvents, 34 and 35, are shown as filled circles and the "anomalous" ethylene glycol solvent, 38, as an asterisk.

and TMIO have been demonstrated to have very similar radical-trapping reactivities,[6,7,10] the quite remarkable similarity in k_∞ values for **1**$^\bullet$ at 80 °C and for neopentyl at 18 °C suggests that *activation-controlled* trapping rates in noncomplexing, saturated hydrocarbon solvents are determined primarily by entropic factors (which may include the steric accessibility of the N–O$^\bullet$ moiety) rather than by enthalpic factors.

Although none of the saturated hydrocarbon solvents which were employed is particularly viscous at 80 °C, there is, nevertheless, a small but probably significant decrease in k_T/k_C in the more viscous hydrocarbons, viz., cyclohexane ($\eta^{80\,°C} = 0.42$ cP),[66] dodecane ($\eta^{80\,°C} = 0.64$ cP),[66] and cyclooctane ($\eta^{80\,°C} = 0.87$ cP),[66] and for these three solvents, we can calculate that at 80 °C $k_T = 1.46$, 1.54, and $1.60 \times 10^9\ M^{-1}\ s^{-1}$, respectively, on the basis that $k_C = 2.4 \times 10^7\ s^{-1}$.[19] A plot of k_T^{-1} vs η (see eq VIII) for these three solvents yields a straight line with a slope, $k_s\eta = 3.2 \times 10^9\ M^{-1}\ s^{-1}$ cP, which compares favorably with a value of $2.9 \times 10^9\ M^{-1}\ s^{-1}$ calculated via eq VI for a solvent having $\eta = 1.0$ cP.

Figure 3 shows a plot, based on the data given in Table I, of log $((k_T/k_C)/M^{-1})$ at 80 °C vs a^N for 4-amino-Tempo (at room temperature). This data set is considerably more extensive than that shown in Figure 2 but the similarities between the two figures are very evident. Thus, for the nonhydroxylic solvents there is a fairly good linear correlation between the kinetic data and the ^{14}N hyperfine splittings,[67] $\langle r \rangle = 0.961$, while for the hydroxylic solvents the k_T/k_C values are considerably greater than would be predicted from the corresponding a^N values. The similarities between the solvent effects found in the clocking experiments (Figure 3) and in the LFP measurements (Figure 2) are most strikingly demonstrated in Figure 4 which shows a plot of $(k_T/k_C)/M^{-1}$ for the **1**$^\bullet$/TMIO system versus $k_T/(M^{-1}\ s^{-1})$ for the benzyl/Tempo reaction for each solvent common to the two experiments. With the exception of ethylene glycol (in which solvent there appears to be an anomaly in the clocking result)[68] the solvents, both nonhydroxylic and hydroxylic, yield an excellent straight line, $\langle r \rangle = 0.989$, with no solvent lying appreciably further from this line than the combined estimated errors in the measurements of k_T/k_C and k_T. We conclude, therefore, that the kinetics of the **1**$^\bullet \rightarrow$ **2**$^\bullet$ rearrangement are virtually uninfluenced by the solvent.[69] This is important because it demonstrates for the first time that the basic assumption underlying the *radical clocking* concept is correct, viz., the assumption that alkyl radical clocks undergo their rearrangements with rates which are not influenced by the solvent. Thus, the kinetic effect of polar, polarizable, and hydrogen-bonding solvents on the clocking experiments with **1**$^\bullet$ derives principally from the trapping reaction and can presumably be attributed to the association of one or more solvent molecules with the polar, reactive N–O$^\bullet$ moiety.

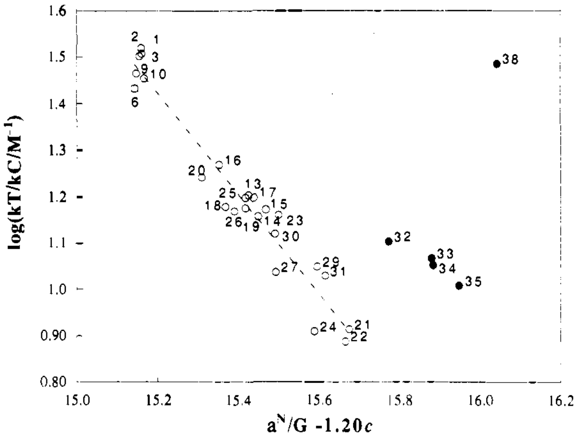

Figure 5. Plot of log $((k_T/k_C)/M^{-1})$ at 80 °C in various solvents versus the nitrogen hyperfine splitting for 4-amino-Tempo[53] "corrected" for the effect of solvent cohesive pressure. Data have been taken from Table I. The hydroxylic solvents are shown as filled circles.

Possible Influence of the Solvent's Cohesive Pressure on NRT. It is well-known that in cases where a set of experimental data give a rather poor "fit" to a one-parameter linear free energy relationship, the quality of the "fit" can usually be improved by the use of an "appropriate" second parameter. A potential second parameter is the solvent's cohesive pressure, c, which is a measure of the total molecular cohesion per unit volume. Cohesive pressure is given by eq IX,[56] where ΔU_v and ΔH_v are, respectively, the

$$c = \frac{\Delta U_v}{V_m} = \frac{(\Delta H_v - RT)}{M_r/\rho} \tag{IX}$$

energy and enthalpy of vaporization of the solvent to a gas at zero pressure, and V_m is the molar volume of the solvent. Thus, the cohesive pressure[70] represents the total strength of the intermo-

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[66] Viscosities at 80 °C have been taken from the sources cited in footnote c of Table IV.

[67] It should be noted that our data do not support suggestions of specially strong binding between nitroxides and diethyl malonate.[26]

[68] There is clearly a discrepancy between the relatively high k_T/k_C values measured for the **1**$^\bullet$/TMIO reaction in ethylene glycol at 80 °C ($\eta \sim 3$ cP)[66] and the relatively low k_T value measured by LFP for the benzyl/Tempo reaction at 18 °C in this solvent ($\eta = 22$ cP). It seems likely that this is due to an anomaly in the clocking reaction arising possibly from a nonhomogeneous solution in which there is a localized "clustering" of the nitroxide and peroxide molecules in this viscous, polar solvent. In this connection, in trial **1**$^\bullet \rightarrow$ **2**$^\bullet$ clocking experiments in glycerol at 80 °C ($\eta^{80\,°C} = 32$ cP)[66] very little rearranged product, **2T**, was formed even with the lowest practical concentrations of TMIO (ca. 5×10^{-2} M); yield ratios were very erratic but indicated that "k_T/k_C" was about an order of magnitude greater than in ethylene glycol or saturated hydrocarbons.

[69] The other clocking reactions shown in Chart I are also unlikely to show large solvent effects because none of these rearrangements would appear to involve dramatic changes in polarity between reactant and product, and hence between reactant and transition state. The largest changes in polarity during rearrangement will probably be for clocks **5**$^\bullet$, **7**$^\bullet$, and **9**$^\bullet$ in which ether-like reactants ($\mu \approx 1.1$ D) are converted to tetrahydrofuran-like products ($\mu \approx 1.7$ D). An examination of the relative k_T/k_C values listed in Table II suggests that there may possibly be a small accelerating effect of the polar solvent CH_2Cl_2 on the rates of cyclization of **5**$^\bullet$, **7**$^\bullet$, and **9**$^\bullet$ relative to the analogous cyclization of the hydrocarbon radical, **3**$^\bullet$, and rearrangement of the hydrocarbon radical, **1**$^\bullet$. The situation with regard to **11**$^\bullet$ is ambiguous since polar solvents may tend to stabilize **11**$^\bullet$ relative to **12**$^\bullet$ + CO_2 and therefore reduce the rate of β-scission while at the same time they may also interfere with the nitroxide trapping reaction. It is clear that more direct and reliable methods for measuring the rates of radical rearrangements and scissions will be required before one can determine whether polar solvents do, or do not, influence these reactions.

[70] Cohesive pressure is sometimes incorrectly referred to as the internal pressure, π, of the solvent.[56] However, π is defined as the change in internal energy of a solvent as it undergoes a very small isothermal expansion, i.e., $\pi = (\partial U/\partial V_m)_T$, which does *not* interrupt all the internal interactions associated with solvent structure. It has been shown that π is mainly a reflection of dispersion, repulsion, and dipole–dipole interactions within the solvent, whereas c also includes specific interactions such as intermolecular hydrogen bonding. Values of π, therefore, approach c only for weakly polar solvents. The Hildebrand solubility parameter, δ, is defined as: $\delta = (c)^{1/2}$.

lecular solvent structure; i.e., it characterizes the amount of energy needed to separate the molecules of a liquid and is therefore a measure of the attractive forces between solvent molecules. In summary, therefore, while solvent polarity reflects the ability of the solvent to interact with a solute, the cohesive pressure is related to the energy required to create a hole in the solvent to accommodate the solute molecule. Polarity (as measured in this instance by a^{N}) and cohesive pressure are therefore complementary terms, so that the rates of the $U^{\bullet} + T^{\bullet}$ reactions might be expected to depend on both quantities.

The effect of an increase in the cohesive pressure will be to increase the rate of any "slow" (activation-controlled) radical/radical coupling reaction because the formation of a covalent bond between two reactants is accompanied by a reduction in solute volume.[71-73] For the clocking data from Table I the best (least-squares) fit for the nonhydroxylic solvents is obtained by plotting log $((k_T/k_C)/M^{-1})$ versus $a^{N}/G - 1.2c/(\text{kcal cm}^{-3})$; see Figure 5. This gives a correlation coefficient, $\langle r \rangle = 0.972$ which can be compared with $\langle r \rangle = 0.961$ obtained for the plot of log $((k_T/k_C)/M^{-1})$ vs a^{N}/G (see Figure 3). In this case, therefore, the introduction of a cohesive pressure term does produce a small improvement in the linear free energy correlation. The cohesive pressure term also moves the data points obtained in hydroxylic solvents quite a bit closer to those obtained in the nonhydroxylic solvents, but they still form a quite distinct group (see Figure 5). Clearly, special solvent effects are at work in hydroxylic solvents, as discussed above.[74]

Unfortunately, "correcting" for the solvents' cohesive pressure does not improve the linear free energy relationship for the benzyl/Tempo LFP system. Taking the kinetic data from Table IV and excluding viscous (7, 8) and hydroxylic (34, 35, 38) solvents, the best fit is given by plotting log $(k_T/M^{-1}\ s^{-1})$ versus $a^{N}/G - 0.69c/(\text{kcal cm}^{-3})$, $\langle r \rangle = 0.987$. For comparison, the plot of log $(k_T/M^{-1}\ s^{-1})$ versus a^{N}/G shown in Figure 2 has $\langle r \rangle = 0.986$. We conclude that the solvent's cohesive pressure either has little effect on the rate of NRT or, more probably, that the effect of the solvent's cohesive pressure is already included in the measured nitrogen hyperfine splitting. Indeed, it is known that a^{N} is markedly influenced by externally applied pressure.[76] Furthermore, the solvents used in this work exhibit a rough correlation between a^{N} and c ($\langle r \rangle = 0.80$ for all solvents).

Why Is NRT a "Slow" Radical/Radical Reaction. Most localized radicals undergo their bimolecular self-reaction at the diffusion-controlled limit even in solvents of low viscosity, and the polarity of the solvent has no effect on the reaction rate. By way of contrast, NRT is significantly slower than the diffusion limit in low viscosity solvents and the rate is slower in polar, polarizable, and hydrogen-bonding solvents than in saturated hydrocarbons. With the more common di-*tert*-alkyl nitroxides such as Tempo and TMIO the "slowness" of NRT might, in principal, have been attributed to steric protection of the $N\text{–}O^{\bullet}$ moiety. However, our LFP results with the sterically unencumbered nitroxide, ABNO, show that although this compound is somewhat more reactive toward the benzyl radical than Tempo it, too, does not react at the diffusion-controlled limit in solvents of low viscosity. Hence, steric hindrance can only be partly responsible for slow NRT by Tempo and TMIO.

Of course, NRT is not unique. As mentioned earlier, the bimolecular self-reactions of many highly delocalized radicals are also known to be "slow". For these reactions, as for NRT, the enthalpic barriers lying in the way of product formation for a caged singlet pair of radicals are less than the activation energies for diffusion together of the singlet pair (which are ca. 2.5–3.5 kcal/mol for common organic solvents with viscosities of 0.4–1.5 cP). The "slowness" of NRT is due, therefore, to an entropic barrier lying between the caged singlet radical pair and the trialkylhydroxylamine product. We suggest that this entropic barrier arises from the loss in entropy which necessarily accompanies the requirement that the unpaired electron must become largely localized on the nitroxide's oxygen atom (i.e., nonpolar, canonical structure A) before bond formation can proceed to completion. In nonviscous, saturated hydrocarbon solvents this need to localize the nitroxide's unpaired electron is presumably the sole origin of the free energy barrier for its reaction with a localized carbon-centered radical. This barrier may, however, be further increased for the trapping of a delocalized carbon-centered radical by the additional need to localize spin. In polar, polarizable, and hydrogen-bonding solvents the dipolar character of the nitroxide's N–O bond (i.e., dipolar, canonical structure B) is further stabilized by associated solvent molecules, some of which must be displaced before the carbon-centered radical can couple with the nitroxide's oxygen atom. In these solvents, reaction is therefore noticeably slower than in the saturated hydrocarbon solvents. The kinetic retardation of NRT by nonhydroxylic, polar, and polarizable solvents could be reasonably well correlated with the solvent's effect on the nitroxide's ^{14}N hyperfine splitting, a^{N}, which provides a rather direct measure of solvent/nitroxide association.

Experimental Section

Materials. Solvents were the purest grade commercially available. They were used without purification except for chloroform (which was percolated through activated basic alumina to remove the ethanol stabilizer) and methyl acrylate (which was purified by rapid distillation immediately prior to use, with only the first 30% being employed). The probe molecule, 1,1-diphenylethylene, used in the LFP studies of nonyl and neopentyl radicals, was percolated through activated basic alumina and distilled (Kugelrohr) immediately prior to use.

9-Azabicyclo[3.3.1]nonane-*N*-oxyl (ABNO)[40] was prepared in fair yield (50–70%) and good purity (98% by LC–MS after hexane recrystallization) from 9-azabicyclo[3.3.1]nonane[40] using the H_2O_2/sodium tungstate oxidation method described by Solomon and co-workers for the preparation of 1,1,3,3-tetramethylisoindoline-2-oxyl (TMIO).[77] The previously studied self- and solvent reactions[40] of ABNO were minimized by storing it in the solid state (−28 °C) and by using only freshly prepared solutions.

Tempo (Aldrich, Milwaukee, WI) was purified by sublimation and TMIO, which was prepared by the method of Solomon and co-workers,[77] by recrystallization from hexane. Both nitroxides had better than 98% purity by LC–MS. Dibenzyl ketone, didecanoyl peroxide, and dipivalyl peroxide were purified by recrystallization from pentane. Preparations of the diacyl peroxides used in the radical clocking study (cf. Chart 1) have been previously described.[7]

Radical Clocking NRT. In a typical experiment, a reaction mixture made up by adding 0.1 mol equiv of diacyl peroxide to an ice-chilled stock solution of nitroxide (500 μL) was freeze–pump–thaw degassed (three cycles, 0.2 Torr), flame sealed, and heated (72 h at 60 °C, 5 h at 80 °C, or 0.2 h at 126 °C) in a glass ampule. The trialkylhydroxylamine products were then analyzed by reversed-phase HPLC[7] with UV detection at 270 nm. Reaction mixtures from the hex-5-enyl radical, $3^{\bullet}$, were concentrated by evaporation in vacuo before analysis. The methods used to identify and quantify the trialkylhydroxylamine products have been described in earlier publications.[7,16,37] The thermal stabilities of these products were tested for each clock/solvent combination by prolonged heating. The TMIO trapped products of primary alkyl, secondary alkyl, and alkoxycarbonyl radicals were shown to be stable under the reaction conditions employed for the kinetic studies.[23] The "kinetic" products (UT and RT) were also shown to be inert toward the HPLC solvent (70–95% aqueous MeOH, 20 h). In contrast, some of the minor components derived from the nitroxide/peroxide and the radical/solvent reactions were quite rapidly decomposed at the highest experimental temperature

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(71) See, e.g., Neuman, R. C., Jr.; Bussey, R. J. *Tetrahedron Lett.* **1969**, 5859–5862. Neuman, R. C., Jr.; Bussey, R. J. *J. Am. Chem. Soc.* **1970**, *92*, 2440–2445. Newman, R. C., Jr.; Lockyer, G. D., Jr. *J. Am. Chem. Soc.* **1983**, *105*, 3982–3987.

(72) For a review of pressure effects on the rates of radical reactions, see Newman, R. C., Jr. *Acc. Chem. Res.* **1972**, *5*, 381–387.

(73) For more general reviews of pressure effects on reaction rates see, e.g., Asano, T.; LeNoble, W. J. *Chem. Rev.* **1978**, *78*, 407–487. Van Eldik, R.; Asano, T.; LeNoble, W. J. *Chem. Rev.* **1989**, *89*, 549–688.

(74) In this connection, it is also worth noting that a study[75] on the effect of externally applied pressure upon the rate of spin-exchange of 4-oxo-Tempo radicals led to the conclusion that, whereas a diffusion process alone is operating in aprotic solvents, in protic solvents an encounter complex is formed as an intermediate.

(75) Sueishi, Y.; Nishimura, N.; Hirata, K.; Kuwata, K. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 252–254.

(76) Griller, D. *J. Am. Chem. Soc.* **1978**, *100*, 5240–5241.

(77) Griffiths, P. G.; Moad, G.; Rizzardo, E.; Solomon, D. H. *Aust. J. Chem.* **1983**, *36*, 397–401.

(126 °C) and/or by exposure to aqueous methanol. For example, the TMIO–CCl_3 adduct (from alkyl radical/CCl_4 reactions) was partially solvolized during analysis by the HPLC eluent.

Laser Flash Photolysis. The laser flash photolysis apparatus and k_T calibration methods have been adequately described in earlier publications from this laboratory;[6,20] experimental conditions are given in the table footnotes. Quenching rate constants were calculated by least-squares fitting of k_{exptl} vs [T$^\bullet$] data for at least six evenly incremented [T$^\bullet$] over an appropriate range of [T$^\bullet$] (viz., such that the decay or grow-in rate constant, k_{exptl}, was in the range (2–30) × 10^5 s^{-1}). Digitally averaged decay curves from three to six laser flashes were used to determine each k_{exptl} value. The effect of photolytic consumption of nitroxide on the k_{exptl} values was assessed in each solvent by comparing data from repeated sets of laser flashes; no appreciable corrections were required. However, for ABNO (where the nitroxide increments were of necessity very small) and in CH_2Cl_2 as solvent[32] the number of flashes needed to be kept to a practical minimum (viz., three or four) to avoid underestimating k_T.

Acknowledgment. We thank Dr. J. Daroszewski for his help with the statistical calculations and preparation of the figures and the Association for International Cancer Research and the National Foundation for Cancer Research for partial support of this work. K.U.I. also wishes to thank the Alexander von Humboldt Foundation and the organic chemists at the Universities of Freiburg and Essen, Germany, for their generous hospitality during the time that this work was written up.

Registry No. 1, 87110-24-5; **2**, 87110-25-6; TMIO, 80037-90-7; TEMPO, 2564-83-2; ABNO, 31785-68-9; benzyl, 2154-56-5; nonyl, 32757-65-6; neopentyl, 3744-21-6.

Kinetics of Nitroxide Radical Trapping. 2. Structural Effects[1]

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Abstract: Laser flash photolysis and kinetic competition product studies have demonstrated that in isooctane at ambient temperatures the rate constant for coupling of carbon-centered radicals with persistent nitroxides, k_T, depends upon the degree of steric hindrance to coupling and upon the extent of resonance stabilization of the carbon radical. Sterically induced reductions in the magnitude of k_T are observed for changes in both the structure of the nitroxide and the structure of the carbon radical. Thus, for any particular carbon radical k_T is largest for the Bredt's rule protected nitroxides, 9-azabicyclo[3.3.1]nonane-*N*-oxyl (ABNO) and nortropane-*N*-oxyl, while for the "usual" di-*tert*-alkyl nitroxides k_T decreases along the series, 1,1,3,3-tetramethylisoindoline-2-oxyl ≥ 2,2,5,5-tetramethylpiperidin-1-oxyl (Tempo) > di-*tert*-butyl nitroxide, i.e., k_T decreases on going from a five-membered ring to a six-membered ring to a noncyclic structure. Cyclopropyl and triphenylmethyl are trapped at the fastest and slowest rates, respectively, the corresponding k_T values being 3.0 × 10^9 and 1.2 × 10^8 M^{-1} s^{-1} for ABNO and 2.1 × 10^9 and <1 × 10^6 M^{-1} s^{-1} for Tempo. Steric effects in the carbon radicals are more pronounced for Tempo than for ABNO. For example, the ratio of k_T's for the trapping of nonyl and *tert*-butyl is 1.7 for Tempo but 1.3 for ABNO, while for the trapping of benzyl and cumyl the ratio of k_T's is 4.1 for Tempo and 0.9 for ABNO. The effect of resonance stabilization can be illustrated by the k_T values for three sterically unhindered primary radicals, *n*-nonyl, benzyl, and 2-naphthylmethyl, viz., 1.2 × 10^9, 4.8 × 10^8, and 5.7 × 10^7 M^{-1} s^{-1}, respectively, for Tempo and 2.2 × 10^9, 1.2 × 10^9, and 8.1 × 10^8 M^{-1} s^{-1}, respectively, for ABNO.

The trapping of transient carbon-centered radicals, U$^\bullet$, by persistent nitroxides, T$^\bullet$, to afford stable trialkylhydroxylamines, UT (reaction 1) has proven to be a valuable kinetic and mechanistic probe for radical-induced polymerizations,[3-5] radical rearrangements,[6-9] and homolytic dissociations.[10-12] Detailed kinetic analysis of systems in which the nitroxide radical trapping (NRT) reaction occurs in competition with unimolecular and/or other bimolecular reactions of U$^\bullet$[3-14] obviously requires reliable trapping rate constants, k_T. Furthermore, these need to be measured under a variety of conditions and with a variety of U$^\bullet$/T$^\bullet$ combinations.

$$U^\bullet + R_2NO^\bullet \xrightarrow{k_T} UONR_2$$

$$U^\bullet + T^\bullet \xrightarrow{k_T} UT \tag{1}$$

Solvent effects on the kinetics of NRT were analyzed in the preceding paper.[15] Earlier work[6,16] has afforded accurate Arrhenius expressions for the effect of temperature on the rates of trapping of certain alkyl and benzylic radicals by Tempo and the isoindolinoxyl radical TMIO. In the present paper we report k_T measurements which were designed to probe the effects on the kinetics of NRT of (i) resonance stabilization of U$^\bullet$, (ii) steric protection of the radical center in U$^\bullet$, and (iii) steric protection

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