Reactivities of Triarylmethyl and Diarylmethyl Cations with Azide Ion Investigated by Laser Flash Photolysis. Diffusion-Controlled Reactions

Robert A. McClelland,*[,1] V. M. Kanagasabapathy,[1] Narinder S. Banait,[1] and Steen Steenken[2]

Contribution from the Department of Chemistry and Scarborough Campus, University of Toronto, Toronto, Ontario, Canada M5S 1A1, and the Max-Planck-Institut fur Strahlenchemie, D-4330 Mulheim, West Germany. *Received July 18, 1990*

Abstract: By use of the technique of laser flash photolysis, rate constants k_{Az} and k_S have been directly measured for the reactions at 20 °C in acetonitrile–water (AN–W) solutions of varying composition of 18 triarylmethyl and 10 diarylmethyl cations with azide and solvent. The cations have k_S that depend on substituent and vary from $\sim 10^1$ to $\sim 10^7$ s^{-1}. For the more stable ions k_{Az} also varies, increasing with decreased electron donation and also increasing by as much as 10^3 with increasing acetonitrile content. For less stable cations, however, the rate constant becomes independent of substituent. The break occurs when k_S has reached $\sim 10^5$ s^{-1}. The limiting rate constants have magnitudes in the vicinity of 10^{10} M^{-1} s^{-1}; these do depend on solvent and type of cation, with diarylmethyl cations reacting at the limit 1.6 ± 0.2 times faster than triarylmethyl. The data can be fit by a model where there is diffusional encounter of the cation and azide to form an ion pair, with the combination within the ion pair rate-limiting for the more stable cations and the diffusion step rate-limiting for the less stable ones. The limiting rate constants represent the latter, diffusional encounter of the cation and azide. The Debye–Smoluchowski equation for diffusion-controlled reactions predicts rate constants that are larger than observed by factors of 2–2.5 for diarylmethyl and 4 for triarylmethyl. Deviations can be attributed to nonproductive encounters where the anion has approached the cation in the plane of one of the rings and thus cannot form a proper reacting configuration. The difference between the two types of cations is explained by the greater difficulty of achieving this configuration with the more sterically congested triarylmethyl cation. Ratios k_{Az}/k_S obtained from product analysis (competition kinetics) have previously been found to show adherence to the reactivity–selectivity principle. This has been interpreted (Rappoport, Jencks) in terms of the reaction with azide having reached the diffusion limit. The directly measured k_{Az} establish that this is indeed the case. This study also validates the use of azide as a "clock" (Jencks, Richard) for converting such ratios to absolute rate constants through use of a value of 5×10^9 M^{-1} s^{-1} for k_{Az}. The directly measured diffusion-limited k_{Az} are somewhat larger than this, but the differences are small, at most a factor of 4.

Azide ion has been used extensively as a competing nucleophile in solvolysis reactions. Originally used as a probe of reaction mechanism,[3] this system became widely cited in discussions of the reactivity–selectivity principle. When the cation stabilities for S_N1 reactions were measured through values of k_{ion} ($k_{solvolysis}$) for their formation, more reactive cations were found to have lower k_{Az}/k_S ratios, that is, lower selectivity.[3,4] The appropriate equations describing the system are summarized (see eqs 1–3).

$$RX \xrightarrow[-X^-]{k_{ion}} R^+ \begin{cases} \xrightarrow{+SOH,\ -H^+;\ k_S} ROS \\ \xrightarrow{+N_3^-;\ k_{Az}} RN_3 \end{cases} \tag{1}$$

$$\frac{k_{Az}}{k_S} = \frac{(\%\ RN_3)}{(\%\ ROS)}\,\frac{1}{[N_3^-]} \tag{2}$$

$$\frac{k_{Az}}{k_{SOH}} = \frac{(\%\ RN_3)}{(\%\ ROS)}\,\frac{[SOH]}{[N_3^-]} \tag{3}$$

Equations 2 and 3, which apply when $[N_3-] > [RX]$, differ in the units employed for the rate constant for the reaction with solvent, k_S in s^{-1} and k_{SOH} in M^{-1} s^{-1}.

Ritchie, on the other hand, has carried out extensive studies of the reactions of nucleophiles with more stable carbocations and has found no such changes in selectivity. His data can be satisfied by the simple relationship[5]

$$\log (k/k_0) = N_+ \tag{4}$$

where k and k_0 are rate constants for combinations with the nucleophile in question and a reference nucleophile and N_+ is a parameter dependent only on the nucleophile and solvent system. According to this equation, the selectivity k/k_0 is independent of the nature and reactivity of the electrophile.

More recently, there have been suggestions that the adherence to RSP seen with azide is caused by the reactions with this nucleophile having reached the diffusion limit.[6,7] In other words, k_{Az} has become constant and changes in selectivity *must* occur, as changes in reactivity affect only the rate of reaction with the solvent. Diffusion control for the reaction with azide has been used as the basis of a "clock" method for obtaining absolute rate constants. This approach, which has produced important data pertaining to cation reactivity,[7,8] makes the assumption that azide—the "clock"—reacts at the diffusion limit and assigns a value of 5×10^9 M^{-1} s^{-1} for this rate constant to convert rate constant ratios involving azide to individual rate constants.

Recently, the technique of nanosecond laser flash photolysis has been used for the *direct* study of the reactivities of short-lived carbocation intermediates in aqueous and alcohol solutions.[9] In

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[1] University of Toronto.

[2] Max-Planck-Institut fur Strahlenchemie.

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[8] For more recent examples, see: (a) Ta-Shma, R.; Jencks, W. P. *J. Am. Chem. Soc.* **1986**, *108*, 8041–8050. (b) Richard, J. P. *Ibid.* **1986**, *108*, 6819–6820. (c) Fishbein, J. C.; McClelland, R. A. *Ibid.* **1987**, *109*, 2824, 2825. (d) Richard, J. P. *J. Chem. Soc., Chem. Commun.* **1987**, 1768, 1769. (e) Richard, J. P. *J. Am. Chem. Soc.* **1989**, *111*, 1455–1465. (f) Amyes, T. L.; Jencks, W. P. *Ibid.* **1989**, *111*, 7888–7900.

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Table I. Triarylmethyl (T$^+$) and Diarylmethyl (D$^+$) Cations

cation	no.	cation	no.	cation	no.
4,4′,4″-(MeO)$_3$T$^+$	**1**	3-MeOT$^+$	**11**	4-Me-4′-MeOD$^+$	**20**
4,4′-(MeO)$_2$T$^+$	**2**	4-ClT$^+$	**12**	4-F-4′-MeOD	**21**
4-Me-4′-MeOT$^+$	**3**	3-ClT$^+$	**13**	4-MeOD$^+$	**22**
3-Me-4′-MeOT$^+$	**4**	3-CF$_3$T$^+$	**14**	4-Cl-4′-MeOD$^+$	**23**
4-MeOT$^+$	**5**	4-CF$_3$T$^+$	**15**	3,4′-(MeO)$_2$D$^+$	**24**
3,4′-(MeO)$_2$T$^+$	**6**	3,3′-Cl$_2$T$^+$	**16**	3-Cl-4′-MeOD$^+$	**25**
4,4′,4″-Me$_3$T$^+$	**7**	3,3′,3″-Cl$_2$T$^+$	**17**	3-CF$_3$-4′-MeOD$^+$	**26**
4,4′-Me$_2$T$^+$	**8**	4,4′-(CF$_3$)$_2$T$^+$	**18**	4-CF$_3$-4′-MeOD	**27**
4-MeT$^+$	**9**	4,4′-(MeO)$_2$D$^+$	**19**	4,4′-Me$_2$D$^+$	**28**
T$^+$	**10**				

particular, we have reported an investigation of a series of triarylmethyl and diarylmethyl cations in acetonitrile–water (AN–W) mixtures,[9d] with lifetimes varying in an incremental manner from the most reactive cation of the "Ritchie" type, the tris(4-methoxyphenyl)methyl cation with $k_S \approx 10^1$ s^{-1}, through 6 orders of magnitude to cations with $k_S \approx 10^7$ s^{-1}. The series of "stable" cations employed by Ritchie had k_S ranging from $\sim 10^{-5}$ to $\sim 10^1$ s^{-1},[10] so that our series effectively doubles the range of reactivities of cations for which data can be obtained. In this paper, we consider tri- and diarylmethyl cations reacting with azide. The principal objective was to directly measure k_{Az} for less stable cations and thus to test the question as to whether this nucleophile does react at the diffusion limit. The data do indeed show that this assumption is valid for short-lived cations but not for more stable ones. A preliminary account of some of the results with diarylmethyl cations has appeared.[9c]

Experimental Section

Compounds employed as precursors for the cations have been described.[9d] Photolysis experiments were carried out with a KrF-excimer laser flash photolysis apparatus with 20-ns pulse width and 248-nm excitation wavelength. The experimental setup and methods of data handling have been described.[9a] Solvents for the kinetic measurements were prepared by mixing in the appropriate volume ratio water from a Millipore-Q system and spectroscopic grade acetonitrile. Azide solutions were prepared by adding a small amount of a stock solution of 1 M sodium azide in water. The precursor to the cation was dissolved in acetonitrile at a concentration of 0.1–1.0 M, and immediately before photolysis, a small amount of this solution was added to the aqueous acetonitrile solution to give a concentration of $\sim 10^{-4}$ M. The individual kinetic runs obeyed excellent first-order kinetics. Rate constants from replicate measurements agreed within ±3%.

Results

First-order rate constants for the decay of the cations listed in Table I were measured in aqueous AN–W mixtures containing 0–1 mM sodium azide (effectively zero ionic strength). With each system, five to seven solutions were employed and the observed rate constants were plotted against the azide concentration. These plots were linear,[11] and second-order rate constants were calculated as the slopes. These rate constants, as well as values of k_S in each solvent, are given as supplementary material. (Rate constants for triarylmethyl cations in 1/2 (v/v) AN–W can also be found in Table II.) In general, the second-order rate constants had one standard deviation of 5% or better. The exception was 4,4′-Me$_2$D$^+$, whose solvent rate constant is near the limit of experimental measurement. Thus, only small increases in the rate could be tolerated on addition of the nucleophile, with larger errors therefore in the slope. Poor solubilities of the precursors in general prevented study in highly aqueous solutions. The one exception was the diarylmethyl cation 3,4′-(MeO)$_2$D$^+$, whose acetate undergoes especially efficient photoheterolysis[9d] and thus could be examined in 100% water.

The details of the flash photolysis experiments that generate these cations have been discussed. Arguments have also been presented that the species observed and studied is a free ion in the ground state.[9c,d] That is, the ion is identical with the intermediate that is obtained in an appropriate thermal reaction such

Table II. Rate Constants k_S and k_{Az} for Triarylmethyl Cations at 20 °C in 1/2 (v/v) AN–W and the Calculated Ratio k_{-d}/k_c for the Partitioning of the Ion Pair

cation	k_S, s^{-1}	k_{Az}(obsd), M^{-1} s^{-1}	k_{Az}(calcd)[a]	(k_{-d}/k_c)-(calcd)[b]
4,4′4″-(MeO)$_3$T$^+$	1.0×10^1	1.5×10^7	1.8×10^7	290
4,4′-(MeO)$_2$T$^+$	8.6×10^1	9.3×10^7	8.8×10^7	61
4-Me-4′-MeOT$^+$	5.7×10^2	3.8×10^8	3.4×10^8	15
3-Me-4′-MeOT$^+$	1.1×10^3	6.0×10^8	5.2×10^8	9.3
4-MeOT$^+$	1.4×10^3	6.9×10^8	6.1×10^8	7.8
3,4′-(MeO)$_2$T$^+$	1.8×10^3	7.0×10^8	7.2×10^8	6.5
4,4′,4″-Me$_3$T$^+$	3.6×10^3	1.0×10^9	1.1×10^9	3.9
4,4′-Me$_2$T$^+$	1.1×10^4	2.0×10^9	2.0×10^9	1.7
4-MeT$^+$	3.7×10^4	3.0×10^9	3.2×10^9	0.70
T$^+$	1.6×10^5	4.1×10^9	4.4×10^9	0.24
3-MeOT$^+$	1.7×10^5	4.0×10^9	4.4×10^9	0.23
4-ClT$^+$	1.8×10^5	4.8×10^9	4.4×10^9	0.22
3-ClT$^+$	5.1×10^5	5.0×10^9	4.9×10^9	0.10
3-CF$_3$T$^+$	6.8×10^5	4.3×10^9	5.0×10^9	0.08
4-CF$_3$T$^+$	1.1×10^6	5.3×10^9	5.1×10^9	0.058
3,3′-Cl$_2$T$^+$	1.6×10^6	4.8×10^9	5.2×10^9	0.044
3,3′,3″-Cl$_2$T$^+$	4.6×10^6	5.4×10^9	5.3×10^9	0.020
4,4′-(CF$_3$)$_2$T$^+$	8.8×10^6	5.7×10^9	5.3×10^9	0.013

[a] Calculated from eq 7, with use of parameters in text. [b] $(k_{-d}/k_c^0)\cdot(1/k_S^{\alpha})$, with use of parameters in text.

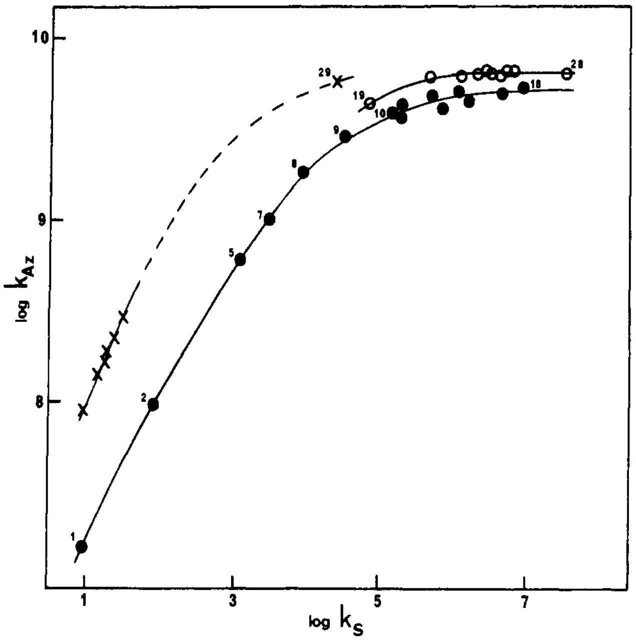

Figure 1. Variation in k_{Az} (M^{-1} s^{-1}) in 1/2 AN–W (v/v) for combination with azide as a function of the rate constant k_S (s^{-1}) for decay in the same solvent. Conditions: 20 °C; ionic strength 0. Key: closed circles, triarylmethyl cations; open circles, diarylmethyl cations. The points × represent rate constants for the 9-xanthylium ion (**29**) and six 9-aryl derivatives in 1/4 AN–W (v/v).[9b]

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[10] Ritchie, C. D. *Can. J. Chem.* **1986**, *64*, 2239–2250.

[11] At the low concentrations of sodium azide employed in these experiments, effects of ionic strength are negligible. Azide is very reactive toward carbocations and does produce significant rate accelerations even when present in small amounts.

as S_N1 solvolysis. Moreover, the ions are all sufficiently long-lived to exist as free ions in these aqueous solutions. There is also the question as to whether the rate constants actually represent cation–nucleophile combinations. In the case of azide, this is shown by the general consistency between the ratios k_{Az}/k_S obtained in the flash photolysis experiments and those measured by product analysis (see later text). In one case, the bis(*p*-methoxyphenyl)methyl cation in the solvent methanol, these ratios have been measured under identical conditions and the agreement is excellent.[9c]

Discussion

Leveling of the Rate Constant for the Reaction with Azide. Figure 1 shows correlations of log k_{Az} with log k_S in the one solvent system. For each cation type the constant k_S qualitatively shows the expected increase with increased electron withdrawal.[12] A dependency on the substituent is also seen in k_{Az}, but only for the more stable cations. For the less stable ions, there is a leveling and k_{Az} becomes essentially constant. For triarylmethyl cations this change occurs when k_S is around 10^5 s^{-1}. With the diarylmethyl cations, only 4,4′-$(MeO)_2D^+$ reacts at a slower rate, and then only slightly. The others all have values of k_{Az} that are the same, despite increases in k_S by almost 2 orders of magnitude. With each system, the rate constants for the more reactive systems are constant within the ±5% experimental error in k_{Az}. They are also within this range of the plateau rate constant calculated by the model discussed in the following text.

The data can be examined in terms of the kinetic scheme[13,14]

$$R^+ + N_3^- \underset{k_{-d}}{\overset{k_d}{\rightleftharpoons}} R^+{\cdot}N_3^- \xrightarrow{k_c} RN_3 \qquad (5)$$

where k_d and k_{-d} are rate constants for diffusional encounter and separation and k_c is the rate constant for combination within the ion pair. To evaluate the fit of the experimental data to this model, k_d and k_{-d} were assumed to be independent of substituent and k_c was assumed to follow a linear free energy relationship in k_S[12]

$$\log k_c = \alpha \log k_S + \log k_c^0 \qquad (6)$$

where α is the slope relating the two and k_c^0 is a constant. A steady-state assumption in the ion pair[15] then produces the equation

$$k_{Az} = \frac{k_d}{1 + \left(\dfrac{k_{-d}}{k_c^0}\right)\left(\dfrac{1}{k_S^{\alpha}}\right)} \qquad (7)$$

The data for the triarylmethyl cations were fit to this equation with the use of nonlinear least squares, giving as the adjustable parameters $k_d = (5.4 \pm 0.3) \times 10^9$ M^{-1} s^{-1}, $\alpha = 0.74 \pm 0.02$, and $k_{-d}/k_c^0 = (1.6 \pm 10^3)$ for 1/2 AN-W. The agreement of the experimental k_{Az} with values calculated from these parameters is illustrated in Table II. The α value of less than unity results principally from the data for the less reactive cations **1**–**7**, being the limiting slope in a plot of log k_{Az} versus log k_S at small k_S. Ritchie has commented with data for the stabilized cations that anionic nucleophiles such as the hydroxide ion have slopes less than unity in correlations with log k_S.[10]

Table III. Rate Constants for the Diffusion-Controlled Reactions of Cations with Azide Ion in Aqueous Acetonitrile (Volume Percent) at 20 °C

% AN	$k_d(Az + Ar_3C^+)$, M^{-1} s^{-1}	$k_d(Az + Ar_2CH^+)$, M^{-1} s^{-1}	D^+/T^+
0		$(7.4 \pm 0.4) \times 10^9$ [a]	
20		$(7.2 \pm 0.3) \times 10^9$	
33	$(5.4 \pm 0.3) \times 10^9$	$(7.3 \pm 0.4) \times 10^9$	1.4
50	$(4.7 \pm 0.2) \times 10^9$	$(7.2 \pm 0.3) \times 10^9$	1.5
67	$(5.2 \pm 0.1) \times 10^9$	$(9.3 \pm 1.1) \times 10^9$	1.8
83	$(7.9 \pm 0.3) \times 10^9$	$(1.2 \pm 0.2) \times 10^{10}$	1.6
93	$(1.0 \pm 0.1) \times 10^{10}$	$(1.9 \pm 0.1) \times 10^{10}$	1.8
99	$(1.1 \pm 0.1) \times 10^{10}$	$(1.8 \pm 0.1) \times 10^{10}$	1.6

[a] Based upon rate constant for the cation 3,4′-$(MeO)_2D^+$ only.

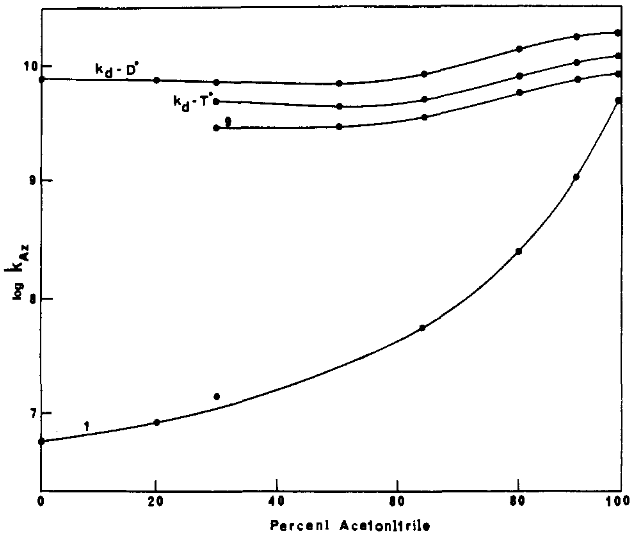

Figure 2. Values of k_{Az} in aqueous acetonitrile solutions (volume percent). The numbers for 4,4′,4″-$(MeO)_3T^+$ (**1**) and 4-MeT^+ (**9**) are directly measured. The values k_d are the constants for the diffusion-limited reactions.

The model is based on a change from activation control, with the second step rate-limiting, to diffusion control, first step rate-limiting, as the cation becomes more reactive. Limiting values of k_{Az} are $K_d k_c$ ($K_d = k_d/k_{-d}$) for $k_{-d} \gg k_c$ and k_d for $k_{-d} \ll k_c$. An analysis of the situation with the triarylmethyl cations in 1/2 AN-W is illustrated in Table II, the ratio k_{-d}/k_c showing the progression from one extreme to the other. The reaction becomes mainly diffusion controlled for triarylmethyl cations more reactive than 3-CF_3T^+ ($k_S > 10^6$ s^{-1}). The change from 100% activation control to 100% diffusion control does not occur suddenly. There is a range, involving cations **4**–**12**, where k_{-d} and k_c are within 1 order of magnitude of one another, so that neither step in eq 5 is entirely rate-limiting. In this region, k_{Az} continues to increase, but less rapidly with respect to k_S than for the more stable cations **1** (4,4′,4″-$(MeO)_3T^+$) and **2** (4,4′-$(MeO)_2T^+$). To explain this, however, it is not necessary to invoke RSP considerations, that is, a change in the inherent selectivity because of the high reactivity of the cation. The behavior is a natural consequence of the changeover to diffusion control.

A changeover to diffusion control was previously observed by Ritchie for azide and PhS^- reacting with *p*-cyano- and *p*-nitrodiazonium ions in methanol and DMSO.[16] The rate constants

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[12] The constant k_S is employed merely as a measure of the effect of the substituents on inherent reactivity of each cation. The analysis of the correlations of k_S with individual substituent constants showed that there was a nonadditivity on multiple substitution; there was also some question as to which is the appropriate substituent scale.[9d]

[13] Rice, S. A. In Diffusion-Limited Reactions. *Comprehensive Chemical Kinetics*; Bamford, C. H., Tipper, C. F. H., Compton, R. G., Eds.; Elsevier: Amsterdam, 1985; Vol. 25, pp 7, 8.

[14] (a) In analyzing the dynamics of ion pairs generated by flash photolysis of electron-donor–electron-acceptor complexes, Masnovi and Kochi invoked a scheme involving "intimate" and "loose" ion pairs.[14b] The model of eq 5 ignores the possibility of such species, since the different ion pairs cannot be distinguished by the data available in this study. It can be noted that "loose" ion pairs were observed on the nanosecond time scale in the experiments of Masnovi and Kochi. Although ion pairs are presumably formed initially, the photoheterolysis systems employed in this study do not require such a species at the completion of the 20-ns laser pulse, the behavior being consistent with the presence of free ions at that time.[9d] (b) Masnovi, J. M.; Kochi, J. K. *J. Am. Chem. Soc.* **1985**, *107*, 7880–7893.

[15] This assumption requires that the ion pair not accumulate to a significant extent during the reaction or, in terms of the rate constants of eq 5, that $k_d[N_3^-] < k_{-d}$ or k_c. On the basis of the data of Masnovi and Kochi,[14a] values of $k_{-d} > 10^9$ s^{-1} are to be expected, particularly for the relatively polar solvents involved in the present study. With azide concentrations less than 1 mM, $k_d[N_3^-] < 10^7$ s^{-1} and steady-state kinetics will be observed. It can be noted that experimentally the kinetics with azide present showed good adherence to a simple exponential rate law. Deviations from such behavior are expected if this assumption is not valid.

Table IV. Calculated Rate Constants for the Diffusion-Controlled Reactions of Cations in Water and Acetonitrile at 20 °C

R^+	Nu	solv	$10^5D_{R^+}$[a]	10^5D_{Nu}[a]	r_o[b]	R[b]	k_d(max)[c,d]	k_d(obs)[d]	k_d(obs)/k_d(max)
T^+	N_3^-	W	0.6	1.6	3.5	8.3	1.4×10^{10}		
D^+	N_3^-	W	0.8	1.6	3.5	8.3	1.5×10^{10}	7.4×10^9	0.49
T^+	N_3^-	AN	1.6	2.1	3.5	15.5	4.3×10^{10}	1.1×10^{10}	0.26
D^+	N_3^-	AN	1.9	2.1	3.5	15.5	4.7×10^{10}	1.8×10^{10}	0.38
D^+	Br^-	AN	1.9	2.3	3.8	15.5	5.0×10^{10}	2.0×10^{10}	0.40

[a] Units of cm^2 s^{-1}. [b] Å. [c] Calculated from eq 8 with $\alpha_R = 4\pi$. [d] M^{-1} s^{-1}.

in these cases were of a similar order of magnitude to those in the limiting region observed here, for example, 1.0×10^{10} M^{-1} s^{-1} for azide plus the two diazonium ions in DMSO. In addition to the magnitudes of the rate constants, the changeover from activation control was seen in a sharp break in the log k–N_+ correlations. (The data of the present study might be argued to show comparatively a more shallow break, but this is somewhat misleading since many more systems near the changeover point were examined than in the Ritchie studies.)

The limiting rate constants, k_d, for both cation types are listed as a function of solvent in Table III. For the triarylmethyl cation, these were obtained as described previously from the three-parameter fit of eq 7 to the experimental data. For the diarylmethyl cations, the value of α was found to have little effect in the fitting procedure and this was fixed at 0.8, the average for Ar_3C^+. There was in fact little difference in the value of k_d derived from this fitting procedure and one obtained by simply averaging the rate constants for Ar_2CH^+ excluding the value for 4,4′-$(MeO)_2D^+$. In 100% water, where only 3,4′-$(MeO)_2D^+$ was studied, k_d was taken to be its value of k_{Az}. The values of k_d are relatively constant from 100 to 50% water and then increase by a factor of ~2.5 on proceeding to 99% acetonitrile. In every solvent where both types of cation were studied, the limit for the diarylmethyl cation was higher than that for the triarylmethyl cation by a factor of 1.6 ± 0.2. These trends are illustrated in Figure 2.

Figure 2 also illustrates the solvent dependency of k_{Az} for two ions that do not react at the diffusion limit. For 4-MeT^+, whose k_{Az} values are about 50% of k_d, a reasonable parallelism with the limit is observed, as is expected since diffusion is partly rate-limiting. For 4,4′,4″-$(MeO)_3T^+$, which reacts in the more aqueous solutions considerably below the limit, no such parallelism exists, with an increase in k_{Az} of approximately 3 orders of magnitude from 100% water to 100% acetonitrile. This undoubtedly reflects the effect of decreasing solvent polarity on k_c, since the combination involves two ions of opposite charge.

Rate Constants for Diffusion-Limited Reactions of Carbocations. The Debye–Smoluchowski equation[17] for the time-independent rate constant for the diffusion-limited reaction of two ions is

$$k_d = \alpha_R NR(D_A + D_B)/1000 \qquad (8)$$

where k_d has units of M^{-1} s^{-1}, N is Avogadro's number, D_A and D_B are the diffusion coefficients of the two ions in units of cm^2 s^{-1}, and R in units of cm is given by

$$R = r_c/[\exp(r_c/r_0) - 1] \qquad (9)$$

where r_0 is the encounter distance, the separation of the ions in contact, and r_c accounts for Coulombic interactions between the two ions. For singly charged ions of opposite charge, the values of r_c at 20 °C are −7.3 Å for water (dielectric constant $\epsilon = 78.5$) and −15.3 Å for acetonitrile ($\epsilon = 37.5$) (with the negative sign arising because of the manner in which eq 9 is written). The quantity α_R in eq 8 can be equated to the solid angle through which encounter of the two ions leads to reaction. For spherically symmetrical ions that react on every encounter this is equal to 4π.

The value of r_0 is normally approximated as the sum of the ionic radii of the reacting ions.[18] For azide, the ionic radius deduced from crystal structures is 1.6 Å;[19] a value obtained through thermochemical consideration of lattice energies,[20] 1.8 Å, is in reasonable agreement. The crystal structure of triphenylmethyl perchlorate shows this to be a propeller-shaped molecule with angles of 31.8° between the plane of each phenyl ring and the plane defined by the central carbon and its three attached carbons.[21] A disordered perchlorate sits above this plane, with a distance of 4.1 Å between the chlorine and the central carbon. Although anions obviously cannot approach this closely in the direction of the plane, this perchlorate obviously models the reacting configuration for a cation–anion combination. Taking an ionic radius for perchlorate of 2.3 Å,[20] then the contact distance for a carbocation in the reacting ion pair can be taken as 1.8 Å.

Diffusion coefficients for ions can be calculated from their limiting single-ion equivalent conductivities, λ_0, using the formula $D = 2.6 \times 10^{-7}\lambda^0$ at 20 °C.[22] For azide, λ_0 in water at 25 °C is 69 cm^2/Ω^{-1} mol^{-1};[23] this can be corrected to a value at 20 °C by multiplying by 0.9, a factor based on the temperature dependencies of other anions and cations.[23] There is no value in the literature for azide in acetonitrile. The Stokes–Einstein equation[24] predicts that the diffusion coefficient (and therefore the conductivity) should be proportional to the inverse of the viscosity of the solution, and with viscosities of water and acetonitrile of 0.890 and 0.344 cP, respectively,[25] the prediction is a factor of 2.58 increase. Conductivities of anions do rise from water to acetonitrile, but the factors are generally smaller—1.29 (Br–), 1.33 (I–), 1.54 (ClO_4–), and 2.55 (picrate),[26] with only picrate, a large, delocalized organic ion, close to the theoretical value. We will assume that the increase for azide will be similar to that of the two halides and use a value of $1.3\lambda_0$ (W) for λ_0 of azide in acetonitrile. Azide is more delocalized than bromide but in terms of its ionic radius it is slightly smaller. Some justification for the assignment for azide comes in the observation that the rate constant for the diffusion-limited reaction of bromide with diarylmethyl cations is 2.0×10^{10} M^{-1} s^{-1} in acetonitrile.[27] This is comparable to the number for azide, indicating that the diffusion coefficients for the two ions must be similar.

Neither diffusion coefficients nor conductivity data are available for the carbocations. These, however, can be modeled by quaternary ammonium ions, with the assumption that a carbocation will behave similarly to an ammonium ion of the same total volume. Although their shapes are different, the two classes of ions are similar in that both are large and relatively poorly solvated, and thus their mobility should be mainly dependent on size. Van der Waals volumes calculated from atomic increments[28] are 233

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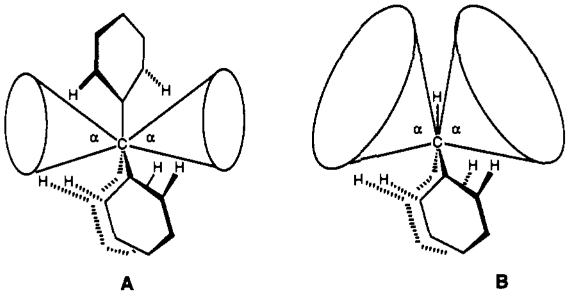

Figure 3. Angles of approach leading to reaction of nucleophiles to triarylmethyl and diarylmethyl cations. The solid angle α in A is $\pi/2$ and in B, π.

Å^3 for Ph_3C^+ and 164 Å^3 for Ph_2CH^+, so that these can be represented by Pr_4N^+ (231 Å^3, $\lambda_0 = 23.4$ (W)[23] and 70.3 (AN)[26]) and Et_4N^+ (163 Å^3, $\lambda_0 = 32.6$ (W)[23] and 84.8 (AN)[26]). These conductivities refer to 25 °C and are adjusted to 20 °C by multiplying by 0.9, as in the previous text.

Results of the calculations are tabulated in Table IV, with k_d(max) the rate constant obtained from eq 8 with $\alpha_R = 4\pi$, that is, if every encounter resulted in reaction. A reasonable assessment of the uncertainties in the various terms suggests that these k_d(max) are reliable to at least ±20%, and in some cases are probably better than that.[29] The uncertainties are certainly not great enough to explain why the values of k_d(obs) are lower than k_d(max). Moreover, they do not explain the lower rate constant for the triarylmethyl cation, since the prediction is that there should be no more than about a 10% difference between this system and a diarylmethyl cation. These deviations are obviously accounted for by recognizing that there is steric hindrance with these unsymmetrical ions, and not every collision will result in reaction. The suggestion is that with a triarylmethyl cation ~25% of the collisions are effective, while a figure of 40–50% applies to a diarylmethyl cation. There is no simple theory to calculate what fraction of the surface area of these ions will lead to reaction. However, examination of simple models suggests that the above numbers are not unreasonable. Moreover, it is also easy to qualitatively visualize why there is a difference between the two types of cation. As represented in Figure 3, a reasonably narrow angle of approach of the nucleophile is required with the triarylmethyl cation in order for it to avoid the aromatic rings. Replacing one of these by hydrogen removes some of this steric obstruction, and reaction can occur through a greater angle.[30]

Azide–Water Selectivities. Ta-Shma and Rappoport (TR) have recently considered the extensive k_{Az}/k_{H_2O} data obtained from competition kinetics that are available in the literature.[6c] They proposed that a plot of log k_{ion} for RCl solvolysis versus log k_{Az}/k_{H_2O} indicated five regions of behavior: (a) a constant selectivity region for very stable cations, as observed by Ritchie, (b) a border region where selectivity decreases more rapidly than reactivity, (c) a region where the reaction with azide has reached diffusion control and selectivity parallels reactivity, (d) a nearly constant low-selectivity region possibly corresponding to a preassociation ion-pair mechanism, and (e) an inverted region where the reaction with azide is mainly S_N2. Regions a–c, which correspond to reactions proceeding by way of free cations, are depicted by the dashed curve in Figure 4.

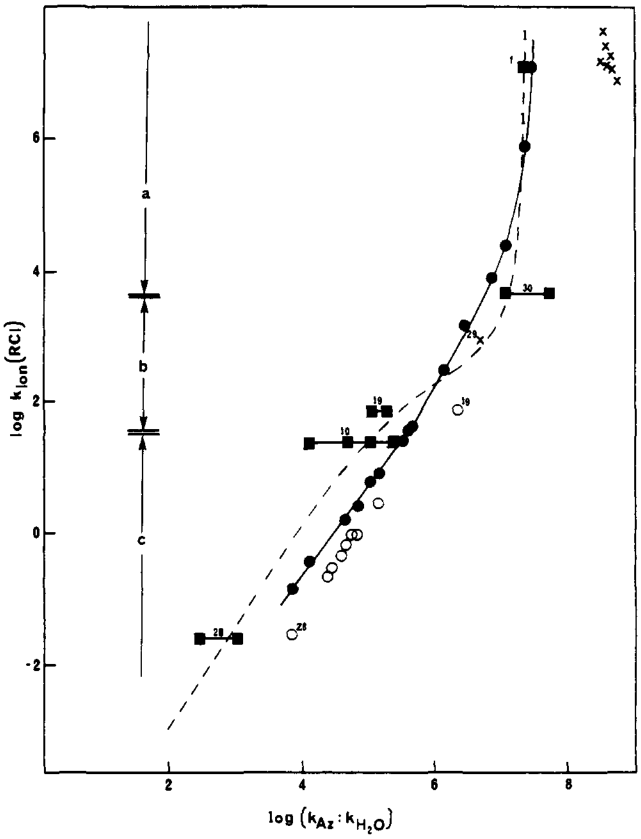

Figure 4. Log k_{ion} for the solvolysis of RCl versus log (k_{Az}/k_{H_2O}). The dashed curve is that drawn by Ta-Shma and Rappoport on the basis of data in 80% acetone at 20 °C.[6c] The solid squares are taken from their compilation of data. Cation **30** is 4-(dimethylamino)phenethyl. Other points refer to directly measured k_{Az}/k_{H_2O} values: solid and open circles, respectively, to triarylmethyl and diarylmethyl cations in 67% acetonitrile at 20 °C (this work) and "X" to xanthylium ions[9b] in 20% acetonitrile at 20 °C. The log k_{H_2O} values have been obtained by dividing k_S by the appropriate concentration of water. Log k_{ion} for these cations has been estimated as described in the text. The solid line has been drawn through the points for the triarylmethyl cations.

To place the directly measured data from the present study on this plot, values of k_{ion} are required for the chloride RCl corresponding to the various cations. These numbers can be estimated through a free energy relationship. The cations **1** (4,4',4''-$(MeO)_3T^+$), **10** (T^+), **19** (4,4'-$(MeO)_2T^+$), and **28** (4,4'-Me_2T^+) were also considered by TR, and a plot of log k_{ion} taken from their compilation versus the directly measured log k_S is reasonably linear.[31] Thus, interpolation using the k_S values for the other cations provides their k_{ion}. Values of k_{Az} and k_S directly measured in 67% acetonitrile were then employed to obtain the selectivity ratio, with the solvent rate constant being converted to second-order units. A comment can be made concerning this last procedure. TR considered data in a variety of solvents and used bimolecular rate constants for the water reaction to correct to their standard solvent, 80% acetone. They admitted some doubt as to the validity of the practice. Our results show very clearly that these second-order rate constants are not constant. This is apparent in the increase in k_S from 100% water to about 80% acetonitrile despite the decrease in water concentration. Values of $k_S/[H_2O]$ actually increase significantly, by ~1 order of magnitude over this range. This is undoubtedly one of the factors

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[29] For a reaction involving the combination of ions of opposite charge, the quantity R in eq 8 is largely determined by the Coulombic term r_c. Thus, errors in r_0 are of lesser importance and the diffusion coefficients are the major source of uncertainty. In water, the quantity $D_A + D_B$ is determined mainly by the value for the more mobile azide ion, whose diffusion coefficient is known. In acetonitrile, the analogy to bromide, whose diffusion coefficient is also known, suggests that value assumed for azide cannot be too much in error. As an example, for the reaction in acetonitrile of Ar_2CH^+ with azide, errors of 25% in D_R^+, 10% in D_{Az}, and 20% in r_0 result in an uncertainty in k_d(max) of 20%. Note that the calculation of r_c uses point charges. The more diffuse nature of the charge in the cations may mean that a lower value of r_c should be used.

[30] (a) Rather than just examining the angle of approach, a model can be envisaged involving competition between diffusional separation in the ion pair and rotation within the solvent cage.[30b] This allows an initially nonproductive encounter to react if the partners rotate to a reactive configuration before separating. (b) Solc, K.; Stockmayer, W. H. *Int. J. Chem. Kinet.* **1973**, *5*, 733–752.

[31] (a) This linear relationship has been suggested by TR to explain the linearity of log k_{ion} and log (k_{Az}/k_{H_2O}) in region c[6c] and also from an analysis of data for the solvolysis of diarylmethyl systems.[31b] (b) Schade, C.; Mayr, H. *Tetrahedron* **1988**, *44*, 5761–5770.

behind the scatter in the TR plot.

Considering the uncertainty in k_{ion} and the different solvents, the data from this work fall quite close to the TR curve (Figure 4). They do, however, indicate that region b is not real. This was a possibility admitted by TR, who proposed this region essentially to fit the points for **10** (T^+), **19** (4,4′-$(MeO)_2D^+$), and **30** (4-$Me_2NC_6H_4CHCH_3^+$) (see Figure 4). The more extensive data from this study, particularly for the triarylmethyl cations, show that there is a single break from the constant selectivity region a to region c. Our data also suggest that there is not a single curve describing the behavior of all cations but there are separate families, for example, triarylmethyl, diarylmethyl, and xanthylium ions. These families are also apparent from the curves in Figure 1. This dependency on the type of cation is undoubtedly another factor in the scatter of the TR plot. A recent example shows how large the deviations can be. The 1-(*p*-methoxyphenyl)-2,2,2-trifluoroethyl cation has a similar $k_{\mathrm{Az}}/k_{\mathrm{S}}$ ratio to its nonfluorinated analogue, the 1-*p*-methoxyphenethyl cation, and yet k_{ion} for the formation of the former is ~6 orders of magnitude smaller.[32]

The "Azide" Clock. As a general conclusion, the assumption of diffusion control in the "azide" clock method is valid but only for cations with k_{S} greater than $10^6\ \mathrm{s}^{-1}$. For cations that are slightly longer lived, k_{Az} will be reasonably close to that for diffusion control, but when k_{S} drops to 10^3–$10^4\ \mathrm{s}^{-1}$, the difference will be large, and values of k_{S} calculated from selectivity ratios with the assumption will be overestimates. The value of $5 \times 10^9\ \mathrm{M}^{-1}\ \mathrm{s}^{-1}$ taken for k_{d}(azide), and admittedly an approximation,[7f,g] is a good choice. The actual numbers are probably slightly larger than this. For example, $7 \times 10^9\ \mathrm{M}^{-1}\ \mathrm{s}^{-1}$ would be an appropriate number for a diarylmethyl cation in 0–50% acetonitrile–water. However, as shown by the results of this study, there are effects of solvent and cation structure, and these are difficult to predict at the theoretical level, particularly the latter effect. The conclusion, however, is that rate constants calculated from selectivity ratios using $k_{\mathrm{Az}} = 5 \times 10^9\ \mathrm{M}^{-1}\ \mathrm{s}^{-1}$ will be within a factor of 4 of the true value, providing the cation is short-lived. In highly aqueous solutions the agreement may even be better.

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Supplementary Material Available: Tables of rate constants k_{Az} and k_{S} for the reactions of triarylmethyl and diarylmethyl cations in acetonitrile–water solutions of varying composition (3 pages). Ordering information is given on any current masthead page.

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Analysis of Asymmetry in the Distribution of Helical Residues in Peptides by ^{1}H Nuclear Magnetic Resonance

M. I. Liff, P. C. Lyu, and N. R. Kallenbach*

Contribution from the Department of Chemistry, New York University, 4 Washington Place, New York, New York 10003.
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Abstract: Peptides that assume full or partial helical structure in aqueous solution have provided useful models for investigating the determinants of α-helical structure. Circular dichroism (CD) spectroscopy, the usual measure of helicity, affords an estimate of the mean helix content when calibrated against suitable standards. Analysis of these systems by means of ^{1}H NMR makes it possible to determine precisely the location and extent of helix structure in a chain. NMR criteria for identifying helical domains include the following: NOE's between adjacent NH protons and between an NH proton at position i and the Cα proton at $i + 3$; values of the three-bond coupling constants $^3J_{\alpha N}$; and the relative chemical shift of the Cα protons. Application of these criteria to members of the series of partially helical synthetic peptides, succinylTyrSerGlu_4Lys_4XXX$Glu_4Lys_4NH_2$, in which sets of three amino acids are inserted between blocks of glutamic acid and lysine side chains, shows that the helix is located preferentially near the N terminus in chains with the central substitution Ala_3,Leu_3, as well as in the parent species lacking any substitution. The degree of helicity rises sharply at the N terminus to a maximum near residue 8 and diminishes gradually from Glu14 to the C terminus. Application of the NMR criteria to the peptide containing Gly_3 reveals very little helical structure in this peptide. These results suggest that helix formation in short chains does not conform to an all-or-none reaction.

Introduction

The α-helix constitutes one of the dominant structural motifs in proteins.[1] Models of the process of forming an α-helix more from initially disordered residues suggest that nucleating a helix is intrinsically more difficult than its propagation;[2] theoretical descriptions introduce two sets of equilibrium constants to take this into account.[2,3] In the notation introduced by Zimm and Bragg,[3] nucleation of a helix by forming the initial peptide hydrogen bond has equilibrium constant $\sigma s \ll 1$, while the propagation of a nucleated helix has a stability constant, s. The fact that certain amino acids tend to occur frequently in the helical regions within proteins of known structure, while others do so rarely,[4] raises the possibility that the sequence of amino acid side chains governs the stability or lack of stability of α-helical structure. The availability of synthetic polypeptides has made it possible to test this proposition experimentally. In an extended investigation, Scheraga's group determined experimental values of σ and s for each of the 20 natural amino acids, by incorporating them at low concentration as "guests" into synthetic copolymers

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