JOC *Featured Article*

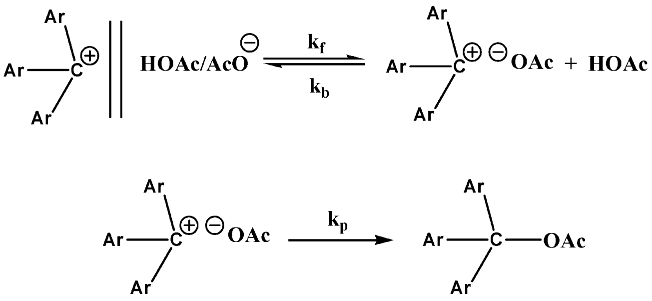
Rapid Formation and Slow Collapse of a Carbocation−Anion Pair to a Neutral Molecule

Weifang Hao and Vernon D. Parker*

Utah State University, Department of Chemistry and Biochemistry, Logan, Utah 84322

vparker@cc.usu.edu

Received November 20, 2007



The 4,4′,4″-trimethoxytrityl cation (TMT^+) was observed to react with acetate ion in acetic acid reversibly to give the corresponding ester (TMT-OAc). The rate of the reaction was found to be independent of [NaOAc] over a 25000-fold range. Similar results were observed in the presence of Bu_4N^+ in acetic acid as well as in HOAc/AN (1/1). It was concluded that $\{TMT^+ (HOAc/AcO^-)\}$ is an ion pair that forms essentially completely from free TMT^+ and $HOAc/AcO^-$ during the time of mixing under stopped-flow conditions. The process which was studied kinetically is the intramolecular collapse of the ion pair to TMT-OAc which takes place in two steps involving a kinetically significant intermediate. The remarkably close resemblance of this reaction to the Winstein scheme for solvolysis reactions is noted. In analogy to the Winstein scheme, it was proposed that the intermediate could be an intimate ion pair formed upon extrusion of solvent from the solvent separated ion pair. The product-forming step could then correspond to the intimate ion pair reacting further to form a covalent bond between the two moieties within the complex. The values of the thermodynamic and the activation parameters as well as the apparent rate constants for the reaction in the presence of either sodium or tetrabutylammonium ions suggest that these counterions play insignificant roles in the reactions. However, the equilibrium constant for the intramolecular step (K_4) was observed to be two times greater in the presence of Bu_4N^+ than in the presence of Na^+. The rate of the reaction in HOAc was observed to be about four times as great as that in HOAc/AN (1/1).

Introduction

The study of the reactions of carbocations with nucleophiles has been a topic of intense interest for more than half a century.[1−18] There appears to be general agreement that the reactions take place in a single rate-determining step accompanied by the formation of a covalent bond between the two moieties. The main recent interest in these reactions has been on developing reactivity scales for both the cations and the nucleophiles.[19,20]

We regard the cation−anion combination reaction as one of the simplest covalent bond forming reactions possible. The reactions result in the formation of a single bond without disrupting any other covalent bonds. This suggests these

---

(1) Turgeon, V. C.; LaMer, V. K. *J. Am. Chem. Soc.* **1952**, *74*, 5988.
(2) Duynstee, E. F. J.; Grunwald, E. *J. Am. Chem. Soc.* **1959**, *81*, 4342.
(3) Diffenback, R. A.; Sano, K.; Taft, R. W. *J. Am. Chem. Soc.* **1966**, *88*, 4747.
(4) Ritchie, C. D.; Skinner, G. A.; Badding, V. G. *J. Am. Chem. Soc.* **1967**, *89*, 2063.
(5) Hill, E. A.; Mueller, W. J. *Tetrahedron Lett.* **1968**, 2565.
(6) Noyce, D. S.; Brauman, S. K. *J. Am. Chem. Soc.* **1968**, *90*, 5218.
(7) Brauman, J. I.; Archie, W. C., Jr. *J. Am. Chem. Soc.* **1970**, *92*, 5981.
(8) Ritchie, C. D.; Virtanen, P. O. I. *J. Am. Chem. Soc.* **1972**, *94*, 4963, 4966.
(9) Bunton, C. A.; Huang, K. *J. Am. Chem. Soc.* **1972**, *94*, 3536.
(10) Ritchie, C. D. *Acc. Chem. Res.* **1972**, *5*, 348.
(11) Ritchie, C. D.; Virtanen, P. O. I. *J. Am. Chem. Soc.* **1973**, *95*, 1882.
(12) Bunton, C. A.; Haung, S. K. *J. Am. Chem. Soc.* **1974**, *96*, 515.

10.1021/jo702492r CCC: $40.75

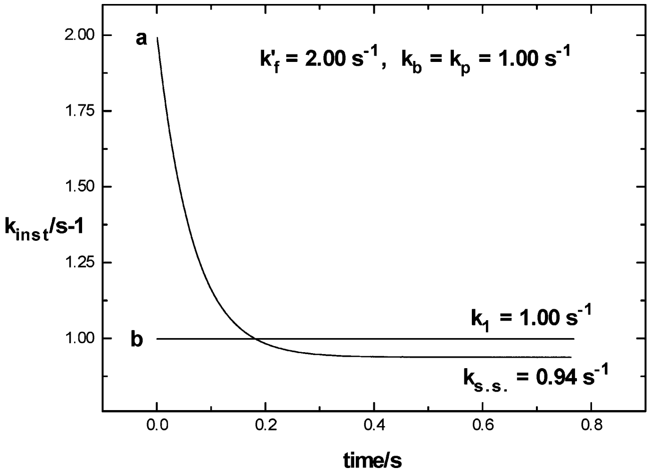
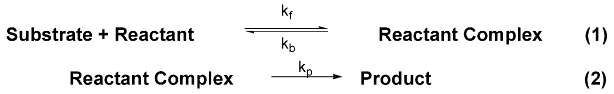


FIGURE 1. IRC plots for pre-association (a) and single-step (b) mechanisms.

reactions as an obvious target for our ongoing research,[21−32] the results of which show that many fundamental organic reactions previously believed to take place in a single step actually take place by a mechanism with more than one transition state.

The ability to distinguish between single-step and more complex reaction mechanisms has been enhanced by the development of instantaneous rate constant (IRC) analysis[33] which allows the course of the reaction to be analyzed in terms of the apparent instantaneous rate constant (k_{inst}) as a function of time. For the single step mechanism in the absence of any complications, k_{inst} is a true constant independent of time. On the other hand, k_{inst} varies with time in the *pre-steady-state time period* for a more complex mechanism and approaches the steady-state value ($k_{\mathrm{s.s.}}$) with increasing time. These relationships are illustrated in Figure 1 for a reaction following the pre-association mechanism (Scheme 1) in which the intermediate reactant complex is kinetically significant. This mechanism was chosen for the illustration since it has been widely discussed[34] and is the simplest complex mechanism involving consecutive reactions.

SCHEME 1



The IRC−time profile for the pre-association mechanism (a) in Figure 1 intercepts the 0 time axis at 2.00, which corresponds to k_f and approaches the steady-state value (0.94 s^{-1}). That for the single-step mechanism (b) ($k_1 = 1.00\ s^{-1}$) is a straight line with zero slope. The ease of distinguishing between the two mechanisms under the conditions of the calculated data is apparent from Figure 1.

The objective of this study was to determine the mechanism of a cation−anion combination reaction. We selected the 4,4′,4″-trimethoxytrityl cation (TMT^+), a carbocation of moderate reactivity toward nucleophiles,[12] as the cationic reactant and acetate ion as the anionic reactant. In order to moderate the rate of the cation−anion combination reaction, we chose acetic acid as the solvent for this study. It is well-known that acetate ion exists in acetic acid as the hydrogen-bonded complex, hydrogen biacetate ion ($HOAc/AcO^-$),[35] and this is expected to markedly affect the nucleophilicity of the ion. Choosing conditions under which the rates of the anion−cation combinations are moderate is of special importance in attempting to determine whether the reactions follow a single step or more complex reaction mechanisms. This is because of the fact that the initial portion of the reaction, i.e., the pre-steady-state time period, must be accessed in order to differentiate between the mechanisms. Since cation−anion combination reactions are inherently rapid reactions, most of the previous kinetic studies have out of necessity been carried out under conditions where the initial time periods could not be accessed.

Results

The reaction between TMT^+ and NaOAc in acetic acid to form the corresponding ester is reversible. The approach to equilibrium is illustrated by the spectra in Figure 2 for the decrease in [TMT^+]. The reversible reaction is illustrated in Scheme 2. No reaction between TMT^+ and acetic acid could be detected in the absence of acetate ion.

Definitions of Rate Constants. A number of different methods were used to obtain rate constants in this work. In order to avoid confusion as to the meaning of the abbreviations used to define the rate constants, the definitions are given below:

k_{inst} = An apparent pseudo first-order rate constant obtained by an IRC procedure over short time intervals. These can be time dependent in the manner illustrated in Figure 1.

$k_{\mathrm{s.s.}}$ = An apparent pseudo first-order rate constant evaluated in the plateau region of the k_{inst}−time profile.

k_N = An apparent pseudo-first-order rate constant evaluated in the conventional way over a segment of the (1 − E.R.)−time profile where E.R. is the extent of reaction. The subscript N signifies the segment number, and k_N can be time dependent.

The Effect of Acetate Ion Concentration on the Reaction Rate. Kinetic experiments were carried out by stopped-flow spectrophotometry under a nitrogen atmosphere in a glove box. Our initial experiments in glacial acetic acid gave rise to

---

(13) Ritchie, C. D. *J. Am. Chem. Soc.* **1975**, *97*, 1170.

(14) Ritchie, C. D.; Sawada, M. *J. Am. Chem. Soc.* **1977**, *99*, 3754.

(15) Ritchie, C. D.; Van Verth, J. E.; Viranen, P. O. I. *J. Am. Chem. Soc.* **1982**, *104*, 3491.

(16) Ritchie, C. D. *J. Am. Chem. Soc.* **1984**, *106*, 7187.

(17) Ritchie, C. D. *Can. J. Chem.* **1986**, *64*, 2239.

(18) Arnett, E. M.; Flowers, R. A.; Ludwig, R. T.; Meekhof, A.; Walek, S. *Pure Appl. Chem.* **1995**, *67*, 729.

(19) Mayr, H.; Kempf, B.; Ofial, A. R. *Acc. Chem. Res.* **2003**, *36*, 66 and references cited therein.

(20) Minegishi, S.; Mayr, H. *J. Am. Chem. Soc.* **2003**, *125*, 286.

(21) Parker, V. D.; Zhao, Y.; Lu, Y.; Zheng, G. *J. Am. Chem. Soc.* **1998**, *120*, 12720.

(22) Lu, Y.; Zhao, Y.; Parker, V. D. *J. Am. Chem Soc.* **2001**, *123*, 5900.

(23) Zhao, Y.; Lu, Y.; Parker V. D. *J. Chem. Soc., Perkin Trans.* **2001**, *2*, 1481.

(24) Parker, V. D.; Zhao, Y. J. *Phys. Org. Chem.* **2001**, *14*, 604.

(25) Zhao, Y.; Lu, Y.; Parker, V. D. *J. Am. Chem. Soc.* **2001**, *123*, 1579.

(26) Lu, Y.; Zhao, Y.; Handoo, K. L.; Parker, V. D. *Org. Biomol. Chem.* **2003**, *1*, 173.

(27) Handoo, K. L.; Lu, Y.; Zhao, Y.; Parker, V. D. *Org. Biomol. Chem.* **2003**, *1*, 24.

(28) Lu, Y.; Handoo, K. L.; Parker, V. D. *Org. Biomol. Chem.* **2003**, *1*, 36.

(29) Parker, V. D.; Lu, Y. *Org. Biomol. Chem.* **2003**, *1*, 2621.

(30) Handoo, K. L.; Lu, Y.; Zhao, Y.; Parker, V. D. *J. Am. Chem. Soc.* **2003**, *125*, 9381.

(31) Parker, V. D.; Lu, Y.; Zhao, Y. *J. Org. Chem.* **2005**, *70*, 1350.

(32) Parker, V. D. *Pure Appl. Chem.* **2005**, *77*, 1823.

(33) Parker, V. D. *J. Phys. Org. Chem.* **2006**, *19*, 714.

(34) Ridd, J. H. *Adv. Phys. Org. Chem.* **1978**, *16*, 1.

(35) Clark, J. H.; Emsley, J. *J. Chem. Soc., Dalton Trans.* **1973**, 2760.

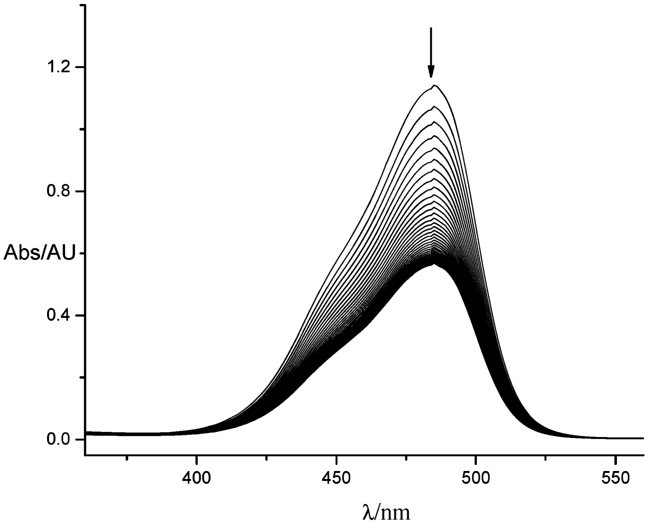


FIGURE 2. Diode-array visible absorption spectra of TMT^+ (0.02 mM) in acetic acid containing sodium acetate (0.01 M): start time, 0 s; cycle time, 2.5 s; total run time, 100 s.

SCHEME 2. Reversible Reaction between TMT^+ and Sodium $HOAc/AcO^-$ in Acetic Acid

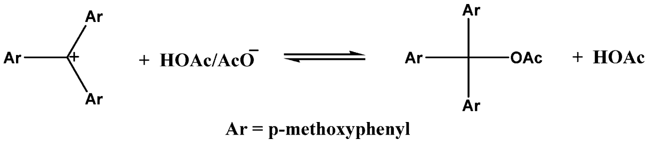


TABLE 1. Effect of Sodium Acetate Concentration on the Apparent Steady-State Rate Constant for the Reaction of TMT^+ with Sodium Acetate in Acetic Acid at 298 K

$[TMT^+]$/mM	[NaOAc]/mM	$k_{s.s.}/s^{-1\,a}$
0.20	500	0.0645
0.20	250	0.0586
0.20	125	0.0597
0.20	10.0	0.0529
0.20	2.50	0.0537
0.010	0.10	0.0593
0.010	0.020	0.0767

[a] $k_{s.s.}$ was evaluated from 200 data points near the half-life of the reaction.

remarkable results. The rate of the reaction was observed to be independent of sodium acetate concentration over a wide range for the reaction of TMT^+ with acetate ion in acetic acid at 298 K (Table 1). [NaOAc] was varied over the entire applicable range, from 0.50 to 0.00002 M with only random variations in $k_{s.s.}$ The data in the last entry in Table 1 where [NaOAc] and $[TMT^+]$ were equal to 0.02 and 0.01 mM, respectively, were subject to significant error due to the small absorbance change for the reaction. The latter data are included to show that the zero-order in [NaOAc] appears to continue as long as there is enough acetate ion present for TMT^+ to completely react.

The data in Table 2 show that the rate of the reaction of TMT^+ with Bu_4N^+ $HOAc/AcO^-$ in acetic acid is also independent of the salt concentration. The value of $k_{s.s.}$ obtained at 480 nm was observed to be constant within experimental error as $[Bu_4N^+\ HOAc/AcO^-]$ was varied from 2 to 20 mM.

The data in Tables 1 and 2 suggest that TMT^+ and $HOAc/AcO^-$ in acetic acid react during the time of mixing. This reaction is reversible (see Figure 1), but because of saturation of equilibrium (3) with respect to $[HOAc/AcO^-]$ there is not a direct relationship between the latter and the concentration of the product (TMT-OAc) at equilibrium. The most likely explanation of zero-order kinetics in acetate ion for this reaction is that $HOAc/AcO^-$ very rapidly interacts with TMT^+ to form an ion-pair, i.e., equilibrium (3) is saturated at all $[HOAc/AcO^-]$ in Table 1 and 2. The ion-pair then reversibly undergoes an intramolecular combination reaction (eq 4) resulting in the formation of the corresponding acetate ester. Since equilibrium (3) is established during the time of mixing in the stopped-flow spectrophotometer, the process that takes place during our kinetic experiments is illustrated by equilibrium (4) (Scheme 3).

TABLE 2. Apparent Steady-State Rate Constants for the Reaction between TMT^+ and Acetate Ion as a Function of $[Bu_4N^+\ HOAc/AcO^-]$ in Acetic Acid at 298 K[a]

$[Bu_4N^+\ HOAc/OAc^-]$/mM	$k_{s.s.}/s^{-1\,b}$	$[TMT\text{-}OAc]_{equil}/[TMT^+]_{equil}$ (= K_4)
20.0	0.0668	1.81
10.0	0.0701	1.89
5.0	0.0710	2.12
2.0	0.0679	1.97

[a] From absorbance−time data at 480 nm. [b] $k_{s.s.}$ was evaluated from 200 data points near the half-life of the reaction.

SCHEME 3. Equilibria Involved in the Reaction of TMT^+ and $HOAc/AcO^-$

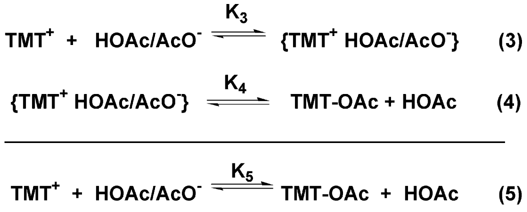


TABLE 3. Ratios of Conventional Pseudo First-Order Rate Constants Evaluated over Initial Data Segments Divided by the Apparent Steady-State Rate Constant ($k_{s.s.} = 0.065\ s^{-1}$) for the Reaction of TMT^+ with $HOAc/AcO^-$ (0.5 M) in Acetic Acid at 298 K

segment/N	$k_N/k_{s.s.}$(21point)	$k_N/k_{s.s.}$(31point)	$k_N/k_{s.s.}$(51point)
1	2.64	2.02	1.51
2	1.12	1.15	1.10
3	1.13	1.09	1.09
4	1.05	1.07	1.07
5	1.09	1.09	1.06
6	1.07	1.07	1.05
7	1.09	1.08	1.05

The Results of Conventional Kinetic Studies of the Combination Reaction in Acetic Acid. The method of data treatment involved evaluating pseudo first-order rate constants over consecutive intervals consisting of three different series of segments. The 21 point procedure included the following segments: data points 1−21(1), 21−41(2), 41−61(3), 61−81(4), 81−101(5), 101−121(6), and 121−141(7) for absorbance−time data obtained by stopped flow spectrophotometry. The 31- and 51-point segments were constructed in the same manner as those in the 21-point procedure. The pseudo first-order rate constants (k_N) evaluated for each time segment are finally divided by the apparent steady-state rate constant ($k_{s.s.}$) calculated from data at times approaching the half-life of the reaction resulting in dimensionless ratios.

The initial rate data in Table 3 were obtained by the consecutive segment treatment of kinetic data for the pseudo-

TABLE 4. Apparent Pseudo-First-Order Rate Constants Ratios Observed for the Reactions of TMT^+ with NaOAc (0.50 M) in Acetic Acid at 298 K

λ/nm	[TMT]/mM	$(k_1(31)/k_{s.s.})^a$	$k_{s.s.}/s^{-1\,b}$	K_4
420	0.10	1.35	0.0646	0.79
430	0.04	1.38	0.0679	0.94
440	0.04	1.67	0.0681	0.83
450	0.02	1.41	0.0729	0.89
460	0.02	1.45	0.0725	0.91
470	0.02	1.44	0.0735	0.93
480	0.02	1.44	0.0711	0.92
490	0.02	1.55	0.0687	0.94
500	0.02	1.72	0.0730	0.92
510	0.02	2.29	0.0650	0.98
520	0.10	2.60	0.0698	0.78

[a] Pseudo-first-order rate constant over the first 31 data points in the 2000 point array divided by $k_{s.s.}$. [b] Evaluated from 200 points near the apparent half-life of the reaction.

first-order reaction of TMT^+ (0.0002 M) with acetate ion (0.50 M) in acetic acid at 298 K. The expected result for a single-step mechanism is that all of the rate constant ratios (the value of the observed pseudo-first-order rate constant divided by $k_{s.s.}$) in Table 3 are expected to be the same and equal to 1.00 within experimental error; i.e., pseudo-first-order rate constants for the single-step mechanism are expected to be time independent. This is equivalent to the straight line with zero slope in Figure 1a. The observed result is that the rate constants in all three sets of data exceed $k_{s.s.}$ by 2.64, 2.02, and 1.51 for the initial 21-, 31-, and 51-point segments, respectively, and the ratios in all three columns approach unity in subsequent segments. The data rule out the simple single-step mechanism for the intramolecular combination reaction between TMT^+ and $HOAc/AcO^-$ in acetic acid.

When an intermediate absorbs in the same spectral region as that where the kinetics of a reaction is monitored, the kinetic results will usually be wavelength dependent. This is because the kinetic analysis assumes that only reactant or product absorb at the wavelength where measurements are made. Conducting kinetic measurements over a range of wavelength then becomes a very effective tool in demonstrating whether a reaction takes place in a single step or by a more complex mechanism. The data in Table 4 summarize the results over the wavelength region from 420 to 520 nm for the reaction of TMT^+ with NaOAc (0.50 M) in acetic acid at 298 K. The variation in the $k_1(31)/k_{s.s.}$ ratio with wavelength suggests that there may be interference from absorbance due to an intermediate since the ratio is otherwise expected to be wavelength independent.

Estimation of the Equilibrium Constant for eq 4. The last columns in Tables 2 and 4 give estimates of K_4 (eq 4), the equilibrium constant for the reaction of the ion pair. These were obtained from the stopped flow experiments and were evaluated as the difference in initial (A_{init}) and infinity absorbances (A_{inf}) divided by (A_{inf}); $(A_{init} - A_{inf})/A_{inf}$). It is of interest to note that K_4 in HOAc at 298 K is about two times as great in the presence of Bu_4N^+ $HOAc/AcO^-$ (2.0 ± 0.1) as compared to that in the presence of Na^+ $HOAc/AcO^-$ (0.89 ± 0.09)

Effect of Cosolvent on the Kinetics of the Reactions of TMT^+ with $HOAc/AcO^-$. Consecutive segment kinetic data for the reaction of TMT^+ (0.02 mM) with $HOAc/AcO^-$ (5.0 mM) in HOAc/AN (1/1 vol) where AN is acetonitrile are summarized in Table 5. The results in the mixed solvent are similar to those in acetic acid in terms of the decrease in the rate constant ratios with the extent of reaction. The greatest difference in the results in the two solvents is that $k_{s.s.}$ in HOAc is about four times greater than in the mixed solvent.

TABLE 5. Ratios of Conventional Pseudo-First-Order Rate Constants Evaluated over Initial Data Segments Divided by $k_{s.s.}$ (0.0155 s^{-1}) for the Reaction of TMT^+ with Acetate Ion in HOAc/AN (1/1 vol) at 298 K

segment/N	$k_N/k_{s.s.}$(21point)	$k_N/k_{s.s.}$(31point)	$k_N/k_{s.s.}$(51point)
1	1.31	1.26	1.21
2	1.24	1.18	1.12
3	1.21	1.11	1.01
4	1.17	1.04	0.98
5	1.04	1.01	0.99
6	1.03	0.98	1.00
7	1.01	0.99	0.99

TABLE 6. Kinetic and Thermodynamic Parameters for the Collapse of $\{TMT^+\ HOAc/AcO^-\}$

solvent	$\Delta H^\ddagger$ kcal mol^{-1}	$\Delta S^\ddagger$ cal $mol^{-1}K^{-1}$	ΔH° kcal mol^{-1}	ΔS° cal mol^{-1} K^{-1}
HOAc	12.7	−21.5	−4.3	−14.3
HOAc/AN (1/1)	13.7	−20.7	−1.4	−5.2

The Effect of Temperature on the Rate and Equilibrium for the Collapse of $\{TMT^+\ HOAc/AcO^-\}$. The kinetics of the collapse of $\{TMT^+\ HOAc/AcO^-\}$ were studied in HOAc and in mixed solvent HOAc/AN (1/1 vol) in the temperature range from 293 to 323 K. The activation and thermodynamic parameters derived from these studies based upon $k_{s.s.}$ data are summarized in Table 6. The corresponding Eyring and van't Hoff plots for the reactions carried out in HOAc are shown in Figure 3 and those obtained from data in mixed solvent are illustrated in Figures S3 and S4 (Supporting Information).

Application of IRC Analysis to the Collapse of $\{TMT^+\ HOAc/AcO^-\}$. The IRC plots shown in Figure 4 are for reaction of TMT^+ with sodium acetate in acetic acid at 298 K for decay of absorbance due to reactant measured at 500 nm. The IRC−time profile for the first 3% of reaction, which was obtained from the fifth-order polynomial smoothed data is illustrated in Figure 4a. The curve appears to intersect the zero time axis at about 0.24 s^{-1} which provides an estimate of k_f in Scheme 4. The IRC−time profile begins to approach a plateau value at about 170 ms. The latter is more clearly illustrated by the IRC−time profile shown in Figure 4b. The latter was obtained using the 51-point sliding procedure described in the experimental section.

The IRC−time profiles shown in Figure 5 were constructed from data obtained at 430 nm during the reaction of TMT^+ (0.04 mM) with sodium acetate (0.5 M) in acetic acid at 298 K. The zero-time intercept in Figure 5a is similar to that observed in Figure 4a. The sine-wave-like behavior in the plateau portion of the IRC−time profile in Figure 5a is often observed in these plots and is due to spectrometer output noise which is not completely smoothed out by the fifth-order polynomial function. The effect of spectrometer output noise is illustrated even more clearly in the plateau regions of Figures 4b and 5b.

Discussion

The reaction coordinate (RC) diagram for the pre-association mechanism is illustrated in Scheme 5. Beginning with separated reactants on the far left, reactant and substrate diffuse and begin to collide resulting in what is called the encounter complex, which amounts to the two reactants in a solvent cage where it

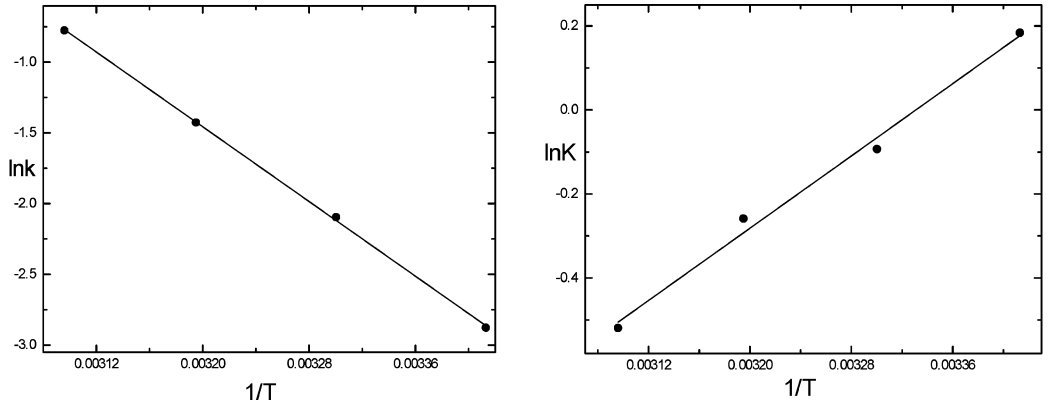


FIGURE 3. Eyring plot (a) for the collapse of the ion pair in acetic acid. Van't Hoff-like plot (b) for equilibrium (4) in HOAc.

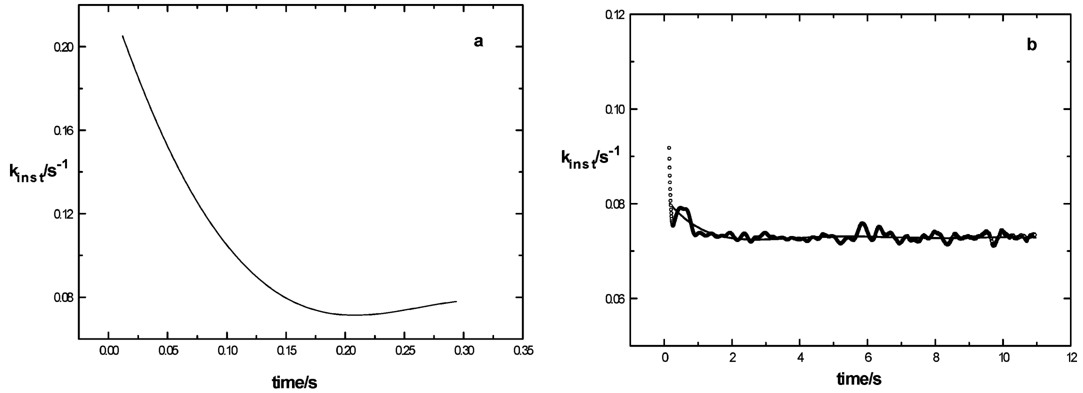


FIGURE 4. IRC time profiles for the reaction of TMT^+ (0.02 mM) with sodium acetate (0.50 M) in acetic acid. Data for the first 3% of the reaction (a) and that over the first-half-life (b).

SCHEME 4. Mechanism of the Combination Reaction

$$\{TMT^+\ HOAc/AcO^-\} \underset{k_b}{\overset{k_f}{\rightleftharpoons}} \text{Reactant Complex}$$

$$\text{Reactant Complex} \xrightarrow{k_p} \text{TMT-OAc} + \text{HOAc}$$

is thought that up to about 10 collisions occur before the reactants separate.[34] The diffusion process is illustrated by a double arrow within a circle on the RC. The encounter complex, which has a lifetime of a nanosecond or less depending upon the solvent, is transformed through the first transition state (TS A) to the reactant complex. We believe that this transformation consists of solvation and geometry changes leading to a configuration ready for covalent bond formation. The latter then is transformed through the second transition state (TS B) to products. This presentation of the RC diagram for pre-association uses the bar graph approach employed by Guthrie[36] in his discussion of reactions passing through tetrahedral intermediates. We use the diffusion element to emphasize how the encounter complex[34] is defined.

All of the kinetic data reported in Tables 1−5 and Figures 3−5 are inconsistent with a single-step mechanism for the reaction between TMT^+ with hydrogen biacetate ion either in the presence of Na^+ or Bu_4N^+ in acetic acid or in mixed solvents. Furthermore, the data are consistent with the pre-association mechanism under all circumstances. The data in Tables 1 and 2 show that the initial reaction takes place during the time of mixing in the stopped-flow spectrophotometer and that the process that can be studied kinetically is the intramolecular collapse of $\{TMT^+\ HOAc/AcO^-\}$ to the product, TMT−OAc (eq 4). The degree of reversibility of this process depends strongly on the solvent composition. The data in Tables 3−5 and in Figures 4 and 5 show that the intramolecular collapse of $\{TMT^+\ HOAc/AcO^-\}$ takes place in at least two steps and that the data are consistent with the reversible consecutive two-step mechanism illustrated in Scheme 4.

Since the mechanism depicted in Scheme 4 is the simplest mechanism consistent with the data, we adopt it for the sake of simplicity since there is no evidence currently available for a more complex mechanism. With the latter in mind, the reaction coordinate diagram illustrated in Scheme 6 was constructed to describe the intramolecular reaction. The reactant in the lower left-hand corner of the diagram is $\{TMT^+\ HOAc/AcO^-\}$. The first transition state (TS#1) lies between the reactant and an intermediate which we refer to as the "Reactant Complex" for which we have no structural data but it is required by the kinetics observed. In the following paragraphs we relate our work to Winstein's scheme for the dissociation of R-X, where R is an alkyl or an arylalkyl group and X is a leaving group, and provide a plausible suggestion for the structure of the "Reactant Complex". The second transition state (TS#2) lies between the "Reactant Complex" and the product TMT-OAc.

The concept of ion pairs in organic reactions owes much to the pioneering work of Winstein's group more than 50 years ago.[37] Using kinetic salt effects, they were able to provide

---

[36] Guthrie, J. P. *J. Am. Chem. Soc.* **1978**, *100*, 5892; **1974**, *96*, 3608; **1973**, *95*, 6999.

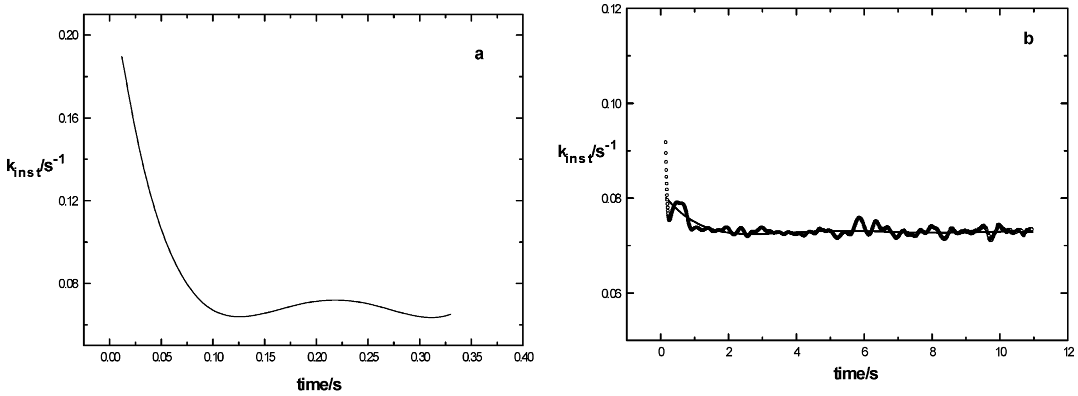
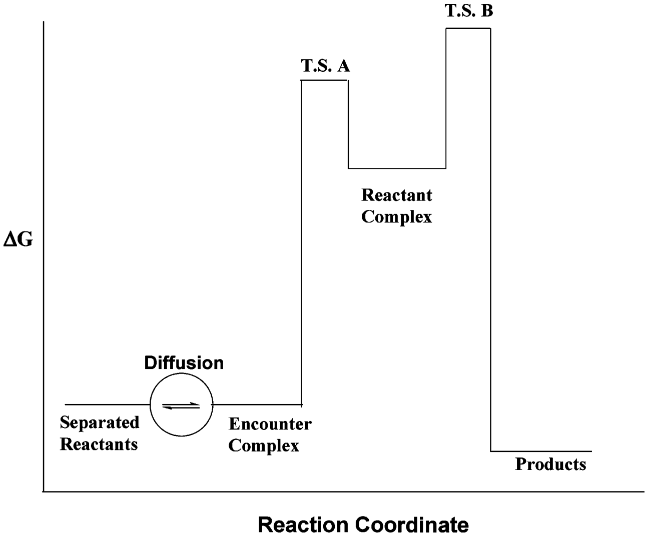


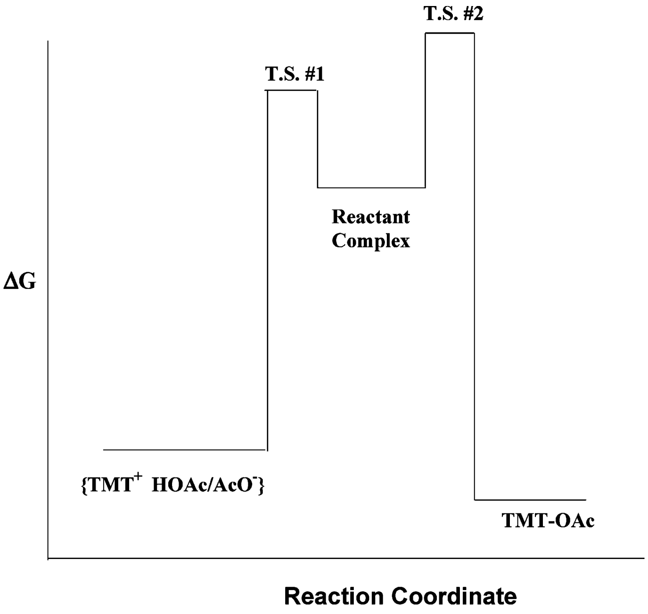
FIGURE 5. IRC time profiles for the reaction of TMT^+ (0.02 mM) with sodium acetate (0.50 M) in acetic acid. Data for the first 3% of the reaction (a) and that over the first half-life (b).

SCHEME 5. Reaction Coordinate Diagram for the Pre-association Mechanism

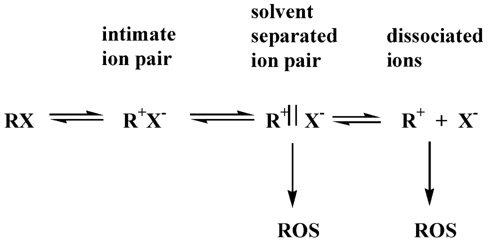


convincing evidence for Scheme 7 for the solvolysis reactions of RX (X = halide or other leaving groups). Ionization to the intimate ion pair which does not undergo solvolysis is the first step in this process. The binding between the ions is weakened and solvent separates the two in the solvent separated ion pair. At this stage R^+ can react irreversibly with solvent to give the substitution product. Alternatively, the solvent separated ion pair can dissociate to the free ions and R^+ can react to form the substitution product. The solvent separated ion pair was observed to undergo exchange with other anions intentionally incorporated in the solution for purposes of studying the process and the substitution reaction could be nearly completely suppressed in the presence of the common ion, X^-.

SCHEME 6. Reaction Coordinate Diagram for the Intramolecular Collapse of {TMT^+ HOAc)/AcO^-} to TMT-OAc and Acetic Acid



SCHEME 7. Winstein Solvolysis Scheme



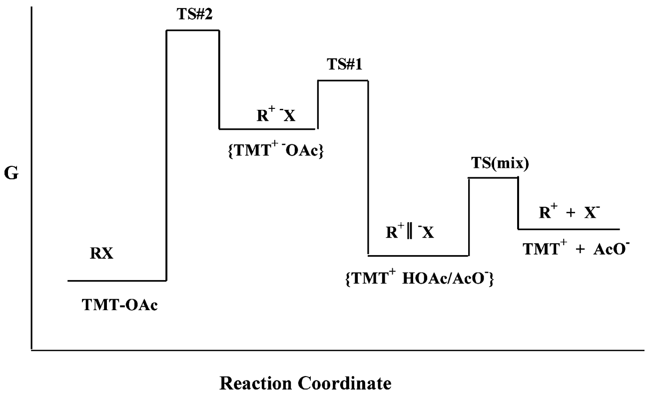
The reaction coordinate diagram (Scheme 8) illustrates the reactions shown in the horizontal line in Scheme 7 compared to the dissociation of TMT−OAc. The free energies (*G*) of wide bars are drawn to approximately correspond to the relative energies of the various species which we are able to estimate from our kinetic data for the reaction of TMT^+ with acetate ion in acetic acid. The designation of the three transition states, TS(mix), TS#1, and TS#2; refer to the TMT^+ system and TS(mix) is labeled to show that this step takes place during the time of mixing in the stopped-flow experiments. The labeling of the other transitions states (TS#1 and TS#2) is consistent with that in Scheme 6.

The correspondence of the reaction coordinate deduced from kinetic data for the dissociation of TMT-OAc in acetic acid to that for the Winstein scheme is truly remarkable. This suggests that {TMT^+ HOAc/AcO^-} is really a solvent (HOAc) separated ion pair and that the "Reactant Complex" is an intimate ion pair. All of our data can be reconciled with this formulation. When considered in this context this work can be considered to be a direct kinetic verification of the Winstein[37] scheme which

---

(37) Winstein, S.; Clippenger, E.; Fainsberg, A. H.; Heck, R.; Robinson, G. C. *J. Am. Chem. Soc.* **1956**, *78*, 328 and references cited therein.

SCHEME 8. Comparison of the Winstein Scheme to the TMT$^+$ System



was based on the more indirect evidence provided by the addition of three different types of salts; (a) a common ion salt (LiX for solvolysis of RX), (b) salts with nonreactive anions (LiY for solvolysis or RX) the effect of which can be attributed to increasing the ionic strength and (c) salts of reactive anions (for example LiN$_3$ for the solvolysis of RX) which result in the formation of a stable compound.

Analysis of $k_{s.s.}$ data in the temperature range from 293 to 323 K resulted in $\Delta H^\ddagger$ and $\Delta S^\ddagger$ equal to 12.7 kcal/mol and −21.5 cal/mol K, respectively. Over the same temperature range, ΔH° and ΔS° for equilibrium (4) were observed to be equal to −4.28 kcal/mol and −14.3 cal/mol K, respectively. It is of interest to note that the cation − anion combination reaction between TMT$^+$ and NaOAc in acetic acid is exothermic ($\Delta H^\circ = -4.28$ kcal/mol) with a significantly large barrier ($\Delta H^\ddagger = 12.7$ kcal/mol, calculated from $k_{s.s.}$ data). Since our evidence strongly suggest that this cation−anion combination is a unimolecular reaction of the solvent separated ion-pair and takes place in two steps, the activation parameters refer to two consecutive transition states. The data are illustrated in Figure 3. The corresponding plots for the reactions in HOAc/AN (1/1) are shown in Figure S3 and S4 (Supporting Information), from which $\Delta H^\ddagger$ and $\Delta S^\ddagger$ were found to be equal to 13.7 kcal/mol and −20.7 cal/mol K, respectively. Values of ΔH° and ΔS° for equilibrium (4) were observed to be equal to −1.40 kcal/mol and −5.2 cal/mol K, respectively. The activation parameters in the mixed solvent in the presence of Bu$_4$N$^+$ ion are very nearly the same as those observed in HOAc in the presence of Na$^+$ ion. On the other hand, both thermodynamic parameters for equilibrium (4) are considerably more negative in the mixed solvent than were observed in HOAc as solvent.

It was mentioned earlier that the changes in the $k_N/k_{s.s.}$ ratios with wavelength in Tables 2 and 3 can be explained by interference from the absorbance by the intermediate. This appears to be consistent with the intermediate being the intimate ion pair {TMT$^+$ $^-$OAc}. We do not find any significant differences in the visible absorption spectrum of {TMT$^+$ HOAc/AcO$^-$} in HOAc/AN (1/1) and of {TMT$^+$ ClO$_4^-$} in CHCl$_3$ or of the former in HOAc (Figure 2). However, it is conceivable that that the spectrum of {TMT$^+$ $^-$OAc} is shifted slightly to lower wavelengths and that the observed absorbance at the higher wavelengths, during the reaction, is more reflective of that of the reactant, {TMT$^+$ HOAc/AcO$^-$}.

Our overall conclusion is that the cation−anion combination reactions of TMT$^+$ with acetate salts in acetic acid involve the formation of {TMT$^+$ HOAc/AcO$^-$}, which we regard as a solvent separated ion-pair, during the time of mixing. The intramolecular collapse of the solvent separated ion-pair then takes place by a two-step mechanism (Scheme 3) involving the formation of a kinetically significant "Reactant Complex" as intermediate which we propose to be the intimate ion pair, {TMT$^+$ $^-$OAc}. This mechanism conforms remarkably well to the Winstein[37] scheme for the ionization of RX (TMT-OAc in this case) as shown in the comparison illustrated in Scheme 7.

In other work, we have proposed that the "Reactant Complex" is a tight complex formed by extrusion of solvent and appropriate geometry changes from the encounter complex or in other cases from the corresponding charge-transfer complex.[26,30,32] It would appear that the latter description can apply equally well to conversion of a solvent separated ion pair to an intimate ion pair. Obviously, our findings are unexpected from studies of carbocation−anion combinations that have appeared in the interim between the 1950s and the present time. Our observation that the HOAc/AcO$^-$ solutions are ideal systems to obtain detailed kinetic and mechanism information on these important reactions will eventually provide the means to greatly increase our knowledge of how these reactions take place. Work in progress is expected to provide more detailed information on this and other cation−nucleophile combination reactions.

Experimental Section

Kinetic Analysis. The appropriate integrated rate law for the pseudo first-order reversible reaction (6) is given by eq 7 where $A_o{}^R$, $A_{eq}{}^R$, and $A_t{}^R$ are the reactant absorbances at zero time, at equilibrium and at time (t), respectively. Equation 7 is directly applicable at wavelengths where the reactant is the only absorbing species. Under these circumstances $A_{eq}{}^R$ is directly measured as the plateau absorbance at long times.

$$\mathrm{R} \underset{k'}{\overset{k}{\rightleftharpoons}} \mathrm{P} \qquad (6)$$

$$\ln\left[\frac{A_o{}^R - A_{eq}{}^R}{A_t{}^R - A_{eq}{}^R}\right] = (k + k')t \qquad (7)$$

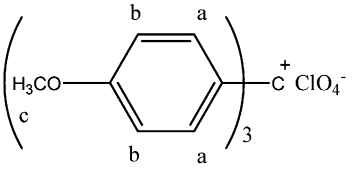
The first step in our analysis is to convert the ($A_o{}^R - A_{eq}{}^R$)−time profile to an extent of reaction−time profile by dividing ($A_t{}^R - A_{eq}{}^R$) by ($A_o{}^R - A_{eq}{}^R$) at each time point in the absorbance−time array. Any kinetic operations on the extent of reaction time profile defined in this way give results equivalent to those when using the pseudo first-order relationship but in this case the apparent rate constant is equal to the sum of forward and reverse rate constants, $k_{app} = (k + k')$.

Experimental Procedure for Kinetic Studies. Solvents and Reactants. Acetic acid and acetonitrile were of the highest purity level commercially available and distilled before use. Sodium acetate was ACS reagent grade and used without further purification.

Bu$_4$N$^+$(HOAc/AcO$^-$). A 40% aqueous solution of Bu$_4$NOH (0.008 mol) was allowed to react with 2 equiv of HOAc (0.016mol) in CH$_2$Cl$_2$ at room temperature. After stirring for about 30 min, anhydrous sodium sulfate (about 10 g) was added to remove most of the water. The CH$_2$Cl$_2$ solution was filtered through anhydrous sodium sulfate before removing the solvent under vacuum. The resulting white solid (Bu$_4$N$^+$ HOAc/OAc$^-$, 0.0048 mol) was washed thoroughly with anhydrous ether and the residual ether was removed under vacuum.

Preparation of 4,4′,4″-Trimethoxytrityl Perchlorate. 4,4′,4″-Trimethoxy-trityl chloride (1mmol) was allowed to react with silver perchlorate (1mmol) in acetonitrile (50 mL) at room temperature.

After the precipitation of silver chloride, the solution was filtered to remove AgCl, and the solvent was removed under vacuum and dried to gave a red solid (0.89 mmol TMT^+ ClO_4^-) identified by it is ^{1}HNMR spectrum (solvent: $CD_3CO_2D/CDCl_3 = 1/2$). The signals at 1.881 to 1.856, 11.533 and 7.254 are due acetic acid and $CHCl_3$, respectively. The ^{1}HNMR assignments are summarized below; and the spectrum is illustrated in Figure S5 (Supporting Information).



a: 7.465, 7.436 b: 7.162, 7.132 c: 3.928

Kinetic Measurements. A Hi-Tech Scientific SF-61 Stopped Flow Spectrophotometer with a Techne Flow Cooler FC-200 thermostat to control the temperature of the cell block within ± 0.2 °C in a glove box under a nitrogen atmosphere was used for kinetic measurements. Data, 2000 points over a time range about 10% greater than the first half-life, were collected under pseudo first-order conditions at 298 K.

Kinetic Procedure. The stopped-flow instrument used a single-beam light path. This necessitated subtraction of background absorbance which was obtained by having pure solvent in the reactant syringe and the excess reagent in the other syringe in the same concentration used in the kinetic experiments. Three background shots were recorded before each set of kinetic shots and all data points were averaged. A minimum of twenty shots under kinetic conditions were recorded in each set of measurements. The kinetic absorbance−time curves were first averaged, background absorbance was subtracted and the zero time absorbance (Abs_o) was calculated by a linear least-squares procedure using the first seven data points. The absorbance−time arrays were converted to $(1 - E.R.)$/time profiles in the manner described in the previous section. The reactant extinction coefficient was calculated from Abs_o and the known reactant concentration.

Data Handling Procedures. The procedures used have been described in detail.[24,33] Additional information specific to the IRC procedure are presented here. The application of the IRC method on calculated data (Figure 1) was used to illustrate the response of the single step and the pre-association mechanisms. The application of the method is somewhat more complex on experimental data since calculating IRC between successive points amplifies the effect of instrumental noise.[33] We have found that smoothing $(1 - E.R.)$ time profiles by fitting to fifth order polynomial equations does not give noticeable distortion in the data as long as the fit is limited to the first 3% of the profile (or if the initial 3% of the data are excluded and the remainder of the profile is fit precisely by that treatment).[33] An alternative method to approximate IRC is to carry out a sliding 51 point analysis in which the IRC for the midpoint of the initial interval (point 26) is estimated from the pseudo first-order rate constant derived from the 51 data points. The IRC for subsequent points (27 to 1975 for a 2000 point array) are obtained by sequentially sliding the data segment analyzed by one point. The IRC for point 27 is obtained from the points ranging from 2 to 52 that for point 28 from points ranging from 3 to 53, and so forth until IRC for point 1976 are obtained from the data segment from point 1950 to 2000. The disadvantage of the latter method is that IRC for short times are not available from the analysis.

Acknowledgment. We are grateful to the National Science Foundation (CHE-0313615) for support of this work. We thank a manuscript reviewer for suggesting the analogy with the Winstein scheme for solvolysis of RX.

Supporting Information Available: Tables of kinetic data and figures of instantaneous rate constant analysis. ^{1}H NMR spectrum of $TMT^+ClO_4^-$ in $CD_3CO_2D/CDCl_3$ (1/2) and ^{1}HNMR spectrum of the equilibrium reaction mixture in HOAc. This material is available free of charge via the Internet at http://pubs.acs.org.

JO702492R