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Application of the N_T Solvent Nucleophilicity Scale To Attack at Phosphorus: Solvolyses of *N,N,N′,N′*-Tetramethyldiamidophosphorochloridate†

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The specific rates of solvolysis of *N,N,N′,N′*-tetramethyldiamidophosphorochloridate have been measured at 25.0 °C in 31 solvents. Analysis with the extended Grunwald−Winstein equation leads to sensitivities toward changes in solvent nucleophilicity (l) of 1.20 ± 0.07 and toward changes in solvent ionizing power (m) of 0.69 ± 0.04. The correlation is improved by omission of the four data points for 2,2,2-trifluoroethanol−ethanol mixtures (F-test value from 155 to 320) with very small reductions in both l and m values. Activation parameters are reported for eight of the solvolyses. The l and m values are very similar to those previously reported for solvolyses of several arenesulfonyl chlorides, consistent with a concerted substitution process. This assignment is supported by a large k_{Cl}/k_F ratio for hydrolysis and a corresponding ratio for hydroxide-assisted hydrolysis of 178. The stereochemistry of nucleophilic attack at tetracoordinate phosphorus(V) is discussed.

The solvent nucleophilicity scale (N_T)[1] based on the logarithm of the ratio of the specific rate of solvolysis of the *S*-methyldibenzothiophenium ion in the solvent under consideration (k) relative to that in 80% ethanol (k_0) has been found to be very useful in considerations of the extent of nucleophilic assistance from the solvent within the rate-determining step of a variety of solvolyses.[2]

For substrates with an initially positive leaving group, leaving as a neutral molecule, one-term linear free energy correlations can be carried out against the N_T scale. For the more commonly studied situation of an initially neutral substrate and an anionic leaving group, the correlations can be carried out by using an extended form of the Grunwald−Winstein equation.[3,4] This involves a linear combination of terms governed by N_T and Y_X values (eq 1), where Y_X is the solvent ionizing power

$$\log(k/k_0) = lN_T + mY_X + c \qquad (1)$$

scale[5] for a leaving group X.[6] The coefficients l and m represent the sensitivities to changes in N_T and Y_X, respectively, and c is a constant (residual) term. For mechanistic investigations of solvolysis reactions, the extended Grunwald−Winstein equation has been found to be easier to apply and to give more useful information than the application of multiparameter equations based on nonsolvolytic solvent−solute properties.[2]

At one extreme, the solvolyses analyzed have involved alkyl derivatives (RX) undergoing rate-determining ionization. The l values of up to about 0.6 have been rationalized in terms of a variable nucleophilic solvation of the incipient carbocation.[7−9] This situation, for the specific case of tertiary alkyl derivatives, has recently been reviewed and a continuation of the use of the term "nucleophilic solvation" was proposed.[10] The solvolyses of methyl and primary alkyl derivatives involve an S_N2 mechanism and the l values are closer to unity[2] (the standard solvolysis of a methyl derivative having by definition a sensitivity to changes in the N_T value of unity). Evidence for both the change in mechanism and the transition state structure variation within the S_N2 region was obtained by application of eq 1 to a study of the solvolyses of a series of para-substituted benzyl *p*-toluenesulfonates.[11]

The N_T scale, in conjunction with the Y_{Cl} scale, has also been applied to the solvolyses involving nucleophilic substitution at the acyl carbon of chloroformate esters.[12] Evidence was found for two pathways. One pathway involves addition−elimination (association−dissociation),

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(1) Kevill, D. N.; Anderson, S. W. *J. Org. Chem.* **1991**, *56*, 1845.
(2) Kevill, D. N. In *Advances in Quantitative Structure−Property Relationships*; Charton, M., Ed.; Jai Press: Greenwich, CT, 1966; Vol. 1, pp 81−115.
(3) Winstein, S.; Grunwald, E.; Jones, H. W. *J. Am. Chem. Soc.* **1951**, *73*, 2700.
(4) Schadt, F. L.; Bentley, T. W.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1976**, *98*, 7667.
(5) Grunwald, E.; Winstein, S. *J. Am. Chem. Soc.* **1948**, *70*, 846.
(6) Bentley, T. W.; Llewellyn, G. *Prog. Phys. Org. Chem.* **1990**, *17*, 121.
(7) Kevill, D. N.; Abduljaber, M. H. *Croat. Chim. Acta* **1992**, *65*, 539.
(8) Kevill, D. N.; D'Souza, M. J. *J. Chem. Res. Synop.* **1993**, 174.
(9) Kevill, D. N.; Abduljaber, M. H. *J. Org. Chem.* **2000**, *65*, 2548.
(10) Richard, J. P.; Toteva, M. M.; Amyes, T. L. *Org. Lett.* **2001**, *3*, 2225.
(11) Kevill, D. N.; D'Souza, M. J.; Ren, H. *Can. J. Chem.* **1998**, *76*, 751.

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with the addition step rate-determining and *l* values in the region of 1.7 to 1.8. The other pathway involves a rate-determining loss of chloride ion assisted by a nucleophilic solvation of the developing acylium ion with, in some instances, loss of carbon dioxide to yield a relatively stable carbocation from which the observed products result.[12e,13] Substitution of sulfur for either or both oxygens leads to a movement toward the ionization pathway.[12b,14]

Having demonstrated that the extended Grunwald−Winstein equation can be a useful tool in studies of solvolysis reactions occurring at either sp^3- or sp^2-hybridized carbon, we have moved on to a consideration of its applicability to nucleophilic substitution reactions occurring at a heteroatom within an organic structure. The nucleophilic substitution reactions at the sulfur of arenesulfonyl chlorides have been reviewed and strong evidence for a concerted S_N2 attack at sulfur was presented.[15] An analysis in terms of eq 1 of the specific rates of solvolysis available for *p*-methoxy- and *p*-methylbenzenesulfonyl chlorides[16] gave good correlations (multiple correlation coefficients of 0.959 and 0.967) with *l* values of 1.10 and 1.25 and *m* values of 0.61 and 0.62, respectively.[17] These values are both just a little higher than the values obtained from an analysis of the specific rates of S_N2 solvolyses of methyl *p*-toluenesulfonate in terms of N_T and Y_{OTs} values. The average *l*/*m* ratio of 1.8 is identical with the value for the methyl *p*-toluenesulfonate solvolyses. Further studies of solvolyses occurring at sulfur are currently under way.

A study has also been published of the solvolyses of two diaryl phosphorochloridates.[18] The treatment in terms of the extended Grunwald−Winstein equation was less successful than the previous analyses of solvolyses at sp^3- or sp^2-hybridized carbon or at sulfur. The data were also analyzed in terms of rate−product correlations by using third-order rate coefficients. Although this approach had previously been successful for several solvolyses including those of *p*-nitrobenzoyl chloride[19] and *p*-nitrobenzenesulfonyl chloride,[20] it was found that third-order rate coefficients, estimated by using product selectivities, did not, for solvolyses of diphenyl phosphorochloridate, always agree with the experimental first-order rate coefficients. The partial failure of both approaches suggested that there are additional factors, possibly unusually strong initial state effects,[18] that need to be considered for these solvolyses.

In the present paper we report the solvolyses of an acid chloride of phosphoric acid containing two *N*,*N*-dimethylamino groups rather than two aryloxy groups, *N*,*N*,*N*′,*N*′-tetramethyldiamidophosphorochloridate (TMDAPC, $(Me_2N)_2POCl$), also known as tetramethylphosphorodiamidic chloride. This compound is of special interest since several conflicting reports concerning its hydrolysis and the influence of added nucleophiles upon the hydrolysis have been presented. Hall[21] studied the hydrolysis and found essentially no acceleration on adding sodium hydroxide; on this basis, an ionization mechanism was proposed. Hall and Lueck[22] subsequently showed electrophilic catalysis by mercury(II) ion but no corresponding catalysis to the reaction, under identical conditions, of diethyl phosphorochloridate. In this second publication, a reexamination of the role of sodium hydroxide in TMDAPC solvolysis found a modest acceleration. This acceleration was confirmed[23] and acceleration by azide[24,25] or fluoride ion was demonstrated in a subsequent study by Traylor and Westheimer. From a study of the hydrolysis of several phosphoramidochloridates, Crunden and Hudson[24] had earlier concluded that TMDAPC solvolyzed by a predominantly bimolecular mechanism, but with bond breaking running ahead of bond making. This description was supported by Traylor and Westheimer.[23]

These suggestions of a mechanism for reaction at phosphorus with bond breaking running ahead of bond making and the observation that the hydrolysis was catalyzed by mercury(II) ion under conditions where a phosphorochloridate diester, the type of compound previously analyzed,[18] was not susceptible to electrophilic catalysis prompted us to carry out a detailed study of the specific rates of solvolysis of TMDAPC, with analyses in terms of the extended Grunwald−Winstein equation (eq 1) using N_T[1,2] and Y_{Cl}[6,8] values.

Results

The specific rates of solvolysis of TMDAPC have been determined in 33 solvents at 25.0 °C. The solvents consisted of ethanol, methanol, 2,2,2-trifluoroethanol (TFE), water, and binary mixtures of water with ethanol, methanol, acetone, TFE, 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP), and dioxane, plus four binary mixtures of TFE and ethanol. The specific rates of solvolysis are presented in Table 1, together with N_T[1,2] and Y_{Cl}[6,8] values.

For seven of the solvents, specific rates of solvolysis were measured at three or four additional temperatures (for H_2O at only two additional temperatures because a literature value[23] of comparable precision and at an appropriate temperature was already available). These values are reported in Table 2 and, together with the values at 25.0 °C from Table 1, they are used to calculate the energies and entropies of activation, also reported in Table 2. The values estimated from a literature report[24]

(12) (a) Kevill, D. N.; D'Souza, M. J. *J. Chem. Soc., Perkin Trans. 2* **1997**, 1721. (b) Kevill, D. N.; D'Souza, M. J. *J. Org. Chem.* **1998**, *63*, 2120. (c) Kevill, D. N.; Kim, J. C.; Kyong, J. B. *J. Chem. Res. Synop.* **1999**, 150. (d) Kyong, J. B.; Kim, Y.-G.; Kim, D. K.; Kevill, D. N. *Bull. Korean Chem. Soc.* **2000**, *21*, 662. (e) Kyong, J. B.; Park, B.-C.; Kim, C.-B.; Kevill, D. N. *J. Org. Chem.* **2000**, *65*, 8051.

(13) (a) Kevill, D. N.; Weitl, F. L. *Tetrahedron Lett.* **1971**, 707. (b) Kevill, D. N.; Kyong, J. B.; Weitl, F. L. *J. Org. Chem.* **1990**, *55*, 4304.

(14) (a) Kevill, D. N.; Bond, M. W.; D'Souza, M. J. *J. Org. Chem.* **1997**, *62*, 7869. (b) Kevill, D. N.; D'Souza, M. J. *Can. J. Chem.* **1999**, *77*, 1118.

(15) Gordon, I. M.; Maskill, H.; Ruasse M.-F. *Chem. Soc. Rev.* **1989**, *18*, 123.

(16) (a) Koo, I. S.; Bentley, T. W.; Kang, D. H.; Lee, I. *J. Chem. Soc., Perkin Trans. 2* **1991**, 175. (b) Koo, I. S.; Bentley, T. W.; Llewellyn, G.; Yang, K. *J. Chem. Soc., Perkin Trans. 2* **1991**, 1175. (c) Forbes, R. M.; Maskill, H. *J. Chem. Soc., Chem. Commun.* **1991**, 854.

(17) Kevill, D. N.; D'Souza, M. J. *Collect. Czech. Chem. Commun.* **1999**, *64*, 1790.

(18) Bentley, T. W.; Ebdon, D.; Llewellyn, G.; Abduljaber, M. H.; Miller, B.; Kevill, D. N. *J. Chem. Soc., Dalton Trans.* **1997**, 3819.

(19) Bentley, T. W.; Jones, R. O. *J. Chem. Soc., Perkin Trans. 2* **1993**, 2351.

(20) Bentley, T. W.; Jones, R. O.; Koo, I. S. *J. Chem. Soc., Perkin Trans. 2* **1994**, 753.

(21) Hall, H. K., Jr. *J. Org. Chem.* **1956**, *21*, 248.

(22) Hall, H. K., Jr.; Lueck, C. H. *J. Org. Chem.* **1963**, *28*, 2818.

(23) Traylor, P. S.; Westheimer, F. H. *J. Am. Chem. Soc.* **1965**, *87*, 553.

(24) Crunden, E. W.; Hudson, R. F. *J. Chem. Soc.* **1962**, 3591.

(25) Samuel, D.; Westheimer, F. H. *Chem. Ind. (London)* **1959**, 51.

TABLE 1. Specific Rates of Solvolysis of Tetramethyldiamidophosphorochloridate[a] in a Variety of Pure and Mixed Solvents at 25.0 °C, and the N_T and Y_{Cl} Values for the Solvents

solvent[b]	10^5k, s^{-1} [c]	N_T[d]	Y_{Cl}[e]
100% EtOH	1.15 ± 0.05	0.37	−2.52
90% EtOH	6.48 ± 0.12	0.16	−0.94
80% EtOH	12.8 ± 0.50	0.00	0.00
70% EtOH	25.1 ± 1.0	−0.20	0.78
60% EtOH	38.9 ± 1.3	−0.38	1.38
40% EtOH	114 ± 4	−0.74	2.75
20% EtOH	333 ± 5	−1.16	4.09
100% H_2O	798 ± 17	−1.38	4.57
100% MeOH	6.07 ± 0.24	0.17	−1.17
90% MeOH	15.7 ± 0.8	−0.01	−0.18
80% MeOH	28.7 ± 1.3	−0.06	0.67
60% MeOH	79.3 ± 1.9	−0.54	2.07
40% MeOH	204 ± 8	−0.87	3.25
20% MeOH	361 ± 14	−1.23	4.10
80% acetone	5.92 ± 0.14	−0.37	−0.83
60% acetone	30.9 ± 0.9	−0.52	0.95
40% acetone	105 ± 3	−0.83	2.46
20% acetone	308 ± 18	−1.11	3.77
100% TFE	0.084 ± 0.005	−3.93	2.81
97% TFE[f]	0.216 ± 0.010	−3.30	2.83
90% TFE[f]	0.596 ± 0.021	−2.55	2.85
80% TFE[f]	1.87 ± 0.03	−2.19	2.90
70% TFE[f]	4.92 ± 0.12	−1.98	2.96
50% TFE[f]	20.2 ± 0.7	−1.73	3.16
80T−20E[g]	0.295 ± 0.014	−1.76	1.89
60T−40E[g]	0.485 ± 0.011	−0.94	0.63
40T−60E[g]	0.873 ± 0.023	−0.34	−0.48
20T−80E[g]	1.02 ± 0.05	0.08	−1.42
70% HFIP[f]	2.09 ± 0.15	−2.94	3.83
50% HFIP[f]	3.91 ± 0.24	−2.49	3.80
60% dioxane	30.9 ± 1.1	−0.54	
40% dioxane	101 ± 5	−0.84	
20% dioxane	324 ± 12	−1.12	3.71

[a] Substrate concentration of 0.0068 mol dm^{-3}. [b] Unless otherwise indicated, on a vol/vol basis, at 25.0 °C, with the other component water. [c] With associated standard deviations. [d] From refs 1 and 2. [e] From refs 6 and 8. [f] Solvent prepared on weight/weight basis. [g] T−E are 2,2,2-trifluoroethanol−ethanol mixtures.

TABLE 2. Specific Rates of Solvolysis of Tetramethyldiamidophosphorochloridate[a] at Various Temperatures (T) and the Calculated Enthalpies ($\Delta H^{\ddagger}$) and Entropies ($\Delta S^{\ddagger}$) of Activation

solvent[b]	T, °C	10^5k, s^{-1} [c]	$\Delta H_{298}^{\ddagger}$,[d] kcal mol^{-1}	$\Delta S_{298}^{\ddagger}$,[d] cal mol^{-1} K^{-1}
100% EtOH	65.0	27.4 ± 1.0		
	55.0	12.6 ± 0.3		
	45.0	6.15 ± 0.18		
	35.0	2.75 ± 0.11	15.2 ± 0.1	−30.3 ± 0.4
80% EtOH	65.0	389 ± 12		
	55.0	198 ± 10		
	45.0	88.5 ± 3.6		
	35.0	38.0 ± 1.4	16.4 ± 0.3	−21.2 ± 0.9
100% H_2O	18.1	405 ± 14[e]		
	10.0	180 ± 6[f]		
	0.0	56.5 ± 2.8[g,h]	16.5 ± 0.1	−12.6 ± 0.3
100% MeOH	55.0	75.0 ± 1.0		
	45.0	33.6 ± 1.1		
	35.0	13.8 ± 0.7	15.8 ± 0.2	−24.8 ± 0.7
80% acetone	55.0	91.9 ± 3.7		
	45.0	41.9 ± 1.8		
	35.0	16.5 ± 0.3	17.2 ± 0.2	−20.1 ± 0.7
97% TFE[i]	65.0	8.04 ± 0.17		
	55.0	3.11 ± 0.09		
	45.0	1.49 ± 0.06		
	35.0	0.528 ± 0.023	17.4 ± 0.2	−26.0 ± 0.9
60T-40E[j]	65.0	15.9 ± 0.5		
	55.0	7.05 ± 0.28		
	45.0	3.10 ± 0.09		
	35.0	1.21 ± 0.05	16.9 ± 0.1	−26.1 ± 0.3
99.3% HCO_2H[k]	25.0	0.47	16.1	−28.9

[a−c] See footnotes to Table 1. [d] Calculations also include the value at 25.0 °C (from Table 1) and are presented with associated standard error. [e] A k value of 421 × 10^{-5} s^{-1} has been reported at 17.9 °C (ref 24). [f] Value from ref 23. [g] A value of 50.5 × 10^{-5} s^{-1} has been reported at 0.6 °C and in the presence of 0.046 mol dm^{-1} $NaClO_4$ (ref 21). [h] Values of 53.6(±1.7) × 10^{-5} s^{-1} and 56.6(±1.6) × 10^{-5} s^{-1} in the presence of 0.0082 and 0.0192 mol dm^{-3} NaCl, respectively. [i] On a weight/weight basis. [j] TFE−ethanol mixtures. [k] Values calculated from Arrhenius activation energy and preexponential factor reported in ref 24.

of specific rates of solvolysis in 99.3% formic acid are also included in Table 2.

Discussion

When the progress of the reaction is followed in terms of acid production, there are two important differences for solvolyses of TMDAPC relative to the earlier study of the solvolyses of diaryl phosphorochloridates. For the diesters, the organic product formed from nucleophilic attack by water titrates as acid under the usual titration conditions and, indeed, the intermediate position at completion of reaction between 1 equiv of acid being produced (all reaction with the alcohol component) and 2 equiv of acid being produced (all reaction with the water component) gives a convenient and accurate way of assessing the product partitioning in aqueous−alcohol solvents.[26] In the presently reported study of the solvolyses of TMDAPC, the hydrolysis product $(Me_2N)_2POOH$ behaves as a neutral species. Heath[27] has determined a pK_a value of 6.76 and it has been suggested[24] that it exists as the zwitterion, with protonation at the nitrogen. Accordingly, in hydroxylic solvents, the initial solvolysis produces exactly 1 equiv of titratable acid, independent of solvent composition.

A second difference is that a subsequent acid-catalyzed amide solvolysis proceeds at a comparable rate in some of the solvents. Fortunately, this is not the case in highly aqueous solvents. Also, for almost all of the usually studied less-aqueous compositions, the kinetics of acid production can be analyzed by the Guggenheim method,[28,29] so as to give the required specific rate of solvolysis of TMDAPC. Previous studies[27] on the hydrolysis of dimethylamides of phosphoric acids have shown that the initial product from $(Me_2N)_2POOH$ solvolysis loses the second dimethylamino group faster than the initial replacement. The relevance of these subsequent reactions to the experimental determination of the specific rates of solvolysis of TMDAPC is discussed within the Experimental Section. The overall solvolysis pattern is outlined in Scheme 1.

In the present paper, we are concerned with the specific rates of the solvolyses represented as the first step within Scheme 1. These are reported for studies at 25.0 °C in Table 1 and at other temperatures in Table 2. The activation parameters (Table 2) show entropies of activa-

(26) Dostrovsky, I.; Halmann, M. *J. Chem. Soc.* **1953**, 502.
(27) Heath, D. F.; Casapieri, P. *Trans. Faraday Soc.* **1951**, *47*, 1093.
(28) Guggenheim, E. A. *Philos. Mag.* **1926**, *2*, 538.
(29) Frost, A. A.; Pearson, R. G. *Kinetics and Mechanism*, 2nd ed.; Wiley: New York, 1961; pp 49−50.

SCHEME 1

(1) $(Me_2N)_2POCl \xrightarrow[slow]{SOH / H_2O} (Me_2N)_2POOS + (Me_2N)_2POOH + HCl$

with Y representing either S or H, this is followed by:

(2) $(Me_2N)_2POOY \xrightarrow[slow]{H^+, SOH / H_2O} (CH_3)_2\overset{+}{N}H_2 + Me_2NPO(OY)_2$ *(3 possibilities)*

(3) $Me_2NPO(OY)_2 \xrightarrow[fast]{H^+, SOH / H_2O} (CH_3)_2\overset{+}{N}H_2 + (YO)_3PO$ *(4 possibilities)*

tion in the range of −20 to −30 cal mol^{-1} K^{-1}, consistent with a bimolecular solvolysis, but not helpful in deciding whether the process involves association−dissociation (addition−elimination) or a concerted S_N2 attack. Although initial reports had favored an ionization mechanism,[21,22] subsequent studies produced results considered to be more consistent with a predominantly bimolecular mechanism with bond breaking running ahead of bond making.[23,24] A recent qualitative observation,[30] confirmed by quantitative measurements in the present study, that the solvolysis of TMDAPC proceeds very slowly in the highly ionizing but poorly nucleophilic 2,2,2-trifluoroethanol (TFE) is also strongly indicative of a bimolecular attack in the rate-determining step of the solvolysis.

A useful tool for quantitatively estimating the rate-controlling influence of nucleophilic participation by solvent during a solvolysis reaction involves the application of the extended Grunwald−Winstein equation (eq 1).[1,2] The sensitivity to changes in solvent nucleophilicity (l) will be close to unity, or even higher, if covalent attachment of solvent, functioning as a nucleophile, is involved in the slow step. Lower values for l (up to about 0.6) have been considered to represent nucleophilic solvation of a developing carbocation. Application of eq 1 to the solvolyses of diphenyl phosphorochloridate and the di-*p*-chloro derivative led to only moderately good correlations, with dispersal for different binary solvent mixtures. The l and m values of 1.72 ± 0.18 and 0.68 ± 0.06 and of 1.79 ± 0.20 and 0.58 ± 0.08, respectively, were very similar to values reported for bimolecular solvolyses of alkyl and aryl chloroformate esters, believed to solvolyze by an addition−elimination mechanism, with the addition being rate-determining. However, the poor quality of the plots [multiple correlation coefficient (R) values of 0.885 and 0.863, respectively] suggested the need for caution in interpreting these values. Certainly, the values strongly suggest a rate-determining attack by solvent, but it would be unwise to try to make a more detailed assignment of mechanism based only on these plots.

Surprisingly, the correlation of the specific rates of solvolysis of TMDAPC, in essentially the same solvents, gives a much improved correlation. Indeed, the measures of goodness of fit are comparable to those which have

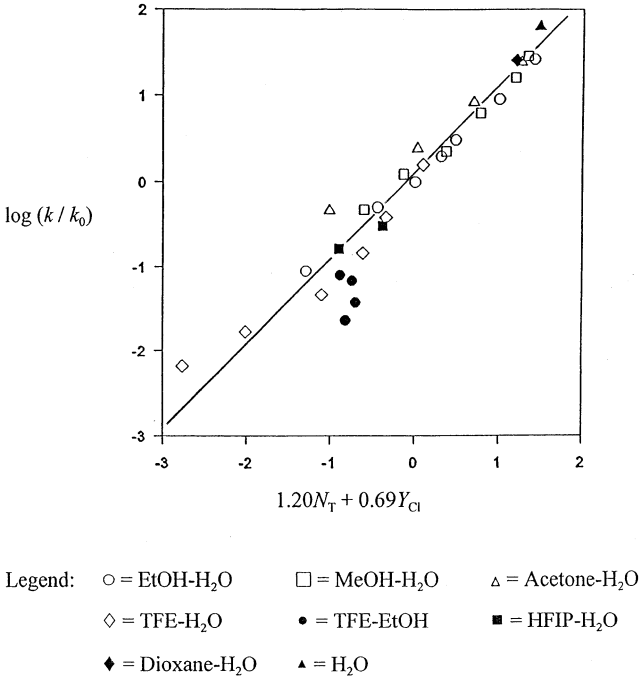

FIGURE 1. Plot of log(k/k_0) for solvolyses of *N*,*N*,*N*′,*N*′-tetramethyldiamidophosphorochloridate at 25.0 °C against ($1.20N_T + 0.69Y_{Cl}$).

recently been obtained[12] for treatments of the solvolyses of chloroformate esters in terms of eq 1. For 31 solvents, values were obtained of 1.20 ± 0.07 for l, 0.69 ± 0.04 for m, and 0.03 for c; the standard error of the estimate was 0.32, the R value was 0.9578, and the F-test value was 155. Inspection of the plot corresponding to this correlation (Figure 1) showed that the four data points for solvolyses in TFE−ethanol mixtures lay below the plot. Recalculation with omission of these points led to values for l of 1.14 ± 0.05, for m of 0.63 ± 0.03, and for c of 0.17; the standard error of the estimate was 0.21, the R value was 0.9817, and the F-test value improved to 320.

The l and m values obtained are essentially identical with those recently reported,[17] after an analysis in terms of eq 1, for the specific rates of solvolysis of *p*-methylbenzenesulfonyl chloride (l = 1.25 ± 0.15, m = 0.62 ± 0.04) and *p*-methoxybenzenesulfonyl chloride (l = 1.10 ± 0.17, m = 0.61 ± 0.04). The history of studies of nucleophilic attack at the sulfur of arenesulfonyl chlorides has parallels to that for attack at the phosphorus of TMDAPC, with initial suggestions of the operation of S_N1-type mechanisms now considered highly unlikely to be correct. Recent interpretations for attack at sulfur have been in terms of bimolecular attack, but with some degree of uncertainty as to whether this is concerted or stepwise. Koo, Bentley, and co-workers[16a,b] suggested that both mechanisms can operate, with the concerted mechanism favored in the more polar solvents. A fairly recent review[15] favored an interpretation in terms of a concerted bimolecular displacement (S_N2) mechanism, involving attack by solvent at sulfur. Our analyses[17] were considered to be consistent with such an explanation. The close similarity of both the l and the m values for attack at sulfur to those for the attack at the phosphorus of TMDAPC gives an indication that the solvolyses of TMDAPC could also be concerted.

(30) Timperley, C. M.; Bird, M.; Borderick, J. F.; Holden, I.; Morton, I. J.; Matthew, J. W. *J. Fluorine Chem.* **2000**, *104*, 215.

Downward Deviation of TFE−Ethanol Data Points. As can be seen in Figure 1, there are appreciable deviations from the plot for the solvolytic data in TFE−ethanol mixtures with the largest deviations for the 80% TFE−20% ethanol and 60% TFE−40% ethanol points. Using the actual k and k_0 (80% ethanol) values together with the l and m values obtained from the correlation analysis (27 solvents), together with the standard values for Y_{Cl},[6,8] we can calculate the value of N_T that would put these points on the correlation line. Values are obtained of −2.63 in 80% TFE−20% ethanol (80T-20E) and −1.75 in 60% TFE−40% ethanol (60T−40E), compared to the standard tabulated values of −1.76 and −0.94, respectively.[1,2]

The values obtained can also be compared to those for solvolyses of chloroformate esters. For the *p*-nitrobenzyl,[12e] ethyl,[12b] and phenyl[12a] esters, which are believed to solvolyze in all but the most ionizing solvents by an addition−elimination mechanism with addition rate-determining, the identically calculated N_T values are in the range of −2.00 to −2.12 for 80T−20E. For the 60T−40E binary mixture, an additional specific rate value is available for the methyl ester[12c] and the values for the four substrates are within the narrow range of −1.14 to −1.24. Several other chloroformate esters are believed to solvolyze by an ionization mechanism with assistance from nucleophilic solvation and isopropyl chloroformate[12d] and ethyl chlorothioformate[12b] have calculated N_T values of −3.02 ± 0.02 in 80T−20E and −1.86 ± 0.06 in 60T−40E. Very similar values are calculated for *N*,*N*-dimethylcarbamoyl chloride[32a] and for the corresponding *N*,*N*-diphenyl[32b] and *N*-phenyl-*N*-methyl derivatives.[32c] Values are also available for 4-(chloroformyl)morpholine.[33] The four sets of N_T values for the carbamoyl chlorides are in the range of −2.4 to −3.1 for 80T−20E and −1.4 to −2.2 for 60T−40E.

The values for TMDAPC are within the ranges of values obtained for chloroformate esters. It is tempting to assume that steric factors lead to these reduced N_T values. The standard values are for attack at the methyl carbon of the *S*-methyldibenzothiophenium ion. One can visualize that, on going to more crowded situations, solvents containing a water component are less disadvantaged than the binary TFE−ethanol mixtures. This cannot be the full story, however, because phenyl chlorodithioformate[14b] and *N*,*N*-dimethylthiocarbamoyl chloride,[34] containing the bulkier thiocarbonyl group in place of carbonyl, solvolyze in TFE−ethanol mixtures with the data from these solvents close to the correlation line. Indeed, insofar as small deviations of the N_T values from the standard values occur, they are in the opposite direction from those obtained for chloroformate esters (calculated N_T values of −1.45 ± 0.25 in 80T−20E and −0.70 ± 0.03 in 60T−40E).

Further, the deviations do not appear to require a change in the position of nucleophilic attack from the sp^3 carbon of the standard methyl derivative to the sp^2 carbon of the carbonyl group or to a heteroatom because the largest deviations we have observed have been for the nucleophilic solvations involved in cyclopropylcarbinyl bromide and cyclobutyl bromide solvolyses,[9] with N_T values of −3.35 ± 0.35 for 80T−20E and −2.11 ± 0.10 in 60T−40E. It would appear that there must be several factors involved in establishing the magnitude of the deviations in TFE−ethanol mixtures, probably including steric effects and, especially for ionization reactions, the extent of charge delocalization at the transition state.

One important conclusion that can be drawn from the elusive nature of the deviations for TFE−ethanol mixtures is that one should resist the urge to over-interpret Grunwald−Winstein correlations. Another conclusion is that, since a wide variety of solvent systems are available, it might be advisable to exclude from the calculations solvolyses in TFE−ethanol mixtures, at least until the nature of the deviations is better understood.

The actual deviations in the linear free energy plots depend not only on the variation of the appropriate N_T value from the standard, but also upon the sensitivity of the solvolysis under study to the variation of this parameter (l value). For studies with chloroformate esters, the deviations of N_T values are greater for the ionization mechanisms but the l value is appreciably lower. One can calculate weighted N_T values based on solvolyses of chloroformate esters and carbamoyl chlorides, which could then be used in studies of other solvolyses of this type of substrate. Since the usual aim of an application of the extended Grunwald−Winstein equation is to assist in a determination of reaction mechanism, it would not be helpful to have independent N_T values for each of the two basic mechanisms. For 80T−20E, the average values are −2.07 for addition−elimination and −2.84 for ionization, and using a weighting factor of 3.5 (the ratio of average l values), one arrives at a compromise N_T value of −2.24. The corresponding values for 60T−40E are −1.19 and −1.80, for a weighted average of −1.33. The weighted averages of −2.24 and −1.33 can be compared to standard values of −1.76 and −0.94, respectively.

Mechanism of Nucleophilic Displacement of Halide Ion at Tetracoordinate Phosphorus. In solution this is usually assumed to be bimolecular in character and an $S_N2(P)$ designation has been proposed.[35,36] It is frequently unclear as to whether this relates to the classical S_N2 mechanism for nucleophilic attack at carbon or to the addition−elimination (association−dissociation) pathway with a pentacoordinated intermediate, or whether no precise assignment is intended. Rahil and Haake[37] suggested restricting $S_N2(P)$ to the concerted process and using $S_N2I(P)$ for reaction proceeding via an intermediate. This does not appear to have gained acceptance, however. The recently recommended IUPAC nomenclature[38] would

(31) (a) Tonnett, M. L.; Hambly, A. N. *Aust. J. Chem.* **1971**, *24*, 703. (b) Vizgert, R. V. *Russ. Chem. Rev.* **1963**, *33*, 182 and references therein.

(32) (a) Kevill, D. N.; Oldfield, A. J.; D'Souza, M. J. *J. Chem. Res. Synop.* **1996**, 122. (b) D'Souza, M. J.; Kevill, D. N.; Bentley, T. W.; Devaney, A. C. *J. Org. Chem.* **1995**, *60*, 1632. (c) Kevill, D N.; Best, B. J.; D'Souza, M. J. *Org. React. (Tartu)* **1997**, *31*, 55.

(33) Kevill, D. N.; Casamassa, A. J.; D'Souza, M. J. *J. Chem. Res. Synop.* **1996**, 472.

(34) Kevill, D. N.; Rudolph, T. M.; D'Souza, M. J. *J. Phys. Org. Chem.* **2000**, *13*, 192.

(35) Dostrovsky, I.; Halmann, M. *J. Chem. Soc.* **1953**, 516.

(36) (a) Emsley, J.; Hall, D. *The Chemistry of Phosphorus*; Harper and Row: New York, 1976; Chapter 8. (b) Kirby, A. J.; Warren, S. G. *The Organic Chemistry of Phosphorus*; Elsevier: Amsterdam, The Netherlands, 1967; pp 276−364. (c) Thatcher, G. R. J.; Kluger, R. *Adv. Phys. Org. Chem.* **1989**, *25*, 99.

(37) Rahil, J.; Haake, P. *J. Am. Chem. Soc.* **1981**, *103*, 1723.

(38) Guthrie, R. D.; Jencks, W. P. *Acc. Chem. Res.* **1989**, *22*, 343.

require A_ND_N and $A_N + D_N$, but this has also not gained wide acceptance. It has been suggested[39] that both of these mechanisms and also the $S_N1(P)$ (or $D_N + A_N$), proceeding through a metaphosphate intermediate, have been observed for nucleophilic substitution at phosphorus under appropriate conditions of substrate and nucleophile. It has been proposed that concerted mechanisms are favored by the presence of a good leaving group[39,40] and a weak nucleophile.[41]

In the present investigation of solvolyses of TMDAPC, we have weakly nucleophilic solvent molecules displacing the chloride ion, a relatively good leaving group. The sensitivities toward changes in solvent nucleophilicity (1.14 ± 0.05) and solvent ionizing power (0.63 ± 0.03) are virtually identical with those recently reported for solvolyses of arenesulfonyl chlorides,[17] where there is independent evidence favoring a bimolecular concerted process.[15] Further support for a concerted process comes from a comparison with the corresponding phosphorofluoridate. In unassisted hydrolysis, the tetramethyldiamidophosphorofluoridate is extremely slow and Heath has shown that, for reaction with OH^- in H_2O, the kinetics can be followed in terms of second-order kinetics without the need to consider any background solvolysis. From second-order rate coefficients reported[27] at 28.1 and 42.3 °C, a value at 10.0 °C of 1.57×10^{-5} L mol^{-1} s^{-1} can be calculated. This can be compared with a second-order rate coefficient of 280×10^{-5} L mol^{-1} s^{-1} for reaction of TMDAPC with aqueous NaOH.[23] The corresponding k_{Cl}/k_F ratio is therefore 178, consistent with a mechanism in which there is appreciable carbon−halogen bond fission at the transition state of the rate-determining step. The observation that the second-order reaction swamps out background hydrolysis for the fluoro compound but the background hydrolysis is a little over 50% of the total reaction in the presence of 0.50 M NaOH for the chloro compound requires that a considerably larger k_{Cl}/k_F ratio would apply for the specific rates of neutral hydrolysis. Consistent with this conclusion, for the neutral hydrolyses of diisopropyl esters, values are obtained at 25.0 °C of 81×10^{-4} s^{-1} for the phosphorochloridate[42] and 1.7×10^{-6} s^{-1} for the phosphorofluoridate,[43] for a k_{Cl}/k_F ratio of 5000, resulting primarily from a higher activation energy for the fluoro compound.[44]

For both acylic esters and fully alkylated amides of phosphorohalidates, it appears that the k_{Cl}/k_F ratios are best rationalized in terms of a concerted $S_N2(P)$ mechanism. If an addition−elimination pathway[45] was to be followed, it would have to be a version with the expulsion of the halide at least partially rate-determining.

A more subtle way of testing leaving-group effects is by using heavy-atom isotope effects. Use of both ^{15}N and ^{18}O kinetic isotope effects for the loss of *p*-nitrophenoxide ion during hydrolysis of stable cobalt complexes of *p*-nitrophenyl phosphate indicated substantial cleavage of the carbon−oxygen bond at the transition state of the rate-determining step, supporting the proposed[39,46] concerted mechanism for displacement of the aryloxide anion.

Dostrovsky and Halmann[47] presented compelling evidence for the absence of an intermediate that could relatively rapidly equilibrate and return to reactants by showing the absence of ^{18}O exchange during solvolysis of $(EtO)_2POCl$ in ^{18}O-enriched water and during solvolysis of $(EtO)_2P^{18}OCl$ in normal water. Any intermediate would have to have a large bias toward progressing toward solvolysis products, a situation that would be close to the favored concerted pathway. For the hydrolysis of diisopropyl phosphorochloridate in H_2O or D_2O at 25.14 °C, a k_H/k_D value of 1.25 was observed.[42] This value is not very far removed from those obtained[23] for the hydrolyses of TMDAPC in 100% H_2O or 100% D_2O at 10.0 °C of 1.34 and in 50% dimethoxyethane with 50% H_2O or 50% D_2O at 30.0 °C of 1.30. These values are exactly of the magnitude (1.28 ± 0.06) previously observed for several S_N1 and S_N2 reactions of alkyl chlorides.[48,49] Unfortunately, solvent isotope effects have proven to be rather insensitive to transition state variation when used as a mechanistic probe.[50]

Stereochemical studies of nucleophilic substitution at tetrahedral phosphorus(V) have led to complete inversion, complete retention, or only marginal stereospecificity. The pathways followed are a rather delicate function of nucleophile, leaving group, and reaction conditions.[51]

The first demonstration of a highly stereospecific reaction at tetrahedral phosphorus(V) was for the methoxide exchange reaction, in methanol, of methyl ethylphenylphosphinate. The kinetics were simultaneously followed in terms of loss of the ^{14}C-labeled methoxy group from the ester and racemization. The factor of 2 favoring racemization showed conclusively that each act of substitution was with inversion.[52] Inversion of configuration was also found in several reactions of phosphorochloridates or phosphorothiochloridates with hydroxide or alkoxide ions and it was pointed out that several related reactions for which retention of configuration had been observed may actually have involved a double displacement.[53]

The inversion mechanism is believed to involve an in-line mechanism with entering and leaving groups in apical positions. The mechanism can be concerted or it can involve a bipyramid intermediate that must then eject the leaving group faster than any reorganization of the ligands (such as in a Berry pseudorotation[54]). There are, however, many unambiguous examples of reactions

(39) Rawlings, J.; Hengge, A. C.; Cleland, W. W. *J. Am. Chem. Soc.* **1997**, *119*, 542.
(40) Hoff, R. H.; Hengge, A. C. *J. Org. Chem.* **1998**, *63*, 6680.
(41) Herschlag, D.; Jencks, W. P. *J. Am. Chem. Soc.* **1989**, *111*, 7587.
(42) Dostrovsky, I.; Halmann, M. *J. Chem. Soc.* **1953**, 502.
(43) Waters, W. A.; de Worms, C. G. M. *J. Chem. Soc.* **1949**, 926.
(44) Halmann, M. *J. Chem. Soc.* **1959**, 305.
(45) (a) Westheimer, F. H. *Pure Appl. Chem.* **1977**, *49*, 1059. (b) Westheimer, F. H. *Chem. Rev.* **1981**, *81*, 313.
(46) (a) Williams, A. *Chem. Soc. Rev.* **1994**, *23*, 93. (b) Ba-Saif, S. A.; Waring, M. A.; Williams, A. *J. Am. Chem. Soc.* **1990**, *112*, 8115. (c) Davis, A. M.; Hall, A. D.; Williams, A. *J. Am. Chem. Soc.* **1988**, *110*, 5105. (d) Bourne, N.; Chrystiuk, E.; Davis, A. M.; Williams, A. *J. Am. Chem. Soc.* **1988,** *110*, 1890.
(47) Dostrovsky, I.; Halmann, M. *J. Chem. Soc.* **1956**, 1004.
(48) Thornton, E. R. *Solvolysis Mechanisms*; Ronald: New York, 1964; pp 212−226.
(49) Schowen, R. L. *Prog. Phys. Org. Chem.* **1972**, *9*, 275.
(50) Blandamer, M. J.; Scott, J. M. W.; Robertson, R. E. *Prog. Phys. Org. Chem.* **1985**, *15*, 149.
(51) Hall, C. R.; Inch, T. D. *Tetrahedron* **1980**, *36*, 2059.
(52) (a) Green, M.; Hudson, R. F. *Proc. Chem. Soc.* **1962**, 307. (b) Hudson, R. F.; Green, M. *Angew. Chem.* **1963**, *75*, 47.
(53) Hall, C. R.; Inch, T. D. *J. Chem. Soc., Perkin Trans. 1* **1979**, 1104.
(54) Berry, R. S. *J. Chem. Phys.* **1960**, *32*, 933.

proceeding with retention of configuration. Here, the attack has been postulated as apical to a nonleaving group followed by pseudorotation so as to put the leaving group in an apical position.[55] The retention mechanism can be especially favored when geometric constraints seriously hinder the in-line attack, as with four-, five-, or six-membered rings[55] or when a short tether is present in an application of the endocyclic restriction test.[56]

Corriu[57,58] has pointed out that there are several stereochemical similarities to an attack at the more thoroughly studied silicon. He is in agreement with other workers as regards the inversion mechanism but he prefers a retention mechanism in which the nucleophilic attack is equatorial rather than apical.[59] He formulated[57] a general rule that retention is favored by a strong nucleophile, with a concentrated charge, in conjunction with a poor leaving group, while inversion is favored by a good leaving group coupled with a weak nucleophile, with a delocalized negative charge. The conditions for inversion are essentially those put forward as favoring a concerted mechanism.[39−41] In this connection, it is noteworthy that, for reactions of cyclic halogenophosphates with aryloxide in THF, a retention pathway is followed that involves the fastest reaction for the fluoro compound with slightly slower reaction for either the chloro or bromo compound. This situation is reminiscent of bimolecular solvolyses of haloformate esters[60] or nucleophilic aromatic substitutions,[61] where an addition−elimination pathway, with addition rate-determining, is followed. In contrast, several reactions proceeding with inversion showed similar rates for the chloro and bromo compounds and considerably slower reactions for the fluoro compound,[58] consistent with extensive bond-breaking to the leaving group at the transition state.

An interesting observation is that by Mikolajczyk and co-workers[62] for the alkaline solvolysis of the cyclic thioesters, 2-halogeno-4-methyl-2-thio-1,3,2-dioxaphosphorinans. For the bromo and chloro derivatives, inversion was observed but this changed to retention for the fluoro derivative. This can be very nicely rationalized in terms of a concerted in-line inversion $S_N2(P)$ pathway for the chloro and bromo compounds. This pathway will show a large decrease in rate on going to the fluoro compound, such that the favored pathway can become one involving addition−elimination and retention. The retention pathway could be with an apical loss of the fluoride ion being accompanied by attack apical to a nonleaving group, followed by pseudorotation,[55] or being accompanied by equatorial attack.[57,58]

Conclusions

The solvolyses of TMDAPC can be followed in terms of acid production for almost all commonly used solvents. A subsequent acid-assisted amide solvolysis leads to dimethylamine, which neutralizes previously produced acid (Scheme 1). Fortunately, the amide solvolyses are, under the experimental conditions, relatively slow for all solvents except those with a very high percentage of acetone or dioxane and accurate specific rates for the first step can usually be obtained from an application of the Guggenheim method. Activation parameters show moderate values for the energy of activation and strongly negative values for the entropy of activation, suggesting a bimolecular process but not allowing any distinction between concerted and stepwise processes.

An analysis in terms of the extended Grunwald−Winstein equation leads to *l* and *m* values (1.14 and 0.63, respectively) which are essentially identical with those for the solvolyses of arenesulfonyl chlorides, where there is fairly good independent evidence for a concerted pathway.

The *l* values are considerably lower than values of 1.72 ± 0.18 and 1.79 ± 0.20 reported[18] for solvolyses of diphenyl phosphorochloridate and di(*p*-chlorophenyl) phosphorochloridate, respectively. The reason for this variation in value is not clear but analyses of preliminary results[63] for dimethyl phosphorochloridate and dimethyl phosphorothiochloridate lead to *l* and *m* values much closer to those for TMDAPC solvolyses, suggesting a perturbing influence of the aromatic rings. However, there must be some mechanistic differences between hydrolyses of the acid chlorides of the diamides and of the diesters of phosphorus(V) as is illustrated by the accelerating influence of mercury(II) perchlorate on TMDAPC hydrolysis but not on diethyl phosphorochloridate hydrolyses.[22]

Despite the lack of acceleration by mercury(II) on hydrolyses of diethyl phosphorochloridate paralleling the behavior of butyl chloroformate and the *l* values for diphenyl phosphorochloridate being similar to values obtained in bimolecular solvolyses of chloroformate esters,[12] there is one important difference between the solvolyses of chloroformate esters and either TMDAPC or phosphorochloridates in that the k_{Cl}/k_F leaving-group effect for bimolecular haloformate solvolyses is small (usually just below unity) but the ratio is of appreciable value for acyclic phosphorohalidate solvolyses. The lack of ^{18}O exchange in hydrolysis of diethyl phosphorochloridate is also best explained[47] in terms of a concerted pathway.

There are, however, cyclic phosphorohalidates for which the k_{Cl}/k_F ratio in nucleophilic substitution is of exactly the value expected for an addition−elimination pathway, with addition rate-determining, and these react with retention of configuration. Closely related compounds can show large k_{Cl}/k_F ratios under the same reaction conditions and these proceed with inversion.[57,58,62] A reasonable interpretation is that unconstrained solvolyses with replacement of halogen at a tetracoordinate phosphorus(V) usually proceed with inversion of config-

(55) (a) De Bruin, K. E.; Zon, G.; Naumann, K.; Mislow, K. *J. Am. Chem. Soc.* **1969**, *91*, 7027. (b) Rowell, R.; Gorenstein, D. G. *J. Am. Chem. Soc.* **1981**, *103*, 5894.

(56) Tollefson, M. B.; Li, J. J.; Beak, P. *J. Am. Chem. Soc.* **1996**, *118*, 9052.

(57) Corriu, R. J. P.; Dutheil, J. P.; Lanneau, G. F.; Ould-Kada, S. *Tetrahedron* **1979**, *35*, 2889.

(58) Corriu, R. J. P.; Dutheil, J. P.; Lanneau, G. *Tetrahedron* **1981**, *37*, 3681.

(59) (a) Westheimer, F. H. *Acc. Chem. Res.* **1968**, *1*, 70. (b) Mislow, K. *Acc. Chem. Res.* **1970**, *3*, 321. (c) Trippett, S. *Pure Appl. Chem.* **1974**, *40*, 595.

(60) Kevill, D. N.; D'Souza, M. J. *J. Chem. Soc., Perkin Trans. 2* **2002**, 240.

(61) (a) Miller, J. *Nucleophilic Aromatic Substitution*; Elsevier: Amsterdam, The Netherlands, 1968. (b) Bunnett, J. F.; Garbisch, E. W., Jr.; Pruitt, K. M. *J. Am. Chem. Soc.* **1957**, *79*, 385.

(62) Mikolajczyk, M.; Krzywanski, J.; Ziemnicka, B. *Tetrahedron Lett.* **1975**, *19*, 1607.

(63) Carver, J. S. M.S. Thesis, Northern Illinois University, DeKalb, IL, 1998.

uration in a concerted pathway, but it is possible, by the imposition of geometric constraints,[55,56] to change the stereochemistry to retention and there is evidence[57,58] that at least some of these reactions proceeding with retention involve a stepwise (addition−elimination) pathway.

Experimental Section

The *N*,*N*,*N*′,*N*′-tetramethyldiamidophosphorochloridate (98+%) was used without further purification. Solvents were purified and the kinetic runs carried out as previously described.[1,9]

In many instances, the calculations of specific rates of solvolysis of TMDAPC were complicated by the observed acid titer rising to a maximum value and then showing a slow falloff in value, such that at 10 half-lives the observed titer was slightly less than that estimated for the acid production from the initial solvolysis reaction (Scheme 1). Only in solvents rich in acetone or dioxane was it not possible to treat this perturbation of the infinity titer by application of the Guggenheim method.[28,29] In 90% dioxane, no acid development was observed and, in 80% dioxane, it rose to only 30% of the theoretical maximum value and then decreased. In 90% acetone, it rose to only 12% of the maximum value before decreasing.

By following the decrease in the acid concentration occurring immediately after 10 half-lives for solvolysis of the TMDAPC, it was possible to obtain an approximate specific rate for loss of acid and then to compare this with the specific rate for solvolysis of TMDAPC. For solvents rich in water the ratio (expressed as a percentage and at 25.0 °C) was very low: for example, 0.1% in 100% H_2O and 0.6% in 20% ethanol. It increases with increasing alcohol content to approximately 1.4% in 80% methanol and to about 5% in 80% ethanol, 70% TFE, and 80% TFE. In 80% acetone, the value is 28% and this represents a situation very close to the limit as regards analysis with the Guggenheim method.

The Guggenheim analysis of the data was used in the modified treatment (so as to give the true infinity titer that would have been observed in the absence of perturbation) that we recently described and applied in analyses of the solvolyses of cyclopropylcarbinyl bromide.[9] As previously, this infinity titer value was then used to calculate from all valid points of duplicate runs (before the need to consider the incursion of the perturbation) an average value for the specific rate of solvolysis and the associated standard deviation.[1] Although it was not strictly necessary to use this method for solvents rich in water, it was for uniformity applied to the calculation of all of the reported specific rates of solvolysis.

The simple and multiple regression analyses were performed with use of the ABSTAT statistical package (Anderson-Bell, Arvada, CO).

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