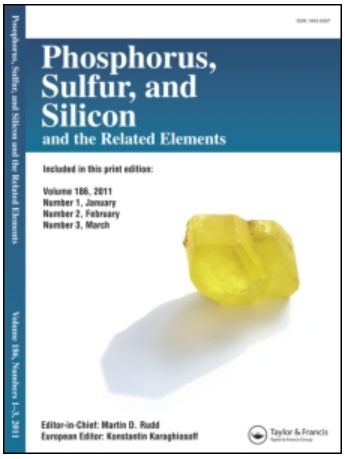

Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

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Online publication date: 03 July 2010

To cite this Article Koh, Han Joong , Kang, Suk Jin and Kevill, Dennis N.(2010) 'Rate and Product Studies in the Solvolyses of Two Cyclic Phosphorochloridate Esters', Phosphorus, Sulfur, and Silicon and the Related Elements, 185: 7, 1404 — 1415
To link to this Article: DOI: 10.1080/10426500903061525
URL: http://dx.doi.org/10.1080/10426500903061525

Phosphorus, Sulfur, and Silicon, 185:1404–1415, 2010

ISSN: 1042-6507 print / 1563-5325 online
DOI: 10.1080/10426500903061525

RATE AND PRODUCT STUDIES IN THE SOLVOLYSES OF TWO CYCLIC PHOSPHOROCHLORIDATE ESTERS

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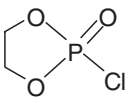
Kinetic and product studies of the solvolyses of acyclic phosphorochloridates are extended to two cyclic diesters, 2-chloro-1,3,2-dioxaphospholane-2-oxide (1) and 2-chloro-5,5-dimethyl-1,3,2-dioxaphosphorinane-2-oxide (2). Slightly faster solvolyses are observed for 1 than for the acyclic dimethyl phosphorochloridate (3), and 2 solvolyzes somewhat slower than 3. An extended Grunwald–Winstein equation treatment shows similar sensitivities to changes in solvent nucleophilicity and solvent ionizing power for 1, 2, and 3, and a concerted S_N2 attack is proposed in each case. Product studies for the solvolyses of 2 in aqueous alcohols are presented.



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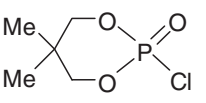

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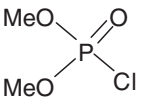

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Keywords Cyclic phosphorochloridates; extended Grunwald–Winstein equation; solvolysis

INTRODUCTION

The extended Grunwald–Winstein equation[1–3] is used to correlate the specific rates of solvolysis reactions in terms of solvent ionizing power[2,4,5] and solvent nucleophilicity.[3,6,7] In Equation (1), k and k_o represent the specific rates of solvolysis in a given solvent and in the standard solvent (80% ethanol), respectively; l represents the sensitivity to changes

Received 13 March 2009; accepted 22 May 2009.

Presented, in part, at the 17th International Conference on Phosphorus Chemistry (ICPC-17), April 15–21, 2007, Xiamen, China, and briefly summarized in the proceedings of the conference: H. J. Koh, S. J. Kang, and D. N. Kevill, *Phosphorus, Sulfur, and Silicon*, **183**, 364 (2008). H.J.K. thanks Chonju National University of Education for the granting of a sabbatical leave during the time that a portion of this research was carried out. Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research. D.N.K. thanks Professor H. Mayr (Universität München) for hospitality during the time this manuscript was being prepared.

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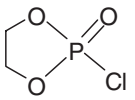
in solvent nucleophilicity (N_T); m represents the sensitivity to changes in solvent ionizing power (Y_X for a leaving group X); c represents a constant (residual) term.

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

The scale was initially developed for nucleophilic attack at sp^3-carbon, but it has been successfully applied to attack at sp^2-carbon[8] and at phosphorus[9,10] and sulfur.[11] The previous studies of attack at phosphorus have included rate and product studies of the solvolytic attack on dialkyl[10] and diaryl[12] phosphorochloridates, and a direct displacement (S_N2) reaction was proposed as the pathway.

In the present article, these studies are extended to the solvolyses of two cyclic phosphorochloridate esters, 2-chloro-1,3,2-dioxaphospholane-2-oxide (**1**) and 2-chloro-5,5-dimethyl-1,3,2-dioxaphosphorinane-2-oxide (**2**), and the specific rates (first-order rate coefficients) and product studies are compared to those previously recorded for the open chain analog, dimethyl phosphorochloridate (**3**).



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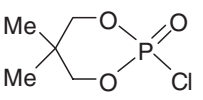

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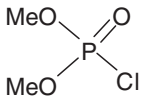


(**3**)

This study is of especial interest since there is a considerable amount of evidence that nucleophilic attack at the phosphorus of a five-membered ring diester can show quite different characteristics to attack at situations with other ring sizes or at open chain analogs. Large[13,14] (sometimes enormous[13]) accelerations have been observed, and, in contrast to the usually observed inversion, several nucleophilic substitution reactions of 2-chloro-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide (a dimethyl derivative of **1**) have been shown[15] to give predominantly retention of configuration. In this context, it will be of interest to examine the relative rates of reaction of **1**, **2**, and **3** under solvolytic conditions and, where possible, to compare the product partitioning behavior in binary water–alcohol solvents.

RESULTS

The specific rates of solvolysis of **1** and **2** have been measured in a wide range of solvents, including binary mixtures of water with 2,2,2-trifluoroethanol (TFE) and 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP). The values at 25.0°C for **1** and the values at 50.0°C for **2** are reported in Table I, together with the literature values for N_T[3,7] and Y_{Cl}[2,16] used in the multiple regression correlations. Values determined at other temperatures and the calculated activation parameters are reported in Table II for **1** and in Table III for **2**. The calculations include also the appropriate specific rate value from Table I, and are based on four temperatures, except for **2** in 100% ethanol, where reaction at 30°C was too slow for convenient measurement. Table II also includes calculated specific rate values for **2** at 25.0°C, obtained by extrapolation from the measurements at higher temperatures.

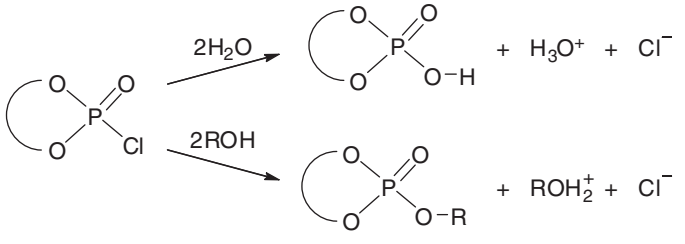
Attempts to obtain the product partitioning for **1** from infinity titers failed due to the relatively rapid solvolyses leading to appreciable reaction before homogeneity was achieved. The slower solvolyses of **2** did not have this problem, and infinity titers, at 50.0°C, could be conveniently used to establish the product partitioning ratio. Product formation via reaction with water produces two equivalents of strong acid, and reaction with an alcohol produces only one equivalent of strong acid (titration in acetone against

Table I Specific rates of solvolysis (k) of 2-chloro-1,3,2-dioxaphospholane-2-oxide (**1**)[a] at 25.0°C and 2-chloro-5,5-dimethyl-1,3,2-dioxaphosphorinane-2-oxide (**2**)[a] at 50.0°C

Solvent[b]	10^2k(**1**), s^{-1} [c] 25.0°C	10^4k(**2**), s^{-1} [c] 50.0°C	N_T[d]	Y_{Cl}[e]
100% EtOH	0.378 ± 0.003	0.458 ± 0.005	0.37	−2.52
90% EtOH	1.86 ± 0.03	1.23 ± 0.01	0.16	−0.94
80% EtOH	3.28 ± 0.04	2.02 ± 0.01	0.00	0.00
70% EtOH	5.32 ± 0.11	2.78 ± 0.01	−0.20	0.78
60% EtOH	10.7 ± 0.1	3.38 ± 0.03	−0.38	1.38
50% EtOH	15.9 ± 0.1	4.32 ± 0.08	−0.58	2.02
40% EtOH	20.8 ± 0.4	5.62 ± 0.05	−0.74	2.75
20% EtOH	44.5 ± 1.7	8.66 ± 0.04	−1.16	4.09
100% H_2O		14.3 ± 0.7	−1.38	4.57
100% MeOH	0.487 ± 0.003	0.964 ± 0.008	0.17	−1.17
90% MeOH	2.25 ± 0.05	1.95 ± 0.05	−0.01	−0.18
80% MeOH	4.80 ± 0.03	3.01 ± 0.04	−0.06	0.67
70% MeOH	9.05 ± 0.04	3.97 ± 0.01	−0.40	1.46
60% MeOH	19.3 ± 0.4	4.82 ± 0.06	−0.54	2.07
40% MeOH		7.06 ± 0.04	−0.87	3.25
20% MeOH		10.1 ± 0.1	−1.23	4.10
90% Acetone	0.0977 ± 0.0009		−0.35	−2.39
80% Acetone	0.699 ± 0.002	0.965 ± 0.006	−0.37	−0.83
70% Acetone	1.64 ± 0.02	1.72 ± 0.04	−0.42	0.17
60% Acetone	3.82 ± 0.06	2.52 ± 0.03	−0.52	0.95
50% Acetone	5.16 ± 0.08	3.22 ± 0.02	−0.70	1.73
40% Acetone	17.9 ± 0.4	3.93 ± 0.05	−0.83	2.46
20% Acetone	38.8 ± 0.8	7.93 ± 0.03	−1.11	3.77
97% TFE[f]	0.0113 ± 0.0007		−3.30	2.83
90% TFE[f]	0.0641 ± 0.0004		−2.55	2.85
80% TFE[f]	0.385 ± 0.006	0.122 ± 0.002	−2.19	2.90
70% TFE[f]	0.887 ± 0.006	0.323 ± 0.005	−1.98	2.96
50% TFE[f]	2.59 ± 0.04	0.800 ± 0.008	−1.73	3.16
90% HFIP[f]	0.104 ± 0.006		−3.84	4.31
70% HFIP[f]	0.554 ± 0.008	0.127 ± 0.004	−2.94	3.83
50% HFIP[f]	1.71 ± 0.02	0.341 ± 0.008	−2.49	3.80

[a]Substrate concentration of 0.0065 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. 3 and 7.
[e]From refs. 2 and 16.
[f]Solvent prepared on a weight/weight basis.

sodium methoxide in methanol, using resorcinol blue as an indicator). The situation is summarized in Equation (2). If a water alcohol solvent is used, the equation, as presented,



(**2**)

Table II Specific rates and activation parameters for the solvolysis of 2-chloro-1,3,2-dioxaphospholane-2-oxide (**1**) in pure and aqueous solvents

Solvent	Temp °C	10^2 k,s^{-1}[a]	$\Delta H^{\neq}_{298}$[b] (kcal/mol)	$\Delta S^{\neq}_{298}$[b] (cal·mol^{-1} K^{-1})
100% EtOH	35.0	0.545 ± 0.007	7.3 ± 0.1	−45.1 ± 0.3
	45.0	0.840 ± 0.003		
	55.0	1.28 ± 0.02		
80% EtOH[c]	35.0	4.17 ± 0.06	4.9 ± 0.1	−49.0 ± 0.3
	45.0	5.56 ± 0.01		
	55.0	7.70 ± 0.03		
100% MeOH	35.0	0.701 ± 0.002	9.1 ± 0.2	−38.9 ± 0.6
	45.0	1.22 ± 0.01		
	55.0	2.14 ± 0.01		
90% Acetone[c]	35.0	0.155 ± 0.002	9.7 ± 0.1	−39.8 ± 0.4
	45.0	0.272 ± 0.003		
	55.0	0.478 ± 0.008		
97% TFE[d]	35.0	0.0221 ± 0.0004	11.3 ± 0.1	−38.7 ± 0.3
	45.0	0.0434 ± 0.0003		
	55.0	0.0695 ± 0.0008		
90% HFIP[d]	35.0	0.144 ± 0.003	6.3 ± 0.1	−51.1 ± 0.3
	45.0	0.204 ± 0.003		
	55.0	0.305 ± 0.003		

[a]With associated standard deviation.
[b]Values at 25.0°C, from Table I, also used in the calculation; the activation parameters are accompanied by the standard error.
[c]On a volume/volume basis at 25.0°C.
[d]On a weight/weight basis.

Table III Specific rates of solvolysis of 2-chloro-5,5-dimethyl-1,3,2-dioxaphosphorinane-2-oxide (**2**) and the calculated enthalpies ($\Delta H^{\neq}$) and entropies ($\Delta S^{\neq}$) of activation

Solvent	Temp.°C	10^5 k,s^{-1} [a]	$\Delta H^{\neq}{}_{323}{}^{b}$ Kcal mol^{-1}	$\Delta S^{\neq}{}_{323}{}^{b}$ cal mol^{-1} K^{-1}
100% EtOH	60.0	7.08 ± 0.04	8.8 ± 0.1	−51.3 ± 0.2
	40.0	2.84 ± 0.03		
	25.0	(1·34)[c]		
80% EtOH[d]	60.0	41.1 ± 0.3	14.8 ± 0.1	−29.7 ± 0.2
	40.0	9.27 ± 0.06		
	30.0	4.07 ± 0.06		
	25.0	(2·69)[c]		
100% H_2O	60.0	293 ± 4	16.7 ± 0.1	−20.2 ± 0.3
	40.0	57.1 ± 0.4		
	30.0	22.5 ± 0.1		
	25.0	(14·3)[c]		
100% MeOH	60.0	19.3 ± 0.4	15.3 ± 0.1	−29.8 ± 0.2
	40.0	4.25 ± 0.05		
	30.0	1.80 ± 0.02		
	25.0	(1·18)[c]		

[a]With associated standard deviation.
[b]Values at 50.0°C, from Table I, also used in the calculation; the activation parameters are accompanied by the standard error.
[c]Calculated from the values at other temperatures, using the Arrhenius equation.
[d]On a volume/volume basis at 25.0°C (the other component is water).

Table IV Selectivity values (S)[a] for solvolyses at 50.0°C of 2-chloro-5,5-dimethyl-1,3,2-dioxaphosphorinane-2-oxide (**2**) in binary mixtures of water with ethanol, methanol, or 2,2,2-trifluoroethanol and a comparison with the S values from solvolyses of dimethyl phosphorochloridate (**3**) at 25.0°C

Solvent[b]	%Ester[c]	S(**2**)	S(**3**)[d]
90% EtOH	84.6	2.0	0.36
80% EtOH	61.8	1.3	0.46
70% EtOH	50.7	1.4	0.56
60% EtOH	40.3	1.5	
50% EtOH	29.7	1.4	
40% EtOH	24.5	1.6	
20% EtOH	13.4	2.0	
90% MeOH	89.8	2.2	0.85
80% MeOH	79.8	2.3	0.84
70% MeOH	66.4	1.9	
60% MeOH	50.8	1.6	
40% MeOH	28.2	1.3	
20% MeOH	15.6	1.7	
80% TFE	15.1	0.23	[e]
70% TFE	3.8	0.09	[e]
50% TFE	1.3	0.07	[e]

[a]As defined in Eq. (3).

[b]Aqueous ethanol and methanol on a volume/volume basis at 25.0°C and aqueous TFE on a weight/weight basis.

[c]Molar percentage of ester formed in competition with the acid.

[d]Values from ref. 10.

[e]Only very small amounts of ester formed, and the S value was too low to be determined by the titration technique.

is simplified in that the second solvent molecule, used to extract the proton from the molecule serving as the nucleophile, could be either water or alcohol. Further, the amounts of each of the two shown protonated solvent species will be determined by a rapid equilibration within the mixed solvent.

The partitioning ratio ([ester]/[acid]) is used in conjunction with the molar composition ratio for the solvent involved ([H_2O]/[ROH]) to calculate the selectivity value (**S**), defined as in Equation (3).

$$S = \frac{[\text{ester in product}]}{[\text{acid in product}]} \cdot \frac{[H_2O \text{ in solvent}]}{[\text{ROH in solvent}]} \tag{3}$$

Values for the percentages of reaction proceeding with ester formation (x%) for solvolyses of **2**, at 50.0°C, in mixtures of water with ethanol, methanol, or TFE, are reported in Table IV. The product ratios (x/100–x) are then used within Equation (3) to give the S values, which are also present within Table IV.

DISCUSSION

The kinetic studies of the solvolyses of **1** and **2** over a wide range of hydroxylic solvents, including the important water–fluoroalcohol systems,[3] involved 28 solvents for **1**, at 25.0°C, and 27 solvents for **2**, at 50.0°C (Table I). Application of Equation (1)

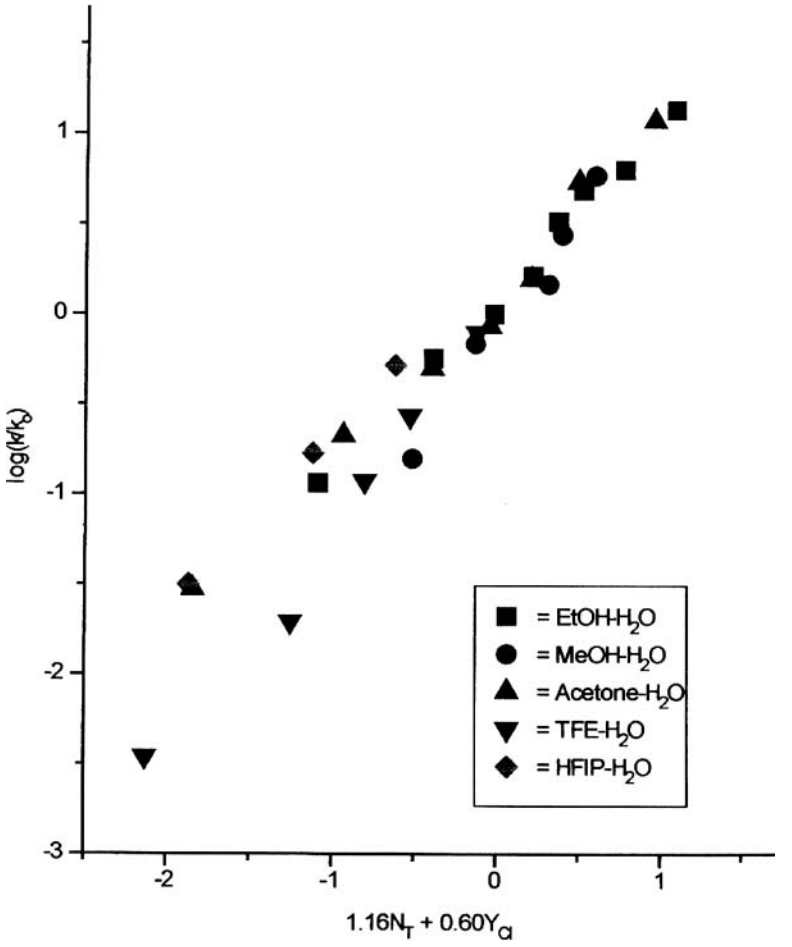


Figure 1 Plot of log (k/k_o) for solvolyses of **1** at 25.0°C against ($1.16N_T+0.60Y_{Cl}$).

to the data (Figures 1 and 2) led to the sensitivities (l) towards changes in solvent nucleophilicity and to the sensitivities (m) towards changes in solvent ionizing power reported in Table V. For both solvolyses, the correlation has a multiple correlation coefficient (R) of 0.974. The c values (residuals) were low at 0.04 ± 0.05 for **1** and 0.09 ± 0.06 for **2**. The l/m ratios, considered to be a useful tool in assigning mechanism,[17] were at values of 1.93 and 2.40, respectively—within the range of values for solvolyses believed to involve S_N2 attack at phosphorus or sulfur (1.67 to 2.70 for the examples in Table V). The other substrates included in the table for comparison are *N*,*N*,*N*′,*N*′-tetramethyldiamidophosphorochloridate,[9] dimethyl phosphorochloridate (**3**),[10] diphenylphosphinyl chloride,[18] *p*-methoxybenzenesulfonyl chloride,[17] 2-propanesulfonyl chloride,[11] and *N*,*N*-dimethylsulfamoyl chloride.[11]

The l and m values for solvolyses of **1** and **2** are similar to those for the other solvolyses listed in Table V, they do not give any indication for special effects in either of the solvolyses, and they, like the l/m ratio,[18] are consistent with an S_N2 pathway. In particular, the l and m values are very similar for **1** and **3**. In Table VI, the specific rate

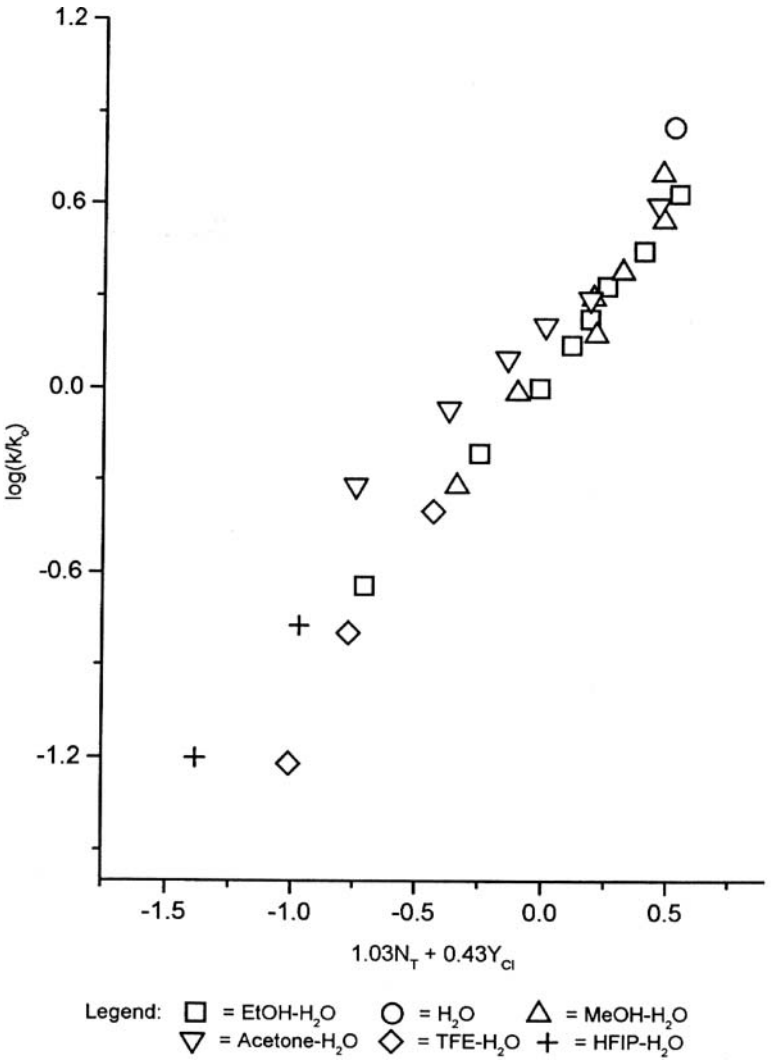


Figure 2 Plot of log (k/k_o) for solvolyses of **2** at 50.0°C against ($1.03N_T+0.43Y_{Cl}$).

values for **1** and **2** are compared with those determined[10] earlier for **3**. For **2**, values were measured primarily at 50.0°C, but for four of the solvolyses, values were calculated for 25.0°C by extrapolation of data measured at higher temperatures (Table III), and for three of these a corresponding specific rate value was available[10] for solvolysis of **3**.

The fastest solvolyses were those of **1**, which reacted from twice as fast as **3** in 90% acetone up to almost 80 times faster in 70% HFIP. Considering the wide variation in the type of hydroxylic solvent involved, the extent of the variation in relative reactivities is rather small, consistent with the similar *l* and *m* values for the two processes. The larger k(**1**)/k(**3**) ratios in aqueous–fluoroalcohol solvents is due to the low nucleophilicity of these solvents, coupled with a higher sensitivity to changes in solvent nucleophilicity for solvolyses of **3** (1.27) than for solvolyses of **1** (1.16).

Table V Grunwald–Winstein correlations for solvolyses at phosphorus and sulfur

Substrate	n^a	T°C	l^b	m^b	R^c	l/m
$(Me_2N)_2POCl$[d]	31	25.0	1.20 ± 0.07	0.69 ± 0.04	0.958	1.74
3[e]	18	25.0	1.27 ± 0.14	0.47 ± 0.08	0.941	2.70
$(MeO)_2PSCl$[e]	28	25.0	1.17 ± 0.07	0.56 ± 0.03	0.966	2.09
Ph_2POCl[f]	27	25.0	1.42 ± 0.10	0.54 ± 0.07	0.956	2.63
1[g]	28	25.0	1.16 ± 0.06	0.60 ± 0.03	0.974	1.93
2[g]	27	50.0	1.03 ± 0.05	0.43 ± 0.02	0.974	2.40
p-$MeOC_6H_4SO_2Cl$[h]	38	25.0	1.07 ± 0.08	0.60 ± 0.03	0.967	1.78
i-$PrSO_2Cl$[i]	19	45.0	1.28 ± 0.05	0.64 ± 0.03	0.988	2.00
Me_2NSO_2Cl[i]	32	25.0	1.20 ± 0.04	0.72 ± 0.03	0.985	1.67

[a]Number of data points.
[b]From Eq. (1), and with associated standard error.
[c]Multiple correlation coefficient.
[d]From ref. 9.
[e]From ref. 10.
[f]From ref. 18.
[g]This work.
[h]From ref. 17.
[i]From ref. 11.

The three available rate ratios for **2** relative to **3** are in the 0.01 to 0.05 range. Overall, the data of Table VI show that there are no very large differences in rate when **1**, **2**, and **3** are solvolyzed under conditions of identical solvent and temperature, with **1** reacting slightly faster than **3**, which in turn reacts somewhat faster than **2**.

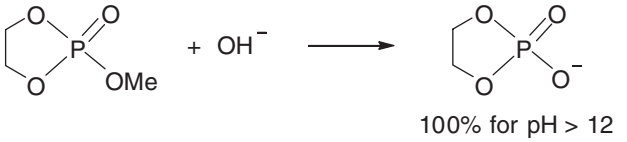
Table VI A comparison of the specific rates of solvolysis, at 25.0°C, of dimethyl phosphorochloridate (**3**), 2-chloro-1,3,2-dioxaphospholane-2-oxide (**1**), and 2-chloro-5,5-dimethyl-1,3,2-dioxaphosphorinane-2-oxide (**2**)

Solvent[a]	$k(\mathbf{1})/k(\mathbf{3})^b$	$k(\mathbf{2})/k(\mathbf{3})^b$
100% EtOH	12.8	0.045
90% EtOH	11.6	
80% EtOH	11.5	0.0095
70% EtOH	12.8	
100% MeOH	4.3	0.011
90% MeOH	7.3	
80% MeOH	9.7	
90% Acetone	2.0	
80% Acetone	4.1	
70% Acetone	5.1	
60% Acetone	7.6	
97% TFE	31.4	
90% TFE	35.8	
80% TFE	32.3	
70% TFE	25.5	
50% TFE	13.9	
70% HFIP	78.3	
50% HFIP	58.0	

[a]On volume/volume basis, except TFE-H_2O mixtures on a weight/weight basis.
[b]The $k(\mathbf{1})$ values from Table I, the $k(\mathbf{2})$ values from Table III, and the $k(\mathbf{3})$ values from ref. 10.

Earlier studies[19–24] of the rates of other nucleophilic substitution reactions of cyclic esters of phosphoric acid found that rings with six or seven members reacted at about the same rate as similar acyclic esters,[22–24] consistent with the present study. However, it was also found that reactions involving five-membered rings were enormously accelerated.

In particular, the rate measurements for the oxygen exchange of the corresponding acids (in H_2O^{18}) and the hydrolysis of the methyl esters (the chlorine of **1**, replaced by a methoxy group) indicated a 10^7 rate difference for exchange and a 10^6 rate difference for hydrolysis, favoring the reactions of the ethylene phosphate derivative.[19–21] The ring-opening reactions were also very fast, which was readily explained in terms of the relief of strain within the five-membered ring, but a different approach was needed to explain the competitive exocyclic hydrolyses with retention of the ring structure (Scheme 1).



Scheme 1

Westheimer[20] proposed that the hydrolytic replacement of an exocyclic substituent (OH by a labeled $O^{18}H$ group[14] or OCH_3 by an OH group[19]), under either acid or basic conditions, involves an ionic pentacoordinate trigonal bipyramid intermediate. This undergoes a favorable reduction in ring strain during the progress of the reaction through the involvement of pseudorotations. The hydrolyses with ring opening do not require pseudorotations, and they were proposed to proceed through an intermediate resembling an S_N2 transition state, situated along an alternative reaction channel.

The proposal of intermediates in these substitution pathways differs from our recent suggestions that several acyclic phosphorochloridates undergo solvolysis by S_N2 attack at phosphorus with displacement of chloride ion, in a concerted process.[9,10,18] The two viewpoints are easily reconciled since concerted pathways would be much more favorable for a relatively good leaving group, such as chloride, compared to a relatively poor leaving group, such as hydroxide or methoxide. For the latter, a process involving addition (association) to give an intermediate, eventually followed by loss of the leaving group (dissociation), could well be the most favorable pathway. Indeed, in the extreme case, with only extremely poor leaving groups available, one would expect to observe only an equilibrium addition as, for example, in the hydration of aldehydes and ketones.

An important observation in this regard was that by Mikolajczyk and coworkers[25] for the basic solvolyses of 2-halogeno-4-methyl-2-thio-1,3,2-dioxaphosphorinans. They observed inversion of configuration for the bromo and chloro compounds but retention for the fluoro compound. This can be rationalized in terms of S_N2 attack for the chloro and bromo compounds but an addition–elimination pathway for the fluoro compound, due to the much poorer fluoride leaving group. Similarly, Corriu and coworkers[26] found that reactions of cyclic halogenophosphorochloridates with aryloxide in tetrahydrofuran all showed an excess of retention of configuration, in conjunction with the reaction of the fluoro compound showing a greater degree of retention than either the chloro or bromo compound. Also, for reactions with lithium or sodium *p*-methylphenoxide in acetonitrile-d_3 or acetone-d_6, the fluoro compound reacted slightly faster than the chloro compound (k_F/k_{Cl} values of

1.1 to 2.5).[27] This behavior is similar to that observed for several nucleophilic substitution reactions of haloformates (ROCOX)[28] or halobenzenes,[29] where strong evidence exists for an addition–elimination pathway. Mechanistic studies of nucleophilic displacement of halide ion from tetracoordinate phosphorus, including a discussion of the work by Corriu and Mikalajczyk, have recently been reviewed.[9]

Specific rates at temperatures other than the ones used to obtain the values in Table I, together with the enthalpies and entropies of activation, are reported for six solvolyses of **1** in Table II and for four solvolyses of **2** in Table III. The enthalpies of activation are lower for the solvolyses of **1**, 4.9 to 11.3 kcal mol^{-1}, than for the solvolyses of **2**, 8.8 to 16.7 kcal mol^{-1}. The higher specific rates for **1** to be expected based on these values are, however, moderated by generally less favorable (highly negative) entropies of activation of −38.9 to −51.1 cal mol^{-1} K^{-1} for **1**, compared to values of -20.2 to -51.3 cal mol^{-1} K^{-1} for **2** (with three of the four values for **2** in the −20 to −30 cal mol^{-1} K^{-1} range). With this balancing of effects, the solvolyses of **1**, at 25.0°C, proceed, relative to those of **2** and using the data of Table VI, about 300 times faster in ethanol, about 400 times faster in methanol, and about 1200 times faster in 80% ethanol. These are appreciable values, but they are considerably lower than the values of in excess of a million observed for catalyzed hydrolyses of related acids and esters.[20] The appreciably negative entropies of activation for **1** and **2** are consistent with the proposed lack of ring opening. Reaction with ring opening would be expected to have a less negative, possibly positive, entropy of activation, especially for opening of the five-membered ring of **1**. Further, such ring-opening reaction would be expected to favor considerably faster reaction for **1** and **2** than for **3**, as opposed to the only modestly higher solvolysis rates for **1** relative to **3** and for **3** relative to **2** (Table VI).

The selectivity values [*S*, Equation (3)] for **2**, at 50.0°C, in mixtures of water with alcohol, were almost constant, with a range of 1.3 to 2.3, in ethanol/water and methanol/water, containing from 90% to 20% (by volume) alcohol. For both mixed systems, a slight fall in values as the alcohol content was decreased was reversed at about the 40% alcohol content (Table IV). In all determinations, there was a slight preference for reaction with alcohol rather than water. In contrast, the *S* values previously determined, at 25.0°C, for solvolyses of **3** have values somewhat below unity, 0.36 to 0.85, indicating a faster reaction with the water component. The influence of the 25.0°C difference in temperature is probably slight,[30] and it appears that in the balance between steric effects and nucleophilicity,[3] both higher for ethanol and methanol, the tying back of the two alkoxy substituents in a ring leads to solvent nucleophilicity effects dominating for **2**, whereas the reverse is true for **3**, with its two methoxy substituents.

In the TFE/water mixtures, as one would expect, there is a considerable preference for reaction with water, with TFE having both a much larger steric effect and a much lower nucleophilicity.[3] The *S* values are towards the lower limit for determination by the titration technique, and, indeed, the even lower values for **3** (again consistent with a larger influence of the steric effect) could not be determined.[10]

CONCLUSIONS

Under identical conditions, at 25.0°C, the solvolyses of 2-chloro-1,3,2-dioxaphospholane-2-oxide (**1**), with the chlorine situated on the phosphorus of a five-membered diester ring, proceeded two to 80 times faster than those studied earlier for the open chain dimethyl phosphorochloridate (**3**).[10] In turn, **3** reacted faster, by factors

of 20 to 100, than in four corresponding solvolyses of 2-chloro-5,5-dimethyl-1,3,2-dioxaphosphorinane-2-oxide (**2**).

Correlations (Table V) using the extended Grunwald–Winstein equation [Eq. (1)] led to sensitivities towards changes in solvent nucleophilicity (l) of 1.16 ± 0.06 (at 25.0°C) for **1** and 1.03 ± 0.05 (at 50.0°C) for **2**, similar to the value[10] of 1.27 ± 0.14 (at 25.0°C) for **3**. The corresponding sensitivities towards changes in solvent ionizing power (m) of 0.60 ± 0.03 for **1** and 0.43 ± 0.02 for **2** are also similar to the value of 0.47 ± 0.08 for **3**.

Consideration of both the relative rates and the Grunwald–Winstein equation correlations suggests that the solvolyses of **1** can be best rationalized in terms of the S_N2 attack at phosphorus usually proposed[10] for solvolytic displacement of chloride from phosphorus.

Selectivity values [Eq. (3)] for **2**, show that, in ethanol/water and methanol/water, there is a slight preference for the alcohol to function as the nucleophile. In contrast, the S values[10] for solvolyses of **3** (at a 25.0°C lower temperature) show a slight preference for reaction with the water component. As one would expect from its low solvent nucleophilicity,[3] TFE in TFE/water mixtures competes only poorly against the water component for reaction with **2**. The rather small differences in S values for solvolyses of **2** and **3** can be rationalized in terms of reduced steric interactions when the attack is at the phosphorus of a tied-back ring system in **2**.

EXPERIMENTAL

The 2-chloro-1,3,2-dioxaphospholane-2-oxide (**1**, Aldrich Technical Grade) and 2-chloro-5,5-dimethyl-1,3,2-dioxaphosphorinane-2-oxide (**2**, Aldrich 96%) were used as received. Compound **1** was reported to contain up to 10% of 2-chloro-1,3,2-dioxaphospholane, a cyclic phosphorochloridite with the same structure as **1**, except that there is no oxygen atom attached to the phosphorus. Phosphorochloridites solvolyze extremely rapidly. For example, the ethanolyses of the dimethyl and diethyl esters [$(RO)_2PCl$; R = Me or Et] have been shown to be "practically instantaneous at 0°C."[31] Accordingly, the impurity in **1** will have solvolyzed completely at 25.0°C before homogeneity is established and before the kinetic runs were initiated. Solvents were purified as previously described.[7]

The kinetic runs were carried out as previously reported,[32] except that, for solvolyses of **1**, 12 μL of a stock solution in acetonitrile were added to 12.5 mL of temperature-equilibrated solvent. Values reported are averages of duplicate determinations. The multiple regression analyses were carried out using commercially available statistical packages.

The product studies for solvolyses of **2**, based on infinity titers, were also determined as previously reported.[10]

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