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Kinetics and Mechanism of the Pyridinolysis of Ethylene Phosphorochloridate in Acetonitrile

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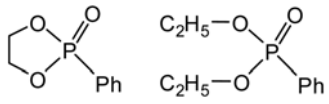
The nucleophilic substitution reactions of ethylene phosphorochloridate (**2**) with X-pyridines are investigated kinetically in acetonitrile at –20.0 °C. The free energy correlations for substituent X variations in the nucleophiles exhibit biphasic concave upwards with a break point at X = 3-Ph. Unusual positive ρ_X (= +2.49) and negative β_X (= –0.41) values are obtained with the weakly basic pyridines, and rationalized by the isokinetic relationship with isokinetic temperature at $t_{ISOKINETIC}$ = 6.6 °C. The pyridinolysis rate of **2** with a cyclic five-membered ring is forty thousand times faster than its acyclic counterpart (**3:** diethyl chlorophosphate) because of great positive value of the entropy of activation of **2** ($\Delta S^{\neq}$ = +49.2 eu) compared to negative value of **3** ($\Delta S^{\neq}$ = –44.1 eu) over considerably unfavorable enthalpy of activation of **2** ($\Delta H^{\neq}$ = 28.4 kcal mol^{-1}) compared to **3** ($\Delta H^{\neq}$ = 6.3 kcal mol^{-1}). Great enthalpy and positive entropy of activation are ascribed to sterically congested transition state (TS) and solvent structure breaking in the TS. A concerted mechanism involving a change of nucleophilic attacking direction from a frontside attack with the strongly basic pyridines to a backside attack with the weakly basic pyridines is proposed.

Key Words : Phosphoryl transfer reaction, Pyridinolysis, Ethylene phosphorochloridate, Biphasic concave upward free energy correlation, Isokinetic relationship

Introduction

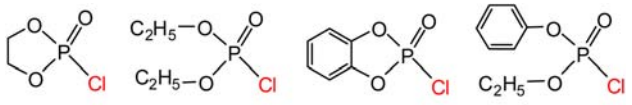
It is known that a cyclic five-membered ring phosphate ester is strained and it hydrolyzes millions times faster than its acyclic counterpart.[1] The rate of base catalyzed hydrolysis of a cyclic five-membered ring of 2-oxo-2-phenyl-1,3,2-dioxaphospholane (**I**) is 1.48 × 10^6 times faster than its acyclic counterpart of diethyl phenylphosphonate (**II**) at 25.4 °C (Scheme 1).[2]

The anilinolysis rate ($C_6H_5NH_2$) of a cyclic five-membered ring of ethylene phosphorochloridate (**2**)[3a] is 4.18 × 10^3 times faster than its acyclic counterpart of diethyl chlorophosphate (**3**),[3b] and that of a cyclic five-membered ring of 1,2-phenylene phosphorochloridate (**6**)[3c] is 1.53 × 10^5 times faster than its acyclic counterpart of phenyl ethyl chlorophosphate (**7**) in acetonitrile (MeCN) at 55.0 °C (Scheme 2).[3d]



I II

Scheme 1. Cyclic five-membered ring of 2-oxo-2-phenyl-1,3,2-dioxaphospholane (**I**) and its acyclic counterpart of diethyl phenylphosphonate (**II**).



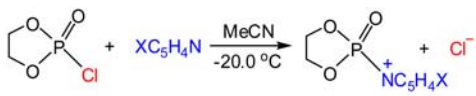
2 3 6 7

Scheme 2. Cyclic five-membered rings of ethylene (**2**) and 1,2-phenylene (**6**) phosphorochloridate, and their acyclic counterparts of diethyl (**3**) and phenyl ethyl (**7**) chlorophosphate.

Continuing the kinetic study of the aminolysis of phosphorus ester involving a cyclic five-membered ring, the nucleophilic substitution reactions of ethylene phosphorochloridate (**2**) with substituted pyridines (XC_5H_4N) are investigated kinetically in MeCN at –20.0 ± 0.1 °C (Scheme 3) to gain further information into the reactivity and mechanism depending on the variation of the two ligands, R_1O and R_2O, as well as to compare the relevant pyridinolyses of dimethyl [**1:** $(MeO)_2P(=O)Cl$],[4a] diethyl [**3:** $(EtO)_2P(=O)Cl$],[4a] diisopropyl [**4:** $(i\text{-}PrO)_2P(=O)Cl$],[4b] and Y-aryl phenyl [**5**: $(PhO)(YC_6H_4O)P(=O)Cl$][4c] chlorophosphates in MeCN.

Results and Discussion

The reactions were carried out under pseudo-first-order conditions with a large excess of pyridine. The observed pseudo-first-order rate constants (k_{obsd}) for all the reactions obeyed eq. (1) with negligible k_0 (≈ 0) in MeCN. The second-order rate constants were determined with at least five pyridine concentrations. The linear plots of eq. (1) suggest a lack of any base-catalysis or side reactions, and the overall reaction is described by Scheme 3.



X = 4-MeO, 4-Me, 3-Me, H, 3-Ph, 3-MeO, 3-Cl, 3-Ac, 4-Ac, 3-CN, 4-CN

Scheme 3. The studied reaction system.

Table 1. Second-order rate constants ($k_2 \times 10^2/M^{-1}\ s^{-1}$) of the reactions of ethylene phosphorochloridate (**2**) with XC_5H_4N in MeCN at –20.0 ºC

X	4-MeO	4-Me	3-Me	H	3-Ph	3-MeO	3-Cl	3-Ac	4-Ac	3-CN	4-CN
$k_2 \times 10^2$	300 ± 1	80.1 ± 0.4	22.5 ± 0.2	9.98 ± 0.05	5.01 ± 0.01	6.75 ± 0.05	25.6 ± 0.1	32.1 ± 0.1	60.5 ± 0.3	86.1 ± 0.6	152 ± 1

$$k_{obsd} = k_0 + k_2[XC_5H_4N] \quad (1)$$

The second-order rate constants [k_2 ($M^{-1}\ s^{-1}$)] are summarized in Table 1. The Brönsted β_X value was calculated by correlating log k_2(MeCN) with pK_a(H_2O),[5] which was justified theoretically and experimentally.[6] The substituent effects of the nucleophiles upon the pyridinolysis rates do not correlate with those for a typical nucleophilic substitution reaction: (i) for more basic pyridines (X = 4-MeO, 4-Me, 3-Me, H, 3-Ph), the stronger nucleophile leads to a faster rate in line with a typical nucleophilic substitution reaction, resulting in negative ρ_X (= –5.39) and positive β_X (= +1.06) values; (ii) for less basic pyridines (X = 3-Ph, 3-MeO, 3-Cl, 3-Ac, 4-Ac, 3-CN, 4-CN), on the contrary, the weaker nucleophile leads to a faster rate, resulting in unusual positive ρ_X (= +2.49) and negative β_X (= –0.41) values. Thus, the Hammett (Fig. 1; log k_2 vs σ_X) and Brönsted [Fig. 2; log k_2 *vs* pK_a(X)] plots are biphasic concave upwards with a break point at X = 3-Ph, giving minimum rate constant.

The unusual positive ρ_X and negative β_X values with the weakly basic pyridines can be occurred because of (i) desolvation of ground state (GS), (ii) imbalance of transition state (TS), or (iii) isokinetic relationship: (i) The discrete linear free energy relationships are reported because of a desolvation step prior to the rate-limiting nucleophilic attack with a smaller value of β_X when the nucleophile is anion and the solvent is polar protic, e.g., water.[7] However, in the present work, the positive ρ_X (and negative β_X) value with the less basic pyridines are not ascribed to a desolvation step prior to the rate-limiting nucleophilic attack, since the pyridine nucleophile is neutral and the MeCN solvent is dipolar aprotic. (ii) The authors reported that the sign of ρ_X changes from positive for the relatively strong electron-donating Y substituents to negative for the more electron-withdrawing substituents of the reactions of 1-(Y-phenyl) ethyl chlorides with X-anilines in methanol.[8] The anilinolyses of Y-benzhydryl chlorides in MeOH-MeCN also exhibited the change of the sign of ρ_X depending on Y substituents.[9] The positive ρ_X values were interpreted in terms of a TS structure in which nearly complete bond formation between the nucleophile and cation formed in an ion-pair pre-equilibrium is coupled with a TS imbalance phenomenon, advocated by Jencks[10] and Bernasconi.[11] In the present work, however, the positive ρ_X value is inadequate to a TS imbalance phenomenon, since an ion-pair pre-equilibrium cannot occur taking into account the substrate. (iii) For a large number of reaction series, it is found that $\delta\Delta H^{\neq}$ and $\delta\Delta S^{\neq}$ are proportional, resulting in isokinetic relationship.[12] The observed second-order rate constants with 3-methoxy, 4-acetyl, and 4-cyano pyridines at –20.0 ºC, –15.0 ºC, and –10.0 ºC, and enthalpies and entropies of activation are summarized in Table 2. The ρ_X value decreases as the reaction temperature becomes higher as seen in Figure 3. Thus, the isokinetic temperature, according to eq. (2), is $T_{ISOKINETIC}$ = 279.7 K = 6.6 ºC (Fig. 4) where the ρ_X value is null, based on $\Delta H^{\neq}$ = 23.0 and $\Delta S^{\neq}$ = +27 with X = 3-MeO; $\Delta H^{\neq}$ = 11.8 and $\Delta S^{\neq}$ = –13 for X = 4-Ac; $\Delta H^{\neq}$ = 5.1 kcal/mol and $\Delta S^{\neq}$ = –37 eu with X = 4-CN.

$$\delta\Delta G^{\neq} = \delta\Delta H^{\neq} - T\delta\Delta S^{\neq} = 0;\ \text{when}\ \delta\Delta H^{\neq} = T_{ISOKINETIC}\delta\Delta S^{\neq} \quad (2)$$

The isokinetic relationships for the pyridinolyses of tetracoordinated phosphorus are also observed when the reaction

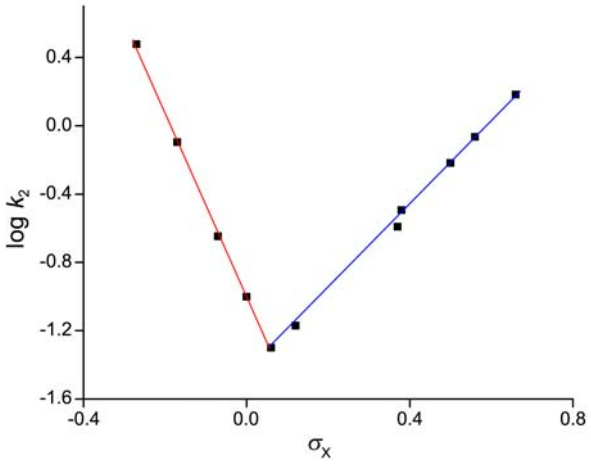


Figure 1. The Hammett plot (log k_2 *vs* σ_X) of the reactions of ethylene phosphorochloridate (**2**) with X-pyridines in MeCN at –20.0 ºC. The values of ρ_X are –5.39 ± 0.02 (r = 0.999) with X = (4-MeO, 4-Me, 3-Me, H, 3-Ph) and 2.49 ± 0.03 (r = 0.999) with X = (3-Ph, 3-MeO, 3-Cl, 3-Ac, 4-Ac, 3-CN, 4-CN).

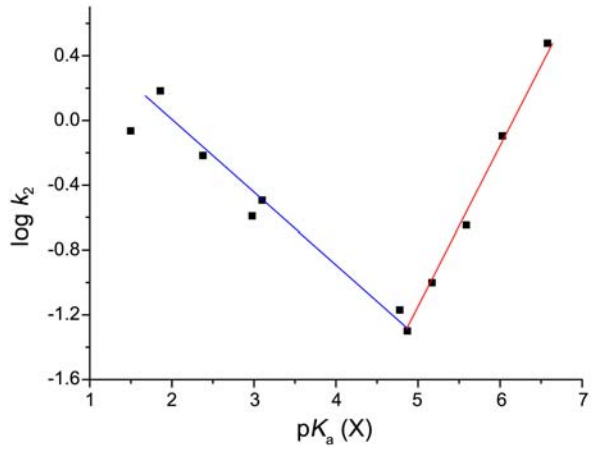


Figure 2. The Brönsted plot [log k_2 *vs* pK_a(X)] of the reactions of ethylene phosphorochloridate (**2**) with X-pyridines in MeCN at –20.0 ºC. The values of β_X are 1.06 ± 0.05 (r = 0.998) with X = (4-MeO, 4-Me, 3-Me, H, 3-Ph) and –0.41 ± 0.14 (r = 0.974) with X = (3-Ph, 3-MeO, 3-Cl, 3-Ac, 4-Ac, 3-CN, 4-CN).

Table 2. Second-order rate constants at –20.0, –15.0, and –10.0 °C, and enthalpy and entropy of activation for the reactions of ethylene phosphorochloridate (**2**) with X-Pyridines (X =3-MeO, 4-Ac and 4-CN) in MeCN

X	$k_2 \times 10^2$ (M^{-1} s^{-1})			$\Delta H^{\neq}$ (kcal mol^{-1})	$\Delta S^{\neq}$(eu)
	–20.0 °C	–15.0 °C	–10.0 °C		
3-MeO	6.75 ± 0.05	17.4 ± 0.1	39.8 ± 0.1	23.0 ± 0.7	+27 ± 3
4-Ac	60.5 ± 0.3	99.6 ± 0.2	153 ± 1	11.8 ± 0.4	–13 ± 2
4-CN	152 ± 1	185 ± 1	233 ± 2	5.1 ± 0.3	–37 ± 1

temperature is considerably low. The pyridinolysis of dimethyl phosphinic chloride [$(Me)_2P(=O)Cl$] yielded positive ρ_X (= +0.16) and negative β_X (= –0.03) values with the weakly basic pyridines in MeCN at 25.0 °C, giving $T_{ISOKINETIC}$ = 249.4 K = 23.8 °C,[13a] while that of methyl phenyl phosphinic chloride [MePhP(=O)Cl] yielded positive ρ_X (= +2.94) and negative β_X (= –0.48) values with the strongly basic pyridines in MeCN at 20.0 °C, giving $T_{ISOKINETIC}$ = 287.5 K = 14.4 °C.[13b] It seems that the pyridinolysis of tetracoordinated phosphorus shows the isokinetic relationship in MeCN at the very low temperature when the free energy correlation exhibits biphasic concave upwards (or downwards) with min (or max) rate constant.

The second-order rate constants (k_2) with unsubstituted pyridine (C_5H_5N) at 35.0 °C, natural bond order (NBO) charges at the reaction center P atom in the gas phase [B3LYP/6-311+G(d,p) level of theory],[14] Brönsted coefficients (β_X), and cross-interaction constant (CIC; ρ_{XY})[15] for the pyridinolyses of five $(R_1O)(R_2O)P(=O)Cl$-type chlorophosphates in MeCN are summarized in Table 3. When the magnitude of the positive charge of the reaction center P atom in the substrate plays an important role to determine the pyridinolysis rate, the sequence of the pyridinolysis rate should be **4** > **3** > **5** > **1** > **2**. On the other hand, when the steric effects of the two ligands (R_1O and R_2O) play an important role, the sequence of the rate should be **1** > **2** ≈ **3** > **4** > **5**.

However, the observed sequence of the pyridinolysis rates is **2** >> **5** > **1** > **3** > **4**, giving the relative rate ratio of 331,000(**2**):27.7(**5**):6.7(**1**):5.5(**3**):1(**4**). The sequence of the pyridinolysis rates does not have consistency with the magnitude of the positive charge of the reaction center P or steric effects of the two ligands. This suggests that the pyridinolysis rates of chlorophosphates are not dependent upon one dominant factor, while the anilinolysis rates of chlorophosphates are predominantly dependent upon the steric effects over the inductive effects.[3]

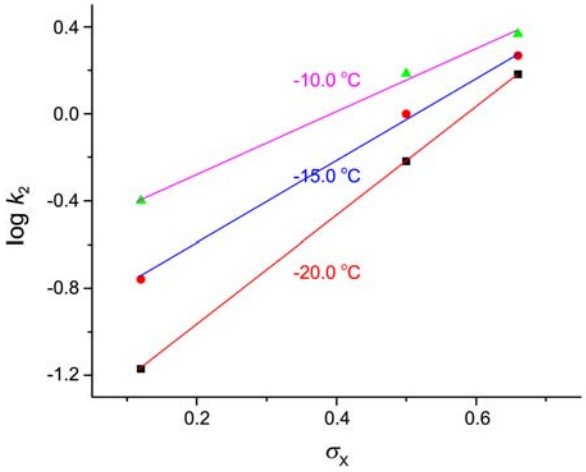


Figure 3. The Hammett plots of log k_2 *vs* σ_X for the reactions of ethylene phosphorochloridate (**2**) with X = 3-MeO, 4-Ac, and 4-CN pyridines in MeCN. The ρ_X values are 1.44±0.04 (r = 0.998), 1.92±0.03 (r = 0.999), and 2.51± 0.01 (r = 1.000) at 10.0, 15.0, and 20.0 °C, respectively.

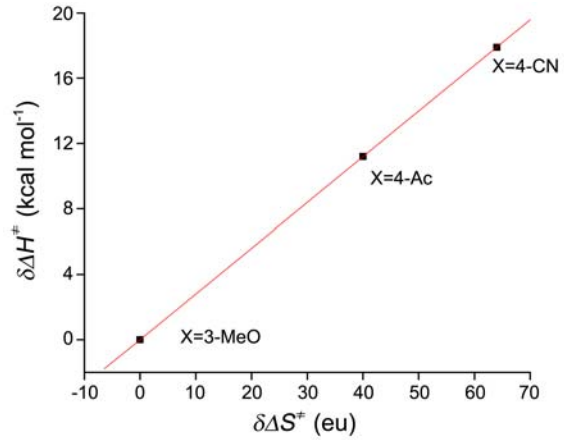


Figure 4. Isokinetic relationship for the reactions of ethylene phosphorochloridate (**2**) with 3-MeO, 4-Ac and 4-CN pyridines in MeCN, giving the slope of $T_{ISOKINETIC}$ = 279.7 K = 6.6 °C (r = 1.000).

Table 3. Summary of the second-order rate constants ($k_2 \times 10^3/M^{-1}$ s^{-1} with C_5H_5N at 35.0 °C), NBO charges at the reaction center P atom, brönsted coefficients (β_X), and cross-interaction constant (ρ_{XY}) for the Pyridinolyses (XC_5H_4N) of **1-5** in MeCN

Substrate	$k_2 \times 10^3$[a]	Charge at P	β_X	ρ_{XY}	Ref
1: $(MeO)_2P(=O)Cl$	64.7	2.226	0.63[e]	–	4a
2: $cC_2H_4O_2P(=O)Cl$	3,180,000[b]	2.196	1.06 /–0.41	–	this work
3: $(EtO)_2P(=O)Cl$	52.8	2.236	0.73[e]	–	4a
4: $(i\text{-}PrO)_2P(=O)Cl$	9.60	2.269	1.05[f] / 0.39[g]	–	4b
5: $(PhO)(YC_6H_4O)P(=O)Cl$	266[c]	2.230[d]	0.16-0.18[h]	–0.15[h]	4c

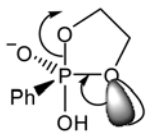
[a]Second-order rate constant with unsubstituted pyridine (X = H) at 35.0 °C. [b]Extrapolated value in the Arrhenius plot with kinetic data: k_2 = 99.8 (± 0.5), 289 (± 1), and 885 (± 4) × 10^{-3} M^{-1} s^{-1} at –20.0, –15.0, and –10.0 °C, respectively. [c]Extrapolated value in the Arrhenius plot with kinetic data: k_2 = 37.1, 94.0, and 135 × 10^{-3} M^{-1} s^{-1} at 5.0, 15.0, and 25.0 °C, respectively, from ref. 1a. [d]The value with Y = H. [e]The value at 35.0 °C. [f]The value at 35.0 °C. X = (4-MeO, 4-Me, 3-Me, H, 3-Ph). [g]The value at 35.0 °C. X = (3-Ph, 3-MeO, 3-Cl, 3-Ac, 4-Ac, 3-CN, 4-CN). [h]The value at 25.0 °C.

The relative rate ratio of cyclic substrate (**2**) and its acyclic counterpart (**3**) are huge: $k_2(\mathbf{2})/k_2(\mathbf{3}) = 6.02 \times 10^4$. These results suggest that the major factor to determine the pyridinolysis rate of a cyclic substrate is different from that of its acyclic counterpart. The activation parameters and the changes in the activation parameters from a cyclic substrate to its acyclic counterpart for the pyridinolyses (C_5H_5N) of **2** and **3** at 35.0 °C, and hydrolyses of **I** and **II** at 25.4 °C[2] are summarized in Table 4. The change in the Gibbs free energy of activation, $\delta\Delta G^{\neq}(\mathbf{2} \rightarrow \mathbf{3}) = \Delta G^{\neq}(\mathbf{3}) - \Delta G^{\neq}(\mathbf{2}) = 19.9\text{-}13.2 \approx 7$ kcal/mol is obtained. The Gibbs free energy of activation difference ($\delta\Delta G^{\neq}$) can be divided into the enthalpy ($\delta\Delta H^{\neq}$) and entropy of activation difference ($\delta\Delta S^{\neq}$): (i) the enthalpy of activation difference, $\delta\Delta H^{\neq}(\mathbf{2} \rightarrow \mathbf{3}) = \Delta H^{\neq}(\mathbf{3}) - \Delta H^{\neq}(\mathbf{2}) = 6.3\text{-}28.4 \approx -22$ kcal/mol, indicates that the pyridinolysis of **3** is much more favorable than that of **2**; (ii) in contrast to the enthalpy of activation difference, the entropy of activation difference, $\delta\Delta S^{\neq}(\mathbf{2} \rightarrow \mathbf{3}) = \Delta S^{\neq}(\mathbf{3}) - \Delta S^{\neq}(\mathbf{2}) = -44.1 - (+49.2) \approx -93$ eu, equivalent to $-T\delta\Delta S(\mathbf{2} \rightarrow \mathbf{3}) = -328.15 \times (-93.3) \times 10^{-3} \approx +29$ kcal/mol, indicates that the pyridinolysis of **2** is much more favorable than that of **3**. The pyridinolysis rate of **2** involving a cyclic five-membered ring is forty thousand times faster than its acyclic counterpart **3** [$\delta\Delta G^{\neq}(\mathbf{2} \rightarrow \mathbf{3}) \approx 7$ kcal/mol] due to great *positive* value of the entropy of activation of **2** compared to negative value of **3** [$-T\delta\Delta S^{\neq}(\mathbf{2} \rightarrow \mathbf{3}) \approx +29$ kcal/mol] over considerably unfavorable enthalpy of activation of **2** compared to **3** [$\delta\Delta H^{\neq}(\mathbf{2} \rightarrow \mathbf{3}) \approx -22$ kcal/mol]. Thus, the authors conclude that the faster pyridinolysis rate of cyclic substrate of **2** than its acyclic counterpart of **3** is ascribed to favorable entropy of activation term over unfavorable enthalpy of activation term. The same trends were also found for the anilinolyses of two pairs of cyclic substrates (**2** and **6**) and their acyclic counterparts (**3** and **7**).[3]

The base catalyzed hydrolysis rate of a cyclic five-membered ring of **I** is million times faster than its acyclic counterpart of **II**, resulting in $\delta\Delta G^{\neq}(\mathbf{III}) = \Delta G^{\neq}(\mathbf{II}) - \Delta G^{\neq}(\mathbf{I}) \approx 8$ kcal/mol at 25.4 °C.[2] The faster hydrolysis rate of cyclic substrate (**I**) compared to that of its acyclic counterpart (**II**) is predominantly ascribed to the enthalpy of activation term of $\delta\Delta H^{\neq}(\mathbf{III}) = \Delta H^{\neq}(\mathbf{II}) - \Delta H^{\neq}(\mathbf{I}) = +6$ kcal/mol in addition to minor positive contribution of the entropy of activation term of $\delta\Delta S^{\neq}(\mathbf{III}) = \Delta S^{\neq}(\mathbf{II}) - \Delta S^{\neq}(\mathbf{I}) \approx -8$ eu, equivalent to $-T\delta\Delta S\ (\mathbf{III}) = -298.55 \times (-8.2) \times 10^{-3} \approx +2$ kcal/mol. These results suggest that the reason of the faster pyridinolysis rate of **2** compared to that of **3** is different from the reason of the faster hydrolysis of **I** compared to that of **II**. The Gibbs free energy of activation difference of 8.4 kcal/mol of base catalyzed hydrolysis of **I** is thought to be derived from both a ring strain effect (~5.2 kcal/mol) and a stereoelectronic effect (~3.2 kcal/mol). The release of the ring strain is attributed to forming the trigonal bipyramidal penta-coordinate (TBP-5C) intermediate, resulting in spanning the five-membered ring in an apical-equatorial position (Scheme 4). The stereoelectronic effect is attributed to the two lone pairs on the basal ring oxygen oriented partially anti-periplanar to the apical ring ester bond leaving group, displayed with the arrows in Scheme 4.[1b,2]

In the present work, much greater value of the enthalpy of activation of **2** [$\Delta H^{\neq}(\mathbf{2}) = 28.4$ kcal/mol] compared to that of **3** [$\Delta H^{\neq}(\mathbf{3}) = 6.3$ kcal/mol] suggests that the absence of the release of the ring strain and stereoelectronic effect of the lone pairs of oxygen in the TS. The authors, thus, suggest that the five-membered ring is not in an apical-equatorial position, which has been observed in the base catalyzed hydrolysis of **I** (see Scheme 4), but an equatorial position in the TS.[3a] Accordingly, the steric congestion between cyclic five-membered ring and pyridine nucleophile becomes greater in the TS, resulting in greater value of the enthalpy of activation. Great positive value of the entropy of activation [$\Delta S^{\neq}(\mathbf{2}) = +49.2$ eu] suggests that the TS structure is much less ordered compared to the GS structure. Taking into account the molecularity of two, great positive entropy of activation must be ascribed to enormous degree of solvent structure breaking in the TS.[3a]

A concerted mechanism with an early TS involving backside nucleophilic attack TSb towards the Cl leaving group (Scheme 5) was proposed on the basis of small negative CIC ($\rho_{XY} = -0.15$)[15] and small values of Brönsted coefficients ($\beta_X = 0.16\text{-}0.18$) for the pyridinolysis of **5**.[4c] The reaction mechanism of S_N2 was proposed for the pyridinolysis of **1** and **3** with both frontside TSf and backside attacks TSb (Scheme 5), and the fraction of a frontside attack is more or less greater than that of a backside attack, on the basis of



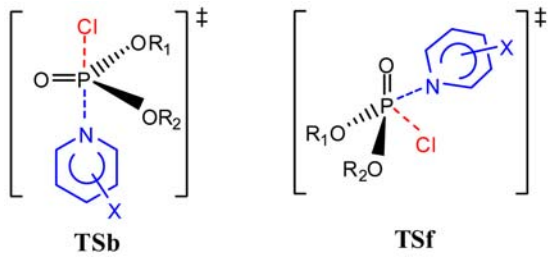
Intermediate

Scheme 4. TBP-5C intermediate of base catalyzed hydrolysis of **I**.

Table 4. Activation parameters[a] and changes in activation parameters from cyclic substrates to their acyclic counterparts for the Pyridinolyses (C_5H_5N) of **2** and **3** in MeCN, and base catalyzed Hydrolyses of **I** and **II**

Substrate	$\Delta H^{\neq}$ (kcal mol^{-1})	$\Delta S^{\neq}$ (cal mol^{-1}K^{-1})	$\Delta G^{\neq}$ (kcal mol^{-1})	$\delta\Delta H^{\neq}$ (kcal mol^{-1})	$\delta\Delta S^{\neq}$ (cal mol^{-1}K^{-1})	$-T\delta\Delta S^{\neq}$ (kcal mol^{-1})	$\delta\Delta G^{\neq}$ (kcal mol^{-1})
2: $cC_2H_4O_2P(=O)Cl$	28.4	+49.2	13.2	–22	–93	29	7
3: $(EtO)_2P(=O)Cl$	6.3	–44.1	19.9				
I: $cC_2H_4O_2P(=O)Ph$	3.6	–37.2	14.7	6	–8	2	8
II: $(EtO)_2P(=O)Ph$	9.6	–45.4	23.1				

[a]The values of activation parameters of **2** and **3** are at 35.0 °C, and those of **I** and **II** are at 25.4 °C.[2]



Scheme 5. Backside attack TSb and frontside attack TSf.

the magnitudes of β_X values.[4a] A concerted S_N2 mechanism was proposed and biphasic concave upward free energy correlations was rationalized by a change of nucleophilic attacking direction from a frontside attack TSf (β_X = 1.05) with the strongly basic pyridines to a backside attack (TSb; β_X = 0.39) with the weakly basic pyridines for the pyridinolysis of **4**.[4b] In the present work, accordingly, the authors propose a concerted mechanism involving a change of nucleophilic attacking direction from a frontside attack TSf (β_X = 1.06) with the strongly basic pyridines to a backside attack (TSb; β_X = –0.41) with the weakly basic pyridines. It is worthy to note that a frontside attack TSf yields greater magnitudes of ρ_X and β_X values compared to a backside attack.[16]

Experimental Section

Materials. Ethylene phosphorochloridate (commercially available) was used for kinetic studies without further purification. The HPLC grade acetonitrile (less than 0.005% water content), diethyl ether and *n*-hexane were used without further purification.

Kinetic Measurement. Rates were measured conductometrically as previously described.[3,4,13,16] [Substrate] = 5.0×10^{-4} M and [X-pyridine] = 0.10-0.30 M were used for the present work. Pseudo-first-order rate constant values were the average of at least three runs that were reproducible within ± 3%.

Product Analysis. Ethylene phosphorochloridate was reacted with excess pyridine, for more than 15 half-lives at –20.0 °C in MeCN. Solvent was removed under reduced pressure. The product was isolated after treatment with ether and acetonitrile, and then dried under reduced pressure. The analytical and spectroscopic data of the product are summarized as follows:

$[(C_2H_4O_2)P(=O)NC_5H_5]^+Cl^-$. Colorless oily liquid; ^{1}H NMR (400 MHz, MeCN-d_3) δ 3.63-4.16 (aliphatic, 4H, m), 7.89-8.68 (aromatic, 5H, m); ^{13}C NMR (100 MHz, $CDCl_3$ & TMS) δ 66.33-66.83 (aliphatic, 2C, m), 125.89-144.11 (aromatic, 5C, m); ^{31}P NMR (162 MHz, $CDCl_3$ & TMS) δ –13.84 (P=O, 1P, s); GC-MS for $C_7H_9NO_3P^+$(EI, *m/z*), 187 (M^+).

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References

1. (a) Westheimer, F. H. *Acc. Chem. Res*. **1968**, *1*, 70. (b) Gorenstein, D. G. *Chem. Rev.* **1987**, *87*, 1047.
2. Yang, J. C.; Gorenstein, D. G. *Tetrahedron* **1987**, *43*, 479.
3. (a) Barai, H. R.; Lee, H. W. *Bull. Korean Chem. Soc*. **2011**, *32*, **in press**. (b) Dey, N. K.; Hoque, M. E. U.; Kim, C. K.; Lee, B. S.; Lee, H. W. *J. Phys. Org. Chem.* **2008**, *21*, 544. (c) Barai, H. R.; Lee, H. W. *Bull. Korean Chem. Soc*. **2011**, *32*, 3355. (d) Hoque, M. E. U.; Dey, N. K.; Kim, C. K.; Lee, B. S.; Lee, H. W. *Org. Biomol. Chem.* **2007**, *5*, 3944.
4. (a) Dey, N. K.; Hoque, M. E. U.; Kim, C. K.; Lee, H. W. *J. Phys. Org. Chem.* **2010**, *23*, 1022. (b) Hoque, M. E. U.; Lee, H. W. *Bull. Korean Chem. Soc*. **2011**, *32*, 3505. (c) Guha, A. K.; Lee, H. W.; Lee, I. *J. Org. Chem*. **2000**, *65*, 12.
5. The pK_a(H_2O) values of X-pyridines were taken from: (a) Fischer, A.; Galloway, W. J.; Vaughan, J. *J. Chem. Soc.* **1964**, 3591. (b) Dean, J. A. *Handbook of Organic Chemistry*; McGraw-Hill: New York, 1987; Chapter 8.
6. (a) Lee, I.; Kim, C. K.; Han, I. S.; Lee, H. W.; Kim, W. K.; Kim, Y. B. *J. Phys. Chem. B* **1999**, *103*, 7302. (b) Coetzee, J. F. *Prog. Phys. Org. Chem.* **1967**, *4*, 45.
7. (a) Jencks, W. P.; Brant, S. R.; Gandler, J. R.; Fendrich, G.; Nakamura, C. *J. Am. Chem. Soc*. **1982**, *104*, 7045. (b) Onyido, I.; Swierczek, K.; Purcell, J.; Hengge, A. C. *J. Am. Chem. Soc*. **2005**, *127*, 7703.
8. Lee, I.; Lee, W. H.; Lee, H. W.; Bentley, T. W. *J. Chem. Soc., Perkin Trans. 2* **1993**, 141.
9. Chang, S.; Koh, H. J.; Lee, B. S.; Lee, I. *J. Org. Chem*. **1995**, *60*, 7760.
10. Jencks, W. P. *Chem. Rev.* **1985**, *85*, 511.
11. (a) Bernasconi, C. F. *Acc. Chem. Res.* **1987**, *20*, 301. (b) Bernasconi, C. F. *Adv. Phys. Org. Chem.* **1992**, *27*, 119.
12. Gilliom, R. D. *Introduction to Physical Organic Chemistry*; Addison-Wesley; Philippines, 1970; pp 167-169.
13. (a) Dey, N. K.; Adhikary, K. K.; Kim, C. K.; Lee, H. W. *Bull. Korean Chem. Soc*. **2010**, *31*, 3856. (b) Adhikary, K. K.; Lee, H. W. *Bull. Korean Chem. Soc.* **2011**, *32*, 1945.
14. Hehre, W. J.; Random, L.; Schleyer, P. V. R.; Pople, J. A. *Ab Initio Molecular Orbital Theory*; Wiley: New York, 1986; Chapter 4.
15. (a) Lee, I. *Chem. Soc. Rev.* **1990**, *19*, 317. (b) Lee, I. *Adv. Phys. Org. Chem.* **1992**, *27*, 57. (c) Lee, I.; Lee, H. W. *Collect. Czech. Chem. Commun*. **1999**, *64*, 1529.
16. Adhikary, K. K.; Lee, H. W.; Lee, I. *Bull. Korean Chem. Soc*. **2003**, *24*, 1135.