

## Kinetics and Mechanism of the Pyridinolysis of Dimethyl Isothiocyanophosphate in Acetonitrile

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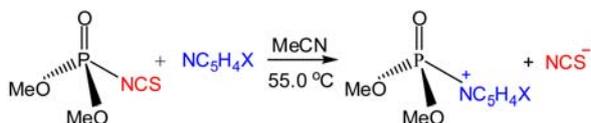
The kinetics and mechanism of the pyridinolysis ( $\text{XC}_5\text{H}_4\text{N}$ ) of dimethyl isothiocyanophosphate are investigated in acetonitrile at 55.0 °C. The Hammett and Brønsted plots for substituent X variations in the nucleophiles exhibit two discrete slopes with a break region between X = 3-Ac and 4-Ac. These are interpreted to indicate a mechanistic change at the break region from a concerted to a stepwise mechanism with a rate-limiting expulsion of the isothiocyanate leaving group from the intermediate. The relatively large  $\beta_X$  values imply much greater fraction of frontside nucleophilic attack TSf than that of backside attack TSb. The steric effects of the two ligands play an important role to determine the pyridinolysis rates of isothiocyanophosphates.

**Key Words :** Phosphoryl transfer reaction, Pyridinolysis, Dimethyl isothiocyanophosphate, Biphasic discrete free energy relationship

### Introduction

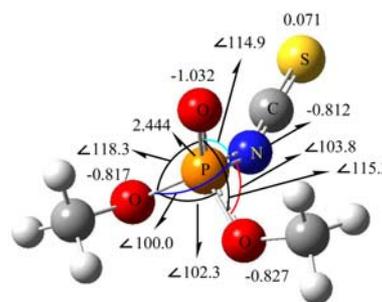
Surprising substituent effects of the nucleophiles (and substrates) on the pyridinolyses of diethyl [2;  $(\text{EtO})_2\text{P}(=\text{O})\text{NCS}$ ]<sup>1</sup> and Y-aryl phenyl [3;  $(\text{YC}_6\text{H}_4\text{O})(\text{PhO})\text{P}(=\text{O})\text{NCS}$ ]<sup>2</sup> isothiocyanophosphates involving a leaving group of isothiocyanate ( $\text{NCS}^-$ ) were found in acetonitrile (MeCN) at 55.0 °C in this lab. To extend the phosphoryl transfer reactions involving a leaving group of isothiocyanate, the kinetic studies on the pyridinolysis of dimethyl isothiocyanophosphate (**1**) have been carried out in MeCN at 55.0 ± 0.1 °C (Scheme 1). The interest is centered into the mechanistic change and/or transition state (TS) structure variation associated with the substituent X changes in the nucleophiles by determining the Hammett ( $\rho_X$ ) and Brønsted ( $\beta_X$ ) coefficients. The kinetic results of the pyridinolysis of **1** are compared with those of diethyl,<sup>1</sup> Y-aryl phenyl<sup>2</sup> isothiocyanophosphates, and their counterparts involving a leaving group of chloride, dimethyl [1';  $(\text{MeO})_2\text{P}(=\text{O})\text{Cl}$ ],<sup>3</sup> diethyl [2';  $(\text{EtO})_2\text{P}(=\text{O})\text{Cl}$ ],<sup>3</sup> and Y-aryl phenyl [3'];  $(\text{YC}_6\text{H}_4\text{O})(\text{PhO})\text{P}(=\text{O})\text{Cl}$ ]<sup>4</sup> chlorophosphates with regard to the leaving group mobility, selectivity parameter, steric effects of the two ligands, and mechanism.

The B3LYP/6-311+G(d,p) geometries, bond angles, and natural bond order (NBO) charges of **1** in the gas phase are shown in Figure 1.<sup>5</sup> The MO theoretical structure shows that the three oxygens and nitrogen have more or less distorted



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

**Scheme 1.** The pyridinolysis of dimethyl isothiocyanophosphate (**1**) in MeCN at 55.0 °C.



**Figure 1.** The B3LYP/6-311+G(d,p) geometries of dimethyl isothiocyanophosphate (**1**) in the gas phase.

tetrahedral geometry with the phosphorus atom at the center. The degree of distortion of **1** ( $\Delta\delta_{\text{GS}} = 0.39$ ) is similar to **2** ( $\Delta\delta_{\text{GS}} = 0.38$ ) and smaller than **3** ( $\Delta\delta_{\text{GS}} = 0.42$ ) due to larger size of the two phenoxy ligands compared to the two methoxy (and ethoxy) ligands.<sup>6</sup>

### 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 ( $k_{\text{obsd}}$ ) for all the reactions obeyed Eq. (1) with negligible  $k_0$  ( $\approx 0$ ) in MeCN. The second-order rate constants ( $k_2$ ) were determined with at least five pyridine concentrations. The linear plots of Eq. (1) suggest a lack of any base-catalysis or side reaction, and the overall reaction is described by Scheme 1.

$$k_{\text{obsd}} = k_0 + k_2 [\text{XC}_5\text{H}_4\text{N}] \quad (1)$$

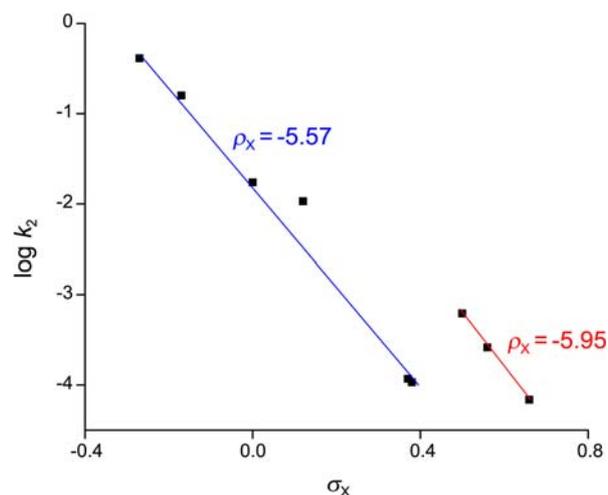
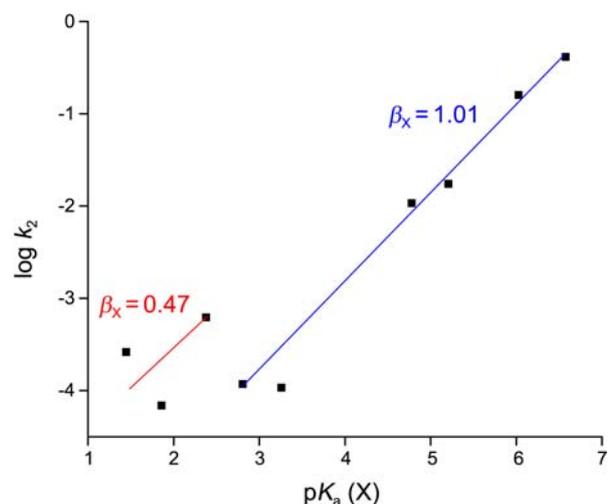
The second-order rate constants [ $k_2$  ( $\text{M}^{-1} \text{s}^{-1}$ )] are summarized in Table 1. The Brønsted  $\beta_X$  value was calculated by correlating  $\log k_2(\text{MeCN})$  with  $\text{p}K_{\text{a}}(\text{H}_2\text{O})$ .<sup>7</sup> This procedure of using  $\text{p}K_{\text{a}}(\text{H}_2\text{O})$  instead of  $\text{p}K_{\text{a}}(\text{MeCN})$  values of X-pyridines has been shown to be justified theoretically and

**Table 1.** The Second-Order Rate Constants ( $k_2 \times 10^3/\text{M}^{-1} \text{s}^{-1}$ ) of the Reactions of Dimethyl Isothiocyanophosphate (**1**) with  $\text{XC}_5\text{H}_4\text{N}$  in MeCN at 55.0 °C

X	4-MeO	4-Me	H	3-MeO	3-Cl	3-Ac	4-Ac	3-CN	4-CN
$k_2 \times 10^3$	412 ± 1	159 ± 1	17.3 ± 0.1	10.7 ± 0.1	0.117 ± 0.001	0.107 ± 0.001	0.618 ± 0.002	0.261 ± 0.001	0.0685 ± 0.0002

experimentally since there is a practically constant difference between the two sets of  $\text{p}K_{\text{a}}$ 's in  $\text{H}_2\text{O}$  and in MeCN for various X-pyridines so that the slopes in the two solvents differ insignificantly.<sup>8</sup> The pyridinolysis rates are not consistent with a typical nucleophilic substitution reaction. The rate becomes slower with a weaker nucleophile for X = (4-MeO, 4-Me, H, 3-MeO, 3-Cl, 3-Ac). However, the rate with X = 4-Ac is unusually 5.8 times faster than with X = 3-Ac in spite of greater basicity of 3-acetylpyridine compared to 4-acetylpyridine. After a break region, the rate becomes slower with a weaker nucleophile for X = (4-Ac, 3-CN, 4-CN). Thus, both the Hammett (Fig. 2;  $\log k_2$  vs  $\sigma_{\text{X}}$ ) and Brønsted [Fig. 3;  $\log k_2$  vs  $\text{p}K_{\text{a}}(\text{X})$ ] plots for substituent X variations in the nucleophiles exhibit two discrete slopes with a break region between X = 3-Ac and 4-Ac, giving  $\rho_{\text{X}} = -5.57 \pm 0.25$  ( $r = 0.989$ ) and  $-5.95 \pm 0.01$  ( $r = 0.999$ ), and  $\beta_{\text{X}} = 1.01 \pm 0.21$  ( $r = 0.993$ ) and  $0.47 \pm 0.61$  ( $r = 0.451$ ) with X = (4-MeO, 4-Me, H, 3-MeO, 3-Cl, 3-Ac) and X = (4-Ac, 3-CN, 4-CN), respectively. The magnitudes of the Hammett coefficient with more basic pyridines are slightly smaller than that with less basic pyridines. However, the Brønsted coefficient with more basic pyridines is slightly greater than that with less basic pyridines. It needs to be stressed that the Brønsted coefficient with more basic pyridines should be slightly smaller than that with less basic pyridines since the magnitude of Hammett coefficient is proportional to that of the Brønsted coefficient. Herein, the problem is ascribed to the different sequence of  $\sigma_{\text{X}}$  and  $\text{p}K_{\text{a}}(\text{X})$  values: X = 4-Ac [ $\sigma_{\text{X}} = 0.50$ ,  $\text{p}K_{\text{a}}(\text{X}) = 2.38$ ]; 3-CN [ $\sigma_{\text{X}} = 0.56$ ,  $\text{p}K_{\text{a}}(\text{X}) = 1.45$ ]; and 4-CN [ $\sigma_{\text{X}} = 0.66$ ,  $\text{p}K_{\text{a}}(\text{X}) = 1.86$ ], giving poor correlation coefficient for Brønsted plot with less basic pyridines (*vide infra*). Biphasic free energy relationships, the two discrete slopes with a break region between X = 3-Ac and 4-Ac, were also found for the pyridinolysis of **2** in MeCN at 55.0 °C. These kinetic results strongly suggest: (i) a change of the reaction mechanism from more basic to less basic pyridines; (ii) the same mechanism for both **1** and **2**.

The second-order rate constants ( $k_2$ ) with unsubstituted pyridine ( $\text{C}_5\text{H}_5\text{N}$ ) at 55.0 °C, NBO charges at the reaction center P atom in the gas phase [B3LYP/6-311+G(d,p) level of theory],<sup>5</sup> summations of Taft's steric constants of the two ligands [ $\Sigma E_{\text{S}} = E_{\text{S}}(\text{R}_1) + E_{\text{S}}(\text{R}_2)$  from  $E_{\text{S}}(\text{R}_i) = 0.00(\text{Me})$ ,  $-0.07(\text{Et})$ , and  $-2.48(\text{Ph})$ ],<sup>9</sup> Brønsted coefficients ( $\beta_{\text{X}}$ ), and cross-interaction constants (CICs,  $\rho_{\text{XY}}$ )<sup>10</sup> for the pyridinolyses ( $\text{XC}_5\text{H}_4\text{N}$ ) of **1-3** and **1'-3'** in MeCN are summarized in Table 2. The pyridinolysis rate ratios of  $k(\mathbf{1}')/k(\mathbf{1}) = 7.7$ ,  $k(\mathbf{2}')/k(\mathbf{2}) = 12$ , and  $k(\mathbf{3}')/k(\mathbf{3}) = 257$  indicate that chloride is better leaving group compared to isothiocyanate and that the leaving group mobility is strongly dependent upon the nature of the two ligands. The magnitude of the NBO charge of the reaction center P atom does not play any role to

**Figure 2.** The Hammett plots ( $\log k_2$  vs  $\sigma_{\text{X}}$ ) of the reactions of dimethyl isothiocyanophosphate (**1**) with X-pyridines in MeCN at 55.0 °C.**Figure 3.** The Brønsted plots [ $\log k_2$  vs  $\text{p}K_{\text{a}}(\text{X})$ ] of the reactions of dimethyl isothiocyanophosphate (**1**) with X-pyridines in MeCN at 55.0 °C.

determine the leaving group mobility. The relative rates of 5.7(**1**):2.9(**2**):1(**3**) indicate that the steric effects of the two ligands are the predominant factor to decide the reactivities of isothiocyanophosphates, *i.e.*, the greater the two ligands, the rate becomes slower. The degree of steric effects of the two ligands on the pyridinolysis rates of isothiocyanophosphates can be qualitatively estimated by the Taft's eq. of  $\log k_{\text{H}} = \delta \Sigma E_{\text{S}} + C$ , giving  $\delta = 0.13$  ( $r = 0.934$ ).<sup>9,11</sup> The pyridinolysis rates of chlorophosphates are also qualitatively dependent upon the steric effects of the two ligands, when excluding diphenyl chlorophosphate (**3'** with Y = H), giving  $\delta = 0.72$  ( $r = 0.904$ ) with **1'**,<sup>3</sup> **2'**,<sup>3</sup> dibutyl [(BuO)<sub>2</sub>P(=O)Cl],<sup>12</sup>

**Table 2.** Summary of the Second-Order Rate Constants ( $k_2$  with  $C_5H_5N$ ), NBO Charges at the Reaction Center P Atom, Summations of Taft's Steric Constants ( $\Sigma E_s$ ) of the Two Ligands, Brønsted coefficients ( $\beta_X$ ), and CICs ( $\rho_{XY}$ ) for the Pyridinolyses of **1-3** and **1'-3'** in MeCN

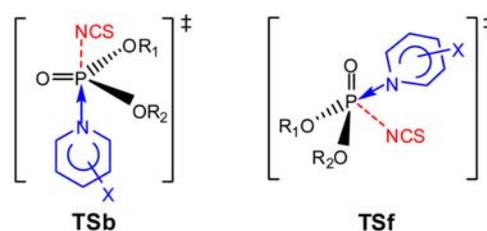
Substrate	$k_2 \times 10^{3a}$	Charge at P	$-\Sigma E_s^e$	$\beta_X$	$\rho_{XY}$
<b>1:</b> (MeO) <sub>2</sub> P(=O)NCS	17.3	2.444	0.00	1.01/0.47 <sup>f</sup>	–
<b>2:</b> (EtO) <sub>2</sub> P(=O)NCS	8.87	2.451	0.14	0.97/0.63 <sup>f</sup>	–
<b>3:</b> (YC <sub>6</sub> H <sub>4</sub> O)(PhO)P(=O)NCS	3.02 <sup>b</sup>	2.454 <sup>b</sup>	4.96 <sup>b</sup>	1.13-1.28/0.08-0.22 <sup>g</sup>	-1.42/-1.81/3.16/1.40 <sup>h</sup>
<b>1':</b> (MeO) <sub>2</sub> P(=O)Cl	134	2.226	0.00	0.63	–
<b>2':</b> (EtO) <sub>2</sub> P(=O)Cl	107 <sup>c</sup>	2.236	0.14	0.73	–
<b>3':</b> (YC <sub>6</sub> H <sub>4</sub> O)(PhO)P(=O)Cl	775 <sup>b,d</sup>	2.230 <sup>b</sup>	4.96 <sup>b</sup>	0.16-0.18	-0.15

<sup>a</sup>The second-order rate constant with unsubstituted pyridine in MeCN at 55.0 °C. <sup>b</sup>The value with Y = H. <sup>c</sup>Extrapolated value in the Arrhenius plot with kinetic data:  $k_2 = 37.9, 52.8,$  and  $78.2 \times 10^{-3} M^{-1} s^{-1}$  at 25.0, 35.0, and 45.0 °C, respectively. See ref. 3. <sup>d</sup>Extrapolated value in the Arrhenius plot with kinetic data:  $k_2 = 37.1, 94.0,$  and  $135 \times 10^{-3} M^{-1} s^{-1}$  at 5.0, 15.0, and 25.0 °C, respectively. See ref. 4. <sup>e</sup>Note that the value of  $\Sigma E_s$  is not ' $E_s(R_1O) + E_s(R_2O)$ ' but ' $E_s(R_1) + E_s(R_2)$ ' since the data of Taft's steric constants of R<sub>1</sub>O are not available. <sup>f</sup>X = (4-MeO, 4-Me, H, 3-MeO, 3-Cl, 3-Ac)/(4-Ac, 3-CN, 4-CN). <sup>g</sup>X = (4-MeO, 4-Me, 3-Me, H, 3-Ph)/(3-Ac, 3-Cl, 4-Ac, 4-CN). <sup>h</sup>Stronger nucleophiles and weaker electrophiles/weaker nucleophiles and weaker electrophiles/stronger nucleophiles and stronger electrophiles/weaker nucleophiles and stronger electrophiles.

and diisopropyl [(*i*-PrO)<sub>2</sub>P(=O)Cl]<sup>13</sup> chlorophosphates in MeCN at 35.0 °C. The very fast pyridinolysis rate of **3'** is unusual. The steric effects of the two ligands on the pyridinolysis rates of chlorophosphates are much greater than those of isothiocyanophosphates.

The pyridinolyses of **1'-3'** involving the chloride leaving group yielded linear free energy relationships for substituent X (and Y) variations in the nucleophiles (and substrates) whereas those of **1-3** involving the isothiocyanate leaving group yielded biphasic free energy correlations for substituent X (and Y) variations in the nucleophiles (and substrates). The substituent effects on the pyridinolyses of **1-3** are more significant than those of **1'-3'**. A concerted mechanism with both frontside and backside nucleophilic attack was proposed for the reactions of **1'** and **2'** on the basis of the magnitudes of relatively large  $\beta_X$  [= 0.63(**1'**) and 0.73(**2'**)] values.<sup>3</sup> A concerted mechanism with an early TS involving backside nucleophilic attack towards the Cl leaving group was proposed on the basis of small negative CIC ( $\rho_{XY} = -0.15$ )<sup>10</sup> and small values of Brønsted coefficients ( $\beta_X = 0.16-0.18$ ) for the pyridinolysis of **2'**.<sup>4</sup>

The change of the leaving group from chloride to that of a lower leaving ability, isothiocyanate, can cause a change in mechanism from a concerted to a stepwise process with a rate-limiting breakdown of the intermediate. This is in accord with the well established trend of the mechanistic change depending on the leaving group ability: the lower the leaving ability of the leaving group, the greater is the tendency for a stepwise mechanism with a rate-limiting expulsion of the leaving group from the intermediate.<sup>14</sup> The free energy correlations of the pyridinolyses of **3** involving isothiocyanate leaving group are biphasic concave upwards with X while biphasic concave downwards with Y, and proposed mechanisms were as follows on the basis of the values of selectivity parameters ( $\rho_X$  and  $\beta_X$ ) and sign of the CICs ( $\rho_{XY}$ ), divided into four groups: (i) for stronger nucleophiles and weaker electrophiles, a concerted process with a frontside nucleophilic attack TSf (Scheme 2); (ii) for weaker nucleophiles and weaker electrophiles, a concerted process with a backside attack TSb (Scheme 2); (iii) for stronger nucleophiles and stronger electrophiles, a stepwise mech-

**Scheme 2.** Backside attack TSb and frontside attack TSf.

anism with a rate-limiting leaving group departure from the intermediate involving a frontside attack TSf; and (iv) for weaker nucleophiles and stronger electrophiles, a stepwise mechanism with a rate-limiting leaving group departure from the intermediate involving a backside attack TSb.

In the present work of **1**, the Hammett and Brønsted plots for substituent X variations in the nucleophiles show two discrete slopes with relatively large  $\beta_X$  values:  $\beta_X = 1.01$  and  $0.47$  with more basic (X = 4-MeO, 4-Me, H, 3-MeO, 3-Cl, 3-Ac) and less basic pyridines (X = 4-Ac, 3-CN, 4-CN), respectively, as observed in the pyridinolysis of **2**. Note that the two  $\beta_X$  values are comparable regardless of the nature of the substituent X, more basic or less basic pyridines (*vide supra*).<sup>15</sup> The discrete two slopes with X in the nucleophiles and biphasic concave downward free energy relationships with Y in the substrates values were observed for the reactions of Y-O-aryl methyl phosphonochloridothioates [Me(YC<sub>6</sub>H<sub>4</sub>O)P(=S)Cl] with X-pyridines in MeCN, and proposed mechanisms were as follows on the basis of the magnitudes of selectivity parameters ( $\rho_X$ ,  $\rho_{XY}$ , and  $\beta_X$ ) and sign of the CICs ( $\rho_{XY}$ ): (i) for stronger nucleophiles and weaker electrophiles, a concerted process (or a stepwise mechanism with a rate-limiting bond formation) involving a backside attack TSb; (ii) for weaker nucleophiles and weaker electrophiles, a stepwise mechanism with a rate-limiting leaving group departure from the intermediate involving a frontside attack TSf; (iii) for stronger nucleophiles and stronger electrophiles, a stepwise mechanism with a rate-limiting leaving group departure from the intermediate involving a backside attack TSb; and (iv) for weaker nucleophiles and stronger electrophiles, a stepwise mechanism with

**Table 3.** Activation Parameters of the Reactions of Dimethyl Isothiocyanophosphate (1) with XC<sub>5</sub>H<sub>4</sub>N in MeCN

X	<i>t</i> /°C	<i>k</i> <sub>2</sub> × 10 <sup>3</sup> /M <sup>-1</sup> s <sup>-1</sup>	Δ <i>H</i> <sup>‡</sup> /kcal mol <sup>-1</sup>	-Δ <i>S</i> <sup>‡</sup> /cal mol <sup>-1</sup> K <sup>-1</sup>
4-MeO	35.0	253 ± 1	4.3 ± 0.2	47 ± 1
	45.0	332 ± 1		
	55.0	412 ± 1		
H	35.0	7.03 ± 0.05	8.4 ± 0.2	41 ± 1
	45.0	11.4 ± 0.1		
	55.0	17.3 ± 0.1		
4-Ac	35.0	0.228 ± 0.001	9.4 ± 0.8	45 ± 3
	45.0	0.410 ± 0.003		
	55.0	0.618 ± 0.002		

a rate-limiting leaving group departure from the intermediate involving frontside attack TSf.<sup>16</sup>

In the present work, thus, the authors propose a concerted S<sub>N</sub>2 mechanism (or a stepwise mechanism with a rate-limiting bond formation step) for more basic pyridines and a stepwise mechanism with a rate-limiting leaving group departure from the intermediate for less basic pyridines on the basis of the pyridinolysis mechanism of *Y-O*-aryl methyl phosphonochloridothioates, showing same free energy relationship as the present work with X. The relatively large β<sub>X</sub> values imply much greater fraction of frontside nucleophilic attack TSf than that of backside attack TSb.

Activation parameters, enthalpies and entropies of activation, are determined for 3 cases as shown in Table 3. The enthalpies of activation are relatively low (4-9 kcal mol<sup>-1</sup>), especially for the reaction with strong nucleophile, and entropies of activation are relatively large negative values (41-47 cal mol<sup>-1</sup> K<sup>-1</sup>). The relatively low of activation enthalpy and large negative value of activation entropy are typical for the aminolyses of P=O systems.

### Experimental Section

**Materials.** HPLC grade MeCN (less than 0.005% water content) was used without further purification. The X-pyridines (GR grade) were used without further purifications. The substrate was synthesized as previously mentioned way,<sup>1,2,17</sup> where methyl dichlorophosphate was taken into a round-bottomed flask with MeCN as solvent. Equivalent amount of potassium thiocyanate solution were taken into another flask with 25 mL acetonitrile. Then the potassium thiocyanate solution was added to methyl dichlorophosphate solution dropwise with a vigorous stirring on a cooling bath at -5.0 °C. The reaction was allowed for 5 hr after completion of addition of potassium thiocyanate. Then the reaction system allowed rising its temperature up to room condition (24.0 °C) to reach in equilibrium. Solvent was evaporated under reduced pressure and 30 mL ethyl ether was added to it. Insoluble potassium chloride was removed by filtration. The product was isolated by column chromatography using 50% ethylacetate and *n*-hexane after evapo-

ration of ether under evacuated pressure. Product was finally isolated by removing solvent under vacuum using oil diffusion pump. The analytical data of the substrates are given below (see Supporting Information):

**(CH<sub>3</sub>O)<sub>2</sub>P(=O)NCS:** Reddish brown colored oily liquid; <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>) δ 3.87 (OCH<sub>3</sub>, d, 6H, *J* = 12.6 Hz); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 55.46 (OCH<sub>3</sub>, aliphatic, 2C, d, *J* = 12.9 Hz), 176.28 (NCS, 1C, s); <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>) δ -10.12 (1P, s); ν<sub>max</sub> (Thin film), 2966 cm<sup>-1</sup> (C-H, str. aliphatic), 1977 cm<sup>-1</sup> (NCS, broad str. region), 1271 cm<sup>-1</sup> (P=O str.), 1030 cm<sup>-1</sup> (P-O-Alph str.); *m/z* 167 (M<sup>+</sup>).

**Kinetic Procedure.** Rates were measured conductometrically at 55.0 °C using a computer controlled conductivity bridge constructed in this laboratory. Pseudo-first-order rate constants, *k*<sub>obsd</sub>, were measured by using curve-fitting method in ORIGIN program. Pseudo-first-order rate constants were determined with large excess of pyridines in acetonitrile; [Substrate] = 3 × 10<sup>-3</sup> M and [X-Pyr] = 0.10-0.25 M. Pseudo-first-order rate constants were reproducible within ± 3%.

**Product Analysis.** Dimethyl isothiocyanophosphate (0.005 moles) were reacted with pyridine (0.005 M) in acetonitrile at 55.0 °C. After more than 15 half-lives, product was isolated by solvent washing using ethylacetate - *n*-hexane mixture (30%) with several attempts. Finally, the product was isolated by washing with *n*-hexane. The respective analytical data of the product gave the following results (see Supporting Information):

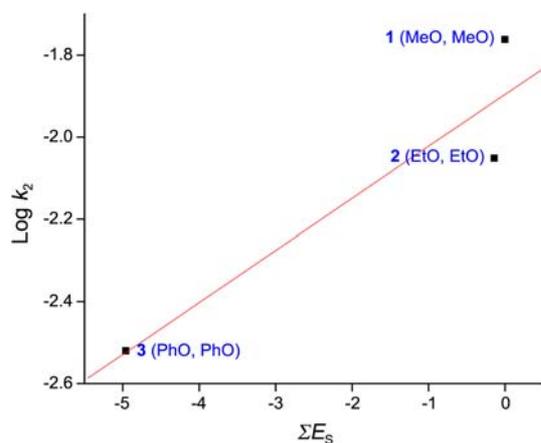
**[(CH<sub>3</sub>O)<sub>2</sub>P(=O) N<sup>+</sup>C<sub>5</sub>H<sub>5</sub>]<sup>-</sup>NCS:** Yellow gummy liquid; <sup>1</sup>H NMR (400 MHz, CD<sub>3</sub>CN) δ 3.65, 4.40 (OCH<sub>3</sub>, m, 6H), 8.05, 8.53 and 8.79 (Arom., m, Pyr 5H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 48.22, 52.98 (OCH<sub>3</sub>, aliphatic, 2C), 127.55-147.34 (Arom., m, 5C), 202.57 (NCS, 1C, s); <sup>31</sup>P NMR (162 MHz, CD<sub>3</sub>CN) δ -2.31 (1P, s, P=O); ν<sub>max</sub> (Thin film), 3058 cm<sup>-1</sup> (C-H, str. aromatic), 2953-2851 cm<sup>-1</sup> (C-H, str. aliphatic), 2054 cm<sup>-1</sup> (NCS, broad str. region), 1258 cm<sup>-1</sup> (P=O str.); 1188, 1035, 970 cm<sup>-1</sup> (P-O-Alph str.); LC-MS, *m/z*, 246 (M).

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### References and Notes

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- The "Degree of distortion" (Δ*δ*<sub>GS</sub>) of substrate with tetraordinated phosphorus from the regular tetrahedral structure is defined as eq. Δ*δ*<sub>GS</sub> = Σ [|θ<sub>*i*</sub> - θ<sub>*j*</sub>|/θ<sub>*i*</sub>] = Σ |θ<sub>*i*</sub> - 109.5|/109.5 by the authors. The Σ means the sum of all six bond angles, θ<sub>*i*</sub> is the calculated bond angle using the B3LYP/6-311+G(d,p) level, and θ<sub>*i*</sub> is the

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**Figure R1.** The plot of  $\log k_2$  with unsubstituted pyridine against  $\Sigma E_s$  for the pyridinolyses of **1-3** in MeCN at  $55.0^\circ\text{C}$ , giving the slope of  $\delta = 0.13 \pm 0.19$  ( $r = 0.934$ ). The number of the substrate and two ligands are displayed next to the corresponding point.