Kinetics and Mechanism of the Pyridinolysis of Aryl Phenyl Isothiocyanophosphate in Acetonitrile

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The kinetics and mechanism of the pyridinolysis (XC_5H_4N) of Y-aryl phenyl isothiocyanophosphates (**1**; $(YC_6H_4O)(C_6H_5O)P(=O)NCS$) are investigated in acetonitrile at 55.0 °C. The Hammett plots for substituent (Y) variations in the substrate (log k_2 *vs* σ_Y) exhibit a convex upward biphasic type with breaks at Y = H. For electron-donating Y groups the Hammett coefficients, ρ_Y, are positive and cross-interaction constant ρ_{XY} is negative, while those for electron-withdrawing Y groups ρ_Y values are negative with a positive ρ_{XY}. These results are interpreted to indicate mechanistic change at the breakpoint ($\sigma_Y = 0$) from a concerted to a stepwise mechanism with rate-limiting expulsion of the $^-$NCS group from a trigonal bipyramidal pentacoordinated (TBP-5C) intermediate. Biphasic plots of log k_2 *vs* σ_X or pK_a(X) with steeper slopes for the more basic nucleophiles are obtained suggesting an equatorial nucleophilic attack in contrast to an apical attack for the less basic nucleophiles with smaller magnitude of ρ_X or β_X.

Key Words : Pyridinolysis, Aryl phenyl isothiocyanophosphates, Cross-interaction constant

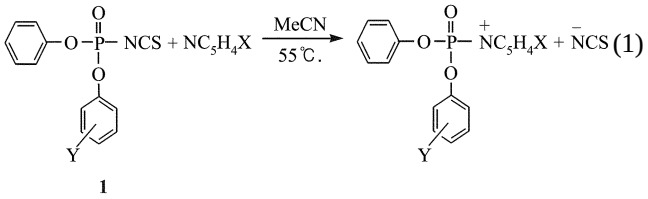
Introduction

Phosphoryl transfers from phosphate monoesters and diesters are an important class of reaction that is involved in many aspects of chemistry and biochemistry ranging from organic synthesis through enzyme catalyzed reactions such as DNA replication and repair.[1] A considerable amount of work has been carried out to clarify the problem whether the phosphoryl transfer reactions proceed concertedly with a single transition state (TS) or stepwise with a pentacoordinated phosphorane intermediate.[1,2]

In our previous works[3] the aminolyses of diphenyl chlorophosphate and 4-chlorophenyl Y-substituted phenyl chlorophosphates have been studied in acetonitrile. The anilinolysis of diphenyl chlorophosphate[3a] proceeds through a concerted pathway but unexpectedly with a late TS. The anilinolysis of 4-chlorophenyl Y-phenyl chlorophosphates[3c] proceeds through a concerted pathway with a relatively larger magnitude of ρ_X and β_X values indicating a larger degree of bond formation than diphenyl chlorophosphate in the TS. The pyridinolysis of diphenyl chlorophosphate[3b] proceeds concertedly with an early TS in which the extent of both bond formation and leaving group departure is small.

A dramatic result was found recently in the investigation of the reactions of Z-aryl bis(4-methoxyphenyl) phosphates, $(4\text{-}MeOC_6H_4O)_2P(=O)OC_6H_4Z$, with X-pyridines, ($XC_5H_4N$), in acetonitrile.[4] In the case of the more basic phenolate leaving groups, the mechanism changes from a concerted process for the less basic pyridines to a stepwise process with rate-limiting formation of a trigonal bipyramidal pentacoordinated (TBP-5C) intermediate for the more basic pyridines. In the case of the less basic phenolate leaving groups, the reaction proceeds through a direct backside attack TBP-5C.

In this work we extend our studies of the mechanism of phosphoryl transfer reactions to the pyridinolysis of Y-aryl phenyl isothiocyanophosphate (**1**) in acetonitrile at 55 °C, eq. 1.



(1)

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X = 4-OCH_3, 4-CH_3, 3-CH_3, H, 3-C_6H_5, 3-$COCH_3$, 3-Cl, 4-$COCH_3$, 4-CN

Y = 4-OCH_3, 4-CH_3, H, 3-OCH_3, 4-Cl

Isothiocyanophosphates are used in various organic synthesis. Liang and coworkers[5] reported new derivatizing reagents for C-terminal peptide sequencing at low nanomole levels and they showed that diphenyl isothiocyanophosphate is one of the superior reagents due to its double function of activation and derivatization. Diphenyl isothiocyanophosphate is also used as an automated carboxy-terminal sequence analysis of peptides and proteins.[6] Kristian and coworkers[7] have developed a new simple method for preparation of α-isothiocyanatoethers from $P(=O)(NCS)_3$ or $(PhO)_2P(=O)NCS$ with an equimolar mixture of aldehydes and alcohols.

Our interest in the present work is centered in the mechanistic change and / or TS structure variation associated with the substituent changes in the substrate (Y) and nucleophile (X) in the phosphoryl transfer involving isothiocyanate leaving group, $^-$NCS , by determining the Hammett (ρ_X, ρ_Y) and Brönsted coefficients (β_X), and cross-interaction constants[8] (ρ_{XY}) in eqs. 2 where X and Y denote the substituents in the nucleophile and the substrate, respectively.

$$\log (k_{XY}/k_{HH}) = \rho_X\sigma_X + \rho_Y\sigma_Y + \rho_{XY}\sigma_X\sigma_Y \quad (2a)$$

$$\rho_{XY} = \partial\rho_Y/\partial\sigma_X = \partial\rho_X/\partial\sigma_Y \quad (2b)$$

It should be noted that the previous studies[4] were concerned with the mechanistic changes due to the substituent variations in the nucleophile (X) and the leaving group (Z), in contrast to the substituent changes in the nucleophile (X) and the substrate (Y) in the present work.

Results and Discussion

The pseudo-first-order rate constants observed (k_{obsd}) were found to follow eq. 3 for all the reactions under pseudo-first-order condition with a large excess of pyridine

$$k_{obsd} = k_0 + k_2[Py] \quad (3)$$

nucleophile. The k_0 values were negligible ($k_0 \approx 0$) in acetonitrile. The second-order rate constants, k_2 ($M^{-1}s^{-1}$), collected in Table 1 were determined for at least five pyridine concentrations, [Py]. The overall reaction is described by eq. 1 without any complications arising from side reactions.

The rate constants k_2 are subjected to Hammett correlation (Figures 1 and 2) and the Hammett coefficients ρ_X and ρ_Y are determined as summarized in Table 2. In addition, the Brönsted coefficients (β_X) are derived from the slopes of the

Table 1. Second-Order Rate Constants, $k_2 \times 10^4$ ($M^{-1}s^{-1}$), for the Reactions of Y-Aryl Phenyl Isothiocyanophosphates with X-Pyridines in Acetonitrile at 55.0 °C

X \ Y	4-OCH_3	4-CH_3	H	3-OCH_3	4-Cl
4-OCH_3	382	611	1750	988	230
4-CH_3	85.9	116	255	151	50.9
3-CH_3	62.2	81.0	170	95.6	35.5
H	9.65	13.6	30.2	17.4	6.72
3-C_6H_5	4.21	6.54	13.9	7.80	3.45
3-$COCH_3$	0.469	0.701	2.23	1.19	0.555
3-Cl	0.402	0.653	1.86	0.746	0.417
4-$COCH_3$	0.353	0.606	1.37	0.682	0.408
4-CN	0.322	0.543	1.14	0.600	0.326

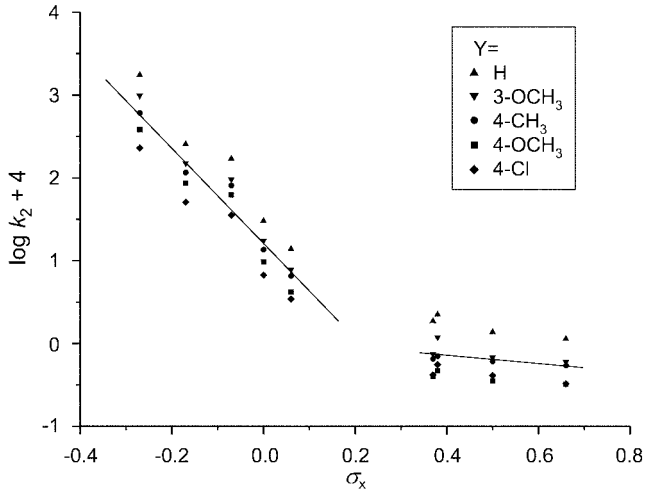


Figure 1. The Hammett plots for the reactions of Y-aryl phenyl isothiocyanophosphates with X-pyridines in acetonitrile at 55.0 °C.

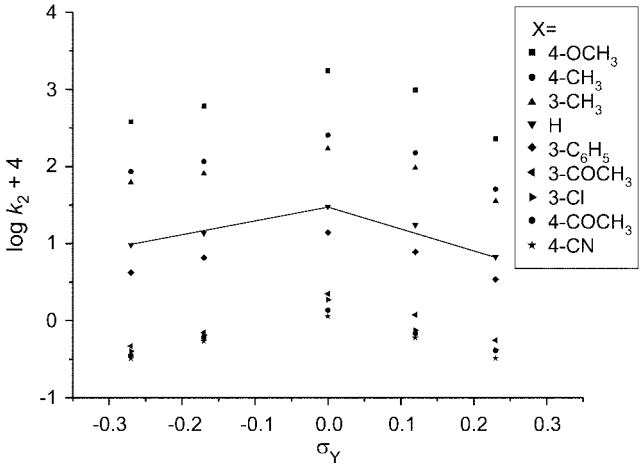


Figure 2. The Hammett plots for the reactions of Y-aryl phenyl isothiocyanophosphates with X-pyridines in acetonitrile at 55.0 °C.

Table 2. Selectivity Parameters[a] for the Reactions of Y-Aryl Phenyl Isothiocyanophosphates with X-Pyridines in Acetonitrile at 55.0 °C

Y	X = 4-OCH_3–3-C_6H_5		X = 3-$COCH_3$–4-CN	
	ρ_X	β_X	ρ_X	β_X
4-OCH_3	−5.75 ± 0.21 (0.972)[b]	1.21 ± 0.21 (0.993)	−0.46 ± 0.04 (0.882)	0.12 ± 0.01 (0.990)
4-CH_3	−5.79 ± 0.19 (0.977)	1.22 ± 0.10 (0.994)	−0.33 ± 0.02 (0.954)	0.08 ± 0.01 (0.996)
H	−6.12 ± 0.19 (0.980)	1.28 ± 0.11 (0.993)	−0.90 ± 0.06 (0.933)	0.22 ± 0.02 (0.994)
3-OCH_3	−6.14 ± 0.18 (0.982)	1.28 ± 0.10 (0.994)	−0.69 ± 0.11 (0.721)	0.20 ± 0.06 (0.917)
4-Cl	−5.38 ± 0.18 (0.978)	1.13 ± 0.09 (0.994)	−0.58 ± 0.07 (0.828)	0.15 ± 0.03 (0.954)

X \ Y	4-OCH_3 − H	H − 4-Cl
	ρ_Y	ρ_Y
4-OCH_3	2.47 ± 0.03 (0.998)[b]	3.81 ± 0.17 (0.963)
4-CH_3	1.78 ± 0.04 (0.995)	3.03 ± 0.11 (0.975)
3-CH_3	1.65 ± 0.04 (0.993)	2.94 ± 0.09 (0.984)
H	1.86 ± 0.03 (0.997)	2.82 ± 0.08 (0.984)
3-C_6H_5	1.92 ± 0.01 (0.999)	2.62 ± 0.05 (0.992)
	ρ_{XY} = −1.42 ± 0.18 (0.957)	ρ_{XY} = +3.16 ± 0.18 (0.960)
3-$COCH_3$	2.56 ± 0.06 (0.992)	2.62 ± 0.03 (0.997)
3-Cl	2.49 ± 0.03 (0.998)	2.83 ± 0.05 (0.995)
4-$COCH_3$	2.17 ± 0.01 (0.999)	2.29 ± 0.02 (0.998)
4-CN	2.02 ± 0.02 (0.999)	2.36 ± 0.01 (0.999)
	ρ_{XY} = −1.81 ± 0.04 (0.983)	ρ_{XY} = +1.40 ± 0.07 (0.951)

[a]The σ values were taken from Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165. The β_X values were determined using pK_a values in water. The pK_a values of pyridines in water at 25 °C were taken from: (i) Dean, J. A. *Handbook of Organic Chemistry*; McGraw-Hill: New York, 1987; Chapter 8. (ii) The pK_a values of X = *m*-C_6H_5 and X = *p*-CH_3CO were taken from Koh, H. J.; Han, K. L.; Lee, H. W.; Lee, I. *J. Org. Chem.* **1998**, *63*, 9834. [b]Correlation coefficient.

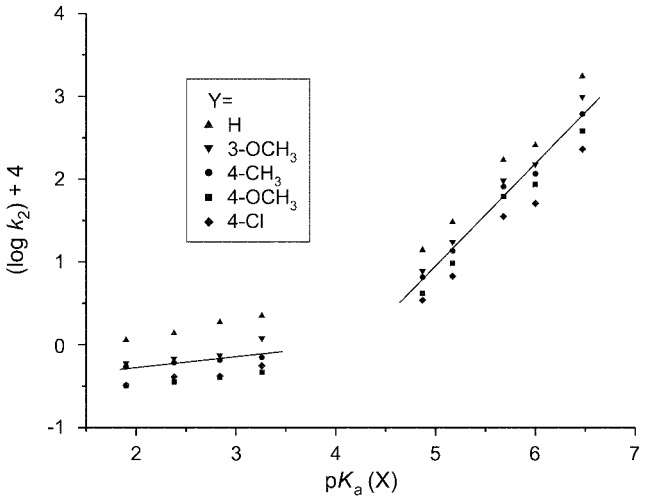


Figure 3. The Brönsted plots for the reactions of Y-aryl phenyl isothiocyanophosphates with X-pyridines in acetonitrile at 55.0 °C.

plots of log k_2(MeCN) against pK_a(X in H_2O) in Figure 3, and are also shown in Table 2. This procedure of using the pK_a(H_2O) instead of pK_a(MeCN) values of pyridines has been shown to be justified since there is a practically constant difference between the two sets of pK_a's in H_2O and in MeCN for various substituted pyridines so that the slopes (β_X) in the two solvents differ insignificantly.[9]

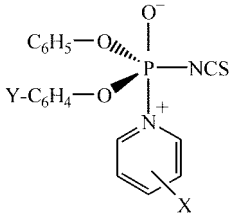
Examination of Figures 1-3 reveals that all the plots are biphasic with break points at $\sigma_X \cong 0.2$ and $\sigma_Y = 0$ in the substituent variation of the nucleophile and substrate, respectively. For the more basic (stronger) nucleophiles (X = 4-OCH_3-3-C_6H_5) the magnitude of ρ_X (= −5.4 to −6.1) and β_X (= 1.1-1.3) are larger than those for the less basic (weaker) nucleophiles (ρ_X = −0.3 to −0.9 ; β_X = 0.1-0.2 for X = 3-$COCH_3$-4-CN). Strikingly the sign of slope (ρ_Y) in the plot of log k_2 *vs* σ_Y changes from positive (= 1.6-2.6) for electron donor Y to negative (ρ_Y = −2.3 to −3.8) for electron acceptor Y with a convex upward Hammett plot (Figure 2). This type of Hammett plot normally suggests a mechanistic change at the breakpoint.[10] We propose the changeover from a concerted (for $\sigma_Y < 0$) to a stepwise mechanism with rate-limiting expulsion of the leaving group, $^-$NCS, in a trigonal bipyramidal pentacoordinated (TBP-5C) intermediate (for $\sigma_Y > 0$), based on the following grounds: The positive sign of ρ_Y indicates negative charge development in the TS on the reaction center, P. This is accompanied with a negative sign of the cross-interaction constant ρ_{XY}, which is indicative of a concerted (S_N2) process[8] or a rate-limiting bond making process in an adduct (or intermediate) formation.[11] In the latter case, however, the magnitude of ρ_{XY} tends to be rather small. For example, addition of amines ($XRNH_2$) to olefines ($YC_6H_4C_aH{=}C_bZ,Z'$) in acetonitrile proceeds by a concerted formation of the $C_\alpha - N$ and $C_\beta - H$ bonds in a single-step process leading to a neutral product.[11] For the olefines with various activating (electron-acceptor) groups (Z,Z'), the reactions of benzylamines have led to the ρ_{XY} values of −0.31 (Z,Z' = CN,CN),[11b] −0.33 (1,2-$(CO)_2C_6H_4$),[11c] −0.40 (NO_2, H)[11a] and −0.52 (NO_2, C_6H_5).[11d] Again, for the rate-limiting formation of a tetrahedral intermediate in the pyridinolysis of phenacyl bromides in acetonitrile the ρ_{XY} value reported is *ca* +0.1.[12] Thus, the magnitude of ρ_{XY} value is small, either negative or positive, in the rate-limiting bond formation process. In contrast, however, in the concerted, S_N2, process the ρ_{XY} observed exhibited a rather large negative value. For the S_N2 processes involving aminolysis of benzyl, benzenesulfonyl and benzoyl halides, the ρ_{XY} values reported range from −0.6 to −1.7.[8a,b] The ρ_{XY} values obtained in the present work, −1.42 and −1.81, are therefore in favor of the concerted (S_N2) mechanism rather than a simple rate-limiting addition mechanism. Additional support for this conclusion is provided by the large $\beta_X(\beta_{nuc})$ values (1.1-1.3) for the more basic pyridine nucleophiles which are considered to be more likely to give stepwise mechanism than less basic nucleophiles.[4,13,14] In a stepwise mechanism, however, the large β_X value is an indication of a rate-limiting leaving group expulsion process,[13] for which ρ_{XY} is not negative but positive as in the present case.

More importantly, this proposal of the concerted mechanism for the reactions of substrates with electron-donating groups ($\sigma_Y < 0$ and $\rho_Y > 0$) are in accord with the well known experimental and theoretical results[15] that the concerted process is favored over the stepwise mechanism by the push provided by the groups that remain behind. In the present case, electron donating Y groups in the substrate provide such a push to expel the leaving group, $^-$NCS, and increase the possibility of the reaction proceeding by a concerted mechanism.

In summary, the large negative ρ_{XY} values coupled with positive ρ_Y and large β_X values (for the more basic pyridines) support a concerted process, an associative S_N2 process with a greater degree of bond-making than bond-cleavage in the TS.

As to the biphasic plots of log k_2 *vs* σ_X or pK_a(X), we propose the front side (equatorial) attack TS for more basic nucleophiles and backside (apical) attack TS for less basic pyridines.[4,14] It is well known that a weakly basic group has a greater apicophilicity so that apical approach is favored for such nucleophiles.[4,14,16] Since the apical bonds are longer than the equatorial bonds,[4,14] the apical nucleophilic attack should lead to a looser P–N bond in the TBP-5C structure and hence a smaller magnitude of β_X as well as ρ_X is obtained.[4]

Now for the pyridinolysis of substrates with electron-withdrawing groups, we obtained negative ρ_Y values. The negative slope suggests either positive charge development, or alternatively, a reduction of negative charge at the reaction center, P, in the TS. The electron-withdrawing groups by depleting electrons from the reaction center, P, retard the rate of leaving group departure and a negative ρ_Y results. This means that rate-limiting cleavage of the P–NCS bond from a TBP-5C intermediate (**2**) occurs in the TS since the departure of $^-$NCS leaving group leaves behind a partial positive charge in the reaction center, P, in the TS which is stabilized by the oxygen lone pairs (O^-) but is destabilized by the electron attraction from the positive charge on the nitrogen



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(N^+) and electron-withdrawing Y substituent. On balance, the destabilization of developing positive charge on P is stronger than the stabilization by the oxygen lone pairs so that the leaving group expulsion is hindered in the TS with the resulting rate retardation. This proposal is supported by the large positive ρ_{XY} values (+3.16 and +1.40) for the reactions of the substrates with electron-withdrawing substituents.[15] For the rate-limiting breakdown of TBP-5C intermediate, the ρ_{XY} values were found to be relatively large positive: ρ_{XY} = +0.88, for the anilinolysis of cinnamoyl chlorides ($YC_6H_4CH{=}CHCOCl$) in acetonitrile,[17] and +0.53 for the reactions of *S*-phenyl benzoates ($YC_6H_4C(=O)SC_6H_5$) with benzylamines in acetonitrile.[18] Another good example is the aminolysis of phenyl dithiobenzoates ($YC_6H_4C(=S)SC_6H_5$) in acetonitrile: the ρ_{XY} values are +0.7 (partially large, for rate-limiting expulsion of the leaving group from a zwitterionic intermediate, $T^{\pm}$) and +0.06 (small, for rate-limiting formation of $T^{\pm}$) for the aminolysis with anilines and benzylamines, respectively.[19] Chloride should be a far better leaving group than isothiocyanate. The anilinolysis of Y-aryl phenyl chlorophosphate has been shown to proceed by a concerted (S_N2) mechanism with ρ_{XY} = −1.31.[3a] Change of the leaving group from Cl^- to that of a lower leaving ability, $^-$NCS, causes a change in mechanism from a concerted to a stepwise process with rate-limiting breakdown of the TBP-5C 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 rate-limiting expulsion of the leaving group from the intermediate.[1a,b,13d,15a,20] Here again, the large and small magnitudes of ρ_X and β_X values for the more basic and less basic nucleophiles, respectively, can be interpreted to indicate formation of the intermediate with equatorial and apical P–N (nucleophile) bonds, respectively.[4,14]

The mechanistic change from a concerted for the substrate with electron-donating Y substituent to a stepwise with rate-limiting breakdown of the TBP-5C intermediate for electron-withdrawing Y can be represented schematically as shown in Figure 4. An electron-donor Y raises the lone pair level on oxygen atoms (n_O) which results in a greater vicinal $n_O \rightarrow \sigma^*_{P\text{-}N}$ charge transfer interactions[21] so that bond cleavage of the P–NCS bond is facilitated[22] and leads to a concerted process. In contrast, an electron-acceptor Y depresses the n_O level resulting in a weaker $n_O \rightarrow \sigma^*_{P\text{-}N}$ vicinal charge transfer interactions and stabilization of the intermediate.[16b,23] This

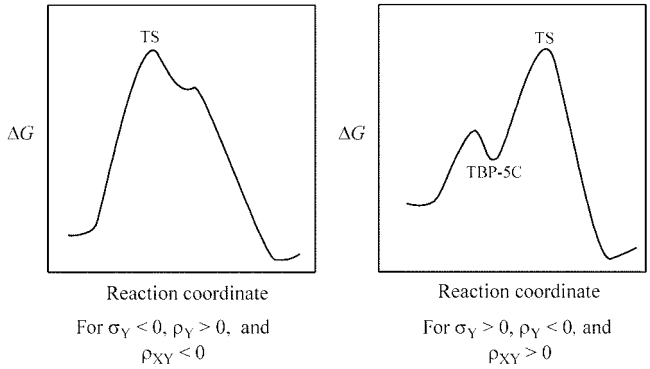

Figure 4. Schematic presentation of the effect of substituent Y in the substrate.

Table 3. Activation Parameters[a] for the Reactions of Y-Aryl Phenyl Isothiocyanophosphates with X-Pyridines in Acetonitrile

X	Y	t/°C	$k_2 \times 10^4$/ $M^{-1}s^{-1}$	$\Delta H^{\neq}$/ kcal mol^{-1}	$-\Delta S^{\neq}$/ cal $mol^{-1}K^{-1}$
4-CH_3	4-OCH_3	45	64.7	6.0 ± 0.5[b]	50 ± 2[b]
		55	85.9		
		65	121		
3-CH_3	H	45	121	6.9 ± 0.3	46 ± 1
		55	170		
		65	246		
3-Ph	3-OCH_3	45	5.24	8.4 ± 0.1	47 ± 1
		55	7.80		
		65	12.2		
3-$COCH_3$	4-Cl	45	0.336	10.1 ± 0.1	47 ± 1
		55	0.555		
		65	0.920		

[a]Calculated by the Eyring equation. [b]Standard deviation.

will lead to a stepwise mechanism with rate-limiting expulsion of the leaving group. In effect, an electron-donor enhances the expulsion of the leaving group while an electron-acceptor depresses it.

The activation parameters, $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$, determined with rate constants at three temperatures are summarized in Table 3. The $\Delta H^{\ddagger}$ values are somewhat higher but $\Delta S^{\ddagger}$ values are less negative than the corresponding values for the reactions with better leaving group (Cl^-), *e.g.* $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ values are 10.1 kcal mol^{-1} and −47 eu for **1** ($^-$NCS leaving group with Y = 4-Cl and X = 3-$COCH_3$) whereas those are 4.2 kcal mol^{-1} and −59 eu for Y-aryl phenyl chlorophosphate (Cl^- leaving group with Y = 4-Cl and X = H).[3a] This is consistent with the stronger P–NCS than P–Cl bond which should be partially cleaved in the TS.

Summary

The kinetic studies of the reactions between Y-aryl phenyl isothiocyanophosphate (**1**) and pyridines (XC_5H_4N) in acetonitrile at 55.0 °C have been carried out. The Hammett plots for substituent (Y) variations in the substrate (log k_2 *vs* σ_Y) show a nonlinear, convex upward curve with breaks at Y

= H. For electron-donating groups ($\sigma_Y < 0$) the Hammett coefficients ρ_Y are positive and ρ_{XY} is negative while those for electron-withdrawing groups ($\sigma_Y > 0$) are negative ($\rho_Y < 0$) with a positive ρ_{XY}. These are interpreted to indicate a concerted mechanism for the reactions with positive slopes ($\rho_Y > 0$) and a stepwise mechanism with rate-limiting breakdown of the TBP-5C intermediate for the reactions with negative slopes ($\rho_Y < 0$). Biphasic plots are also obtained with log k_2 *vs* σ_X or pK_a(X) plots with steeper slopes for basic nucleophiles than weakly basic nucleophiles. The larger magnitudes of ρ_X and β_X for stronger nucleophiles are considered to arise from the front side (equatorial) nucleophilic attack, whereas the smaller values arise from the back side (apical) nucleophilic attack in the TS.

Experimental Section

Materials. GR grade pyridines were used without further purification. HPLC grade acetonitrile (water content is less than 0.005%) was used without further purification, except drying over molecular sieve, storing under nitrogen atmosphere, and then distilled before use. Y-Aryl phenyl isothiocyanophosphates were prepared by the following two steps. In step 1, Y-aryl phenyl chlorophosphate[24] was prepared by reacting phenyl dichlorophosphate with substituted phenol for six hours in the presence of triethylamine in methylene chloride on an ice bath as reported.[3a] In step 2, Y-aryl phenyl isothiocyanophosphates[25] were synthesized by reacting Y-aryl phenyl chlorophosphate with potassium thiocyanate for four hours in acetonitrile on an ice bath. The substrates were isolated in the similar way described in step 1 and were identified by TLC, IR, ^{1}H-NMR, ^{13}C-NMR and GC-MS. GR Grade diphenyl chlorophosphate, phenyl dichlorophosphate, 4-chlorophenyl dichlorophosphate and potassium thiocyanate were used without further purification. The physical constants after column chromatography (silicagel/ethylacetate + *n*-hexane) were as follows;

4-Methoxyphenyl phenyl isothiocyanophosphate. Liquid. δ_H ($CDCl_3$), 200 MHz., 6.72-7.4 (aromatic-H, 9H, m), 3.79 (OCH_3 str. 3H, s); δ_C ($CDCl_3$), 50 MHz., 112-154 (C=C, aromatic, 12C, m/w), 156 (NCS, 1C, w), 53 (OCH_3, 1C, s); ν_{max} (neat), 3065-2985 (C-H, str. aromatic), 2835 (C-H str. aliphatic), 1977 (N=C=S, str.), 1587, 1502, 1250 (P-O-Ph), 1311 (P=O str.); *m*/*z*, 321 (M^+).

4-Methylphenyl phenyl isothiocyanophosphate. Liquid. δ_H ($CDCl_3$), 200 MHz., 7.14-7.50 (aromatic-H, 9H, m), 2.34 (CH_3 str. 3H, s); δ_C ($CDCl_3$), 50 MHz., 117-150 (C=C, aromatic, 12C, m/w), 132 (NCS, 1C, w), 18.2 (CH_3, 1C, s); ν_{max} (neat), 3042-3073 (C-H, str. aromatic), 2928 (C-H str. aliphatic), 1993 (N=C=S, str.), 1587, 1503, 1487, 1181 (P-O-Ph), 1311 (P=O str.); *m*/*z*, 305 (M^+).

Diphenyl isothiocyanophosphate. Liquid. δ_H ($CDCl_3$), 200 MHz., 7.15-7.40 (aromatic-H, 10H, s); δ_C ($CDCl_3$), 50 MHz., 117-147 (C=C, aromatic), 128 (NCS); ν_{max} (neat), 3065-3073 (C-H, str. aromatic), 1985 (N=C=S, str.), 1587, 1487, 1200 (P-O-Ph), 1311 (P=O str.); *m*/*z*, 291 (M^+).

3-Methoxyphenyl phenyl isothiocyanophosphate. Liquid. δ_H ($CDCl_3$), 200 MHz., 6.72-7.5 (aromatic-H, 9H, m/s), 3.79 (OCH_3 str. 3H, s); δ_C ($CDCl_3$), 50 MHz., 103-158 (C=C, aromatic, 12C, m/w), 124 (NCS, 1C, w), 53 (OCH_3, 1C, s); ν_{max} (neat), 3071-2946 (C-H, str. aromatic), 2838 (C-H str. aliphatic), 1980 (N=C=S, str.), 1621, 1502, 1458, 1290 (P-O-Ph), 1317 (P=O str.); *m*/*z*, 321 (M^+).

4-Chlorophenyl phenyl isothiocyanophosphate. Liquid. δ_H ($CDCl_3$), 200 MHz., 7.18-7.4 (aromatic-H, 9H, m/s); δ_C ($CDCl_3$), 50 MHz., 117-148 (C=C, aromatic, 12C, m/w), 129 (NCS, 1C, w); ν_{max} (neat), 3103-3062 (C-H, str. aromatic), 1955 (N=C=S, str.), 1600, 1497, 1450 (P-O-Ph), 1311 (P=O str.); *m*/*z*, 325 (M^+).

Kinetics measurement. Rates were measured conductometrically at 55.0 °C for the reactions of aryl phenyl isothiocyanophosphate with pyridines using a computer controlled conductivity bridge constructed in this laboratory. Pseudo-first-order rate constants, k_{obsd}, were measured by using curve fitting method in ORIGIN program (version 5.1) or Guggenheim method.[26] Pseudo-first-order rate constants were determined with large excess of nucleophiles, [substrate] = 1×10^3 M and [nucleophile] = 0.1-0.5 M. Pseudo-first-order rate constant values were average of three runs which were reproducible within ± 3%.

Product analysis. 4-Methoxyphenyl phenyl isothiocyanophosphate was refluxed with excess pyridine for more than 15 half-lives at 55 °C in acetonitrile. Acetonitrile was evaporated under reduced pressure. 4-Methoxyphenyl phenyl phosphoropyridinium thiocyanate was isolated by removing excess pyridine using column-chromatography technique. It is important to notice that the product was collected from the upper most part silica-gel of the column by washing with acetonitrile solvent. Then solvent was evaporated under reduced pressure. The physical constants after column chromatography (silica-gel/ethyl acetate + *n*-hexane) were as follows:

$[(4\text{-}OCH_3C_6H_4O)(C_6H_5O)P(=O)(NC_5H_5)]^+(NCS)^-$. Liquid. δ_H (DMSO), 200 MHz., 6.76-8.6 (including pyridine aromatic-H, 14H, m/w), 3.6 (OCH_3, 3H, s); δ_C (DMSO), 50 MHz., 118-153 (including pyridine aromatic-C, 17C, w), 112 (NCS, 1C, w), 53.5 (OCH_3, 1C, s); ν_{max} (neat), 2958-3103 (C-H str., aromatic), 2843 (C-H str., aliphatic), 2070 (SCN), 1717 (C-N str., aromatic), 1602, 1510, 1379 (P-O-Ph), 1250 (P=O).

4-Chlorophenyl phenyl isothiocyanophosphate was refluxed with excess pyridine as described above.

$[(4\text{-}ClC_6H_4O)(C_6H_5O)P(=O)(NC_5H_5)]^+(NCS)^-$. Liquid. δ_H ($CDCl_3$), 200 MHz., 7.076-7.345 (including pyridine aromatic-H, 14H, m/w); δ_C ($CDCl_3$), 50 MHz., 120.485-150.5 (including pyridine aromatic-C, 17C, w); ν_{max} (neat), 3071-3098 (C-H str., aromatic), 2865 (C-H str., aliphatic), 1583, 1496, 1306 (P-O-Ph), 1187 (P=O).

4-Chlorophenyl phenyl isothiocyanophosphate was refluxed with excess 4-methylpyridine as described above.

$[(4\text{-}ClC_6H_4O)(C_6H_5O)P(=O)(4\text{-}CH_3NC_5H_5)]^+(NCS)^-$. Liquid. δ_H ($CDCl_3$), 200 MHz., 7.08-8.40 (including pyridine aromatic-H, 14H, m/w), 2.61 (CH_3, 3H, s); δ_C ($CDCl_3$), 50 MHz., 120.26-152.25 (including pyridine aromatic-C, 17C,

w), 159.25 (NCS, 1C, w), 22.38 (CH_3, 1C, s); ν_{max} (neat), 3066-3093 (C-H str., aromatic), 2865 (C-H str., aliphatic), 2065 (NCS str.), 1589, 1485, 1310 (P-O-Ph), 1165 (P=O). δ_p ($CDCl_3$), 162 MHz., –5.77 (P=O, 1P, s).

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