DOI 10.5012/bkcs.2011.32.7.2339

Kinetics and Mechanism of the Pyridinolysis of *O,O*-Dimethyl *S*-Aryl Phosphorothioates in Dimethyl Sulfoxide

Hasi Rani Barai and Hai Whang Lee*

*Department of Chemistry, Inha University, Incheon 402-751, Korea. *E-mail: hwlee@inha.ac.kr*
Received May 22, 2011, Accepted May 27, 2011

Kinetic studies for the reactions of *O,O*-dimethyl Z-*S*-aryl phosphorothioates with X-pyridines have been carried out in dimethyl sulfoxide at 85.0 ºC. The Hammett and Brönsted plots for substituent X variations in the nucleophiles are biphasic concave upwards with a break point at X = H, while those for substituent Z variations in the leaving groups are linear. The negative sign of the cross-interaction constant (ρ_{XZ}) implies that the reaction proceeds through a concerted mechanism for both the strongly and weakly basic pyridines. The magnitude of ρ_{XZ} (= –0.35) for the strongly basic pyridines is greater than that (ρ_{XZ} = –0.15) for the weakly basic pyridines, indicating a change of the nucleophilic attacking direction from frontside for the strongly basic pyridines to backside for the weakly basic pyridines. The early transition state is proposed on the basis of the absence of positive deviations from both the Hammett and Brönsted plots for the strong π-acceptor, X = 4-Ac, and small values of ρ_{XZ} and β_X.

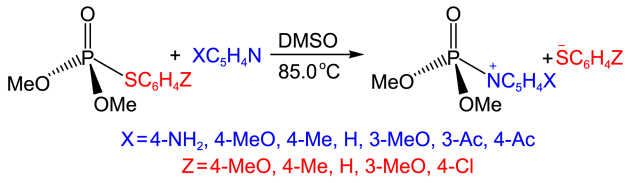
Key Words : Biphasic concave upward free energy correlation, Phosphoryl transfer reaction, Pyridinolysis, *O,O*-Dimethyl Z-*S*-aryl phosphorothioates

Introduction

Phosphoryl transfer reactions have been studied extensively of their importance to biochemistry and organometallic chemistry, and usefulness in synthesis. Two main types of displacement processes are reported regarding the phosphoryl species; either stepwise (A_N+D_N) through a trigonal bipyramidal pentacoordinate (TBP-5C) intermediate or a concerted process (A_ND_N).[1]

This lab reported various types (pyridinolysis,[2] anilinolysis,[3] benzylaminolysis,[4] and theoretical study[5]) of phosphoryl and thiophosphoryl transfer reactions to clarify the mechanism and to gain the systematic information; the thio effects and steric effects of the two ligands (R_1 and R_2) on reactivity, electrophilicities of substrates, leaving group mobilities, substituent effects and deuterium kinetic isotope effects on mechanism. The authors' studies on the pyridinolyses are focused mainly on R_1R_2P(=O or S)Cl-type substrates involving the Cl leaving group in acetonitrile (MeCN),[2a,d,f-i] and sometimes on R_1R_2P(=O or S)LG-type substrates involving the Z-substituted thiophenoxide (SC_6H_4Z),[2e] phenoxide (OC_6H_4Z),[2b] anilinide (NHC_6H_4Z),[2i] and isothiocyanate (NCS)[2c] leaving groups (LGs) in MeCN or DMSO. Herein, the authors reported that the substituent effects of the nucleophiles (X) and/or substrates (Y) and/or leaving groups (Z) upon the pyridinolysis mechanism were more dramatic than those upon the anilinolysis mechanism.

In this work, the kinetic studies of the reactions of *O,O*-dimethyl Z-*S*-aryl phosphorothioates with X-pyridines in dimethyl sulfoxide at 85.0 ± 0.1 ºC (Scheme 1) are reported to gain further systematic information into the phosphoryl transfer reactions and the substituent effects of the nucleophiles and leaving groups on the reaction mechanism, as well as to compare the relevant pyridinolyses of dimethyl chlorophosphate [$(MeO)_2P(=O)Cl$],[2g] *O,O*-diphenyl Z-*S*-aryl phosphorothioates [$(C_6H_5O)_2P(=O)SC_6H_4Z$],[2e] and Y-aryl phenyl chlorophosphates [$(YC_6H_4O)(C_6H_5O)P(=O)Cl$][2a] in MeCN. The MO theoretical [B3LYP/6-311+G(d,p)] structure of *O,O*-dimethyl *S*-phenyl phosphorothioate in the gas phase shows that the three oxygens and sulfur have a near tetrahedral geometry with the phosphorus atom at the center.



Scheme 1. The studied reaction system.

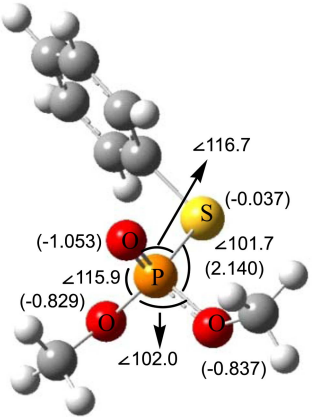


Figure 1. The B3LYP/6-311+G(d,p) geometry of *O,O*-dimethyl *S*-phenyl phosphorothioate in the gas phase.

Results and Discussion

The pseudo-first-order rate constants observed (k_{obsd}) for all reactions obey eq. (1) with negligible k_0 (= 0) in MeCN. The second-order rate constants were determined with at least five pyridine concentrations [XC_5H_4N]. No third-order or higher-order terms were detected, and no complications were found in the determination of k_{obsd} or in the linear plot of eq. (1). This suggests that there is no base-catalysis or noticeable side reactions, and the overall reaction follows the reaction path given by Scheme 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, together with selectivity parameters, ρ_X, β_X, ρ_Z, and ρ_{XZ}. The substituent effects in the nucleophiles and leaving groups on the rates are in accord with those for a typical nucleophilic substitution reaction with positive charge development at the nucleophilic N atom ($\rho_X < 0$ and $\beta_X > 0$) and negative charge development at the leaving group S atom ($\rho_Z > 0$) in the transition state (TS). However, the Hammett and Brönsted plots for substituent X variations in the nucleophiles are biphasic concave upwards with a break point at X = H (Figs. 2 and 3), while the Hammett plot for substituent Z variations in the leaving groups are linear. Herein, the β_X values were determined using pK_a values in water; the slopes from the plots of log k_2(DMSO) against pK_a(H_2O). Justification of this procedure has been experimentally and theoretically provided.[6]

The cross-interaction constants (CICs; ρ_{XZ}), eqs. (2), are determined, where X and Z represent the substituents in the nucleophile and leaving group, respectively.[9] The sign and magnitude of the CICs have made it possible to correctly interpret the reaction mechanism and degree of tightness of the TS, respectively. In general, the ρ_{XZ} has a negative value in a concerted S_N2 and a stepwise mechanism with a rate-limiting bond formation. However, it has a positive value for a stepwise mechanism with a rate-limiting leaving group expulsion from the intermediate. The magnitude of ρ_{XZ} is inversely proportional to the distance between the nucleophile and leaving group through the reaction center; the

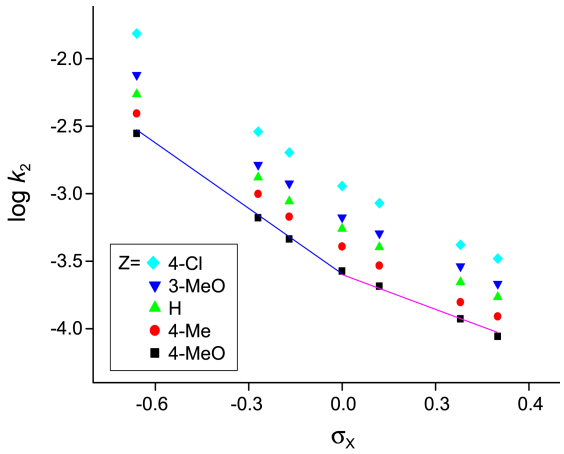


Figure 2. The Hammett plots (log k_2 *vs* σ_X) of the reactions of *O,O*-dimethyl Z-*S*-aryl phosphorothioates with X-pyridines in DMSO at 85.0 °C.

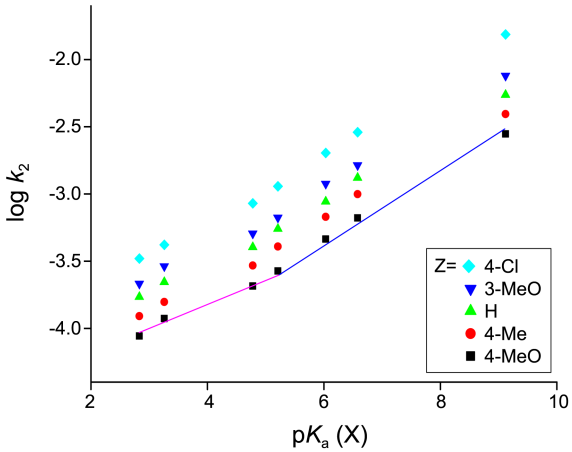


Figure 3. The Brönsted plots [log k_2 *vs* pK_a(X)] of the reactions of *O,O*-dimethyl Z-*S*-aryl phosphorothioates with X-pyridines in DMSO at 85.0 °C.

Table 1. Second-Order Rate Constants ($k_2 \times 10^4/M^{-1}$ s^{-1}) and Selectivity Parameters[a] of the Reactions of *O,O*-Dimethyl Z-*S*-Aryl Phosphorothioates with X-Pyridines in DMSO at 85.0 °C

X \ Z	4-MeO	4-Me	H	3-MeO	4-Cl	ρ_Z[b]
4-NH_2	28.0 ± 0.3	39.3 ± 0.1	54.6 ± 0.3	76.0 ± 0.9	154 ± 0.6	1.35 ± 0.08
4-MeO	6.63 ± 0.01	9.98 ± 0.08	13.2 ± 0.04	16.4 ± 0.2	28.8 ± 0.01	1.14 ± 0.06
4-Me	4.61 ± 0.05	6.74 ± 0.03	8.78 ± 0.03	11.9 ± 0.02	20.2 ± 0.04	1.17 ± 0.05
H	2.67 ± 0.02	4.06 ± 0.04	5.49 ± 0.08	6.67 ± 0.05	11.4 ± 0.3	1.13 ± 0.06
3-MeO	2.06 ± 0.02	2.93 ± 0.02	4.01 ± 0.01	5.09 ± 0.03	8.52 ± 0.19	1.13 ± 0.05
3-Ac	1.18 ± 0.01	1.57 ± 0.05	2.21 ± 0.03	2.90 ± 0.02	4.19 ± 0.02	1.05 ± 0.02
4-Ac	0.877 ± 0.01	1.23 ± 0.01	1.71 ± 0.02	2.15 ± 0.08	3.30 ± 0.03	1.07 ± 0.03
$-\rho_X$[c,d]	1.56 ± 0.02	1.51 ± 0.02	1.54 ± 0.03	1.61 ± 0.02	1.73 ± 0.04	ρ_{XZ}[c,i] =
β_X[c,e]	0.259 ± 0.022	0.250 ± 0.026	0.255 ± 0.021	0.267 ± 0.017	0.288 ± 0.010	–0.35 ± 0.06
$-\rho_X$[f,g]	0.959 ± 0.01	1.04 ± 0.01	1.01 ± 0.01	0.974 ± 0.01	1.10 ± 0.02	ρ_{XZ}[f,j] =
β_X[f,h]	0.190 ± 0.029	0.206 ± 0.028	0.201 ± 0.029	0.193 ± 0.030	0.219 ± 0.017	–0.15 ± 0.04

[a]The σ values were taken from ref. 7 and pK_a values of pyridines in water were taken from ref. 8. [b]Correlation coefficients, *r*, are better than 0.973. [c]For X = 4-NH_2, 4-MeO, 4-Me, H. [d]$r \geq 0.998$. [e]$r \geq 0.999$. [f]For X = H, 3-MeO, 3-Ac, 4-Ac. [g]$r \geq 0.999$. [h]$r \geq 0.994$. [i]$r = 0.987$. [j]$r = 0.987$.

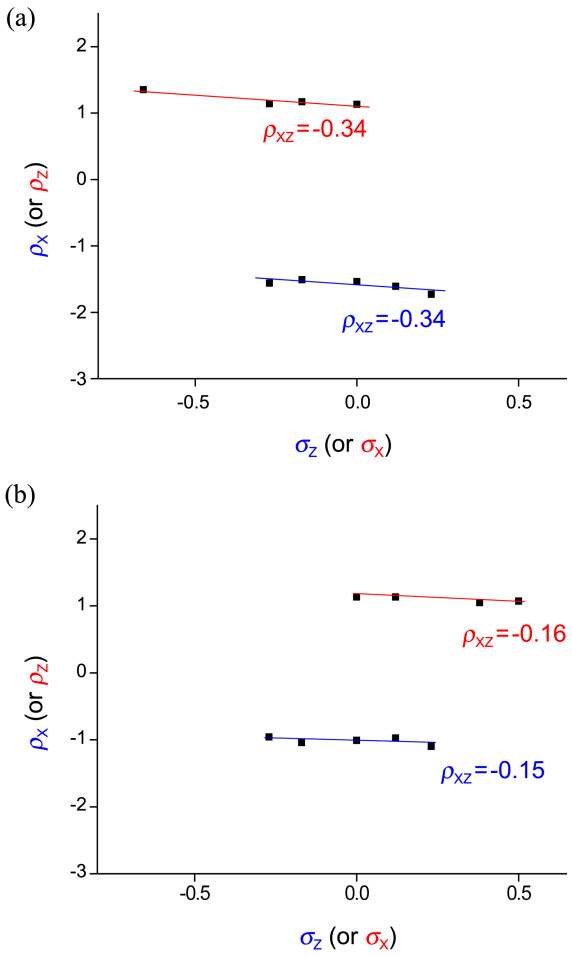


Figure 4. Determination of ρ_{XZ} (= $\partial\rho_Z/\partial\sigma_X = \partial\rho_X/\partial\sigma_Z$) according to eq. (2b) of the reactions of *O,O*-dimethyl *Z*-*S*-aryl phosphorothioates with X-pyridines in DMSO at 85.0 °C. The obtained CIC values by multiple regressions are: (a) ρ_{XZ} = –0.35 ± 0.06 with the strongly basic pyridines (X = 4-NH_2, 4-MeO, 4-Me, H) and (b) ρ_{XZ} = –0.15 ± 0.04 with the weakly basic pyridines (X = H, 3-MeO, 3-Ac, 4-Ac).

tighter the TS, the greater the magnitude of the CIC.[9]

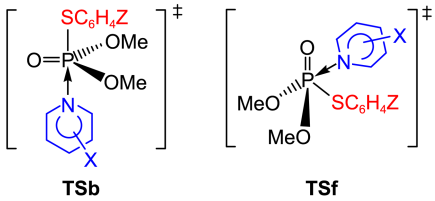
$$\log(k_{XZ}/k_{HH}) = \rho_X\sigma_X + \rho_Z\sigma_Z + \rho_{XZ}\sigma_X\sigma_Z \quad (2a)$$

$$\rho_{XZ} = \partial\rho_X/\partial\sigma_Z = \partial\rho_Z/\partial\sigma_X \quad (2b)$$

Despite the biphasic concave upward Hammett and Brönsted plots for substituent X variations in the nucleophiles with a break point at X = H, the sign of the CICs, ρ_{XZ}, is negative for both the strongly and weakly basic pyridines (Table 1 and Fig. 4). The authors propose a concerted mechanism for the studied reaction system on the basis of the negative sign of CICs, ρ_{XZ}, and relatively small magnitudes of β_X values, regardless of the nature of substituent X. The magnitude of ρ_{XZ} (= –0.35) for the strongly basic pyridines is greater than that (ρ_{XZ} = –0.15) for the weakly basic pyridines, which means that the distance between X and Z for the strongly basic pyridines is shorter than for the weakly basic pyridines. As seen in Table 1, the greater values of β_X (= 0.250-0.288) for the strongly basic pyridines than those (β_X = 0.190-0.219) for the weakly basic pyridines may also suggest the greater degree of bond formation for the strongly basic pyridines than for the weakly basic pyridines, in line with the prediction from the magnitudes of CICs.

Assuming that the pyridine nucleophile attacks backside towards the Z-thiophenoxide leaving group in the TBP-5C TSb (Scheme 2) where both the nucleophile and leaving group occupy the apical positions. The small negative value of ρ_{XZ} (= –0.15) for the weakly basic pyridines is consistent with a backside attack where the nucleophile and leaving group are far apart. However, the magnitude of ρ_{XZ} (= –0.35) for the strongly basic pyridines is too large to be substantiated by a backside attack TSb. The somewhat large magnitude of ρ_{XZ} implies that the nucleophile and leaving group are in close enough proximity to interact strongly. Thus, it is the proposal of the authors that the reaction for the strongly basic pyridines proceeds through a frontside attack TSf (Scheme 2), resulting in larger magnitudes of ρ_{XZ} and β_X.[10] It needs to be stressed that the large magnitudes of the ρ_{XZ} values ($|\rho_{XZ}| \geq 0.5$) were obtained due to the frontside nucleophilic attack.[11]

In general, the nonlinear free energy correlation of a concave upward plot is diagnostic of a change in the reaction mechanism where the reaction path is changed depending on the substituents, while nonlinear free energy correlation of the concave downward plot is diagnostic of a rate-limiting



Scheme 2. Backside attack TSb and frontside attack TSf.

Table 2. Summary of the NBO Charges on the P Reaction Center, Second-Order Rate Constants ($k_2 \times 10^3$/M^{-1} s^{-1}), and Selectivity Parameters for the Reactions of $R_1R_2P(=O)LG$-type Substrates with X-Pyridines

LG	R_1	R_2	charge on P	$k_2 \times 10^3$ (t °C)[a]	solvent	β_X	ρ_{XZ} (or ρ_{XY})	ref.
SC_6H_4Z	MeO	MeO	2.140	0.549 (85.0)	DMSO	0.250-0.288[b]/ 0.190-0.219[c]	–0.35[b]/–0.15[c]	this work
Cl	MeO	MeO	2.226	64.7 (35.0)	MeCN	0.63	–	2g
SC_6H_4Z	C_6H_5O	C_6H_5O	2.140	44.2 (35.0)	MeCN	0.88-0.93	–0.70[d]/+0.76[e]	2e
Cl	YC_6H_4O	C_6H_5O	2.230	135 (25.0)	MeCN	0.16-0.18	(–0.15)	2a

[a]For the reaction of unsubstituted substrate (or leaving group) (Y=H or Z=H) with unsubstituted pyridine (X=H) in a given solvent at a given temperature. [b]For X=4-NH_2, 4-MeO, 4-Me, H. [c]For X=H, 3-MeO, 3-Ac, 4-Ac. [d]For Z=4-Me, H. [e]For Z=H, 4-Cl, 3-Cl.

step change from bond breaking for the weakly basic nucleophiles to bond formation for the strongly basic nucleophiles.[12] In the present work, the nonlinear free energy correlations of biphasic concave upward plots for substituent X variations in the nucleophiles are ascribed to a change in the attacking direction of the nucleophile from a backside (TSb) for the weakly basic pyridines to a frontside attack (TSf) for the strongly basic pyridines.

Table 2 shows the natural bond order (NBO) charges on the reaction center P in the gas phase [calculated at the B3LYP/6-311+G(d,p) level],[13] second-order rate constants in a given solvent at a given temperature, and selectivity parameters, β_X and CICs (ρ_{XZ} or ρ_{XY}), for the two pyridinolysis systems with the Z-thiophenoxide and Cl leaving groups. The pyridinolysis rate with the thiophenoxide leaving group is slower than with the Cl one, as expected from the poorer leaving group mobility of thiophenoxide than that of Cl. The rate ratio of the two systems, $k(SC_6H_5)/k(Cl)$, for R_1=R_2=MeO[14] is much smaller than that for R_1=R_2=PhO. The pyridinolysis rate has no consistency with the NBO charge on the reaction center P, i.e., the greater the positive charge on P, the rate rather becomes slower for both systems. This means that the electrophilicity (or NBO charge on P) of the substrate does not play any role to determine the reactivity. The anilinolysis rate is predominantly dependent upon the steric effects of the two ligands, R_1 and R_2, i.e., the greater the size of the two ligands, the rate consistently becomes slower.[3f-m] However, the pyridinolysis rate does not depend at all on the steric effects of the two ligands, i.e., the greater the size of the two ligands, the rate rather becomes faster as seen in Table 2.

In the pyridinolysis of Y-aryl phenyl chlorophosphates,[2a] a concerted mechanism involving a backside nucleophilic attack was proposed. Herein, the strong π-acceptor substituents, 4-Ac and 4-CN, did not exhibit positive deviations from both the Hammett and Brönsted plots for substituent X variations in the nucleophiles. No positive deviations from both plots were rationalized by the early TS with little positive charge development on the N atom of pyridine.[15] The early TS, the small extent of both the bond formation and leaving group departure, was supported by the small CIC (ρ_{XY} = –0.15)[16] and small β_X (= 0.16-0.18) values.[2a] In the present work, the strong π-acceptor substituent, 4-Ac, does not exhibit positive deviations from both the Hammett and Brönsted plots (Figs. 2 and 3), as observed in the pyridinolysis of Y-aryl phenyl chlorophosphates. As discussed earlier, the backside attack TSb is proposed for the weakly basic pyridines. The small values of β_X (= 0.190-0.219) for the weakly basic pyridines are comparable with those (β_X = 0.16-0.18) of the pyridinolysis of Y-aryl phenyl chlorophosphates. Thus, the authors propose the early TS for the weakly basic pyridines based on the small values of ρ_{XZ} and β_X, and no deviation of the strong π-acceptor substituent, 4-Ac, from the free energy correlations. The authors also propose the early TS for the strongly basic pyridines, since the greater values of ρ_{XZ} and β_X than for the weakly basic pyridines are attributed to a frontside attack TSf. The more or less smaller magnitude of ρ_{XZ} (= –0.35) for the strongly basic pyridines compare to the magnitudes of the ρ_{XZ} values ($|\rho_{XZ}| \geq 0.5$)[2l,8d] for an usual frontside attack is ascribed to the early TS.

Conclusions

The reactions of *O,O*-dimethyl *Z*-*S*-aryl phosphorothioates with X-pyridines are studied kinetically in DMSO at 85.0 ºC. A concerted S_N2 mechanism with the early TS is proposed on the basis of the negative cross-interaction constants, ρ_{XZ}, small values of ρ_{XZ} and β_X, and no positive deviations for the strong π-acceptor, X = 4-Ac, in both the Hammett and Brönsted plots. Biphasic concave upward Hammett and Brönsted plots for substituent X variations in the nucleophiles are rationalized by a change of the nucleophilic attacking direction from frontside for the strongly basic pyridines to backside for the weakly basic pyridines.

Experimental Section

Materials. GR-grade X-pyridines were used without further purification. The GR grade dimethyl sulfoxide was dried over molecular sieves and used after three distillations under reduced pressure prior to use. HPLC grade acetonitrile (less than 0.005% water content), diethyl ether and n-hexane were used without further purification. GR-grade dimethyl chlorophosphate (96%), Z-thiophenols (97-98%), and triethylamine (99%) were used for synthesis of substrate.

Kinetic Measurements. Conductometric rate measurements were carried out using self-made computer-aided automatic A/D converter conductivity bridges. The pseudo-first-order rate constants (k_{obsd}) were determined using large excesses of nucleophiles, [XC_5H_4N] = 0.10-0.30 M and [Substrate] = 3.0×10^{-3} M. Each value (k_{obsd}) of pseudo-first-order rate constant was averaged obtained from more than three runs, which were reproducible within ± 3%.

Syntheses of Substrates. The substrates, *O,O*-dimethyl *Z*-*S*-Phenyl thiophosphates (Z=4-MeO, 4-Me, H, 3-MeO, and 4-Cl) were prepared by reacting dimethyl chlorophosphate (96%) with Z-thiophenols in the presence of triethylamine in acetonitrile on an cooling bath at −10.0 ºC.[2e,17] Triethylamine hydrochloride salt was separated by filtration. The remaining product in acetonitrile was treated with water and ether for work up after removal of solvent under reduced pressure. Ether soluble organic part was dried with anhydrous $MgSO_4$ for about 3 hr. The product mixture was isolated by filtration and finally separated through column chromatography (silica gel/ethyl acetate-*n*-hexane) after removal of solvent. The substrates were characterized by the spectral analysis as follows:

***O*,*O*-Dimethyl *S*-4-methoxyphenyl Phosphorothioate [$(CH_3O)_2P(=O)SC_6H_4$-4-OCH_3]:** Oily colorless liquid; ^{1}H-NMR (400 MHz, $CDCl_3$ & TMS) δ 3.79-3.82 (aliphatic, 9H, m), 6.88 (aromatic, 2H, d, J = 9.2 Hz); 7.45-7.48 (aromatic, 2H, m); ^{13}C-NMR (100 MHz, $CDCl_3$ & TMS) δ 54.16 (aliphatic, 2C, s), 55.34 (aliphatic, 1C, s), 115.09-160.58

(aromatic, 6C, m); ^{31}P-NMR (162 MHz, $CDCl_3$ & TMS) δ 32.24 (P=O, 1P, s); GC-MS (EI, *m*/*z*) 248 (M^+) and Anal. Calcd for $C_9H_{13}O_4PS$: C 43.55, H 5.28, S 12.92. Found: C 43.59, H 5.27, S 13.08.

***O*,*O*-Dimethyl *S*-4-methylphenyl Phosphorothioate [$(CH_3O)_2P(=O)SC_6H_4$-4-CH_3]:** Oily colorless liquid; ^{1}H-NMR (400 MHz, $CDCl_3$ & TMS) δ 2.35 (aliphatic, 3H, s), 3.80-3.83 (aliphatic, 6H, m), 7.17 (aromatic, 2H, d, J = 8.0 Hz); 7.44 (aromatic, 2H, d, J = 6.4 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$ & TMS) δ 21.18 (aliphatic, 1C, s), 54.21 (aliphatic, 2C, s), 130.28 (aromatic, 5C, d, J = 2.3 Hz); 134.63 (aromatic, 1C, d, J = 4.5 Hz); ^{31}P-NMR (162 MHz, $CDCl_3$ & TMS) δ 32.09 (P=O, 1P, s); GC-MS (EI, *m*/*z*) 232 (M^+).

***O*,*O*-Dimethyl *S*-Phenyl Thiophosphate [$(CH_3O)_2P(=O)$-SC_6H_5]:** Oily colorless liquid; ^{1}H-NMR (400 MHz, $CDCl_3$ & TMS) δ 3.79-3.86 (aliphatic, 6H, m), 7.35-7.59 (aromatic, 5H, m); ^{13}C-NMR (100 MHz, $CDCl_3$ & TMS) δ 54.29 (aliphatic, 2C, s), 129.16-134.64 (aromatic, 6C, m); ^{31}P-NMR (162 MHz, $CDCl_3$ & TMS) δ 31.61 (P=O, 1P, s); GC-MS (*m*/*z*) 218 (M^+).

***O*,*O*-Dimethyl *S*-3-methoxyphenyl Phosphorothioate [$(CH_3O)_2P(=O)SC_6H_4$-3-OCH_3]:** Oily colorless liquid; ^{1}H-NMR (400 MHz, $CDCl_3$ & TMS) δ 3.76-3.90 (aliphatic, 9H, m), 6.90-7.29 (aromatic, 4H, m); ^{13}C-NMR (100 MHz, $CDCl_3$ & TMS) δ 54.35 (aliphatic, 2C, s), 55.40 (aliphatic, 1C, s), 115.05-154.19 (aromatic, 6C, m); ^{31}P-NMR (162 MHz, $CDCl_3$ & TMS) δ 31.53 (P=O, 1P, s); GC-MS (EI, *m*/*z*) 248 (M^+).

***O*,*O*-Dimethyl *S*-4-chlorophenyl Phosphorothioate [$(CH_3O)_2P(O)SC_6H_4$-4-Cl]:** Oily colorless liquid; ^{1}H-NMR (400 MHz, $CDCl_3$ & TMS) δ 3.80-3.83 (aliphatic, 6H, m), 7.31-7.33 (aromatic, 2H, m); 7.47-7.49 (aromatic, m); ^{13}C-NMR (100 MHz, $CDCl_3$ & TMS) δ 54.34 (aliphatic, 2C, d, J = 6.1Hz), 94.41-135.82 (aromatic, 6C, m); ^{31}P-NMR (162 MHz, $CDCl_3$ & TMS) δ 30.90 (P=O, 1P, s); GC-MS (EI, *m*/*z*) 252 (M^+) and Anal. Calcd for $C_8H_{10}ClO_2PS$: C 38.03, H 3.99. Found: C 38.23, H 4.05.

Product Analysis. *O,O*-Dimethyl *S*-4-methoxyphenyl phosphorothioate and 4-methylpyridine were reacted for more than 15 half-lives in DMSO at 85.0 °C. The product was extracted by ethyl acetate with several attempts. Solvent was removed under reduced pressure and found gummy product was washed with diethyl ether for several times to remove excess pyridine. Analytical data of the product gave the following results:

[$(CH_3O)_2P(=O)NC_5H_4$-4-CH_3]$^+$(SC_6H_4-4-OCH_3): Gummy brown semisolid; ^{1}H NMR (200 MHz, $CDCl_3$ & TMS) δ 2.59 (aliphatic, 3H, s), 3.46-3.85 (aliphatic, 9H, m), 6.72-6.91 (aromatic, 2H, m), 7.29-7.66 (aromatic, 4H, m), 7.65 (aromatic, 2H, s), 9.08 (aromatic, 2H, d J = 6.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.04 (aliphatic, 1C, s), 55.25 (aliphatic, 3C, s), 114.09 (aromatic, 2C, s), 115.11 (aromatic, 1C, s), δ 128.35 (aromatic, 4C, s), δ 134.14-134.19 (aromatic, 2C, m), 137.48 (aromatic, 1C, s), 145.31 (aromatic C=O, 1C, s); ^{31}P NMR (162 MHz, $CDCl_3$) δ 20.12 (P=O, 1P, s).

Acknowledgments. This work was supported by the Brain Korea 21 Program from National Research Foundation of Korea and Inha University Research Grant.

References and Notes

1. (a) Hudson, R. F. *Structure and Mechanism in Organophosphorus Chemistry*; Academic Press: London, 1965; Chapter 3. (b) Hall, C. R.; Inch, T. D. *Tetrahedron* **1980**, *36*, 2059. (c) Thatcher, G. R. J.; Kluger, R. *Adv. Phys. Org. Chem.* **1989**, *25*, 99. (d) Williams, A. *Concerted Organic and Bio-Organic Mechanisms*; CRC Press: Boca Raton, 2000; Chapter 7-8. (e) Kirby, A. J.; Souza, B. S.; Medeiros, M.; Priebe, J. P.; Manfredi, A. M.; Nome, F. *Chem. Commun.* **2008**, 4428.
2. (a) Guha, A. K.; Lee, H. W.; Lee, I. *J. Org. Chem*. **2000**, *65*, 12. (b) Lee, H. W.; Guha, A. K.; Kim, C. K.; Lee, I. *J. Org. Chem.* **2002**, *67*, 2215. (c) Adhikary, K. K.; Lee, H. W.; Lee, I. *Bull. Korean Chem. Soc*. **2003**, *24*, 1135. (d) Hoque, M. E. U.; Dey, N. K.; Guha, A. K.; Kim, C. K.; Lee, B. S.; Lee, H. W. *Bull. Korean Chem. Soc*. **2007**, *28*, 1797. (e) Adhikary, K. K.; Lumbiny, B. J.; Kim, C. K.; Lee, H. W. *Bull. Korean Chem. Soc*. **2008**, *29*, 851. (f) Lumbiny, B. J.; Adhikary, K. K.; Lee, B. S.; Lee, H. W. *Bull. Korean Chem. Soc*. **2008**, *29*, 1769. (g) Dey, N. K.; Hoque, M. E. U.; Kim, C. K.; Lee, H. W. *J. Phys. Org. Chem.* **2010**, *23*, 1022. (h) Dey, N. K.; Adhikary, K. K.; Kim, C. K.; Lee, H. W. *Bull. Korean Chem. Soc*. **2010**, *31*, 3856. (i) Dey, N. K.; Kim, C. K.; Lee, H. W. *Bull. Korean Chem. Soc*. **2011**, *32*, 709. (j) Hoque, M. E. U.; Dey, S.; Kim, C. K.; Lee, H. W. *Bull. Korean Chem. Soc*. **2011**, *32*, 1138. (k) Guha, A. K.; Hoque, M. E. U.; Lee, H. W. *Bull. Korean Chem. Soc*. **2011**, *32*, 1375. (l) Guha, A. K.; Kim, C. K.; Lee, H. W. *J. Phys. Org. Chem.* **2011**, *24*, 474.
3. (a) Guha, A. K.; Lee, H. W.; Lee, I. *J. Chem. Soc., Perkin Trans. 2* **1999**, 765. (b) Lee, H. W.; Guha, A. K.; Lee, I. *Int. J. Chem. Kinet*. **2002**, *34*, 632. (c) Hoque, M. E. U.; Dey, S.; Guha, A. K.; Kim, C. K.; Lee, B. S.; Lee, H. W. *J. Org. Chem.* **2007**, *72*, 5493. (d) Hoque, M. E. U.; Lee, H. W. *Bull. Korean Chem. Soc.* **2007**, *28*, 936. (e) Dey, N. K.; Han, I. S.; Lee, H. W. *Bull. Korean Chem. Soc.* **2007**, *28*, 2003. (f) Hoque, M. E. U.; Dey, N. K.; Kim, C. K.; Lee, B. S.; Lee, H. W. *Org. Biomol. Chem.* **2007**, *5*, 3944. (g) Dey, N. K.; Hoque, M. E. U.; Kim, C. K.; Lee, B. S.; Lee, H. W. *J. Phys. Org. Chem.* **2008**, *21*, 544. (h) Lumbiny, B. J.; Lee, H. W. *Bull. Korean Chem. Soc*. **2008**, *29*, 2065. (i) Dey, N. K.; Hoque, M. E. U.; Kim, C. K.; Lee, B. S.; Lee, H. W. *J. Phys. Org. Chem.* **2009**, *22*, 425. (j) Dey, N. K.; Kim, C. K.; Lee, H. W. *Bull. Korean Chem. Soc*. **2009**, *30*, 975. (k) Hoque, M. E. U.; Guha, A. K.; Kim, C. K.; Lee, B. S.; Lee, H. W. *Org. Biomol. Chem*. **2009**, *7*, 2919. (l) Dey, N. K.; Lee, H. W. *Bull. Korean Chem. Soc*. **2010**, *31*, 1403. (m) Dey, N. K.; Kim, C. K.; Lee, H. W. *Org. Biomol. Chem*. **2011**, *9*, 717.
4. Adhikary, K. K.; Lee, H. W. *Bull. Korean Chem. Soc*. **2011**, *32*, 1625.
5. (a) Lee, I.; Kim, C. K.; Li, H. G.; Sohn, C. K.; Kim, C. K.; Lee, H. W.; Lee, B. S. *J. Am. Chem. Soc*. **2000**, *122*, 11162. (b) Han, I. S.; Kim, C. K.; Lee, H. W. *Bull. Korean Chem. Soc*. **2011**, *32*, 889.
6. Lee, I.; Hong, S. W.; Koh, H. J.; Lee, B. S.; Lee, H. W. *J. Org. Chem.* **2001**, *66*, 8549.
7. Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165.
8. (a) Albert, A.; Serjeant, E. P. *The Determination of Ionization Constants*, 3rd ed.; Chapman and Hall: New York, 1984; pp 154-155. (b) Dean, J. A. *Handbook of Organic Chemistry*; McGraw-Hill: New York, 1987; Chapter 8. (c) Fischer, A.; Galloway, W. J.; Vaughan, J. *J. Chem. Soc.* **1964**, 3591. (d) Koh, H. J.; Han, K. L.; Lee, I. *J. Org. Chem.* **1999**, *64*, 4783. (e) Koh, H. J.; Han, K. L.; Lee, H. W.; Lee, I. *J. Org. Chem.* **1998**, *63*, 9834.
9. (a) Lee, I. *Chem. Soc. Rev.* **1990**, *9*, 317. (b) Lee, I. *Adv. Phys. Org. Chem.* **1992**, *27*, 57. (c) Lee, I.; Lee, H. W. *Collect. Czech. Chem. Commun.* **1999**, *64*, 1529.

10. The β_X values for both the strongly and weakly basic pyridines are relatively small. The greater β_X values for the strongly basic pyridines than for the weakly basic pyridines would be ascribed to a frontside attack, in which both the pyridine and leaving group occupy the equatorial positions in the TBP-5C TSf. The equatorial bond length is shorter than the apical one and, as a result, the β_X values for a frontside attack are greater than for a backside attack. The TSb would be more or less distorted TBP-5C, whereas the TSf would be significantly distorted TBP-5C; even hard to call TBP-5C and rather similar to *cis*-basal (ref. 1c; p 128).
11. The ρ_{XZ} values greater than ~0.5 suggest that the reactions proceed predominantly by the frontside nucleophilic attack S_N2 pathways; see ref. 2l for detailed discussion.
12. (a) ref 1d; Chapter 7. (b) Ruff, A.; Csizmadia, I. G. *Organic Reactions Equilibria, Kinetics and Mechanism*; Elsevier: Amsterdam, Netherlands, 1994; Chapter 7.
13. Hehre, W. J.; Random, L.; Schleyer, P. V. R.; Pople, J. A. *Ab Initio Molecular Orbital Theory*; Wiley: New York, 1986; Chapter 4.
14. Taking into account the differences of solvent polarity and reaction temperature between the two reactions; DMSO (dielectric constant: ε_r = 46.45) *vs* MeCN (ε_r = 35.94) and 85.0 *vs* 35.0 °C, respectively.
15. The behavior of the strong π-acceptor X-substituent in the Hammett and/or Brönsted plots can be a clue to clarify the reaction mechanism: see refs. 2l and 8e for more detailed discussion.
16. The magnitude of ρ_{XY} = –0.15 is the smallest one that the authors have obtained for the phosphoryl and thiophosphoryl transfer reactions. In contrast, the great magnitude of ρ_{XY} = –1.31 and great secondary inverse deuterium kinetic isotope effects of k_H/k_D = 0.61-0.87 involving deuterated aniline ($XC_6H_4ND_2$) were obtained for the anilinolysis of Y-aryl phenyl chlorophosphates, and a late TS was proposed: see ref. 3a.
17. Torii, S.; Tanaka, H.; Sayo, N. *J. Org. Chem.* **1979**, *44*, 2938.