

Kinetics and Mechanism of the Anilinolysis of Dipropyl Chlorothiophosphate in Acetonitrile

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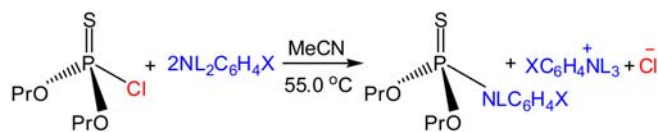
The nucleophilic substitution reactions of dipropyl chlorothiophosphate (**3**) with substituted anilines ($\text{XC}_6\text{H}_4\text{NH}_2$) and deuterated anilines ($\text{XC}_6\text{H}_4\text{ND}_2$) are investigated kinetically in acetonitrile at 55.0 °C. The obtained deuterium kinetic isotope effects (DKIEs; $k_{\text{H}}/k_{\text{D}}$) are primary normal ($k_{\text{H}}/k_{\text{D}} = 1.11\text{--}1.35$). A concerted mechanism involving predominant frontside nucleophilic attack is proposed on the basis of the primary normal DKIEs and selectivity parameters. Hydrogen bonded, four-center-type transition state is proposed. The steric effects of the two ligands on the anilinolysis rates of various substrates are discussed.

Key Words : Phosphoryl transfer reaction, Anilinolysis, Dipropyl chlorothiophosphate, Deuterium kinetic isotope effect, Steric effect

Introduction

The nucleophilic substitution reactions at tetracoordinated phosphorus with anilines have been studied extensively by this lab.¹ Continuing the studies on the phosphoryl and thiophosphoryl transfer reactions, the reactions of dipropyl chlorothiophosphate (**3**) with substituted anilines ($\text{XC}_6\text{H}_4\text{NH}_2$) and deuterated anilines ($\text{XC}_6\text{H}_4\text{ND}_2$) are investigated kinetically in acetonitrile (MeCN) at 55.0 ± 0.1 °C (Scheme 1). The aim of this work is to gain further information into the phosphoryl and thiophosphoryl transfer reactions, as well as to compare with the reaction mechanism and deuterium kinetic isotope effects (DKIEs; $k_{\text{H}}/k_{\text{D}}$) on the anilinolyses of $(\text{R}_1\text{O})(\text{R}_2\text{O})\text{P}(=\text{S})\text{Cl}$ -type chlorothiophosphates: dimethyl [**1**: $(\text{MeO})_2\text{P}(=\text{S})\text{Cl}$],^{1g} diethyl [**2**: $(\text{EtO})_2\text{P}(=\text{S})\text{Cl}$],^{1g} Y-aryl ethyl [**4**: $(\text{EtO})(\text{YC}_6\text{H}_4\text{O})\text{P}(=\text{S})\text{Cl}$],^{1f} and Y-aryl phenyl [**5**: $(\text{PhO})(\text{YC}_6\text{H}_4\text{O})\text{P}(=\text{S})\text{Cl}$],^{1c} chlorothiophosphates. The numbering of the substrates of **1-5** follows the sequence of the size of the two ligands, R_1O and R_2O . The anilinolysis,¹ ethanolysis² and hydrolysis³ rates of various $\text{P}=\text{O}$ and $\text{P}=\text{S}$ substrates are discussed on the basis of the steric effects of the two ligands. Henceforth, for convenience in expressing the substrates, $(\text{R}_1\text{O})(\text{R}_2\text{O})\text{P}(=\text{O})\text{Cl}$ and $(\text{R}_1\text{O})(\text{R}_2\text{O})\text{P}(=\text{S})\text{Cl}$ are denoted as $\text{O}(\text{R}_1\text{O}, \text{R}_2\text{O})$ and $\text{S}(\text{R}_1\text{O}, \text{R}_2\text{O})$, respectively.

The B3LYP/6-311+G(d,p) geometry, bond angles, and natural bond order (NBO) charges of **3** in the gas phase⁴ are shown in Figure 1. The MO theoretical structure shows that



L = H or D
X = 4-MeO, 4-Me, 3-Me, H, 3-MeO, 4-Cl, 3-Cl

Scheme 1. The anilinolysis of dipropyl chlorothiophosphate (**3**) in MeCN at 55.0 °C.

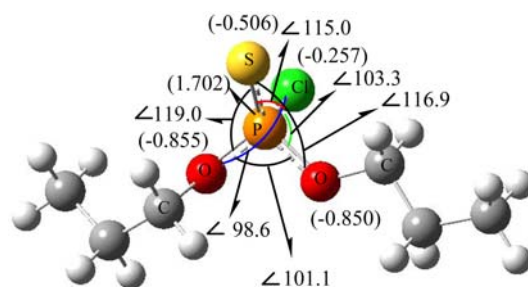


Figure 1. The B3LYP/6-311+G(d,p) geometry of dipropyl chlorothiophosphate (**3**) in the gas phase.

the two oxygens, sulfur, and chlorine have somewhat distorted tetrahedral geometry with the phosphorus atom at the center. The ground state (GS) structure of **3** does not have symmetry plane although it has two same ligands.

Results and Discussion

The observed pseudo-first-order rate constants (k_{obsd}) were found to follow eq. (1) for all the reactions under pseudo-first-order conditions with a large excess of aniline nucleophile. The k_0 values were negligible ($k_0 \approx 0$) in MeCN. The second-order rate constants ($k_{\text{H(D)}}$) were determined for at least five concentrations of anilines. The linear plots of eq. (1) suggest that there are no base-catalysis or noticeable side reactions and that the overall reaction is described by Scheme 1.

$$k_{\text{obsd}} = k_0 + k_{\text{H(D)}}[\text{XC}_6\text{H}_4\text{NH}_2(\text{D}_2)] \quad (1)$$

The k_{H} and k_{D} values are summarized in Table 1, together with the DKIEs ($k_{\text{H}}/k_{\text{D}}$) and the Hammett ρ_X and Brønsted β_X selectivity parameters. The $\text{p}K_{\text{a}}(\text{X})$ values of the X-anilines in water were used to obtain the Brønsted β_X values in MeCN, and this procedure was justified experimentally and theoretically.⁵ The values of $\text{p}K_{\text{a}}(\text{X})$ and σ_X of the deuterated X-anilines are assumed to be identical to those of

Table 1. The Second-Order Rate Constants ($k_{\text{H(D)}} \times 10^4/\text{M}^{-1} \text{s}^{-1}$), Selectivity Parameters (ρ_{X} and β_{X}),^a and DKIEs ($k_{\text{H}}/k_{\text{D}}$) of the Reactions of Dipropyl Chlorothiophosphate (**3**) with $\text{XC}_6\text{H}_4\text{NH}_2(\text{D}_2)$ in MeCN at 55.0 °C

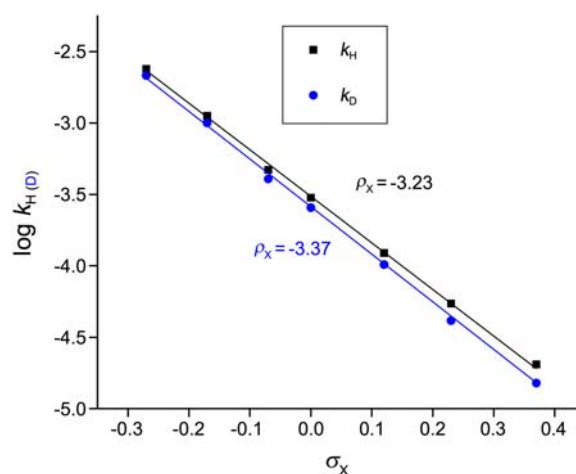
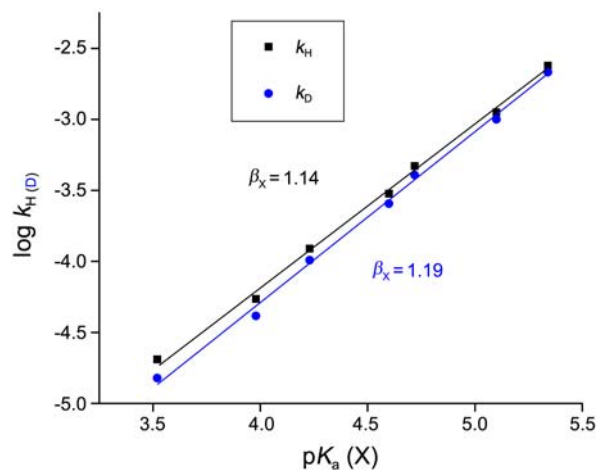
X	$k_{\text{H}} \times 10^4$	$k_{\text{D}} \times 10^4$	$k_{\text{H}}/k_{\text{D}}$
4-MeO	23.9 ± 0.1^b	21.5 ± 0.1	1.11 ± 0.01^g
4-Me	11.2 ± 0.1	10.0 ± 0.1	1.12 ± 0.02
3-Me	4.70 ± 0.03	4.05 ± 0.01	1.16 ± 0.01
H	3.00 ± 0.01	2.55 ± 0.02	1.18 ± 0.01
3-MeO	1.23 ± 0.01	1.02 ± 0.01	1.21 ± 0.02
4-Cl	0.544 ± 0.003	0.413 ± 0.001	1.32 ± 0.01
3-Cl	0.204 ± 0.001	0.151 ± 0.001	1.35 ± 0.01
$-\rho_{\text{X(H and D)}}$	3.23 ± 0.02^c	3.37 ± 0.02^e	
$\beta_{\text{X(H and D)}}$	1.14 ± 0.04^d	1.19 ± 0.04^f	

^aThe σ values were taken from ref. 7. The $\text{p}K_{\text{a}}$ values of X-anilines in water were taken from ref. 8. ^bStandard deviation. ^cCorrelation coefficient, $r = 0.999$. ^d $r = 0.999$. ^e $r = 0.999$. ^f $r = 0.999$. ^gStandard error $\{= 1/k_{\text{D}}[(\Delta k_{\text{H}})^2 + (k_{\text{H}}/k_{\text{D}})^2 \times (\Delta k_{\text{D}})^2]^{1/2}\}$ from ref. 9.

the X-anilines. Perrin and coworkers reported that the basicities of β -deuterated analogs of benzylamine, *N,N*-dimethylaniline and methylamine increase roughly by 0.02 $\text{p}K_{\text{a}}$ units per deuterium, and that these effects are additive.⁶ Thus, the $\text{p}K_{\text{a}}(\text{X})$ values of deuterated X-anilines may be slightly greater than those of X-anilines, however, the difference is too small to be taken into account. Figures 2 and 3 show the Hammett ($\log k_{\text{H(D)}} \text{ vs } \sigma_{\text{X}}$) and Brønsted [$\log k_{\text{H(D)}} \text{ vs } \text{p}K_{\text{a}}(\text{X})$] plots, respectively, for substituent X variations in the nucleophiles. The stronger nucleophile leads to the faster rate as observed in a typical nucleophilic substitution reaction. The primary normal DKIEs ($k_{\text{H}}/k_{\text{D}} > 1$) are observed with all the nucleophiles. The values of DKIEs invariably increase as the nucleophile changes from the strongly to weakly basic anilines; from X = 4-MeO ($k_{\text{H}}/k_{\text{D}} = 1.11$) to X = 3-Cl ($k_{\text{H}}/k_{\text{D}} = 1.35$).

The second-order rate constants (k_{H}) with unsubstituted aniline, NBO charges at the reaction center P atom [B3LYP/6-311+G(d,p) level of theory] in the gas phase,⁴ summations of the Taft's steric constants of R_1 and R_2 [$\Sigma E_{\text{S}} = E_{\text{S}}(\text{R}_1) + E_{\text{S}}(\text{R}_2)$],¹⁰ Brønsted coefficients ($\beta_{\text{X(H)}}$), cross-interaction constants (ρ_{XY}),¹¹ and DKIEs ($k_{\text{H}}/k_{\text{D}}$) of the reactions of **1-5** with $\text{XC}_6\text{H}_4\text{NH}_2(\text{D}_2)$ in MeCN at 55.0 °C are summarized in Table 2.

When the magnitude of the positive charge of the reaction

**Figure 2.** The Hammett plots ($\log k_{\text{H(D)}} \text{ vs } \sigma_{\text{X}}$) of the reactions of dipropyl chlorothiophosphate (**3**) with $\text{XC}_6\text{H}_4\text{NH}_2(\text{D}_2)$ in MeCN at 55.0 °C.**Figure 3.** The Brønsted plots [$\log k_{\text{H(D)}} \text{ vs } \text{p}K_{\text{a}}(\text{X})$] of the reactions of dipropyl chlorothiophosphate (**3**) with $\text{XC}_6\text{H}_4\text{NH}_2(\text{D}_2)$ in MeCN at 55.0 °C.

center P atom (or the inductive effects of the two ligands) is the major factor to determine the anilinolysis rate, the sequence of the anilinolysis rates should be $5 < 1 \approx 4 < 2 \approx 3$. However, the observed sequence is $1 > 2 > 3 \approx 4 > 5$, giving the rate ratio of 9.9(1):5.1(2):3.0(3):2.8(4):1(5). These results are not consistent with expectations for the positive

Table 2. Summary of Second-Order Rate Constants ($k_{\text{H}} \times 10^3/\text{M}^{-1} \text{s}^{-1}$) with $\text{C}_6\text{H}_5\text{NH}_2$, NBO Charges at the Reaction Center P Atom, Summations of the Taft's Steric Constants of R_1 and R_2 [$\Sigma E_{\text{S}} = E_{\text{S}}(\text{R}_1) + E_{\text{S}}(\text{R}_2)$], Brønsted Coefficients ($\beta_{\text{X(H)}}$), Cross-Interaction Constants (ρ_{XY}), and DKIEs ($k_{\text{H}}/k_{\text{D}}$) for the Reactions of **1-5** with $\text{XC}_6\text{H}_4\text{NH}_2(\text{D}_2)$ in MeCN at 55.0 °C

Substrate	$10^3 k_{\text{H}}^a$	charge at P	$-\Sigma E_{\text{S}}^b$	$\beta_{\text{X(H)}}$	ρ_{XY}	$k_{\text{H}}/k_{\text{D}}$	ref.
1: S(MeO,MeO)	1.09	1.687	0.00	0.993	–	0.945-1.06	1g
2: S(EtO,EtO)	0.512	1.701	0.14	0.977	–	1.01-1.10	1g
3: S(PrO,PrO)	0.300	1.702	0.72	1.14	–	1.11-1.35	this work
4: S(EtO,YC ₆ H ₄ O)	0.280^c	1.687^c	2.55^c	1.10-1.19	-0.28	1.06-1.27	1f
5: S(PhO,YC ₆ H ₄ O)	0.101^c	1.661^c	4.96^c	1.34-1.41	-0.22	1.11-1.33	1c

^aThe values with unsubstituted aniline. ^bNote that the value of ΣE_{S} is not $E_{\text{S}}(\text{R}_1\text{O}) + E_{\text{S}}(\text{R}_2\text{O})$ but $E_{\text{S}}(\text{R}_1) + E_{\text{S}}(\text{R}_2)$ since the data of Taft's steric constants of R_iO are not available. ^cThe values with Y = H.

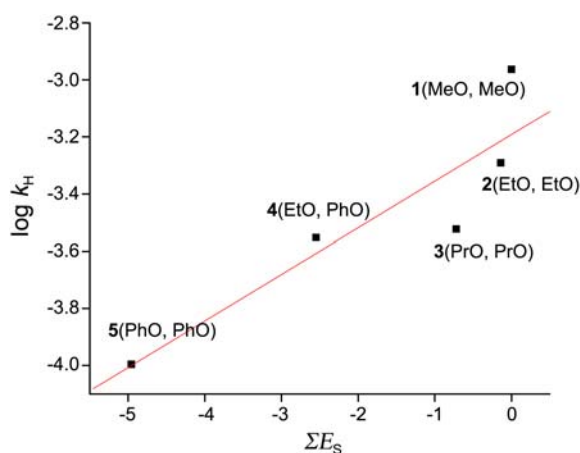


Figure 4. The plot of $\log k_H$ vs ΣE_S , according to Taft eq. (2), for the reactions of **1-5** with $C_6H_5NH_2$ in MeCN at 55.0 °C. The number of substrate and two ligands are displayed next to the corresponding point. The slope of $\delta = 0.16$ ($r = 0.902$) with **1-5**, $\delta = 0.18$ ($r = 0.959$) with **1, 2, 4**, and **5**, and $\delta = 0.21$ ($r = 0.998$) with **1, 4**, and **5** are obtained.

charge at the reaction center P atom, suggesting that the inductive effects of the two ligands do not play any role to decide the reactivity of anilinolysis of $(R_1O)(R_2O)P(=O)Cl$ -type substrates. The sequence of the anilinolysis rates of **1-5** is inversely proportional to the size of the two ligands; the greater the size of the two ligands, the rate becomes slower. These results indicate that the steric effects of the two ligands play an important role to determine the reactivity of the chlorothiophosphates. The Taft's eq. (2) can be used to rationalize the steric effect on the reaction rate where k_H is the second-order rate constant with unsubstituted aniline in MeCN at 55.0 °C, E_S is the Taft's steric constant [$E_S(R) = 0(\text{Me}); -0.07(\text{Et}); -0.36(\text{Pr}); -2.48(\text{Ph})$], ΣE_S is the summation of the steric constants of the two ligands, and δ is the sensitivity coefficient.¹⁰ Figure 4 shows the plot of $\log k_H$ with unsubstituted aniline ($C_6H_5NH_2$) against the summation of the Taft's steric constants of the two ligands of the reactions of five chlorothiophosphates (**1-5**) in MeCN at 55.0 °C, giving the sensitivity coefficients of $\delta = 0.16$ ($r = 0.902$) with five substrates of **1-5**, $\delta = 0.18$ ($r = 0.959$) with

four substrates of **1, 2, 4**, and **5**, and $\delta = 0.21$ ($r = 0.998$) with three substrates of **1, 4**, and **5**.

$$\log k_H = \delta \Sigma E_S + C \quad (2)$$

The sensitivity coefficients of δ for some phosphoryl and thiophosphoryl transfer reactions in a given solvent are summarized in Table 3. The relative reactivities of the reaction system **I-VII** are predominantly dependent upon the steric effects over the inductive effects of the ligands. Herein, it should be noted that the value of ΣE_S is not $E_S(R_1O) + E_S(R_2O)$ but $E_S(R_1) + E_S(R_2)$ for the reaction systems of **II** (**II'**, **II''**) and **IV** (**IV'**), since the data of Taft's steric constants of R_iO are not available. Despite the greater size of R_iO than that of its corresponding R_i , the steric effects of the two ligands on the anilinolysis rates (reaction systems of **I-IV'**) are smaller in $A(R_iO, R_jO)$ than in $A(R_i, R_j)$ where $A = O$ or S : e.g., $k_H[O(\text{Me}, \text{Me})]/k_H[O(\text{Ph}, \text{Ph})] = 4,520^{1d,i}$ while $k_H[O(\text{MeO}, \text{MeO})]/k_H[O(\text{PhO}, \text{PhO})] = 4.8$;^{1a,g} $k_H[S(\text{Me}, \text{Me})]/k_H[S(\text{Ph}, \text{Ph})] = 16^{1e,j}$ while $k_H[S(\text{MeO}, \text{MeO})]/k_H[S(\text{PhO}, \text{PhO})] = 11$.^{1c,g} This means that the intervening oxygen atom between the reaction center phosphorus atom and R_i reduces the steric congestion when the nucleophile attacks the reaction center P atom in the TS.

In the $P=S$ system of **I**, the anilinolysis rates of $S(\text{Et}, \text{Et})$ and $S(i\text{-Pr}, i\text{-Pr})$ are exceptionally slow to be rationalized by the conventional stereoelectronic effects.^{1p,u} In the $P=S$ system of **II**, the anilinolysis rate of $S(\text{EtO}, \text{EtO})$ is somewhat slow^{1g} and that of $S(\text{PrO}, \text{PrO})$ is much slow to be rationalized by the conventional stereoelectronic effects, as seen in Figure 4 and Table 3. In the $P=O$ system of **III**, the anilinolysis rate of $O(\text{Et}, \text{Et})$ is somewhat slow and that of $O(\text{cHex}, \text{cHex})$ is exceptionally slow to be rationalized by the conventional stereoelectronic effects.^{11,o} In the $P=O$ system of **IV**, the anilinolysis rate of $O(\text{EtO}, \text{EtO})$ is somewhat slow and that of $O(i\text{-PrO}, i\text{-PrO})$ is exceptionally slow to be rationalized by the conventional stereoelectronic effects.^{1g,r} These results might indicate that: (i) the steric effects of ethyl, propyl, *i*-propyl, and *cyclo*-hexyl ligands are greater than the reference reaction of Taft's eq. or (ii) another additional factor plays an important role to decide the anilinolysis rate. Thus, further systematic studies are essen-

Table 3. Steric Effects of the Two ligands on the Rates of the Reaction Systems of **I-VII**

no	Reaction system	Solvent	δ
I	$S(\text{Me}, \text{Me}), S(\text{Ph}, \text{Ph}) + \text{anilines}$	MeCN	0.24
II	$S(\text{MeO}, \text{MeO}), S(\text{EtO}, \text{PhO}), S(\text{PhO}, \text{PhO}) + \text{anilines}$	MeCN	0.21 ($r = 0.998$)
II'	$S(\text{MeO}, \text{MeO}), S(\text{EtO}, \text{EtO}), S(\text{EtO}, \text{PhO}), S(\text{PhO}, \text{PhO}) + \text{anilines}$	MeCN	0.18 ($r = 0.959$)
II''	$S(\text{MeO}, \text{MeO}), S(\text{EtO}, \text{EtO}), S(\text{PrO}, \text{PrO}), S(\text{EtO}, \text{PhO}), S(\text{PhO}, \text{PhO}) + \text{anilines}$	MeCN	0.16 ($r = 0.902$)
III	$O(\text{Me}, \text{Me}), O(\text{Me}, \text{Ph}), O(\text{Ph}, \text{Ph}) + \text{anilines}$	MeCN	0.74 ($r = 0.999$)
III'	$O(\text{Me}, \text{Me}), O(\text{Et}, \text{Et}), O(\text{Me}, \text{Ph}), O(\text{Ph}, \text{Ph}) + \text{anilines}$	MeCN	0.57 ($r = 0.895$)
IV	$O(\text{MeO}, \text{MeO}), O(\text{EtO}, \text{PhO}), O(\text{PhO}, \text{PhO}) + \text{anilines}$	MeCN	0.14 ($r = 0.999$)
IV'	$O(\text{MeO}, \text{MeO}), O(\text{EtO}, \text{EtO}), O(\text{EtO}, \text{PhO}), O(\text{PhO}, \text{PhO}) + \text{anilines}$	MeCN	0.12 ($r = 0.967$)
V	$\text{Me}_2\text{P}(=\text{O})\text{OC}_6\text{H}_4\text{-4-NO}_2, \text{MePhP}(=\text{O})\text{OC}_6\text{H}_4\text{-4-NO}_2, \text{Ph}_2\text{P}(=\text{O})\text{OC}_6\text{H}_4\text{-4-NO}_2 + \text{anilines}$	DMSO	0.02 ($r = 0.954$)
VI	$\text{Me}_2\text{P}(=\text{O})\text{OC}_6\text{H}_4\text{-4-NO}_2, \text{MePhP}(=\text{O})\text{OC}_6\text{H}_4\text{-4-NO}_2, \text{Ph}_2\text{P}(=\text{O})\text{OC}_6\text{H}_4\text{-4-NO}_2 + \text{ethanol}$	EtOH	0.48 ($r = 0.953$)
VII	$\text{Me}_2\text{P}(=\text{O})\text{OC}_6\text{H}_4\text{-4-NO}_2, \text{Ph}_2\text{P}(=\text{O})\text{OC}_6\text{H}_4\text{-4-NO}_2 + \text{water}$	water	0.35

tial to clarify the structure and reactivity relationship. In the P=O system of **V**, the sensitivity coefficient of δ is considerably small, however, it is evident that the steric effects are the predominant factor to determine the anilinolysis rate over the inductive effects of the two ligands.^{1m} In the P=O systems of **VI** and **VII**, the ethanolysis and hydrolysis rates are also strongly influenced by the steric effects over the inductive effects of the two ligands.^{2,3} It is worthy of note that the steric effects of the two ligands are no longer dominant factor to determine the pyridinolysis rates of both P=O and P=S systems.¹² Regarding the steric effects of the two ligands, the horizontal approach of the aniline ring should cause excessive steric hindrance in contrast to a much less steric effects in the vertical approach of the pyridine ring.^{10,12a}

The DKIEs are one of the strong tools to clarify the reaction mechanism. The DKIEs have provided a useful means to determine the TS structures in the nucleophilic substitution reactions, and how the reactants, especially through changes in substituents, alter the TS structures. Incorporation of deuterium in the nucleophile has an advantage in that the α -DKIEs reflect only the degree of bond formation. When partial deprotonation of the aniline occurs in a rate-limiting step by hydrogen bonding, the k_H/k_D values are greater than unity, primary normal ($k_H/k_D > 1.0$).¹³ The greater the extent of the hydrogen bond, the value of k_H/k_D becomes greater. In contrast, the DKIEs can only be secondary inverse ($k_H/k_D < 1.0$) in a normal S_N2 reaction, since the N–H(D) vibrational frequencies invariably increase upon going to the TS because of an increase in steric congestion in the bond-making process.¹⁴ The greater the degree of the steric congestion in the TS, the value of k_H/k_D becomes smaller.

The attacking direction of aniline nucleophile can be *semi*-quantitatively divided into three groups on the basis of the magnitudes of the k_H/k_D values: (i) predominant backside attack TSb (Scheme 2) when $k_H/k_D < 1$; (ii) the fraction of the frontside attack TSf (Scheme 2) is greater than that of backside attack TSb when $1.0 < k_H/k_D < 1.1$; (iii) predominant frontside attack TSf when $k_H/k_D > 1.1$.¹⁵

As seen in Table 2, the DKIEs of **1** ($k_H/k_D = 0.945$ -1.06)^{1g} are secondary inverse with the strongly basic anilines and primary normal with the weakly basic anilines, while those of **2** ($k_H/k_D = 1.01$ -1.10),^{1g} **3** ($k_H/k_D = 1.11$ -1.35), **4** ($k_H/k_D = 1.06$ -1.27)^{1f} and **5** ($k_H/k_D = 1.11$ -1.33)^{1c} are primary normal. The CICs are also one of the strong tools to clarify the reaction mechanism.¹¹ The negative values of ρ_{XY} imply that the anilinolyses of **4** and **5** proceed through a concerted S_N2

mechanism.¹¹ The authors accordingly proposed that the anilinolysis of **1** proceeds through a concerted mechanism and the attacking direction gradually changes from backside to frontside as the aniline changes from the strongly basic to weakly basic. A concerted mechanism was proposed for the anilinolysis of **2** in which the fraction of the frontside attack TSf is greater than that of backside attack TSb on the basis of $1.01 < k_H/k_D < 1.10$. A concerted mechanism involving predominant hydrogen-bonded, four-center-type TSf was proposed for the anilinolyses of **4** and **5** on the basis of the large primary normal DKIEs. In the present work, thus, the authors propose a concerted mechanism involving predominant hydrogen-bonded, four-center-type TSf on the basis of the primary normal DKIEs.

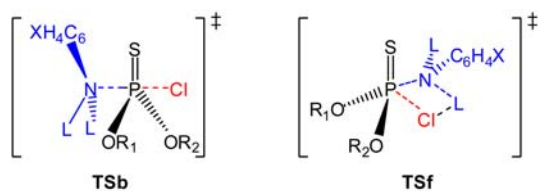
Experimental Section

Materials. Dipropyl chlorothiophosphate (commercially available) and HPLC grade acetonitrile (water content is less than 0.005%) were used for kinetic studies without further purification. Anilines were redistilled or recrystallized before use as previously described.¹ Deuterated anilines were synthesized by heating anilines and deuterium oxide (99.9 atom %D) and one drop of HCl as catalyst at 85 °C for 72 hours, and after numerous attempts, anilines were deuterated more than 98%, as confirmed by ¹H NMR.

Kinetic Procedure. Rates were measured conductometrically at 55.0 °C. The conductivity bridge used in this work was a self-made computer automated A/D converter conductivity bridge. Pseudo-first-order rate constants, k_{obsd} were measured by curve fitting analysis in origin program with a large excess of anilines, [Substrate] = 1×10^3 M and [X-Aniline] = (0.1-0.5) M. Second-order rate constants, k_2 , were obtained from the slope of a plot of k_{obsd} vs. [X-Aniline] with five concentrations of anilines. The k_{obsd} values were the average of three runs, which were reproducible within $\pm 3\%$.

Product Analysis. Dipropyl chlorothiophosphate was reacted with excess 4-methoxyaniline, for more than 15 half-lives at 55.0 °C in MeCN. The 4-methoxyaniline hydrochloride salt was separated by filtration. Acetonitrile was evaporated under reduced pressure. The product was isolated with ether by a work-up process and dried over anhydrous MgSO₄. After filtration the product was isolated by evaporating the solvent under reduced pressure. The analytical and spectroscopic data of the product after column chromatography (silica gel/20% ethyl acetate + *n*-hexane) were:

(PrO)₂P(=S)NHC₆H₄-4-OCH₃. Dark brown gummy-substance; ¹H NMR (400 MHz, CDCl₃) δ 0.87-0.90 (t, $J = 7.6$ Hz, 6H, 2 CH₃, Pr), 1.63-1.68 (m, 4H, 2 CH₂, Pr), 3.74 (s, 3H, OCH₃), 3.94 (d, $J = 6.8$ Hz, 2H, CH₂, Pr), 4.01 (d, $J = 6.8$ Hz, 2H, CH₂, Pr), 6.26 (s, 1H, NH), 6.77 (d, $J = 8.4$ Hz, 2H, phenyl), 6.95 (d, $J = 9.2$ Hz, 2H, phenyl); ¹³C NMR (100 MHz, CDCl₃) δ 10.01 (CH₃, Pr), 23.49 (CH₂, Pr), 55.46 (OCH₃), 68.10 (CH₂, Pr), 114.45, 118.85, 118.93, 132.88, 154.59 (C=C, aromatic); ³¹P NMR (162 MHz, CDCl₃) δ 8.25 (s, 1P, P=S); m/z , 303 (M⁺).



Scheme 2. Backside attack TSb and frontside attack TSf (L = H or D).

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References and Notes

- (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. (n) Barai, H. R.; Lee, H. W. *Bull. Korean Chem. Soc.* **2011**, *32*, 1939. (o) Hoque, M. E. U.; Lee, H. W. *Bull. Korean Chem. Soc.* **2011**, *32*, 1997. (p) Hoque, M. E. U.; Lee, H. W. *Bull. Korean Chem. Soc.* **2011**, *32*, 2306. (q) Adhikary, K. K.; Lumbiny, B. J.; Dey, S.; Lee, H. W. *Bull. Korean Chem. Soc.* **2011**, *32*, 2628. (r) Hoque, M. E. U.; Lee, H. W. *Bull. Korean Chem. Soc.* **2011**, *32*, 3245. (s) Barai, H. R.; Lee, H. W. *Bull. Korean Chem. Soc.* **2011**, *32*, 3355. (t) Barai, H. R.; Lee, H. W. *Bull. Korean Chem. Soc.* **2011**, *32*, 3783. (u) Hoque, M. E. U.; Lee, H. W. *Bull. Korean Chem. Soc.* **2011**, *32*, 3880.
- (a) Dunn, E. J.; Buncel, E. *Can. J. Chem.* **1989**, *67*, 1440. (b) Dunn, E. J.; Moir, R. Y.; Buncel, E.; Purdon, J. G.; Bannard, R. A. *Can. J. Chem.* **1990**, *68*, 1837. (c) Buncel, E.; Albright, K. G.; Onyido, I. *Org. Biomol. Chem.* **2004**, *2*, 601. (d) Onyido, I.; Albright, K.; Buncel, E. *Org. Biomol. Chem.* **2005**, *3*, 1468.
- (a) Williams, A.; Naylor, R. A. *J. Chem. Soc. B* **1971**, 1967. (b) Douglas K. T.; Williams, A. *J. Chem. Soc., Perkin Trans 2* **1976**, 515.
- Hehre, W. J.; Random, L.; Schleyer, P. V. R.; Pople, J. A. *Ab Initio Molecular Orbital Theory*; Wiley: New York, 1986; Chapter 4.
- (a) Ritchie, C. D. in *Solute-Solvent Interactions*, Coetzee, J. F., Ritchie, C. D., Ed.; Marcel Dekker: New York, 1969; Chapter 4. (b) Coetzee, J. F. *Prog. Phys. Org. Chem.* **1967**, *4*, 54. (c) Spillane, W. J.; Hogan, G.; McGrath, P.; King, J.; Brack, C. *J. Chem. Soc., Perkin Trans. 2* **1996**, 2099. (d) Oh, H. K.; Woo, S. Y.; Shin, C. H.; Park, Y. S.; Lee, I. *J. Org. Chem.* **1997**, *62*, 5780.
- (a) Perrin, C. I.; Engler, R. E. *J. Phys. Chem.* **1991**, *95*, 8431. (b) Perrin, C. I.; Ohta, B. K.; Kuperman, J. *J. Am. Chem. Soc.* **2003**, *125*, 15008. (c) Perrin, C. I.; Ohta, B. K.; Kuperman, J.; Liberman, J.; Erdelyi, M. *J. Am. Chem. Soc.* **2005**, *127*, 9641.
- Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165.
- (a) Streitwieser, A., Jr.; Heathcock, C. H.; Kosower, E. M. *Introduction to Organic Chemistry*, 4th ed.; Macmillan: New York, 1992; p 735. (b) The pK_a value of 4-fluoroaniline (4.5) was taken from Zeyer, J.; Wasserfallen, A.; Timmis, K. N. *App. Environ. Microbiol.* **1985**, *50*, 447.
- Crumpler, T. B.; Yoh, J. H. *Chemical Computations and Errors*; John Wiley: New York, 1940; p 178.
- (a) Taft, R. W. *Steric Effect in Organic Chemistry*, ed. Newman, M. S., Wiley: New York, 1956; Chapter 3. (b) Exner, O. *Correlation Analysis in Chemistry: Recent Advances*; Chapman, N. B., Shorter, J., Ed.; Plenum Press: New York, 1978; p 439.
- (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.
- (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. (m) Adhikary, K. K.; Lee, H. W. *Bull. Korean Chem. Soc.* **2011**, *32*, 1945. (n) Hoque, M. E. U.; Lee, H. W. *Bull. Korean Chem. Soc.* **2011**, *32*, 2109. (o) Barai, H. R.; Lee, H. W. *Bull. Korean Chem. Soc.* **2011**, *32*, 2339. (p) Hoque, M. E. U.; Lee, H. W. *Bull. Korean Chem. Soc.* **2011**, *32*, 2805. (q) Hoque, M. E. U.; Lee, H. W. *Bull. Korean Chem. Soc.* **2011**, *32*, 3505. (r) Adhikary, K. K.; Lumbiny, B. J.; Lee, H. W. *Bull. Korean Chem. Soc.* **2011**, *32*, 3743.
- (a) Lee, I.; Koh, H. J.; Lee, B. S.; Lee, H. W. *J. Chem. Soc., Chem. Commun.* **1990**, 335. (b) Lee, I. *Chem. Soc. Rev.* **1995**, *24*, 223. (c) Marlier, J. F. *Acc. Chem. Res.* **2001**, *34*, 283. (d) Westaway, K. C. *Adv. Phys. Org. Chem.* **2006**, *41*, 217. (e) Villano, S. M.; Kato, S.; Bierbaum, V. M. *J. Am. Chem. Soc.* **2006**, *128*, 736. (f) Gronert, S.; Fajin, A. E.; Wong, L. *J. Am. Chem. Soc.* **2007**, *129*, 5330.
- (a) Poirier, R. A.; Youliang, W.; Westaway, K. C. *J. Am. Chem. Soc.* **1994**, *116*, 2526. (b) Yamata, H.; Ando, T.; Nagase, S.; Hanamusa, M.; Morokuma, K. *J. Org. Chem.* **1984**, *49*, 631. (c) Xhao, X. G.; Tucker, S. C.; Truhlar, D. G. *J. Am. Chem. Soc.* **1991**, *113*, 826.
- This lab has cumulated data of DKIEs for the anilinolyses of various kinds of substrates in MeCN and DMSO.