

Kinetics and Mechanism of the Anilinolysis of Dipropyl Chlorophosphate in Acetonitrile

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The kinetic studies on the reactions of dipropyl chlorophosphate (**3O**) with substituted anilines ($\text{XC}_6\text{H}_4\text{NH}_2$) and deuterated anilines ($\text{XC}_6\text{H}_4\text{ND}_2$) have been carried out in acetonitrile at 55.0 °C. The obtained deuterium kinetic isotope effects (DKIEs; $k_{\text{H}}/k_{\text{D}}$) are primary normal ($k_{\text{H}}/k_{\text{D}} = 1.09\text{--}1.01$) with the strongly basic anilines while secondary inverse ($k_{\text{H}}/k_{\text{D}} = 0.74\text{--}0.82$) with the weakly basic anilines. The steric effects of the two ligands on the rates are extensively discussed for the anilinolyses of the $(\text{R}_1\text{O})(\text{R}_2\text{O})\text{P}(=\text{O})$ or $\text{S})\text{Cl}$ -type chlorophosphates and chlorothiophosphates. A concerted mechanism is proposed with a frontside nucleophilic attack involving a hydrogen-bonded four-center-type transition state for the strongly basic anilines and with a backside attack transition state for the weakly basic anilines on the basis of the DKIEs, primary normal and secondary inverse with the strongly and weakly basic anilines, respectively.

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

Introduction

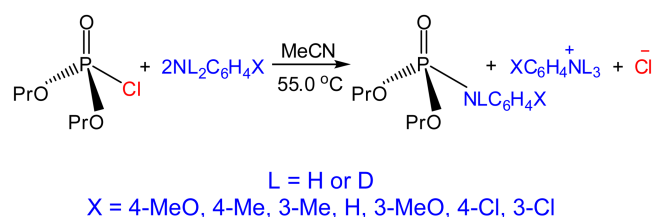
To extend the phosphoryl and thiophosphoryl transfer reactions of anilinolyses,¹ the kinetic studies on the reactions of dipropyl chlorophosphate (**3O**) with substituted anilines ($\text{XC}_6\text{H}_4\text{NH}_2$) and deuterated anilines ($\text{XC}_6\text{H}_4\text{ND}_2$) have been carried out in acetonitrile (MeCN) at 55.0 ± 0.1 °C (Scheme 1). The kinetic data of the present work are compared with those of the anilinolyses of $(\text{R}_1\text{O})(\text{R}_2\text{O})\text{P}(=\text{O})\text{Cl}$ -type chlorophosphates and $(\text{R}_1\text{O})(\text{R}_2\text{O})\text{P}(=\text{S})\text{Cl}$ -type chlorothiophosphates: dimethyl [**1O**: $(\text{MeO})_2\text{P}(=\text{O})\text{Cl}$],^{1g} diethyl [**2O**: $(\text{EtO})_2\text{P}(=\text{O})\text{Cl}$],^{1g} dibutyl [**4O**: $(\text{BuO})_2\text{P}(=\text{O})\text{Cl}$],^{1y} diisopropyl [**5O**: $(i\text{-PrO})_2\text{P}(=\text{O})\text{Cl}$],^{1r} Y-aryl ethyl [**6O**: $(\text{EtO})(\text{YC}_6\text{H}_4\text{O})\text{P}(=\text{O})\text{Cl}$],^{1f} and Y-aryl phenyl [**7O**: $(\text{PhO})(\text{YC}_6\text{H}_4\text{O})\text{P}(=\text{O})\text{Cl}$]^{1a} chlorophosphates; dimethyl [**1S**: $(\text{MeO})_2\text{P}(=\text{S})\text{Cl}$],^{1g} diethyl [**2S**: $(\text{EtO})_2\text{P}(=\text{S})\text{Cl}$],^{1g} dipropyl [**3S**: $(\text{PrO})_2\text{P}(=\text{S})\text{Cl}$],^{1x} dibutyl [**4S**: $(\text{BuO})_2\text{P}(=\text{S})\text{Cl}$],^{1z} Y-aryl ethyl [**6S**: $(\text{EtO})(\text{YC}_6\text{H}_4\text{O})\text{P}(=\text{S})\text{Cl}$],^{1f} and Y-aryl phenyl [**7S**: $(\text{PhO})(\text{YC}_6\text{H}_4\text{O})\text{P}(=\text{S})\text{Cl}$]^{1c} chlorothiophosphates in MeCN. The numbering of the substrates of **1**–**7** follows the sequence of the summation of the Taft's steric constants of the two ligands, R_1 and R_2 .² **O** and **S** represent the chlorophosphate ($\text{P}=\text{O}$ system) and chlorothiophosphate ($\text{P}=\text{S}$ system), respectively. The aim of this work is to examine: (i)

the anilinolysis rate difference between the chlorophosphates and chlorothiophosphates; and (ii) the steric effects of the two ligands on the anilinolysis rates of the chlorophosphates and chlorothiophosphates by means of the Taft's Eq.²

Results and Discussion

The B3LYP/6-311+G(d,p) geometry, bond angles, and natural bond order (NBO) charges of **3O** in the gas phase are shown in Figure 1.³ The MO theoretical structure shows that the three oxygens and chlorine have more or less distorted tetrahedral geometry with the phosphorus atom at the center. The largest and smallest tetrahedral bond angles are 118.3° and 100.3°, respectively. The ground state (GS) structure of **3O** in the gas phase does not have plane of symmetry although it has two same ligands of $(\text{PrO})_2$.

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 with at least five concentrations of anilines. The linear plots of Eq. (1) suggest that there is no base-catalysis or noticeable



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

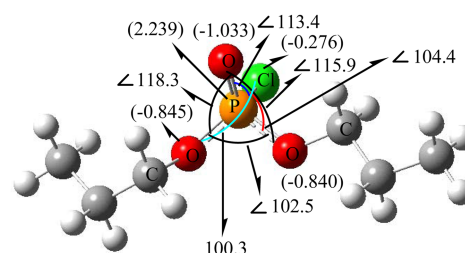


Figure 1. The B3LYP/6-311+G(d,p) geometry of dipropyl chlorophosphate (**3O**) in the gas phase.

Table 1. The Second-Order Rate Constants ($k_{\text{H(D)}} \times 10^3/\text{M}^{-1} \text{s}^{-1}$), Selectivity Parameters (ρ_{X} and β_{X}),^a and DKIEs ($k_{\text{H}}/k_{\text{D}}$) of the Reactions of Dipropyl Chlorophosphate (**30**) with $\text{XC}_6\text{H}_4\text{NH}_2(\text{D}_2)$ in MeCN at 55.0 °C

X	$k_{\text{H}} \times 10^3$	$k_{\text{D}} \times 10^3$	$k_{\text{H}}/k_{\text{D}}$
4-MeO	15.2 ± 0.1^b	13.9 ± 0.1	1.09 ± 0.01^g
4-Me	7.60 ± 0.03	7.18 ± 0.03	1.06 ± 0.01
3-Me	3.32 ± 0.01	3.28 ± 0.01	1.01 ± 0.01
H	2.12 ± 0.01	2.60 ± 0.01	0.815 ± 0.005
3-MeO	0.920 ± 0.004	1.18 ± 0.01	0.780 ± 0.007
4-Cl	0.428 ± 0.001	0.552 ± 0.002	0.775 ± 0.003
3-Cl	0.168 ± 0.001	0.228 ± 0.001	0.737 ± 0.005
$-\rho_{\text{X(H and D)}}$	3.06 ± 0.02^c	2.76 ± 0.03^e	
$\beta_{\text{X(H and D)}}$	1.08 ± 0.04^d	0.98 ± 0.03^f	

^aThe σ values were taken from ref. 6. The $\text{p}K_{\text{a}}$ values of X-anilines in water were taken from ref. 7. ^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. 8.

side reaction and that the overall reaction is described by Scheme 1.

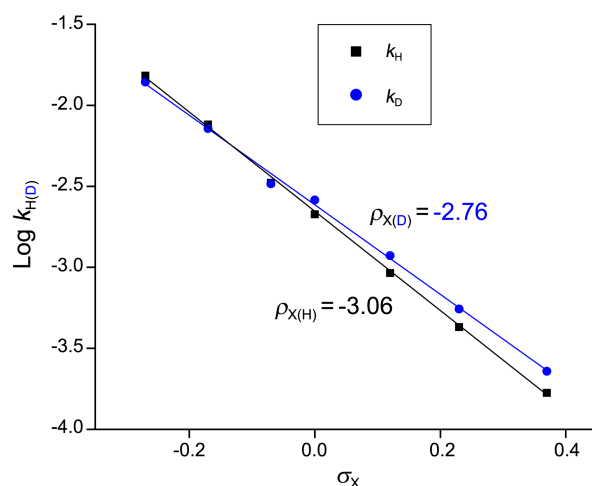
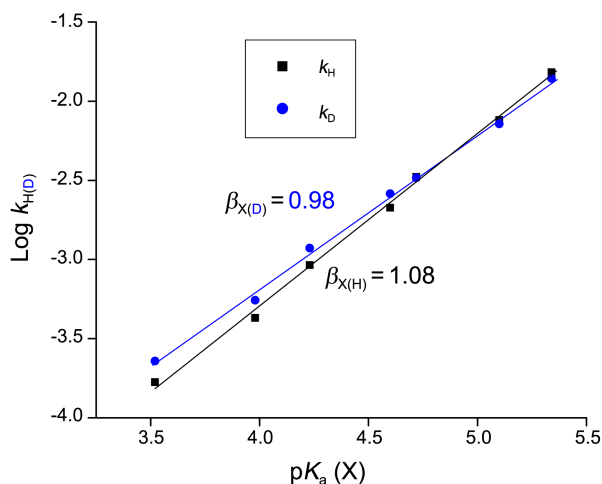
$$k_{\text{obsd}} = k_0 + k_{\text{H(D)}}[\text{XC}_6\text{H}_4\text{NH}_2(\text{D}_2)] \quad (1)$$

The second-order rate constants (k_{H} and k_{D}) are summarized in Table 1, together with the deuterium kinetic isotope effects (DKIEs; $k_{\text{H}}/k_{\text{D}}$) and 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.⁴ 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 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.⁵ 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 with X, respectively. The stronger nucleophile leads to the faster rate as observed in a typical nucleophilic substitution reaction with positive charge development at the nucleophilic N atom in the TS. The DKIEs are primary

Table 2. Summary of the Second-Order Rate Constants ($k_{\text{H}} \times 10^3/\text{M}^{-1} \text{s}^{-1}$) with $\text{C}_6\text{H}_5\text{NH}_2$ at 55.0 °C, 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 ($\beta_{\text{X(H)}}$), DKIEs ($k_{\text{H}}/k_{\text{D}}$), and CICs (ρ_{XY}) for the Reactions of **10-70** with $\text{XC}_6\text{H}_4\text{NH}_2(\text{D}_2)$ in MeCN

Substrate	$k_{\text{H}} \times 10^3^a$	Charge at P	$-\Sigma E_{\text{S}}^c$	$\beta_{\text{X(H)}}$	$k_{\text{H}}/k_{\text{D}}$	ρ_{XY}
10 : $(\text{MeO})_2\text{P}(=\text{O})\text{Cl}$	4.28	2.226	0.00	0.96	0.80-0.98	–
20 : $(\text{EtO})_2\text{P}(=\text{O})\text{Cl}$	2.82	2.236	0.14	1.06	0.71-0.92	–
30 : $(\text{PrO})_2\text{P}(=\text{O})\text{Cl}$	2.12	2.239	0.72	1.08	0.74-1.09	–
40 : $(\text{BuO})_2\text{P}(=\text{O})\text{Cl}$	2.06	2.239	0.78	1.11	0.86-1.10	–
50 : $(i\text{-PrO})_2\text{P}(=\text{O})\text{Cl}$	0.710	2.269	0.94	1.10	0.71-0.95	–
60 : $(\text{EtO})(\text{YC}_6\text{H}_4\text{O})\text{P}(=\text{O})\text{Cl}$	2.00^b	2.233^b	2.55	1.13	1.07-1.28	-0.60
70 : $(\text{PhO})(\text{YC}_6\text{H}_4\text{O})\text{P}(=\text{O})\text{Cl}$	0.891^b	2.230^b	4.96	1.24-1.68	0.61-0.87	-1.31

^aThe values with unsubstituted aniline at 55.0 °C. ^bThe values with Y = H. ^cNote 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.

**Figure 2.** The Hammett plots ($\log k_{\text{H(D)}} \text{ vs } \sigma_{\text{X}}$) of the reactions of dipropyl chlorophosphate (**30**) 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 chlorophosphate (**30**) with $\text{XC}_6\text{H}_4\text{NH}_2(\text{D}_2)$ in MeCN at 55.0 °C.

normal ($k_{\text{H}}/k_{\text{D}} = 1.01\text{-}1.09 > 1$) with more basic anilines (X = 4-MeO, 4-Me, and 3-Me) while secondary inverse ($k_{\text{H}}/k_{\text{D}} = 0.74\text{-}0.82 < 1$) with less basic anilines (X = H, 3-MeO, 4-Cl, and 3-Cl). The values of DKIEs invariably decrease as the aniline becomes less basic. The magnitudes of ρ_{X} and β_{X}

Table 3. Rate Ratios of the Anilinolyses of the P=O systems to their P=S Counterparts in MeCN at 55.0 °C and Differences of NBO Charge at P Atom between P=O and P=S Systems

	1(MeO,MeO)	2(EtO,EtO)	3(PrO,PrO)	4(BuO,BuO)	6(EtO,PhO)	7(PhO,PhO)
$[k_H(\mathbf{O}) \times 10^3]/$ $[k_H(\mathbf{S}) \times 10^3]$	4.28/1.09 = 3.9	2.82/0.512 = 5.5	2.12/0.300 = 7.1	2.06/0.322 = 6.4	2.00/0.280 = 7.1	0.891/0.101 = 8.8
Δ (charge at P)	2.226-1.687 = 0.539	2.236-1.701 = 0.535	2.239-1.702 = 0.537	2.239-1.703 = 0.536	2.233-1.687 = 0.546	2.230-1.661 = 0.569

values with anilines are slightly greater than those with deuterated anilines, suggesting more sensitive to substituent X effect of anilines compared to that of deuterated anilines.

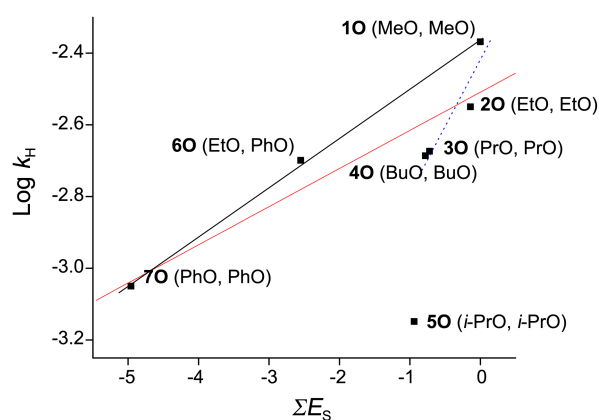
The second-order rate constants (k_H) with unsubstituted aniline ($C_6H_5NH_2$) at 55.0 °C, NBO charges at the reaction center P atom [B3LYP/6-311+G(d,p) level of theory] in the gas phase,³ summations of the Taft's steric constants of R_1 and R_2 [$\Sigma E_S = E_S(R_1) + E_S(R_2)$],² Brønsted coefficients ($\beta_{X(H)}$), DKIEs (k_H/k_D), and cross-interaction constants (CICs; ρ_{XY})⁹ of the reactions of **10-70** with $XC_6H_4NH_2(D_2)$ in MeCN are summarized in Table 2. The Brønsted coefficients ($\beta_{X(H)}$) are in the range of 1.0-1.1, when excluding **7**. There is no correlation between the second-order rate constant and positive charge at the reaction center P atom, implying 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 anilinolysis rates of the P=O systems (chlorophosphates) are 4-9 times faster than their P=S counterparts (chlorothiophosphates) as seen in Table 3. It is well known that the P=O systems are generally more reactive than their P=S counterparts for several reasons, the so-called 'thio effect', which is mainly the electronegativity difference between O and S and favors P=O over P=S.¹⁰ The differences of the NBO charges at the reaction center P atom between P=O and P=S systems are 0.54-0.57 in the gas phase.

The Taft's Eq. (2) can be used to rationalize the steric effects of the two ligands on the reaction rate where k_H is the second-order rate constant with $C_6H_5NH_2$, E_S is the Taft's steric constant [$E_S(R) = 0(\text{Me}); -0.07(\text{Et}); -0.36(\text{Pr}); -0.39(\text{Bu}); -0.47(i\text{-Pr}); -2.48(\text{Ph})$], ΣE_S is the summation of the steric constants of the two ligands, and δ is the sensitivity coefficient.²

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

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 for the anilinolyses of seven $(R_1O)(R_2O)P(=O)Cl$ -type chlorophosphates (**10-70**) in MeCN at 55.0 °C, according to Eq. (2). The substrate of **50** with two *i*-PrO ligands shows great negative deviation from the slope. The substrate **50** has not only the greatest magnitude of the positive charge at the reaction center P atom among seven chlorophosphates but also smaller size of the two ligands compared to **60** and **70**. These indicate that the anilinolysis rate of **50** is exceptionally slow to be rationalized by the conventional stereoelectronic effects.¹¹ At this point, the authors tentatively suggest that the exceptionally slow rate of the anilinolysis of **50** is attributed to an unexpected steric hindrance of the two *i*-PrO ligands

**Figure 4.** The plot of $\log k_H$ with unsubstituted aniline against ΣE_S for the anilinolyses of **10-70** in MeCN at 55.0 °C. The number of the substrate and two ligands are displayed next to the corresponding point.**Table 4.** Comparison of the Sensitivity Coefficients of δ depending on the group (A-D) for the Anilinolyses of Chlorophosphates with those of Chlorothiophosphates^a

Group	Substrates	δ
AO	10 (MeO,MeO), 60 (EtO,PhO), 70 (PhO,PhO)	0.14 (r = 0.999)
AS	1S (MeO,MeO), 6S (EtO,PhO), 7S (PhO,PhO)	0.21 (r = 0.998)
BO	10 (MeO,MeO), 20 (EtO,EtO), 60 (EtO,PhO), 70 (PhO,PhO)	0.12 (r = 0.967)
BS	1S (MeO,MeO), 2S (EtO,EtO), 6S (EtO,PhO), 7S (PhO,PhO)	0.18 (r = 0.959)
CO	10 (MeO,MeO), 20 (EtO,EtO), 30 (PrO,PrO), 40 (BuO,BuO), 60 (EtO,PhO), 70 (PhO,PhO)	0.11 (r = 0.909)
CS	1S (MeO,MeO), 2S (EtO,EtO), 3S (PrO,PrO), 4S (BuO,BuO), 6S (EtO,PhO), 7S (PhO,PhO)	0.16 (r = 0.878)
DO	10 (MeO,MeO), 20 (EtO,EtO), 30 (PrO,PrO), 40 (BuO,BuO)	0.34 (r = 0.928)
DS	1S (MeO,MeO), 2S (EtO,EtO), 3S (PrO,PrO), 4S (BuO,BuO)	0.59 (r = 0.908)

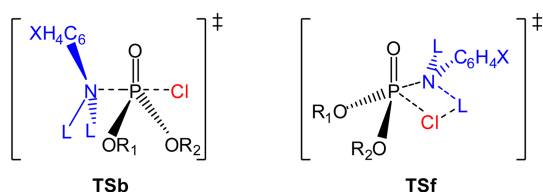
^aThe two ligands of R_1O and R_2O are displayed in parentheses.

which cannot be predicted by the Taft's ΣE_s . It should be noted that the value of ΣE_s is not ' $E_s(R_1O) + E_s(R_2O)$ ' but ' $E_s(R_1) + E_s(R_2)$ ' because of the lack of data of the Taft's steric constant of R_1O .

The sensitivity coefficients of δ with the groups (A-D) for the anilinolyses of **10(S)**-**40(S)**, **60(S)**, and **70(S)** are summarized in Table 4.¹¹ Note that the substrate of **50** (with two *i*-PrO ligands) is not considered in Table 3 because of exceptionally great negative deviation from the slope. It is evident that the anilinolysis rates of both chlorophosphate and chlorothiophosphate systems are predominantly dependent upon the steric effects over the inductive effects of the two ligands. The anilinolysis rate is inversely proportional to the size of the two ligands; the larger the two ligands, the anilinolysis rate becomes slower. The dependences of δ upon the two ligands of both chlorophosphate and chlorothiophosphate systems show quite similar trend; qualitatively with groups C and D, semi-quantitatively with group B, and quantitatively with group A. The δ values of all the groups with the P=S systems are *ca* 1.5 times greater than their P=O counterparts, indicating that the P=S systems are more sensitive to the steric effects of the two ligands compared to the P=O systems.

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 ($k_H/k_D > 1.0$).¹² 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.¹³ 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 involving a hydrogen-bonded four-center-type 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 $k_H/k_D > 1.1$.¹⁴



Scheme 2. Backside attack TSb and frontside attack TSf.

As seen in Table 2, (i) the DKIEs of **10** ($k_H/k_D = 0.80$ - 0.98),^{1g} **20** ($k_H/k_D = 0.71$ - 0.92),^{1g} **50** ($k_H/k_D = 0.71$ - 0.92),^{1r} and **70** ($k_H/k_D = 0.61$ - 0.87)^{1a} are secondary inverse; (ii) those of **40** are secondary inverse ($k_H/k_D = 0.86$ - 0.97) with the strongly basic anilines while primary normal ($k_H/k_D = 1.04$ - 1.10) with the weakly basic anilines;^{1y} (iii) those of **60** ($k_H/k_D = 1.07$ - 1.28) are primary normal.^{1f} In the present work of **30**, the DKIEs are primary normal ($k_H/k_D = 1.01$ - 1.09) with the strongly basic anilines (X = 4-MeO, 4-Me, 3-Me) while secondary inverse ($k_H/k_D = 0.74$ - 0.82) with the weakly basic anilines (X = H, 3-MeO, 4-Cl, 3-Cl). The authors accordingly propose the attacking direction of the aniline nucleophile: (i) predominant backside attack TSb for **10**, **20**, **50**, and **70**; (ii) predominant backside attack TSb with the strongly basic anilines and greater fraction of frontside attack TSf than that of backside attack TSb with the weakly basic anilines for **40**; (iii) predominant frontside attack TSf involving a hydrogen-bonded four-center-type TSf for **60**. In the present work of **30**, predominant backside attack TSb with the weakly basic anilines and greater frontside attack involving a hydrogen-bonded four-center-type TSf than that of backside attack TSb with the strongly basic anilines.

The CIC is also one of the strong tools to clarify the reaction mechanism.⁹ The sign of the CIC (ρ_{XY}) is negative in a normal S_N2 reaction (or in a stepwise reaction with a rate-limiting bond formation), and positive in a stepwise reaction with a rate-limiting leaving group expulsion from the intermediate. The magnitude of the CIC is inversely proportional to the distance between X and Y through the reaction center; the tighter the TS, the greater the magnitude of the CIC. Thus, the authors proposed that the anilinolyses of **60** and **70** proceed through a concerted mechanism on the basis of the negative sign of CIC, and the TS of **70** with $\rho_{XY} = -1.31$ is tighter than that of **60** with $\rho_{XY} = -0.60$.^{1a,f} The authors proposed that the anilinolyses of **10**, **20**, and **40** proceed through a concerted mechanism.^{1g,y} In the case of **50**, a stepwise mechanism with a rate-limiting bond breaking for the strongly basic anilines and with a rate-limiting bond formation for the weakly basic anilines were proposed.^{1r,y} In the present work of **30**, the authors propose a concerted S_N2 mechanism for both the strongly and weakly basic anilines regardless of the DKIEs, primary normal or secondary inverse and the attacking direction of the aniline gradually changes from a frontside involving a hydrogen-bonded four-center-type TSf with the strongly basic anilines to a backside with the weakly basic anilines.

Activation parameters, enthalpy and entropy of activation, are determined of the reaction of dipropyl chlorophosphate (**30**) with $C_6H_5NH_2$ in MeCN (Table S1). The relatively low of activation enthalpy ($6.3 \text{ kcal mol}^{-1}$) and large negative value of activation entropy ($-52 \text{ cal mol}^{-1} \text{ K}^{-1}$) obtained are typical for the aminolyses of P=O systems.

Experimental Section

Materials. Dipropyl chlorophosphate (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 in MeCN. 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] = (0.1-0.3) M. The pseudo-first-order rate constant values (k_{obsd}) were the average of at least three runs that were reproducible within $\pm 3\%$.

Product Analysis. Dipropyl chlorophosphate was reacted with excess aniline, for more than 15 half-lives at 55.0 °C in MeCN. The aniline 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 gave the following results (see supporting information including activation parameters):

(PrO)₂P(=O)NHC₆H₅. Orange-red liquid; ¹H NMR (400 MHz, CDCl₃) δ 0.84-0.96 (m, 6H, 2 CH₃, Pr), 1.63-1.72 (m, 4H, 2 CH₂, Pr), 3.90-3.99 (m, 2H, OCH₂, PrO), 4.02-4.10 (m, 2H, OCH₂, PrO), 6.30 (s, 1H, NH), 6.91-6.96 (t, $J = 8.4$ Hz, 1H, phenyl), 6.99-7.01 (d, $J = 8.4$ Hz, 2H, phenyl), 7.21-7.26 (t, $J = 8.0$ Hz, 2H, phenyl); ¹³C NMR (100 MHz, CDCl₃) δ 10.03 (CH₃, Pr), 23.48, 23.56 (CH₂, Pr), 68.18, 68.24 (OCH₂, PrO), 117.22, 117.29, 121.44, 129.18, 139.75 (C=C, aromatic); ³¹P NMR (162 MHz, CDCl₃) δ 8.15 (s, 1P, P=O); MS (EI) m/z (M⁺) calcd. 257.27, found 257.

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References and Notes

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- Fig. R1 shows the plot of $\log k_{\text{H}}$ with unsubstituted aniline (C₆H₅NH₂) against the summation of the Taft's steric constants of the two ligands for the anilinolyses of six (R₁O)(R₂O)P(=S)Cl-type chlorothiophosphates (**1S-4S**, **6S**, and **7S**) in MeCN at 55.0 °C, according to eq. (2).

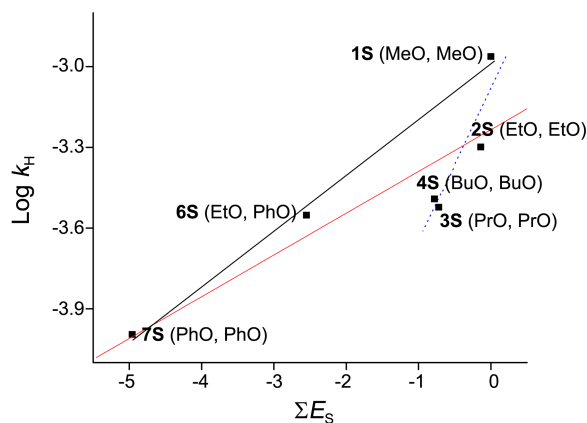


Figure R1. The plot of $\log k_{\text{H}}$ vs ΣE_s for the reactions of **1S-4S**, **6S**, and **7S** with C₆H₅NH₂ in MeCN at 55.0 °C.

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14. This lab has cumulated a lot of data of DKIEs for the anilinolyses of various kinds of substrates in MeCN and DMSO.
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