

Kinetics and Mechanism of Anilinolysis of Phenyl *N*-Phenyl Phosphoramidochloridate in Acetonitrile

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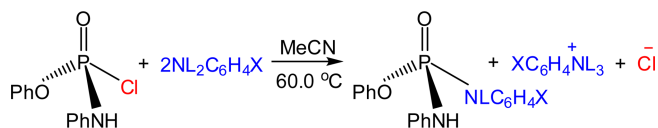
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The kinetic studies on the reactions of phenyl *N*-phenyl phosphoramidochloridate (**8**) with substituted anilines (XC₆H₄NH₂) and deuterated anilines (XC₆H₄ND₂) have been carried out in acetonitrile at 60.0 °C. The obtained deuterium kinetic isotope effects (DKIEs; k_H/k_D) are huge secondary inverse ($k_H/k_D = 0.52$ - 0.69). A concerted mechanism is proposed with a backside attack transition state (TS) on the basis of the secondary inverse DKIEs and the variation trends of the k_H/k_D values with X. The degree of bond formation in the TS is really extensive taking into account the very small values of the DKIEs. The steric effects of the two ligands on the rates are extensively discussed for the aminolyses of the chlorophosphate-type substrates on the basis of the Taft equation.

Key Words : Phosphoryl transfer reaction, Anilinolysis, Phenyl *N*-phenyl phosphoramidochloridate, Deuterium kinetic isotope effect, Steric effect

Introduction

To extend the phosphoryl and thiophosphoryl transfer reactions of anilinolyses, the kinetic studies on the reactions of phenyl *N*-phenyl phosphoramidochloridate (**8**), involving anilino (C₆H₅NH) ligand, with substituted anilines (XC₆H₄NH₂) and deuterated anilines (XC₆H₄ND₂) have been carried out in acetonitrile (MeCN) at 60.0 ± 0.1 °C (Scheme 1). The kinetic data of the present work are compared with those of the anilinolyses of (R₁O)(R₂O)P(=O)Cl-type chlorophosphates: dimethyl [**1**: (MeO)₂P(=O)Cl],^{1a} diethyl [**2**: (EtO)₂P(=O)Cl],^{1a} dipropyl [**3**: (PrO)₂P(=O)Cl],^{1b} dibutyl [**4**: (BuO)₂P(=O)Cl],^{1c} diisopropyl [**5**: (*i*-PrO)₂P(=O)Cl],^{1d} Y-aryl ethyl [**6**: (EtO)(YC₆H₄O)P(=O)Cl],^{1e} and Y-aryl phenyl [**7**: (PhO)(YC₆H₄O)P(=O)Cl]^{1f} chlorophosphates in MeCN. The steric effects of the two ligands on the anilinolysis rates of the eight substrates (**1-8**) are discussed by means of the Taft eq.² The numbering of the substrates of **1-8** follows the sequence of the summation of the Taft steric constants of the two ligands, R₁ and R₂.²



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

Scheme 1. The anilinolysis of phenyl *N*-phenyl phosphoramidochloridate (**8**) in MeCN at 60.0 °C.

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 with at least five concentrations of anilines. The linear plots of Eq. (1) suggest that there is no base-catalysis or noticeable 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_H/k_D) and Hammett ρ_X and Brønsted β_X selectivity parameters. The $\text{p}K_a(\text{X})$ 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.³ The values of $\text{p}K_a(\text{X})$ and σ_X of the deuterated

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_H/k_D) of the Reactions of Phenyl *N*-Phenyl Phosphoramidochloridate (**8**) with XC₆H₄NH₂(D₂) in MeCN at 60.0 °C

X	$k_H \times 10^4$	$k_D \times 10^4$	k_H/k_D
4-MeO	5.50 ± 0.03 ^b	7.92 ± 0.02	0.694 ± 0.004 ^g
4-Me	3.06 ± 0.01	4.60 ± 0.04	0.665 ± 0.006
3-Me	1.48 ± 0.01	2.42 ± 0.01	0.612 ± 0.005
H	1.03 ± 0.01	1.73 ± 0.01	0.595 ± 0.007
4-F	0.780 ± 0.004	1.38 ± 0.01	0.565 ± 0.005
4-Cl	0.273 ± 0.003	0.521 ± 0.004	0.524 ± 0.007
3-Cl	0.115 ± 0.001	0.223 ± 0.001	0.516 ± 0.005
$-\rho_{\text{X(H and D)}}$	2.61 ± 0.02 ^c	2.39 ± 0.02 ^e	
$\beta_{\text{X(H and D)}}$	0.93 ± 0.03 ^d	0.85 ± 0.02 ^f	

^aThe σ values were taken from ref. 6. The $\text{p}K_a$ 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 $\{= 1/k_D[(\Delta k_H)^2 + (k_H/k_D)^2 \times (\Delta k_D)^2]^{1/2}\}$ from ref. 8.

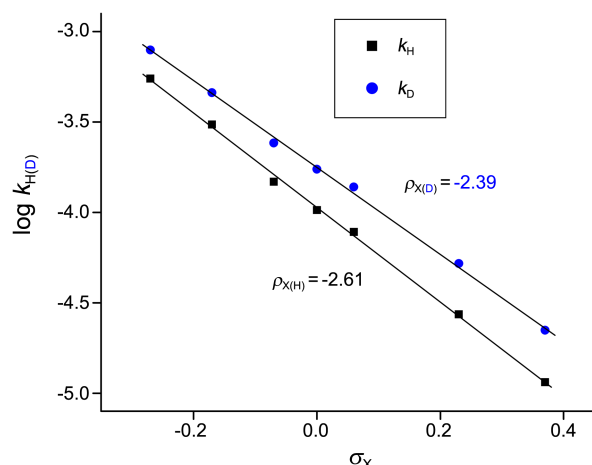


Figure 1. The Hammett plots ($\log k_{\text{H(D)}} \text{ vs } \sigma_{\text{X}}$) of the reactions of phenyl *N*-phenyl phosphoramidochloridate (**8**) with $\text{XC}_6\text{H}_4\text{NH}_2$ (D_2) in MeCN at 60.0 °C.

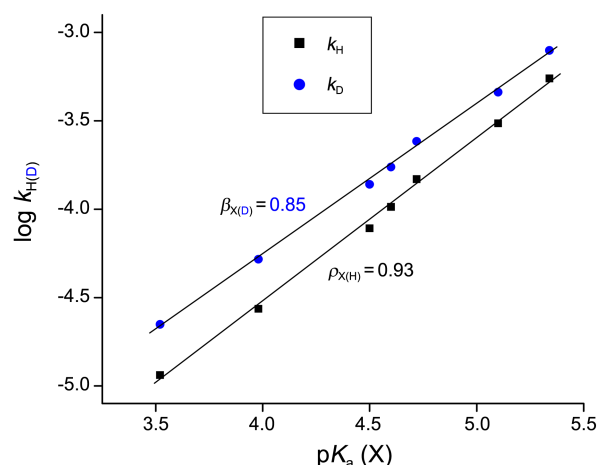


Figure 2. The Brønsted plots [$\log k_{\text{H(D)}} \text{ vs } \text{p}K_{\text{a}}(\text{X})$] of the reactions of phenyl *N*-phenyl phosphoramidochloridate (**8**) with $\text{XC}_6\text{H}_4\text{NH}_2$ (D_2) in MeCN at 60.0 °C.

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.⁴ 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 obtained DKIEs are the largest secondary inverse ($k_{\text{H}}/k_{\text{D}} = 0.52\text{--}0.69 < 1$) for the P=O systems, observed in this lab.⁵ The values of DKIEs invariably decrease as the aniline becomes less basic. The magnitudes of ρ_{X} and β_{X} values with anilines are slightly greater than those with deuterated anilines, suggesting more sensitive to substituent X effects of anilines compared to those of deuterated anilines.

The second-order rate constants (k_{H}) with unsubstituted aniline ($\text{C}_6\text{H}_5\text{NH}_2$) 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,¹⁰ summations of the Taft steric constants of R_1 and R_2 [$\Sigma E_{\text{S}} = E_{\text{S}}(\text{R}_1) + E_{\text{S}}(\text{R}_2)$],² Brønsted coefficients ($\beta_{\text{X(H)}}$ and $\beta_{\text{X(D)}}$), DKIEs ($k_{\text{H}}/k_{\text{D}}$), and cross-interaction constants (CICs; ρ_{XY})¹¹ of the reactions of **1-8** with $\text{XC}_6\text{H}_4\text{NH}_2(\text{D}_2)$ in MeCN are summarized in Table 2. The Brønsted coefficients ($\beta_{\text{X(H)}}$) are in the range of 1.0-1.2, when excluding **7**. There is no correlation between the second-order rate constant (k_{H} with $\text{C}_6\text{H}_5\text{NH}_2$) and positive (NBO) charge at the reaction center P atom in MeCN at 55.0 °C as seen in Figure 3, implying that the inductive effects of the two ligands do not play any role to decide the reactivity of anilinolyses of **1-8**.

The Taft 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 $\text{C}_6\text{H}_5\text{NH}_2$, E_{S} is the Taft steric constant [$E_{\text{S}}(\text{R}) = 0(\text{Me}); -0.07(\text{Et}); -0.36(\text{Pr}); -0.39(\text{Bu}); -0.47(i\text{-Pr}); -2.48(\text{Ph})$], ΣE_{S} is the summation of the steric constants of the two ligands, and δ is the sensitivity coefficient.²

$$\log k_{\text{H}} = \delta \Sigma E_{\text{S}} + C \quad (2)$$

Figure 4 shows the Taft plot of $\log k_{\text{H}}$ with unsubstituted aniline ($\text{C}_6\text{H}_5\text{NH}_2$) against the summation of the Taft steric constants of the two ligands for the anilinolyses of eight (**1-**

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 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 **1-8** with $\text{XC}_6\text{H}_4\text{NH}_2(\text{D}_2)$ in MeCN

Substrate	$k_{\text{H}} \times 10^{3a}$	Charge at P	$-\Sigma E_{\text{S}}^d$	$\beta_{\text{X(H)}}$	$k_{\text{H}}/k_{\text{D}}$	ρ_{XY}
1: $(\text{MeO})_2\text{P}(=\text{O})\text{Cl}$	4.28	2.226	0.00	0.96	0.80-0.98	–
2: $(\text{EtO})_2\text{P}(=\text{O})\text{Cl}$	2.82	2.236	0.14	1.06	0.71-0.92	–
3: $(\text{PrO})_2\text{P}(=\text{O})\text{Cl}$	2.12	2.239	0.72	1.08	0.74-1.09	–
4: $(\text{BuO})_2\text{P}(=\text{O})\text{Cl}$	2.06	2.239	0.78	1.11	0.86-1.10	–
5: $(i\text{-PrO})_2\text{P}(=\text{O})\text{Cl}$	0.710	2.269	0.94	1.10	0.71-0.95	–
6: $(\text{EtO})(\text{YC}_6\text{H}_4\text{O})\text{P}(=\text{O})\text{Cl}$	2.00 ^b	2.233 ^b	2.55	1.09-1.20	1.07-1.28	-0.60
7: $(\text{PhO})(\text{YC}_6\text{H}_4\text{O})\text{P}(=\text{O})\text{Cl}$	0.891 ^b	2.230 ^b	4.96	1.24-1.68	0.61-0.87	-1.31
8: $(\text{PhO})(\text{PhNH})\text{P}(=\text{O})\text{Cl}$	0.0674 ^c	2.176	4.98 ^e	0.93	0.52-0.69	–

^aThe values with unsubstituted aniline at 55.0 °C. ^bThe values with Y = H. ^cExperimental value at 55.0 °C. ^dNote 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 steric constants of R_iO are not available. ^eSee ref. 9.

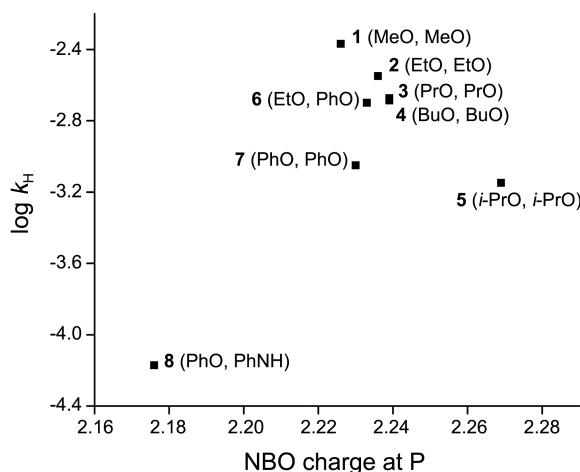


Figure 3. The plot of $\log k_H$ with unsubstituted aniline against NBO charge at the reaction center P atom in the substrate for the anilinolyses of **1-8** in MeCN at 55.0 °C. The number of the substrate and two ligands are displayed next to the corresponding point.

8) substrates in MeCN at 55.0 °C, according to Eq. (2). The anilinolysis rates of **1-4** and **6-8** (excluding **5**) are very roughly dependent upon the steric effects of the two ligands and the rate is inversely proportional to the size of the two ligands. The pyridinolysis rates of **1-4** and **8** are also qualitatively dependent upon the steric effects of the two ligands (see Fig. R1).^{12,13} The anilinolyses of **6** with ethoxy and phenoxy ligands and **7** with two phenoxy ligands show great positive deviations from the plot. The pyridinolysis of **7** also shows exceptionally great positive deviation from the plot.^{12a,13} On the contrary, the anilinolysis of **5** with two *i*-PrO ligands shows great negative deviation from the plot. The substrate of **5** has not only the greatest magnitude of the positive charge at the reaction center P atom among eight substrates but also smaller size of the two ligands compared to **6-8**. These indicate that the anilinolysis rate of **5** is exceptionally slow to be rationalized by the conventional stereoelectronic effects. The pyridinolysis of **5** also shows great negative deviation from the plot.^{12c,13} At this point, the authors tentatively suggest that the exceptionally slow rates of the anilinolysis and pyridinolysis of **5** are attributed to an unexpected steric hindrance of the two *i*-PrO ligands which cannot be predicted by the Taft ΣE_s . The sensitivity coefficient for the anilinolyses of five substrates of **1-4** and **8** gives $\delta = 0.35$ with $r = 0.998$, while that for the pyridinolyses of five substrates of **1-4** and **8** gave $\delta = 0.14$ with $r = 0.963$.¹³ The steric effects of the two ligands on the anilinolysis rates are much greater than those on the pyridinolysis rates. 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 steric constant of R_iO .

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.

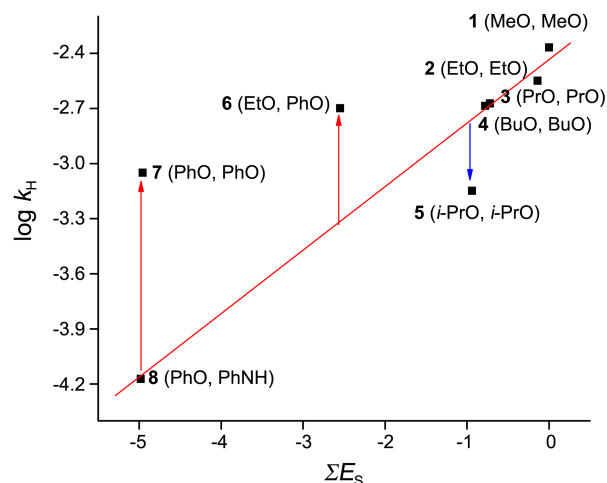
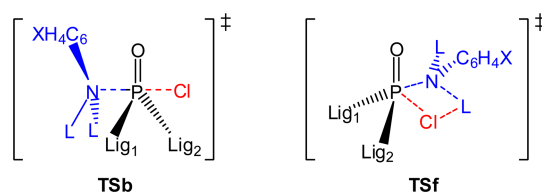


Figure 4. The Taft plot of $\log k_H$ with unsubstituted aniline against ΣE_s for the anilinolyses of **1-8** in MeCN at 55.0 °C. The number of the substrate and two ligands are displayed next to the corresponding point.

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 ($k_H/k_D > 1.0$).¹⁴ 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.¹⁵ The greater the degree of the steric congestion in the TS, the value of k_H/k_D becomes smaller.

Thus, 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 involving a hydrogen-bonded four-center-type TSf when $k_H/k_D > 1.1$.¹⁶

The DKIEs of the anilinolyses of **1-8** are as follows: (i) secondary inverse for **1** ($k_H/k_D = 0.80-0.98$),^{1a} **2** ($k_H/k_D = 0.71-0.92$),^{1a} **5** ($k_H/k_D = 0.71-0.92$),^{1d} **7** ($k_H/k_D = 0.61-0.87$)^{1f} and **8** ($k_H/k_D = 0.52-0.69$); (ii) primary normal ($k_H/k_D = 1.01-1.09$) with the strongly basic anilines while secondary



Scheme 2. Backside attack TSb and frontside attack TSf for the anilinolyses of chlorophosphates. The two ligands are denoted as Lig₁ and Lig₂.

inverse ($k_H/k_D = 0.74-0.82$) with the weakly basic anilines for **3**;^{1b} (iii) 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 for **4**;^{1c} and (iv) primary normal ($k_H/k_D = 1.07-1.28$) for **6**.^{1c} The authors accordingly propose the attacking direction of the aniline nucleophile: (i) predominant backside attack TSb for **1**, **2**, **5**, **7**, and **8**; (ii) predominant backside attack TSb with the weakly basic anilines and grater frontside attack involving a hydrogen-bonded four-center-type TSf than that of backside attack TSb with the strongly basic anilines for **3**; (iii) predominant backside attack TSb with the strongly basic anilines and grater fraction of frontside attack TSf than that of backside attack TSb with the weakly basic anilines for **4**; (iv) predominant frontside attack involving a hydrogen-bonded four-center-type TSf for **6**.

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 **6** and **7** proceed through a concerted mechanism on the basis of the negative sign of CIC, and the TS of **7** with $\rho_{XY} = -1.31$ ^{1f} is tighter than that of **6** with $\rho_{XY} = -0.60$.^{1c} The authors proposed that the anilinolyses of **1**, **2**, **3**, and **4** proceed through a concerted mechanism.^{1a-c} In the case of **5**, 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 on the basis of the variation trends of the values of DKIEs with X.^{1d,17} In the present work of **8**, the authors propose a concerted S_N2 mechanism on the basis of the variation trends of the values of DKIEs with X,¹⁷ and the degree of bond formation in the TS is very extensively taking into account the considerably small values, *i.e.*, huge secondary inverse DKIEs, of $k_H/k_D = 0.52-0.69$.

Activation parameters, enthalpy and entropy of activation, are determined of the reaction of phenyl *N*-phenyl phosphoramidochloridate with $C_6H_5NH_2$ in MeCN (Table S1). The activation enthalpy ($16.0 \text{ kcal mol}^{-1}$) is greater than those ($2-10 \text{ kcal mol}^{-1}$) for typical aminolyses of P=O systems while the magnitude of activation entropy ($-29 \text{ cal mol}^{-1} \text{ K}^{-1}$) is smaller than those (-40 to $-70 \text{ cal mol}^{-1} \text{ K}^{-1}$) for typical aminolyses of P=O systems. This may be ascribed to the greater degree of bond formation of the present work compared to typical P=O systems.

Experimental Section

Materials. Phenyl *N*-phenyl phosphoramidochloridate (99%) and HPLC grade acetonitrile (water content is less than 0.005%) were used 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 $85 \text{ }^\circ\text{C}$ for 72 hr, and after numerous attempts, anilines were deuterated more than 98%, as confirmed by $^1\text{H-NMR}$, $^2\text{D-NMR}$, and GC-MS comparing 4-chloroaniline with deuterated 4-chloroaniline ($4\text{-Cl-C}_6\text{H}_4\text{ND}_2$) (see supporting information).

Kinetic Procedure. Rates were measured conductometrically at $60.0 \text{ }^\circ\text{C}$. 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, $[\text{substrate}] = 1 \times 10^{-3} \text{ M}$ and $[\text{X-aniline}] = (0.1-0.5) \text{ M}$. Second-order rate constants, k_2 , were obtained from the slope of a plot of k_{obsd} vs. $[\text{X-aniline}]$ with at least five concentrations of anilines. 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. Phenyl *N*-phenyl phosphoramidochloridate was reacted with excess 4-methoxyaniline, for more than 15 half-lives at $60.0 \text{ }^\circ\text{C}$ 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 MgSO_4 . 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):

(PhO)(NHPh)P(=O)NHC₆H₄-4-CH₃O: Dark brown solid, mp $160-162 \text{ }^\circ\text{C}$; $^1\text{H NMR}$ (400 MHz , CDCl_3) δ 3.74 (s, 3H, OCH₃), 5.58 (s, 1H, NH), 5.78 (s, 1H, NH), 6.76-6.79 (d, $J = 8.4 \text{ Hz}$, 2H, phenyl), 6.96-7.04 (t, $J = 8.8 \text{ Hz}$, 3H, phenyl), 7.07-7.09 (d, $J = 8.4 \text{ Hz}$, 2H, phenyl), 7.18-7.31 (m, 7H, phenyl); $^{13}\text{C NMR}$ (100 MHz , CDCl_3) δ 55.68 (OCH₃), 114.81, 118.53, 120.76, 120.80, 121.42, 122.58, 125.34, 129.55, 129.93 (C=C, aromatic); $^{31}\text{P NMR}$ (162 MHz , CDCl_3) δ 3.81 (s, 1P, P=O); MS (ESI) m/z 354 (M^+).

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5. The largest secondary inverse DKIE ($k_{iV}/k_D = 0.37$) was obtained for the P=S system in this lab; the anilinolysis of *O*-aryl methyl phosphonochloridothioate [Me(YC₆H₄O)P(=S)Cl] with X = 4-Cl and Y = 4-CN in MeCN at 55.0 °C: Hoque, E. M. U.; Guha, A. K.; Kim, C. K.; Lee, B. S.; Lee, H. W. *Org. Biomol. Chem.* **2009**, *7*, 2919.
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13. Fig. R1 shows the Taft plot of $\log k_{\text{pyr}}$ with unsubstituted pyridine (C₅H₅N) against the summation of the Taft steric constants of the two ligands for the pyridinolyses of seven substrates of **1-5**, **7**, and **8** in MeCN at 35.0 °C.

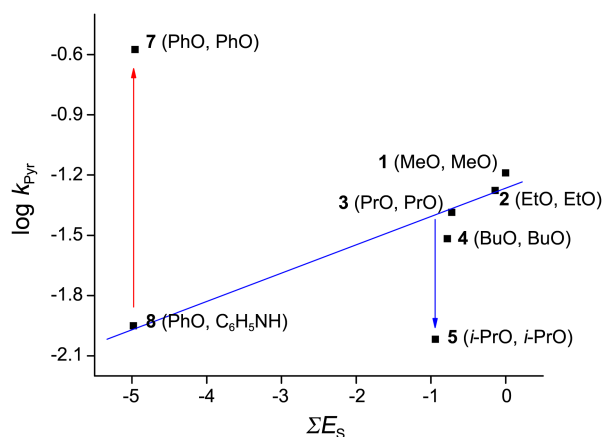


Figure R1. The Taft plot of $\log k_{\text{pyr}}$ vs ΣE_S for the reactions of **1-5**, **7**, and **8** with C₅H₅N in MeCN at 35.0 °C.

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16. This lab has cumulated a lot of data of DKIEs for the anilinolyses of various kinds of substrates in MeCN and DMSO.
17. The values of the secondary inverse DKIEs with X of **1**, **2**, **3**, **4**, **7**, and **8** invariably decrease as the aniline becomes weaker. However, the values of the secondary inverse DKIEs with X of **5** invariably increase and then invariably decrease as the aniline becomes weaker. The values of the primary normal DKIEs with X of **3**, **4** and **6** invariably increase as the aniline becomes weaker.