Kinetics and Mechanism of the Anilinolysis of Diethyl Thiophosphinic Chloride in Acetonitrile

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The nucleophilic substitution reactions of diethyl thiophosphinic chloride with substituted anilines ($XC_6H_4NH_2$) and deuterated anilines ($XC_6H_4ND_2$) are investigated kinetically in acetonitrile at 55.0 °C. The values of deuterium kinetic isotope effects (DKIEs; k_H/k_D) invariably increase from secondary inverse ($k_H/k_D < 1$) to primary normal ($k_H/k_D > 1$) as the nucleophiles change from the strongly basic to weakly basic anilines. The secondary inverse with the strongly basic anilines and primary normal DKIEs with the weakly basic anilines are rationalized by the gradual transition state (TS) variation from a predominant backside attack, via invariably increasing the fraction of a frontside attack, to a predominant frontside attack, in which the reaction mechanism is a concerted S_N2 pathway. A frontside attack involving a hydrogen bonded, four-center-type TS is substantiated by the primary normal DKIEs.

Introduction

Phosphoryl and thiophosphoryl transfer reactions have been studied extensively because of an important class of reaction regarding biological chemistry and usefulness of synthesis. The authors investigated various types of phosphoryl and thiophosphoryl transfer reactions experimentally (anilinolysis,[1] pyridinolysis,[2] and benzylaminolysis[3]) and theoretically.[4] In the present work, the nucleophilic substitution reactions of diethyl thiophosphinic chloride [**2S**; $Et_2P(=S)Cl$] with substituted anilines ($XC_6H_4NH_2$) and deuterated anilines ($XC_6H_4ND_2$) are investigated kinetically in acetonitrile at 55.0 ± 0.1 °C (Scheme 1). The goal of this work is to gain further systematic information into the phosphoryl and thiophosphoryl transfer reactions, as well as to compare the reaction mechanism, stereoelectronic effects of the two ligands, and deuterium kinetic isotope effects (DKIEs; k_H/k_D) of the anilinolyses of dimethyl [**1S**; $Me_2P(=S)Cl$][1j] and diphenyl [**4S**; $Ph_2P(=S)Cl$][1e] thiophosphinic chlorides. The kinetic results of the anilinolyses of their P=O counterparts, dimethyl [**1O**; $Me_2P(=O)Cl$],[1i] diethyl [**2O**; $Et_2P(=O)Cl$],[1l] methyl phenyl [**3O**; $MePhP(=O)Cl$],[1i] and diphenyl [**4O**; $Ph_2P(=O)Cl$][1d] phosphinic chlorides in MeCN are also discussed, together with those (solvolyses and anilinolyses) of the three phosphinates, dimethyl [**1Z**; $Me_2P(=O)OC_6H_4Z$], methyl phenyl [**3Z**; $MePhP(=O)OC_6H_4Z$], and diphenyl [**4Z**; $Ph_2P(=O)OC_6H_4Z$] phosphinates.[1m] The sequence of the substrate number follows the size of the two ligands, R_1 and R_2, as follows: number of the substrate (R_1,R_2); **1S**, **1O**, and **1Z** (Me,Me), **2S** and **2O** (Et,Et), **3O** and **3Z** (Me,Ph), and **4S**, **4O**, and **4Z** (Ph,Ph).

Results and Discussion

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

$$k_{obsd} = k_0 + k_{H(D)}[XC_6H_4NH_2(D_2)] \tag{1}$$

The k_H and k_D values are summarized in Table 1, together with the DKIEs (k_H/k_D) and the Hammett ρ_X and Brönsted β_X coefficients. The pK_a values of the anilines in water are used to obtain the Brönsted β_X values in MeCN, and this procedure was justified experimentally and theoretically.[5] The pK_a and σ values of the deuterated anilines are assumed to be identical to those of the anilines. The pK_a value of deuterated X-aniline may be slightly greater than that of X-aniline, however, the difference is too small to be taken into account.[6] Figures 1 and 2 show the Hammett (log k_2 *vs* σ_X) and Brönsted [log k_2 *vs* pK_a(X)] plots, respectively. The stronger nucleophile leads to the faster rate as observed in a typical nucleophilic substitution reaction. The magnitudes of the ρ_X and σ_X values of the reactions of **2S** with the
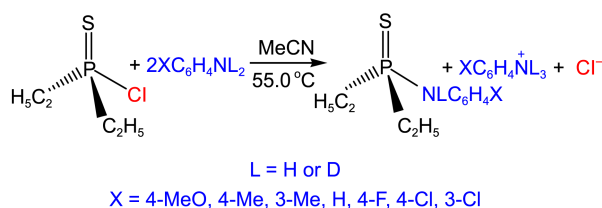
Scheme 1. The studied reaction system.

Table 1. The Second-Order Rate Constants ($k_{H(D)} \times 10^4$/M^{-1} s^{-1}), Selectivity Parameters (ρ_X and β_X),[a] and DKIEs (k_H/k_D) of the Reactions of **2S** (Diethyl Thiophosphinic Chloride) with XC$_6$H$_4$NH$_2$(D$_2$) in MeCN at 55.0 °C

X	$k_H \times 10^4$/M^{-1} s^{-1}	$k_D \times 10^4$/M^{-1} s^{-1}	k_H/k_D
4-MeO	28.2 ± 0.3[b]	31.4 ± 0.2	0.898 ± 0.011[i]
4-Me	12.5 ± 0.1	13.2 ± 0.1	0.947 ± 0.010
3-Me	5.28 ± 0.05	5.38 ± 0.03	0.981 ± 0.011
H	3.30 ± 0.03	2.79 ± 0.03	1.18 ± 0.02
4-F	3.12 ± 0.03	2.46 ± 0.02	1.27 ± 0.02
4-Cl	0.702 ± 0.006	0.525 ± 0.005	1.34 ± 0.02
3-Cl	0.249 ± 0.002	0.182 ± 0.002	1.37 ± 0.02
$-\rho_X$	3.14 ± 0.07[c,d]	3.46 ± 0.05[f,g]	
β_X	1.12 ± 0.06[c,e]	1.22 ± 0.10[f,h]	

[a]The σ values were taken from Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165. The pK_a values of X-anilines in water were taken from Streitwieser, A. Jr.; Heathcock, C. H.; Kosower, E. M. *Introduction to Organic Chemistry*, 4th ed.; Macmillan: New York, 1992; p 735. [b]Standard deviation. [c]Calculated from k_H. [d]Correlation coefficient, r = 0.996. [e]r = 0.996. [f]Calculated from k_D. [g]r = 0.998. [h]r = 0.992. [i]Standard error $\{= 1/k_D[(\Delta k_H)^2 + (k_H/k_D)^2 \times (\Delta k_D)^2]^{1/2}\}$ from Crumpler, T. B.; Yoh, J. H. *Chemical Computations and Errors*; John Wiley: New York, 1940; p 178.

deuterated anilines are somewhat greater than those with the anilines, suggesting more sensitivity to substituent effects of the deuterated anilines compared to anilines, opposite to the other anilinolyses of phosphinic and thiophosphinic chlorides (see Table 2). The values of DKIEs (k_H/k_D) invariably increase from secondary inverse (k_H/k_D < 1) to primary normal (k_H/k_D > 1) as the nucleophiles change from the strongly to weakly basic anilines.

The second-order rate constants (k_H) with unsubstituted aniline at 55.0 °C, summary of summations of inductive effects of the two ligands [$\Sigma\sigma_I = \sigma_I(R_1) + \sigma_I(R_2)$],[7] the natural bond order (NBO) charges at the reaction center P atom in the gas phase [B3LYP/6-311+G(d,p) level of theory],[8] summations of the Taft's steric constants of the two ligands [$\Sigma E_S = E_S(R_1) + E_S(R_2)$],[9] Brönsted coefficient $\beta_{X(H)}$ and $\beta_{X(D)}$, and DKIEs (k_H/k_D) of the reactions of **1S**, **2S**, **4S** (P=S systems),
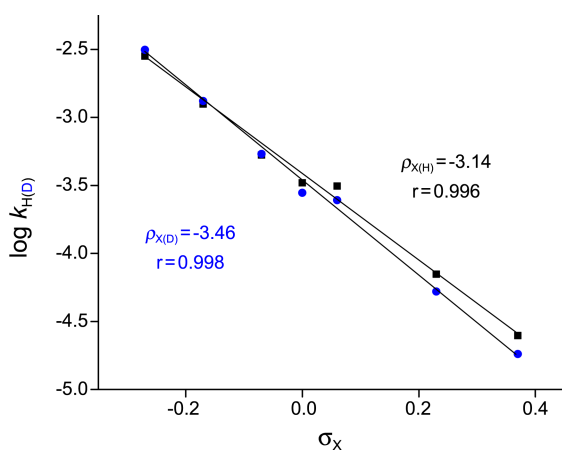
Figure 1. The Hammett plots (log $k_{H(D)}$ *vs* σ_X) of the reactions of **2S** (diethyl thiophosphinic chloride) with XC$_6$H$_4$NH$_2$(D$_2$) in MeCN at 55.0 °C.
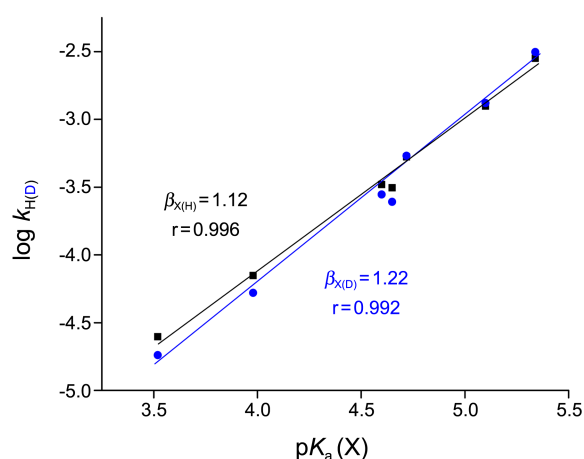
Figure 2. The Brönsted plots [log $k_{H(D)}$ *vs* pK_a(X)] of the reactions of **2S** (diethyl thiophosphinic chloride) with XC$_6$H$_4$NH$_2$(D$_2$) in MeCN at 55.0 °C.

1O, **2O**, **3O**, and **4O** (P=O counterparts) with XC$_6$H$_4$NH$_2$(D$_2$) in MeCN are summarized in Table 2. The reactivity of the P=O system is greater than that of its P=S counterpart, k_H(**1O**)/k_H(**1S**) = 799, k_H(**2O**)/k_H(**2S**) = 573, and k_H(**4O**)/k_H(**4S**) = 2.9. 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 O over S.[10] The natural bond order (NBO) charges of the reaction center P in the gas phase are 1.180(**1S**), 1.208(**2S**), and 1.236(**4S**) (P=S system), and 1.793(**1O**), 1.817(**2O**), 1.821(**3O**), and 1.844(**4O**) (P=O system) which are consistent with the inductive effects of Ph (σ_I = +0.12), Et (σ_I = −0.01), and Me (σ_I = −0.01) ligands. Solely considering the magnitudes of the positive charge of the reaction center P atom in the P=S (and P=O) system, the sequence of the anilinolysis rates should be **1S** < **2S** < **4S** (and **1O** < **2O** < **3O** < **4O**). However, the observed sequence is **1S** >> **4S** > **2S**, giving relative rate ratio of 30(**1S**):1.8(**4S**):1(**2S**) [and **1O** >> **2O** > **3O** >> **4O**, giving relative rate ratio of 4,520(**1O**):109(**2O**):80(**3O**):1(**4O**)]. These results are not in line with expectations from the inductive effects of the ligands, strongly suggesting that the inductive effects of the two ligands do not play any role to decide the reactivity of both the P=S and P=O systems.

Buncel and coworkers reported that the second-order rate constants for the ethanolyses of the three phosphinates, dimethyl [**1Z**; Me$_2$P(=O)OC$_6$H$_4$Z], methyl phenyl [**3Z**; MePhP(=O)OC$_6$H$_4$Z], and diphenyl [**4Z**; Ph$_2$P(=O)OC$_6$H$_4$Z] phosphinates with Z = 4-NO$_2$, gave relative rate ratio of 235(k_{EtO^-} = 230) : 69(k_{EtO^-} = 67.6) : 1(k_{EtO^-} = 0.980 M^{-1} s^{-1}) in anhydrous ethanol at 25.0 °C, resulting in δ = 0.478 (r = 0.953) according to the Taft' eq. (log k_{EtO^-} = $\delta\Sigma E_S$ + C).[11] Williams and coworkers reported that the second-order rate constants for the phosphate catalyzed hydrolyses of the two phosphinates, **1Z** and **4Z** with Z = 4-NO$_2$, gave relative rate ratio of 52($k_{HPO_4^{2-}}$ = 1.06 × 10^{-2}) : 1($k_{HPO_4^{2-}}$ = 2.05 × 10^{-4} M^{-1} s^{-1}) in 10% dioxane-aqueous 0.1 M NaCl at 25.0 °C, resulting in δ = 0.345.[12] The authors reported that the anilinolyses

Table 2. The Summary of Second-Order Rate Constants ($k_H \times 10^3/M^{-1}$ s^{-1}) with $C_6H_5NH_2$ at 55.0 °C, Summations of Inductive Effects of the Two Ligands ($\Sigma\sigma_I$), NBO Charges at Reaction Center P, Summations of the Taft's Steric Constants of the Two Ligands (ΣE_S), $\beta_{X(H \text{ and } D)}$, and k_H/k_D Values of the Reactions of **1S, 2S, 4S, 1O, 2O, 3O** and **4O** with $XC_6H_4NH_2(D_2)$ in MeCN

Substrate	$k_H \times 10^{3a}$	$\Sigma\sigma_I$	charge at P	$-\Sigma E_S$	$\beta_{X(H)}/\beta_{X(D)}$	k_H/k_D	ref
1S; Me$_2$P(=S)Cl	9.79	–0.02	1.180	0.00	1.28/1.22[b]	0.74-0.95[b]	1j
2S; Et$_2$P(=S)Cl	0.330	–0.02	1.208	0.14	1.12/1.22[b]	0.90-1.37[b]	this work
4S; Ph$_2$P(=S)Cl	0.601	0.24	1.236	4.96	1.40/1.40[b]	1.00-1.10[b]	1e
1O; Me$_2$P(=O)Cl	7,820[c]	–0.02	1.793	0.00	1.62/1.56[d]	0.70-0.90[d]	1i
2O; Et$_2$P(=O)Cl	189[e]	–0.02	1.817	0.14	0.56/0.52[f]	0.83-0.97[f]	1l
3O; MePhP(=O)Cl	138	0.11	1.821	2.48	0.88/0.81[b]	1.62-2.10[b]	1i
4O; Ph$_2$P(=O)Cl	1.73	0.24	1.844	4.96	1.69/1.62[b]	1.42-1.82[b]	1d

[a]Values with $C_6H_5NH_2$ at 55.0 °C. [b]Values at 55.0 °C. [c]The value of $k_H = 7.82$ M^{-1} s^{-1} at 55.0 °C was calculated by extrapolation in the Arrhenius plot (r = 0.999) with empirical kinetic data: $k_H = 0.776$ (0.0 °C), 1.01 (5.0 °C) and 1.61 M^{-1} s^{-1} (15.0 °C) from ref. 1i. [d]Values at 15.0 °C. [e]The value of $k_H = 189 \times 10^{-3}$ M^{-1} s^{-1} at 55.0 °C was obtained by extrapolation in the Arrhenius plot (r = 0.999) with kinetic data: $k_H = 117$ (40.0 °C), 162 (50.0 °C), and 211×10^{-3} M^{-1} s^{-1} (60.0 °C) from 1l. [f]Values at 50.0 °C.

($C_6H_5NH_2$) of the three phosphinates, **1Z**, **3Z**, and **4Z** with Z = 4-NO$_2$ in DMSO at 60.0 °C gave a small value of $\delta = 0.021$ (r = 0.954).[1m] It is evident that the sequence of the anilinolysis rates of the phosphinic chlorides, **1O** >> **2O** > **3O** >> **4O**, is inversely proportional to the sizes of the two ligands; Ph,Ph(**4O**) > Me,Ph(**3O**) > Et,Et(**2O**) > Me,Me (**1O**). The plots of log k_H against ΣE_S for the reactions of three phosphinic chlorides (**1O**, **3O**, and **4O**) with $C_6H_5NH_2$ in MeCN at 55.0 °C gave the great sensitivity coefficient of the steric effects of $\delta = 0.737$ (r = 0.999; good linearity).[1i] The anilinolysis rates of four phosphinic chlorides (**1O**, **2O**, **3O**, and **4O**) with $C_6H_5NH_2$ in MeCN at 55.0 °C gave a value of $\delta = 0.572$ (r = 0.895; roughly linear), due to a large negative deviation of **2O** from the slope of $\delta = 0.737$.[1l] These results indicate that the relative reactivities of the phosphinates and phosphinic chlorides are predominantly dependent on steric effects over the inductive effects of the ligands.

In the P=O system, the sequence of the anilinolysis rates (k_H with $C_6H_5NH_2$ in MeCN at 55.0 °C) of the $R_1R_2(P=O)Cl$-type substrates, studied in this lab, is as follows: R_1,R_2($k_H \times 10^3/M^{-1}$ s^{-1}); Me,Me(**1O**; 7,820)[1j] > Et,Et(**2O**; 189)[1l] > Me,Ph(**3O**; 138)[1i] > MeO,MeO(4.28)[1g] > EtO,EtO(2.82)[1g] > EtO,PhO(2.00)[1f] > Ph,Ph(**4O**; 1.73)[1d] > PhO,PhO(0.891)[1a] > cHex,cHex(0.00940).[1n] Dividing the studied substrates into two groups, *a*o-group with $R_1 = R_2$ = alkyl and/or phenyl and *b*o-group with $R_1 = R_2$ = alkoxy and/or phenoxy, the sequence of the rates is as follows: *a*o-group; Me,Me(**1O**; 7,820)[1j] > Et,Et(**2O**; 189)[1l] > Me,Ph(**3O**; 138)[1i] > Ph,Ph(**4O**; 1.73),[1d] and *b*o-group; MeO,MeO(4.28)[1g] > EtO,EtO(2.82)[1g] > EtO,PhO(2.00)[1f] > PhO,PhO(0.891).[1a] It is clear that the anilinolysis rate of both groups becomes slower as the size of the two ligands becomes greater. Herein, the anilinolysis rate of dicyclohexyl phosphinic chloride [cHex$_2$P(=O)Cl] is too slow to be rationalized by the stereoelectronic effects of the two ligands.[1n]

In the P=S system, the sequence of the anilinolysis rates (k_H with $C_6H_5NH_2$ in MeCN at 55.0 °C) of the $R_1R_2(P=S)Cl$-type substrates, studied in this lab, is as follows: R_1,R_2 ($k_H \times 10^3/M^{-1}$ s^{-1}); Me,Me(**1S**; 9.79)[1j] > Me,PhO(7.25)[1k] > MeO,MeO(1.09)[1g] > Ph,Ph(**4S**; 0.601)[1e] > EtO,EtO(0.512)[1g] > Et,Et(**2S**; 0.330) > EtO,PhO(0.280)[1f] > Ph,PhS(0.175)[1h] > PhO,PhO(0.101).[1c] Dividing the studied substrates into two groups, *a*s-group with $R_1 = R_2$ = alkyl and/or phenyl and *b*s-group with $R_1 = R_2$ = alkoxy and/or phenoxy, the sequence of the rates is as follows: *a*s-group; Me,Me(**1S**; 9.79)[1j] > Ph,Ph(**4S**; 0.601)[1e] > Et,Et(**2S**; 0.330), and *b*s-group; MeO,MeO(1.09)[1g] > EtO,EtO(0.512)[1g] > EtO,PhO(0.280)[1f] > PhO,PhO(0.101).[1c] The anilinolysis of Y-O-aryl methyl phosphonochloridothioates [Me(YC$_6$H$_4$O)P(=S)Cl] in MeCN exhibited biphasic concave downwards for substituent X variations in the nucleophiles with a break region[13] and the DKIEs were primary normal ($k_H/k_D = 1.03$-1.30) for stronger nucleophiles and unprecedented large secondary inverse ($k_H/k_D = 0.367$-0.567)[14] for weaker nucleophiles.[1k] In *b*s-group, the rate becomes slower as the size of the two ligands becomes greater as in the P=O system, while, in *a*s-group, the rather faster rate of **4S** (with two phenyl) than **2S** (with two ethyl) is surprising result. The authors conclude that the steric effects of the two ligands on the anilinolysis rate are predominant factor to decide the reactivities of the P=O system with both *a*o- and *b*o-groups and the P=S system with *b*s-group, while one of the major factors in the P=S system with *a*s-group.

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.[15] 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 ($k_H/k_D > 1.0$).[16] 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$_N$2 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.[16] The greater the degree of the steric congestion in the TS, the value of k_H/k_D becomes smaller. In general, the magnitude of β_X value represents the

degree of bond formation, and the greater β_X value is treated as greater degree of bond formation. As seen in Table 2, however, there is no correlation between the magnitudes of β_X and k_H/k_D values.

The DKIEs of **1S** (k_H/k_D = 0.74-0.95),[1j] **1O** (k_H/k_D = 0.70-0.90),[1i] and **2O** (k_H/k_D = 0.83-0.97)[1l] are secondary inverse, while those of **4S** (k_H/k_D = 1.00-1.10),[1e] **3O** (k_H/k_D = 1.62-2.10),[1i] and **4O** (k_H/k_D = 1.42-1.82)[1d] are primary normal. In the present work (**2S**), however, the DKIEs invariably change from secondary inverse (k_H/k_D = 0.898; min at X = 4-MeO) to primary normal (k_H/k_D = 1.37; max at X = 3-Cl) as the substituent X of the nucleophiles change from electron-donating to electron-withdrawing.

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 $k_H/k_D > 1.1$.[17] The authors accordingly proposed that the anilinolyses of **1S**, **1O**, and **2O** proceed through a concerted mechanism involving predominant TSb on the basis of the secondary inverse DKIEs, since the two small ligands readily enable backside nucleophilic attack. On the contrary, a concerted mechanism involving predominant hydrogen-bonded four-center-type TSf was proposed for the anilinolyses of **3O** and **4O** on the basis of the considerably large primary normal DKIEs, since frontside attack is more favorable than backside attack due to the large sizes of the two ligands. Meanwhile, a concerted mechanism with both frontside TSf and backside attack TSb was proposed for the anilinolysis of **4S**, where the fraction of a frontside attack is greater than that of a backside attack on the basis of relatively small primary normal DKIEs.[18]

In the present work, thus, secondary inverse with the strongly basic anilines and primary normal DKIEs with the weakly basic anilines can be rationalized by the gradual TS variation from a predominant backside attack TSb, *via* invariably increasing the fraction of a frontside attack, to a predominant frontside attack TSf, in which the reaction mechanism is a concerted S_N2 pathway.[19] Both the anilinolyses of P=O and P=S systems, the proposed mechanism is generally a normal S_N2 process because of good leaving group ability of Cl.[20] The nucleophilic attacking direction is correlated with the steric effects of the two ligands, R_1 and R_2. The larger the two ligands, the greater steric hindrance occurs, and a frontside attack becomes more favorable. In the P=O system, a backside nucleophilic attack is favorable,
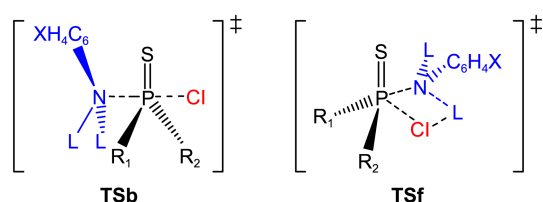
1O and **2O**, until the severe steric hindrance prohibits backside attack and consequently frontside attack becomes predominant, **3O** and **4O**. In the P=S system, **1S** favors a backside attack, **2S** favors both backside and frontside attack, and **4S** favors greater fraction of frontside attack than that of backside attack.

Experimental Section

Materials. HPLC-grade MeCN (water content is less than 0.005%) was 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 with deuterium oxide (99.9 atom % D) and one drop of HCl catalyst at 90 °C for 72 hours, and after numerous attempts, anilines were deuterated more than 98%, as confirmed by ^{1}H NMR. Diethyl thiophosphinic chloride was prepared by the following one step synthetic route.[21] Chlorodiethyl phosphine (97%) was stirred overnight with sulfur in THF. The solvent was removed under reduced pressure and a pale yellow liquid product was isolated through column chromatography (15% ethyl acetate + *n*-hexane). Analytical and spectroscopic data of the product gave the following results:

$(C_2H_5)_2P(=S)Cl$: Pale yellow liquid; ^{1}H NMR (400 MHz, CDCl3) δ 1.26-1.49 (m, 6H, 2 CH3), 2.28-2.41 (m, 4H, 2 CH2); ^{13}C NMR (100 MHz, CDCl3) δ 6.92 (CH3), 32.97, 33.53 (CH2); ^{31}P NMR (162 MHz, CDCl3) δ −132.97 (s, 1P, P=S); *m/z*, 156 (M⁺).

Kinetics Measurement. Rates were measured conductometrically at 55.0 °C as previously described.[1] [Substrate] = 0.001 M and [Nucleophile] = (0.1-0.5) M were used for the present work. Pseudo-first-order rate constant values were the average of three runs that were reproducible within ± 3%.

Product Analysis. Diethyl thiophosphinic chloride was reacted with excess 4-methoxyaniline for more than 15 half-lives at 55.0 °C in MeCN. The 4-methoxy aniline hydrochloride salt was separated by filtration. Acetonitrile was removed 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/30% ethyl acetate + *n*-hexane) gave the following results:

$(C_2H_5)_2P(=S)NHC_6H_4$-4-OCH₃: Dark-brown solid; mp (7980) °C; ^{1}H NMR (400 MHz, CDCl3) δ 1.18-1.27 (m, 6H, 2 CH3), 1.90-2.09 (m, 4H, 2 CH2), 3.77 (s, 3H, CH3O), 4.13 (s, 1H, NH), 6.81 (d, *J* = 6.8 Hz, 2H, phenyl), 6.95 (d, 2H, *J* = 8.8 Hz, phenyl); ^{13}C NMR (100 MHz, CDCl3) δ 6.28 (CH3), 25.39, 26.03 (CH2), 55.49 (OCH3), 114.74, 123.15, 132.83, 156.08 (C=C, aromatic); ^{31}P NMR (162 MHz, CDCl3) δ 80.18 (s, 1P, P=S); *m/z*, 243 (M⁺).

Scheme 2. Backside attack TSb and frontside attack TSf.

References and Notes

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18. This lab has cumulated data of DKIEs for the anilinolyses and benzylaminolyses of various kinds of substrates in MeCN and DMSO.
19. The anilinolyses of dimethyl chlorothiophosphate [$(MeO)_2P$(=S)Cl] ($k_H/k_D = 0.95$-1.1), dicyclohexyl phosphinic chloride ($k_H/k_D = 0.67$-1.05), and *O*-aryl methyl phosphonochloridothioates [$Me(YC_6H_4O)$-P(=S)Cl] ($k_H/k_D = 1.0$-1.3 with the strongly basic anilines and $k_H/k_D = 0.37$-0.57 with the weakly basic anilines), and the present work simultaneously yielded both primary normal and secondary inverse DKIEs. All the other studied P=O and P=S substrates yielded either primary normal or secondary inverse DKIEs.
20. The reactions of *O*-aryl methyl phosphonochloridothioates with the weakly basic anilines proceed through a stepwise mechanism with a rate-limiting bond breaking.
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