

## Theoretical Study of Phosphoryl Transfer Reactions

In-Suk Han, Chan Kyung Kim,\* and Hai Whang Lee\*

Department of Chemistry, Inha University, Incheon 402-751, Korea. \*E-mail: hwlee@inha.ac.kr

Received November 25, 2010, Accepted December 19, 2010

The energetics and transition state (TS) structures of the reactions of six substrates,  $R_1R_2P(=O \text{ or } S)Cl$ -type where  $R_1 = R_2 = \text{Me}$  and/or  $\text{MeO}$ , with ammonia in acetonitrile are theoretically investigated at the level of CPCM-MP2/6-31+G(d) and CPCM-MP2/6-311+G(3df,2p). The degrees of distortion of TS from the ideal trigonal bipyramidal pentacoordinate,  $\Delta\delta_{\#b}$  for a backside and  $\Delta\delta_{\#f}$  for a frontside attack, are calculated. The results of calculation suggest that the feasibility of a frontside attack for  $P=S$  is greater than that for  $P=O$  system when the two ligands,  $R_1$  and  $R_2$ , becomes larger. The experimental and calculated results of anilinolyses of  $R_1R_2P(=O \text{ or } S)Cl$ -type show the consistent tendencies.

**Key Words** : Aminolysis, Phosphoryl transfer Reaction, MO theoretical study, Frontside attack

## Introduction

In previous work, the authors theoretically studied on identity phosphoryl transfer reactions in the gas phase,  $(RO)_2P(=O)Cl + Cl$  when  $R = \text{Me}$  and  $\text{H}$ , by means of RHF, B3LYP, and SCIPCM methods.<sup>1</sup> The bond lengths in the trigonal bipyramidal pentacoordinate transition state (TBP-5C TS) for the reactions of  $R_2P(=O)Y$  with  $Y^-$  ( $R = \text{Me}$  and  $\text{MeO}$ ,  $Y = \text{Cl}$  and  $\text{F}$ ) in the gas phase were theoretically investigated.<sup>2</sup> The calculated results (B3LYP/6-311+G\*\* level)<sup>3</sup> supported the proposed mechanism of the pyridinolysis of *Z*-aryl bis(4-methoxyphenyl) phosphates [(4-MeOC<sub>6</sub>H<sub>4</sub>O)<sub>2</sub>P(=O)(OC<sub>6</sub>H<sub>4</sub>Z)] in acetonitrile (MeCN).<sup>2</sup> The MO theoretical calculation [CPCM-MP2/6-31+G(d) level]<sup>4</sup> of the reactions of dimethyl chloro and chlorothio phosphates with ammonia in MeCN and water were reported to investigate the energetics and TS structures of a backside and frontside nucleophilic attack.<sup>5</sup> Herein, the TS structure for a frontside nucleophilic attack has a very distorted TBP-5C, which is even hard to call TBP-5C. The rotation barriers of ethyl (and/or) phenyl and/or phenoxy in  $R_1R_2P(=O \text{ or } S)Cl$  ( $R_1 = R_2 = \text{EtO}$  and/or  $\text{PhO}$ ) were calculated at the level of RHF/6-31G\*<sup>6</sup> to discuss the steric hindrance of the ligands. The "Degree of distortions" ( $\Delta\delta_{GS}$  and  $\Delta\delta_{\#}$ ) from the regular tetrahedral structure and ideal TBP-5C TS were defined as Eqs. (1) and (2), respectively.<sup>6,7d</sup>

$$\Delta\delta_{GS} = \sum [|\theta_c - \theta_i/\theta_i|] = \sum |\theta_c - 109.5|/109.5 \quad (1)$$

$$\Delta\delta_{\#} = \sum [|\theta_c - \theta_i/\theta_i|]_{e,e} + \sum [|\theta_c - \theta_i/\theta_i|]_{a,e} \quad (2a)$$

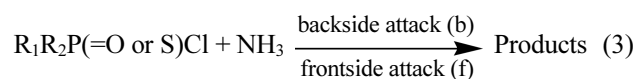
$$= \sum [|\theta_c - 120|/120]_{e,e} + \sum [|\theta_c - 90|/90]_{a,e} \quad (2b)$$

In Eq. (1),  $\Delta\delta_{GS}$  is the degree of distortion from the regular tetrahedral ground state (GS). The  $\Sigma$  means the sum of all six bond angles,  $\theta_c$  is the calculated bond angle using the B3LYP/6-311+G(d,p) level, and  $\theta_i$  is the ideal bond angle (109.5°) of a regular tetrahedral structure. In Eq. (2),  $\Delta\delta_{\#}$  is the degree of distortion from the ideal TBP-5C TS. The first term on the right side is the sum of the bond angle deviations from the ideal bond angle of 120° ( $\theta_e$ ) for the three equatorial

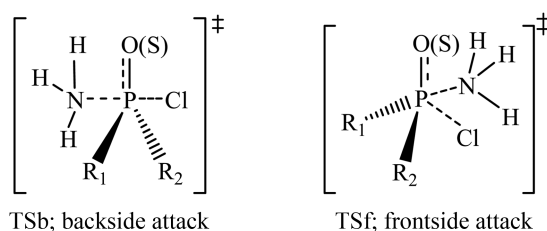
ligands (subscript e,e) and the second term is the sum of six bond angle deviations from the ideal bond angle of 90° ( $\theta_a$ ) between apical and equatorial ligands (subscript a,e).

Various phosphoryl and thiophosphoryl transfer reactions were reported by the authors.<sup>2,5,6-8</sup> The anilinolyses<sup>5,6,7a-j</sup> and pyridinolyses<sup>2,8a,c,e,f,g</sup> of  $R_1R_2P(=O \text{ or } S)Cl$ -type substrates are extensively studied in MeCN. A backside and frontside nucleophilic attack were discussed on the basis of the deuterium kinetic isotope effects (DKIEs;  $k_H/k_D$ ), selectivity parameters ( $\rho_X$ ,  $\rho_Y$ ,  $\beta_X$ , and  $\rho_{XY}$ ) and free energy correlations (linear, biphasic concave upwards/downwards) for variation of substituent X and Y in the nucleophile and substrate, respectively.

To gain further understanding of the mechanism for the phosphoryl and thiophosphoryl transfer reactions, theoretical studies on the reactions of  $R_1R_2P(=O \text{ or } S)Cl$  substrates with ammonia in MeCN are carried out at the level of CPCM-MP2/6-31+G(d) and CPCM-MP2/6-311+G(3df,2p),<sup>9</sup> Eq. (3).



The studied six substrates are as follows: dimethyl phosphinic chloride [ $\text{Me}_2P(=O)Cl$ ]; dimethyl thiophosphinic chloride [ $\text{Me}_2P(=S)Cl$ ]; *O*-methyl methyl phosphonochloridoate [( $\text{MeO}$ ) $\text{MeP}(=O)Cl$ ]; *O*-methyl methyl phosphonochloridothioate [( $\text{MeO}$ ) $\text{MeP}(=S)Cl$ ]; dimethyl chlorophosphate [( $\text{MeO}$ )<sub>2</sub> $P(=O)Cl$ ]; dimethyl chlorothiophosphate [( $\text{MeO}$ )<sub>2</sub> $P(=S)Cl$ ]. The energetics and TS structures of the reactions of the mentioned substrates with ammonia are theoretically investigated for a backside (TSb) and frontside (TSf) nucleophilic attack in MeCN.



## Results and Discussion

Henceforth,  $R_1R_2P(=O \text{ or } S)Cl$  is denoted as O(or S) ( $R_1, R_2$ ) for convenience, and the studied reaction systems can be represented as follows: O(Me,Me), S(Me,Me), O(MeO,Me), S(MeO,Me), O(MeO,MeO), and S(MeO,MeO). Table 1 shows the degree of distortions of GS ( $\Delta\delta_{GS}$ )<sup>7d</sup> from the regular tetrahedral structure [B3LYP/6-311+G(d,p) level of theory] and TS ( $\Delta\delta_{\#b}$  and  $\Delta\delta_{\#f}$  of a backside and frontside nucleophilic attack, respectively) from the ideal TBP-5C [CPCM-MP2/6-311+G(3df,2p) level of theory], summations of inductive effects of the two ligands [ $\Sigma\sigma_1 = \sigma_1(R_1) + \sigma_1(R_2)$ ],<sup>10</sup> natural bond order (NBO) charges on the P atom reaction center in the gas phase [B3LYP/6-311+G(d,p) level of theory],<sup>7d</sup> second-order rate constants ( $k_2$ ) at 55.0 °C, Brønsted coefficients ( $\beta_X$ ), and DKIEs ( $k_H/k_D$ ) involving deuterated anilines ( $XC_6H_4ND_2$ ) for the anilinolyses of  $R_1R_2P(=O \text{ or } S)Cl$  in MeCN. The correlations  $\Sigma\sigma_1$  with the NBO charge on the P atom reaction center do not show good linear. The plots of the NBO charge on P against  $\Sigma\sigma_1$  yield the slopes of 0.586 ( $r = 0.955$ ) and 0.778 ( $r = 0.861$ ) for P=O and P=S systems, respectively. The P=O systems are 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 that favors O over S.<sup>11</sup> The NBO charges on the P atom of P=O systems are greater (ca. 0.5–0.6) than those of their P=S counterparts, implying the electronegativity difference between O and S. The anilinolysis rate decreases as the size of the two ligands becomes larger, which means that the steric hindrance is the predominant factor to determine the reactivity for both P=O and P=S systems. The  $\beta_X$  values obtained from  $k_H$  (with  $XC_6H_4NH_2$ ) are slightly greater than those from  $k_D$  (with  $XC_6H_4ND_2$ ).

The degree of distortion of GS ( $\Delta\delta_{GS}$ ) from the regular tetrahedral structure becomes greater as the size of the two ligands becomes larger. The values of  $\Delta\delta_{GS}$  of P=S systems

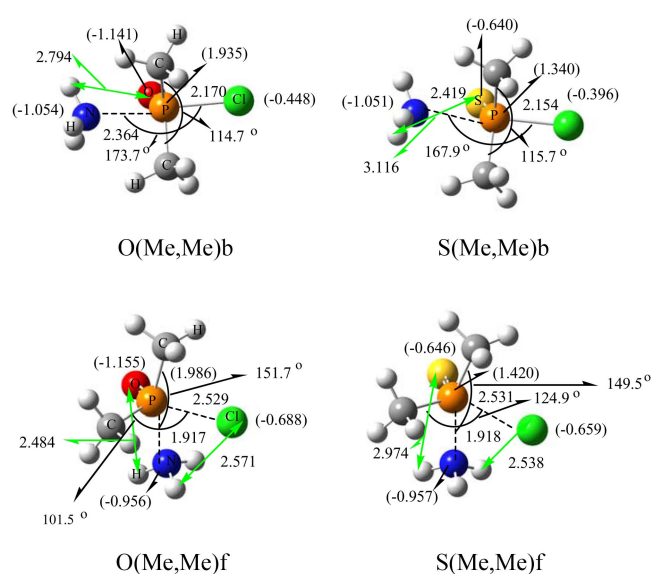
are somewhat greater (0.06–0.08) than those of their P=O counterparts due to the larger size of P=S sulfur compared to that of P=O oxygen. The structures, bond angles (the largest angle is displayed in a backside attack, while the largest and next largest angles are displayed in a frontside attack), atomic charges, and distances between atoms of the TSs, optimized at the CPCM-MP2/6-311+G(3df,2p) level, for the reactions of the six substrates with ammonia for a backside and frontside attack in MeCN are shown in Figures 1–3. The detailed bond angles of a backside and frontside attack TS are summarized in Supporting Information.<sup>12</sup>

In a backside attack, the bond angles of two apical positions are as follows: 173.7° [O(Me,Me)] and 167.9° [S(Me,Me)]; 174.2° [O(MeO,Me)] and 170.1° [S(MeO,Me)]; 173.7° [O(MeO,MeO)] and 170.3° [S(MeO,MeO)]. The bond angles of two apical positions of a backside attack are close to 180° of ideal TBP-5C TS, and the bond angle of two apical positions of P=O system is greater (3.4°–5.8°) than that of its P=S counterpart as expected. Herein, the ammonia nucleophile and Cl leaving group occupy two apical positions, respectively. In a frontside attack, the two apical positions having the largest bond angle are arbitrarily chosen and hence the bond angles of two apical positions are as follows: 151.7° [O(Me,Me)] and 149.5° [S(Me,Me)]; 145.4° [O(MeO,Me)] and 143.8° [S(MeO,Me)]; 143.9° [O(MeO,MeO)] and 141.9° [S(MeO,MeO)]. Then, the ammonia nucleophile occupies apical position while the Cl leaving group occupy equatorial position in TBP-5C. The bond angles of two apical positions of a frontside attack are far from the ideal bond angle 180°, and the bond angle of two apical positions of P=O system is slightly greater (1.6°–2.2°) than that of its P=S counterpart. The  $\Delta\delta_{\#f}$  values are significantly greater than  $\Delta\delta_{\#b}$  values for both P=O and P=S systems, indicating that the degree of distortion of a frontside attack is considerably larger than that of a backside attack from the ideal TBP-5C TS. The  $\Delta\delta_{\#b}$  values of P=S systems are slightly greater than those of P=O systems. The

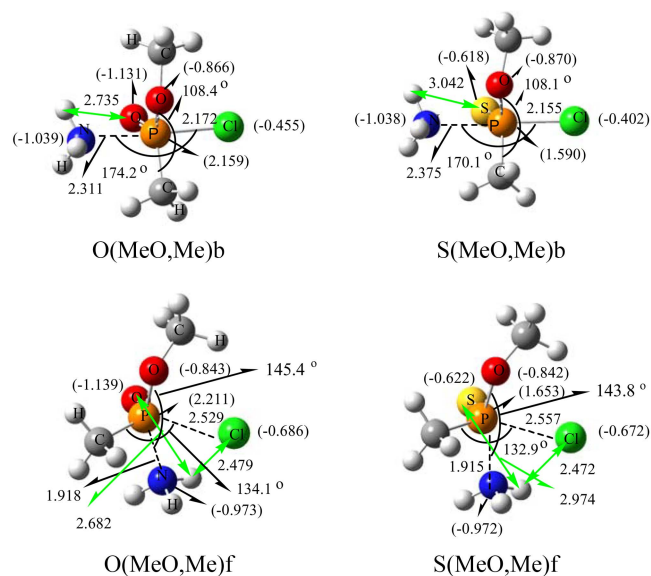
**Table 1.** Summary of Degree of Distortions of GS ( $\Delta\delta_{GS}$ ) and TS ( $\Delta\delta_{\#b}$  and  $\Delta\delta_{\#f}$  of a Backside and Frontside Attack, Respectively), Summations of Inductive Effects of the Two Ligands ( $\Sigma\sigma_1$ ), NBO Charges on Reaction Center P, Second-Order Rate Constants ( $k_2$ ) at 55.0 °C, Brønsted Coefficients ( $\beta_X$ ), and DKIEs ( $k_H/k_D$ ) for the Anilinolyses of  $R_1R_2P(=O \text{ or } S)Cl$  in MeCN

Substrate	$\Delta\delta_{GS}^a$	$\Delta\delta_{\#b}^b$	$\Delta\delta_{\#f}^b$	$\Sigma\sigma_1$	charge on P	$k_2 \times 10^4^c$	$\beta_X$	$k_H/k_D$	ref
O(Me,Me)	0.29	0.43	0.91	−0.02	1.793	78200 <sup>d</sup>	1.62 <sup>e</sup> /1.56 <sup>f</sup>	0.703–0.899	7g
S(Me,Me)	0.36	0.48	0.76	−0.02	1.180	97.9	1.28 <sup>e</sup> /1.22 <sup>f</sup>	0.740–0.945	7h
O(MeO,Me)	0.34	0.62	0.99	0.29	2.019	–	–	–	–
S(MeO,Me)	0.42	0.66	0.90	0.29	1.441	–	–	–	–
O(MeO,MeO)	0.37	0.66	1.02	0.60	2.226	42.8	0.962 <sup>e</sup> /0.907 <sup>f</sup>	0.798–0.979	7e
S(MeO,MeO)	0.44	0.66	1.07	0.60	1.687	10.9	0.993 <sup>e</sup> /0.963 <sup>f</sup>	0.945–1.06	7e
O(EtO,EtO)	0.37	–	–	0.56	2.236	28.2	1.06 <sup>e</sup> /0.993 <sup>f</sup>	0.714–0.919	7e
S(EtO,EtO)	0.43	–	–	0.56	1.701	5.12	0.977 <sup>e</sup> /0.957 <sup>f</sup>	1.01–1.10	7e
O(PhO,PhO)	0.40	–	–	0.80	2.230	8.91	1.36 <sup>e</sup>	0.61–0.87	7a
S(PhO,PhO)	0.48	–	–	0.80	1.661	1.01	1.36 <sup>e</sup>	1.11–1.33	5

<sup>a</sup>B3LYP/6-311+G(d,p) level of theory. The values of  $\Delta\delta_{GS}$  are from ref 7d. <sup>b</sup>CPCM-MP2/6-311+G(3df,2p) level of theory. <sup>c</sup>For the reactions of  $C_6H_5NH_2$  with substrate at 55.0 °C. <sup>d</sup>Extrapolated value from the Arrhenius plot with empirical kinetic data:  $k_H = 0.776$  (0.0 °C), 1.01 (5.0 °C), and 1.61 M<sup>−1</sup> s<sup>−1</sup> (15.0 °C). <sup>e</sup>Calculated with  $k_H$  values. <sup>f</sup>Calculated with  $k_D$  values.

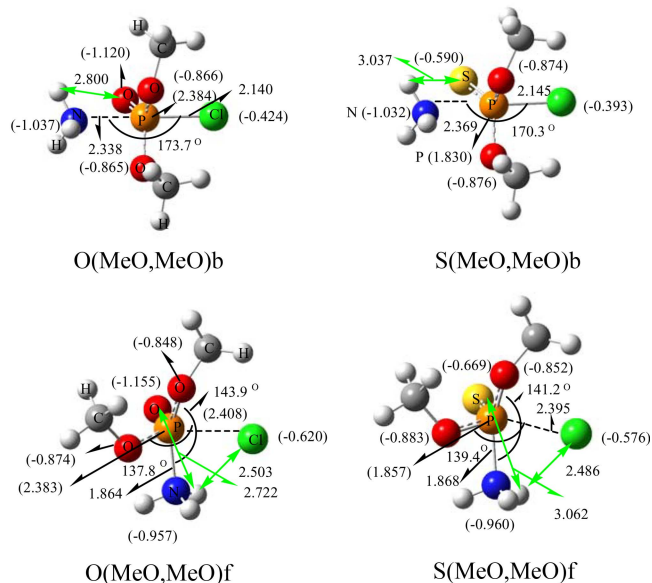


**Figure 1.** The structures, bond angles, atomic charges, and distances between atoms of the TSs, optimized at the CPCM-MP2/6-311+G(3df,2p) level of theory, for the reactions of O(Me,Me)b [ $\text{Me}_2\text{P}(=\text{O})\text{Cl} + \text{NH}_3$ ; backside attack], S(Me,Me)b [ $\text{Me}_2\text{P}(=\text{S})\text{Cl} + \text{NH}_3$ ; backside attack], O(Me,Me)f [ $\text{Me}_2\text{P}(=\text{O})\text{Cl} + \text{NH}_3$ ; frontside attack], and S(Me,Me)f [ $\text{Me}_2\text{P}(=\text{S})\text{Cl} + \text{NH}_3$ ; frontside attack] in MeCN.



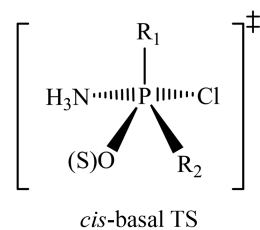
**Figure 2.** The structures, bond angles, atomic charges, and distances between atoms of the TSs, optimized at the CPCM-MP2/6-311+G(3df,2p) level of theory, for the reactions of O(MeO,Me)b [(MeO)MeP(=O)Cl +  $\text{NH}_3$ ; backside attack], S(MeO,Me)b [(MeO)MeP(=S)Cl +  $\text{NH}_3$ ; backside attack], O(MeO,Me)f [(MeO)MeP(=O)Cl +  $\text{NH}_3$ ; frontside attack], and S(MeO,Me)f [(MeO)MeP(=S)Cl +  $\text{NH}_3$ ; frontside attack] in MeCN.

$\Delta\delta_{\text{zf}}$  values of P=O systems show consistency, while those of P=S systems do not show consistency on variation of the size of two ligands. Considering the bond angles of a frontside attack, the TS structure resembles *cis*-basal<sup>13</sup> (square pyramidal) rather than TBP-5C. In *cis*-basal TS, the



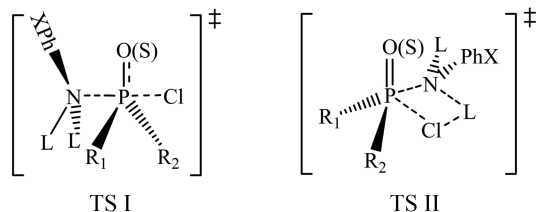
**Figure 3.** The structures, bond angles, atomic charges, and distances between atoms of the TSs, optimized at the CPCM-MP2/6-311+G(3df,2p) level of theory, for the reactions of O(MeO,MeO)b [(MeO)<sub>2</sub>P(=O)Cl +  $\text{NH}_3$ ; backside attack], S(MeO,MeO)b [(MeO)<sub>2</sub>P(=S)Cl +  $\text{NH}_3$ ; backside attack], O(MeO,MeO)f [(MeO)<sub>2</sub>P(=O)Cl +  $\text{NH}_3$ ; frontside attack], and S(MeO,MeO)f [(MeO)<sub>2</sub>P(=S)Cl +  $\text{NH}_3$ ; frontside attack] in MeCN.

nucleophile and leaving groups occupy adjacent positions in square planar and, as a result, retention of stereochemistry is obtained.



The secondary inverse DKIEs ( $k_{\text{H}}/k_{\text{D}} < 1$ ) imply an increase in the N–H(D) vibrational frequencies as a result of steric congestion of the N–H(D) moiety in the TS I involving a backside nucleophilic attack. Thus, the normal  $\text{S}_{\text{N}}2$  anilinolysis involving a backside attack always yields the secondary inverse DKIEs. The primary normal DKIEs ( $k_{\text{H}}/k_{\text{D}} > 1$ ) suggest that partial deprotonation of the aniline occurs in a rate-determining step by hydrogen bonding.<sup>14</sup> To rationalize the primary normal DKIEs, the hydrogen-bonded, four-center-type TS II involving a frontside nucleophilic attack was proposed, in which the nucleophile and leaving group are located adjacent to each other in order to form the hydrogen bond between the hydrogen (or deuterium) atom in the N–H(D) moiety and the leaving group Cl.<sup>2,5-7,15</sup> The real primary normal DKIE due to the hydrogen bond between the hydrogen of the N–H(D) moiety and the leaving group should be greater than the observed value, since the secondary inverse DKIE ( $k_{\text{H}}/k_{\text{D}} < 1$ ) because of the steric hindrance that increases the out-of-plane bending vibrational

frequencies of the other N–H(D) bond.



The reaction mechanism of the anilinolyses of  $R_1R_2P(=O \text{ or } S)Cl$  in MeCN in Table 1 were rationalized mainly based on the cross-interaction constants (CICs),<sup>16</sup> selectivity parameters ( $\rho_X$  and  $\beta_X$ ), and DKIEs. In O(PhO,PhO) and S(PhO,PhO), a concerted  $S_N2$  mechanism was proposed on the basis of a negative  $\rho_{XY}$  value ( $\rho_{XY} = -1.31$  and  $-0.22$ , respectively). In O(Me,Me), S(Me,Me), O(MeO,MeO), S(MeO,MeO), O(EtO,EtO), and S(EtO,EtO), a concerted  $S_N2$  mechanism was proposed on the basis of selectivity parameters ( $\rho_X$  and  $\beta_X$ ) and DKIEs. The attacking direction of aniline nucleophile could be semi-quantitatively divided into four groups on the basis of the magnitudes of the  $k_H/k_D$  values:<sup>17</sup> (group A) a predominant backside attack when  $k_H/k_D < 1$ ;  $k_H/k_D = 0.703\text{--}0.899$  [O(Me,Me)],<sup>7g</sup>  $0.740\text{--}0.945$  [S(Me,Me)],<sup>7h</sup>  $0.798\text{--}0.979$  [O(MeO,MeO)],<sup>7c</sup>  $0.714\text{--}0.919$  [O(EtO,EtO)],<sup>7c</sup> and  $0.61\text{--}0.87$  [O(PhO,PhO)];<sup>7a</sup> (group B) a backside and frontside attack when the  $k_H/k_D$  values change from less than unity to greater than unity;  $0.945\text{--}1.06$  [S(MeO,MeO)];<sup>7c</sup> (group C) the fraction of a frontside attack is greater than that of a backside attack when  $1.0 < k_H/k_D < 1.1$ :  $1.01\text{--}1.10$  [S(EtO,EtO)];<sup>7c</sup> (group D) a predominant frontside attack when  $k_H/k_D > 1.1$ ;  $1.11\text{--}1.33$  [S(PhO,PhO)]<sup>5</sup> (*vide infra*). The fraction of a frontside attack of the P=S system is greater than that of the P=O system because of the greater electrophilicity of reaction center P in P=O compared to P=S system. When the degree of steric hindrance is more or less significant, the lesser electrophilicity of P in P=S leads to a frontside attack with a hydrogen bonded four-center-type TS II rather than a backside attack. Meanwhile, the greater electrophilicity of P in P=O overcomes the steric

hindrance and enables a backside attack until the severe steric hindrance prohibits backside attack and consequently frontside attack becomes predominant. Consequently, a frontside attack with a hydrogen bonded, four-center-type TS II could be an alternative pathway competing with a backside nucleophilic attack when the steric hindrance is great, especially for P=S system with a relatively small electrophilicity.

The energetics of the reactions of six substrates with ammonia in MeCN are summarized in Tables 2 [CPCM-MP2/6-31+G(d) level] and 3 [CPCM-MP2/6-311+G(3df,2p) level]. Calculated activation energy of a backside and frontside attack ( $\Delta E_b^\ddagger$  and  $\Delta E_f^\ddagger$ ) and activation energy difference ( $\delta\Delta E^\ddagger = \Delta E_f^\ddagger - \Delta E_b^\ddagger$ ) with CPCM-MP2/6-311+G(3df,2p) level are all greater than those with CPCM-MP2/6-31+G(d) level. Nevertheless, both results of CPCM-MP2/6-31+G(d) and CPCM-MP2/6-311+G(3df,2p) calculation show the consistent tendencies: (i) a backside attack is more favorable than a frontside attack for all six reactions; (ii) ( $R_1, R_2$ ) changes from (Me,Me) via (MeO,Me) to (MeO,MeO), i.e., the size of the two ligands becomes larger, activation energy of a backside attack ( $\Delta E_b^\ddagger$ ) consistently becomes greater, whereas activation energy of a frontside attack ( $\Delta E_f^\ddagger$ ) consistently becomes smaller; (iii) the size of the two ligands becomes larger, the difference of activation energy barrier ( $\delta\Delta E_b^\ddagger = \Delta E_f^\ddagger - \Delta E_b^\ddagger$ ) between a frontside and backside attack becomes smaller; (iv) the size of the two ligands becomes larger, the decrements of  $\delta\Delta E^\ddagger$  for P=S systems ( $15.26 \rightarrow 10.17 \rightarrow 3.57$  in Table 2 and  $15.97 \rightarrow 11.46 \rightarrow 4.49$  kcal/mol in Table 3) becomes greater than those for P=O systems ( $15.76 \rightarrow 12.70 \rightarrow 6.14$  in Table 2 and  $16.12 \rightarrow 13.07 \rightarrow 6.38$  kcal/mol in Table 3). These calculated results strongly suggest that the feasibility of a frontside attack for P=S system is greater than that of P=O system when the steric hindrance becomes larger (*vide supra*).

Comparing the grouping A, B, C, and D depending on the magnitudes of DKIEs with calculated results: (i) considerably small ligands lead a backside attack regardless of P=O or P=S systems, O(Me,Me) and S(Me,Me). (ii) changing

**Table 2.** Calculated Activation Energy Barriers (kcal/mol) at CPCM-MP2/6-31+G(d) Level of Theory for a Backside and Frontside Attack of the Reactions of  $R_1R_2P(=O \text{ or } S)Cl$  with Ammonia in MeCN

	O(Me,Me)	S(Me,Me)	O(MeO,Me)	S(MeO,Me)	O(MeO,MeO) <sup>d</sup>	S(MeO,MeO) <sup>d</sup>
$\Delta E_b^{\ddagger a}$	3.20	3.02	2.42	2.52	5.13	6.11
$\Delta E_f^{\ddagger b}$	18.97	18.28	15.13	12.69	11.27	9.68
$\delta\Delta E^{\ddagger c}$	15.76	15.26	12.70	10.17	6.14	3.57

<sup>a</sup>Activation energy for a backside attack. <sup>b</sup>Activation energy for a frontside attack. <sup>c</sup> $\delta\Delta E^\ddagger = \Delta E_f^\ddagger - \Delta E_b^\ddagger$ . <sup>d</sup>Ref. 2.

**Table 3.** Calculated Activation Energy Barriers (kcal/mol) at CPCM-MP2/6-311+G(3df,2p) Level of Theory for a Backside and Frontside Attack of the Reactions of  $R_1R_2P(=O \text{ or } S)Cl$  with Ammonia in MeCN

	O(Me,Me)	S(Me,Me)	O(MeO,Me)	S(MeO,Me)	O(MeO,MeO)	S(MeO,MeO)
$\Delta E_b^{\ddagger a}$	3.20	3.50	3.80	3.44	6.17	6.97
$\Delta E_f^{\ddagger b}$	19.32	19.47	16.87	14.90	12.56	11.46
$\delta\Delta E^{\ddagger c}$	16.12	15.97	13.07	11.46	6.38	4.49

<sup>a-c</sup>Same as in Table 2

from O(Me<sub>2</sub>Me) to S(Me<sub>2</sub>Me), the fraction of a backside attack of O(Me<sub>2</sub>Me) ( $k_H/k_D = 0.703-0.899$ ) is greater than that of S(Me<sub>2</sub>Me) ( $k_H/k_D = 0.740-0.945$ ). (iii) changing from O(MeO,MeO) ( $k_H/k_D = 0.798-0.979$ ) to S(MeO,MeO) ( $k_H/k_D = 0.945-1.06$ ) and from O(EtO,EtO) ( $k_H/k_D = 0.714-0.919$ ) to S(EtO,EtO) ( $k_H/k_D = 1.01-1.10$ ), the fraction of a frontside attack is greater than that of a backside attack. (iv) considerably large ligands in P=S system leads to a predominant frontside attack, S(PhO,PhO) ( $k_H/k_D = 1.11-1.33$ ). The calculated results qualitatively (and partially quantitatively) support the proposed mechanism of the anilinolyses of R<sub>1</sub>R<sub>2</sub>P(=O or S)Cl in MeCN.

**Acknowledgments.** This work was supported by Inha University Research Grant.

### References and Notes

1. Lee, I.; Kim, C. K.; Li, H. G.; Sohn, C. K.; Kim, C. K.; Lee, H. W.; Lee, B. S. *J. Am. Chem. Soc.* **2000**, *122*, 11162.
2. Lee, H. W.; Guha, A. K.; Kim, C. K.; Lee, I. *J. Org. Chem.* **2002**, *67*, 2215.
3. (a) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648. (b) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785.
4. Hehre, W. J.; Random, L.; Schleyer, P. V. R.; Pople, J. A. *Ab initio Molecular Orbital Theory*; Wiley: New York, 1986; Chap. 4.
5. Hoque, M. E. U.; Dey, S.; Guha, A. K.; Kim, C. K.; Lee, B. S.; Lee, H. W. *J. Org. Chem.* **2007**, *72*, 5493.
6. Hoque, M. E. U.; Dey, N. K.; Kim, C. K.; Lee, B. S.; Lee, H. W. *Org. Biomol. Chem.* **2007**, *5*, 3944.
7. (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.; Lee, H. W. *Bull. Korean Chem. Soc.* **2007**, *28*, 936. (d) Dey, N. K.; Han, I. S.; Lee, H. W. *Bull. Korean Chem. Soc.* **2007**, *28*, 2003. (e) Dey, N. K.; Hoque, M. E. U.; Kim, C. K.; Lee, B. S.; Lee, H. W. *J. Phys. Org. Chem.* **2008**, *21*, 544. (f) Lumbiny, B. J.; Lee, H. W. *Bull. Korean Chem. Soc.* **2008**, *29*, 2065. (g) Dey, N. K.; Hoque, M. E. U.; Kim, C. K.; Lee, B. S.; Lee, H. W. *J. Phys. Org. Chem.* **2009**, *22*, 425. (h) Dey, N. K.; Kim, C. K.; Lee, H. W. *Bull. Korean Chem. Soc.* **2009**, *30*, 975. (i) Hoque, M. E. U.; Guha, A. K.; Kim, C. K.; Lee, B. S.; Lee, H. W. *Org. Biomol. Chem.* **2009**, *7*, 2919. (j) Dey, N. K.; Lee, H. W. *Bull. Korean Chem. Soc.* **2010**, *31*, 1403. (k) Dey, N. K.; Kim, C. K.; Lee, H. W. *Org. Biomol. Chem.* **2011**, *9*, 717.
8. (a) Guha, A. K.; Lee, H. W.; Lee, I. *J. Org. Chem.* **2000**, *65*, 12. (b) Adhikary, K. K.; Lee, H. W.; Lee, I. *Bull. Korean Chem. Soc.* **2003**, *24*, 1135. (c) 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. (d) Adhikary, K. K.; Lumbiny, B. J.; Kim, C. K.; Lee, H. W. *Bull. Korean Chem. Soc.* **2008**, *29*, 851. (e) Lumbiny, B. J.; Adhikary, K. K.; Lee, B. S.; Lee, H. W. *Bull. Korean Chem. Soc.* **2008**, *29*, 1769. (f) Dey, N. K.; Hoque, M. E. U.; Kim, C. K.; Lee, H. W. *J. Phys. Org. Chem.* **2010**, *23*, 1022. (g) Dey, N. K.; Kim, C. K.; Lee, H. W. *Bull. Korean Chem. Soc.* **2010**, *31*, 3856. (h) Guha, A. K.; Kim, C. K.; Lee, H. W. *J. Phys. Org. Chem.* DOI:10.1002/poc.1788.
9. (a) Barone, V.; Cossi, M. *J. Phys. Chem. A* **1998**, *102*, 1995. (b) Cossi, M.; Rega, N.; Scalmani, G.; Barone, V. *J. Comput. Chem.* **2003**, *24*, 669.
10. Charton, M. *Prog. Phys. Org. Chem.* **1987**, *16*, 287.
11. (a) Hondal, R. J.; Bruzik, K. S.; Zhao, Z.; Tsai, M. D. *J. Am. Chem. Soc.* **1997**, *119*, 5477. (b) Omakor, J. E.; Onyido, I.; vanLoon, G. W.; Buncel, E. *J. Chem. Soc., Perkin Trans. 2* **2001**, 324. (c) Gregersen, B. A.; Lopez, X.; York, D. M. *J. Am. Chem. Soc.* **2003**, *125*, 7178. (d) Onyido, I.; Swierczek, K.; Purcell, J.; Hengge, A. C. *J. Am. Chem. Soc.* **2005**, *127*, 7703. 324.
12. The bond angles calculated at the level of CPCM-MP2/6-31+G(d) and CPCM-MP2/6-311+G(3df,2p) are summarized in Supporting Information.
13. Thatcher, G. R. J.; Kluger, R. *Adv. Phys. Org. Chem.* **1989**, *25*, 99.
14. The secondary normal β-type-DKIEs,  $k_H/k_D > 1$ , involving the rate-limiting leaving group expulsion from the intermediate can be obtained: (i)  $k_H/k_D = 1.03-1.11$  for the reactions of phenylacetyl chlorides with deuterated anilines in MeCN (Lee, H. W.; Lee, J. W.; Koh, H. J.; Lee, I. *Bull. Korean Chem. Soc.* **1998**, *19*, 642); (ii)  $k_H/k_D = 1.04-1.12$  for the reactions of 4-nitrophenyl *N*-phenylcarbamates with deuterated benzylamines in MeCN (Koh, H. J.; Kim, O. S.; Lee, H. W.; Lee, I. *J. Phys. Org. Chem.* **1997**, *10*, 725); (iii)  $k_H/k_D = 1.02-1.11$  for the reactions of benzhydryl chlorides with deuterated pyrrolidine in MeCN (Chang, S.; Koh, H. J.; Lee, B. S.; Lee, I. *J. Org. Chem.* **1995**, *60*, 7760); and (iv) The obtained order of 1.1 is consistent with the typical value of the secondary normal β-DKIEs. (Lowry, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry*, 3rd ed.; Harper and Row: New York, 1987; p 239).
15. (a) Lee, I.; Koh, H. J.; Lee, B. S.; Lee, H. W. *J. Chem. Soc., Chem. Commun.* **1990**, 335. (b) Melander, L., Jr.; Saunders, W. H. *Reaction Rates of Isotopic Molecules*; Wiley-Interscience: New York, 1980.
16. (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.
17. The grouping depending on the magnitude of DKIE seems to be somewhat arbitrary. A lot of DKIEs data for the aminolyses (anilinolysis and benzylaminolyses) of various substrates involving deuterated nucleophiles have been cumulated by the authors, enough to be confident of the grouping.