

## Anilinolysis of Diphenyl Thiophosphinic Chloride and Theoretical Studies on Various $R_1R_2P(O \text{ or } S)Cl^\dagger$

Nilay Kumar Dey, In-Suk Han, and Hai Whang Lee\*

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

Received October 4, 2007

The aminolysis of diphenyl thiophosphinic chloride (**2**) with substituted anilines in acetonitrile at 55.0 °C is investigated kinetically. Kinetic results yield large Hammett  $\rho_X$  ( $\rho_{\text{nuc}} = -3.97$ ) and Brønsted  $\beta_X$  ( $\beta_{\text{nuc}} = 1.40$ ) values. A concerted mechanism involving a partial frontside nucleophilic attack through a hydrogen-bonded, four-center type transition state is proposed on the basis of the primary normal kinetic isotope effects ( $k_H/k_D = 1.0$ -1.1) with deuterated aniline ( $XC_6H_4ND_2$ ) nucleophiles. The natural bond order charges on P and the degrees of distortion of 42 compounds: chlorophosphates  $[(R_1O)(R_2O)P(=O)Cl]$ , chlorothiophosphates  $[(R_1O)(R_2O)P(=S)Cl]$ , phosphonochloridates  $[(R_1O)R_2P(=O)Cl]$ , phosphonochlorothioates  $[(R_1O)R_2P(=S)Cl]$ , chlorophosphinates  $[R_1R_2P(=O)Cl]$ , and chlorothiophosphinates  $[R_1R_2P(=S)Cl]$  are calculated at the B3LYP/6-311+G(d,p) level in the gas phase.

**Key Words** : Anilinolysis of diphenyl thiophosphinic chloride, Frontside nucleophilic attack, Deuterium kinetic isotope effect, NBO charge, Degree of distortion

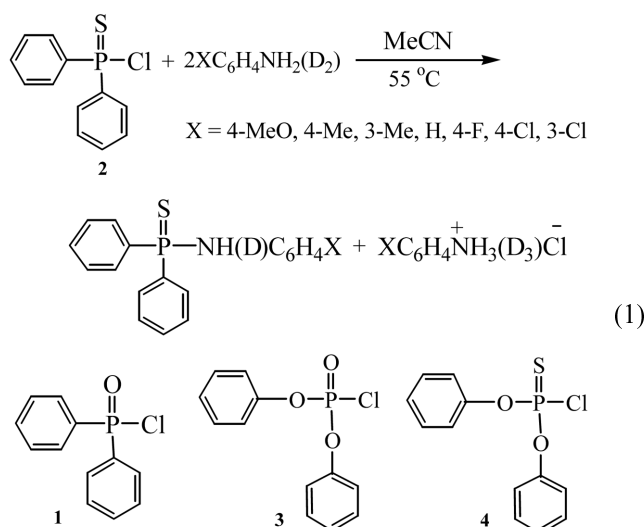
### Introduction

Phosphoryl transfer is an important part of many biological chemistry and organic syntheses.<sup>1</sup> Nucleophilic substitution reactions at phosphorus in tetracoordinate penta-covalent phosphorus esters and related compounds generally proceed either stepwise with a trigonal bipyramidal penta-coordinate (TBP-5C) intermediate or through an  $S_N2$  mechanism with a single transition state (TS).<sup>1b-c,2</sup> When the attacking and leaving groups occupy apical positions [ap(Nu)-ap(Lg)], *i.e.*, backside nucleophilic attack, the configuration is inverted, but when the nucleophile attacks frontside toward the leaving group, the configuration is retained. When backside and frontside nucleophilic attacks occur simultaneously, the relative importance of the reaction pathways leads to products with inversion or retention of configuration depending on the nucleophile, the leaving group, and the reaction conditions.<sup>3</sup>

In our preceding papers,<sup>4</sup> we reported several phosphoryl and thiophosphoryl transfer reactions kinetically and theoretically. Partial frontside nucleophilic attack was suggested for reactions of aryl bis(4-methoxyphenyl) phosphates with less basic pyridines;<sup>4g</sup> aryl phenyl isothiocyanophosphates with more basic pyridines;<sup>4h</sup> aryl phenyl chlorothiophosphates with anilines;<sup>4c</sup> diphenyl phosphinic chlorides with anilines;<sup>4d</sup> diphenyl thiophosphinic chlorides with more basic pyridines;<sup>4i</sup> and aryl ethyl chloro and chlorothio phosphates with anilines.<sup>4e</sup>

In this work, we investigate the aminolysis of diphenyl thiophosphinic chloride (**2**) with substituted anilines and deuterated anilines ( $XC_6H_4NH_2$  and  $XC_6H_4ND_2$ ) in acetonitrile at 55.0 °C, eq. (1), to clarify the phosphoryl transfer mechanism, as well as to compare the reactivity of diphenyl

phosphinic chloride (**1**),<sup>3d</sup> diphenyl chlorophosphate (**3**),<sup>3a</sup> and diphenyl chlorothiophosphate (**4**).<sup>3c</sup>



We also calculate the natural bond order (NBO) charge on P and degree of distortion of various chlorophosphates  $[(R_1O)(R_2O)P(=O)Cl]$ , chlorothiophosphates  $[(R_1O)(R_2O)P(=S)Cl]$ , phosphonochloridates  $[(R_1O)R_2P(=O)Cl]$ , phosphonochlorothioates  $[(R_1O)R_2P(=S)Cl]$ , chlorophosphinates  $[R_1R_2P(=O)Cl]$ , and chlorothiophosphinates  $[R_1R_2P(=S)Cl]$  at the B3LYP/6-311+G(d,p) level<sup>5</sup> to compare the structure-reactivity relationships.

### Results and Discussion

The observed pseudo-first-order rate constants ( $k_{\text{obsd}}$ ) for the reactions obeyed eq. (2) with negligible  $k_0$  ( $= 0$ ) in acetonitrile. The second-order rate constants,  $k_{H(D)}$ , were determined using eq. (2) with at least five aniline concentrations,  $[An]$ . No third-order or higher-order terms were

<sup>†</sup>This paper is dedicated to Professor Sang Chul Shim on the occasion of his honorable retirement.

**Table 1.** Second-Order Rate Constants,  $k_H$  and  $k_D$  ( $\times 10^4/M^{-1}s^{-1}$ ), of the Aminolysis of Diphenyl Thiophosphinic Chloride (**2**) with  $XC_6H_4NH_2$  and  $XC_6H_4ND_2$  in Acetonitrile at 55.0 °C

X	$k_H^a$	$k_D^b$	$k_H/k_D$
4-MeO	$86.6 \pm 2.4^c$	$78.8 \pm 1.7$	$1.10 \pm 0.04$
4-Me	$23.1 \pm 0.6$	$21.2 \pm 0.5$	$1.09 \pm 0.04$
3-Me	$10.7 \pm 0.1$	$10.2 \pm 0.2$	$1.05 \pm 0.02$
H	$6.01 \pm 0.12$	$5.99 \pm 0.15$	$1.00 \pm 0.03$
4-F	$3.78 \pm 0.07$	$3.71 \pm 0.09$	$1.02 \pm 0.03$
4-Cl	$0.572 \pm 0.013$	$0.541 \pm 0.012$	$1.06 \pm 0.03$
3-Cl	$0.246 \pm 0.006$	$0.232 \pm 0.005$	$1.06 \pm 0.04$

<sup>a</sup>Correlation coefficients ( $r$ ) were better than 0.998. <sup>b</sup> $r \geq 0.998$ . <sup>c</sup>Standard deviation.

detected, and no complications were found in the

$$k_{\text{obsd}} = k_0 + k_{H(D)}[\text{An}] \quad (2)$$

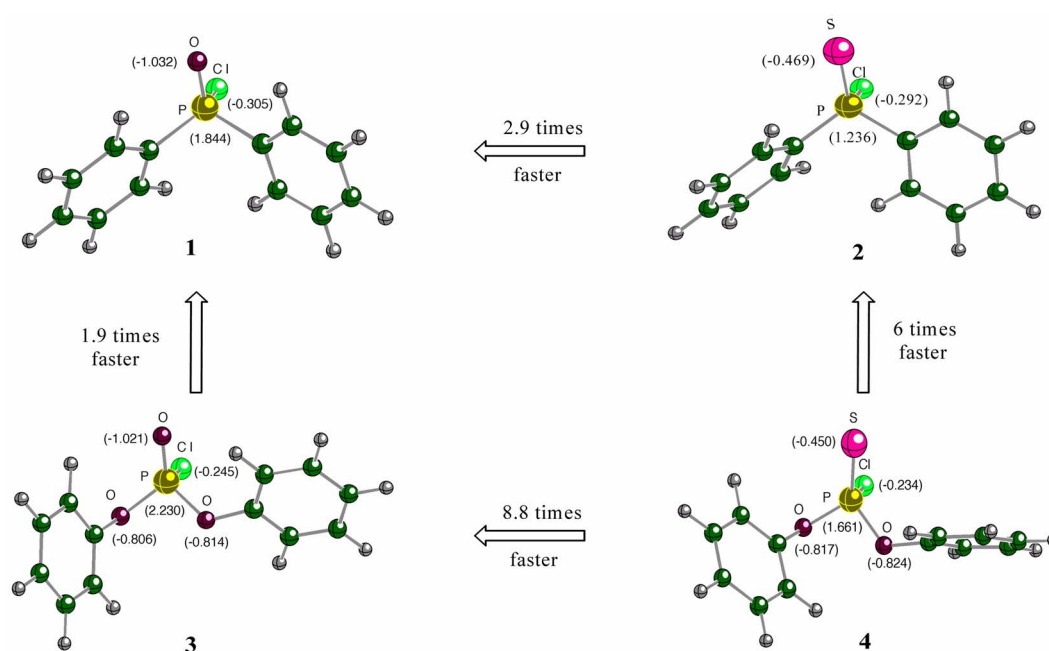
determination of  $k_{\text{obsd}}$  or in the linear plots of eq. (2). This suggests that there is no base-catalysis or noticeable side reaction, and that the overall reactions follow the route given by eq. (1). The  $k_H$  values are summarized in Table 1, together with the  $k_D$  values involving deuterated anilines ( $XC_6H_4ND_2$ ).

In agreement with the trends for typical nucleophilic substitution reactions, the rates are faster with stronger nucleophiles. Figure 1 shows the rate ratios of the aminolysis of **1**, **2**, **3**, and **4** in acetonitrile at 55.0 °C. The reaction rate of **1**<sup>4d</sup> is 2.9 times faster than that of **2**, while the rate of **3**<sup>4a</sup> is 8.8 times faster than that of **4**<sup>4c</sup>. Phosphate systems are more reactive than their thiophosphate counterparts by one or more orders of magnitude,<sup>6</sup> while phosphinate systems are less sensitive to S substitution in the P=O bond compared to phosphate systems,<sup>7</sup> in accordance with our results. 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.<sup>8</sup>

The phenoxy group ( $\sigma_1 = 0.40$ ) has stronger electron-withdrawing ability than the phenyl group ( $\sigma_1 = 0.12$ ).<sup>9</sup> Solely considering the difference of inductive effects between the phenoxy and phenyl groups, the positive charge of the reaction center P in **1** (and **2**) would be smaller than that in **3** (and **4**). Figure 1 shows the NBO charges on reaction center P, 1.844 (**1**), 2.230 (**3**); 1.236 (**2**), 1.661 (**4**). The NBO charges on reaction center P are consistent with the expectations for the inductive effects. If the rate is proportional to the positive charge on reaction center P, the rate ratios should be  $k_{P=O}(\mathbf{1})/k_{P=O}(\mathbf{3}) < 1$  and  $k_{P=S}(\mathbf{2})/k_{P=S}(\mathbf{4}) < 1$ . However, to the contrary, rate ratios of  $k_{P=O}(\mathbf{1})/k_{P=O}(\mathbf{3}) = 1.9$  and  $k_{P=S}(\mathbf{2})/k_{P=S}(\mathbf{4}) = 6$  are obtained. These kinetic results imply that the reaction rate does not depend only on the magnitude of the positive charge on reaction center P.

Selectivity parameters,  $\rho_X$  and  $\beta_X$ , and deuterium kinetic isotope effects (KIEs),  $k_H/k_D$ , are summarized in Table 2. The magnitudes of Hammett  $\rho_X$  ( $-3.97$ ) and Brønsted  $\beta_X$  ( $1.40$ ) values of **2** are both large, suggesting extensive bond formation in the TS. However, these values are somewhat smaller than those of **1**,  $\rho_X(\mathbf{1}) = -4.78$  and  $\beta_X(\mathbf{1}) = 1.69$ ,<sup>4d</sup> indicating a lesser degree of bond-formation in the aminolysis of **2** compared to that of **1**. Figure 2 shows the Brønsted plots of the reactions of **2** with  $XC_6H_4NH_2$  and  $XC_6H_4ND_2$  in acetonitrile. The magnitudes of  $\rho_X$  and  $\beta_X$  values of **2** ( $-3.94$  and  $1.40$ , respectively) with deuterated anilines ( $XC_6H_4ND_2$ ) are nearly the same as those with anilines ( $XC_6H_4NH_2$ ), while the magnitudes of  $\rho_X$  and  $\beta_X$  values of **1** ( $-4.56$  and  $1.62$ , respectively) with deuterated anilines are somewhat smaller than those with anilines. The  $pK_a$  values of anilines in water are used to obtain the Brønsted  $\beta_X$  values and are

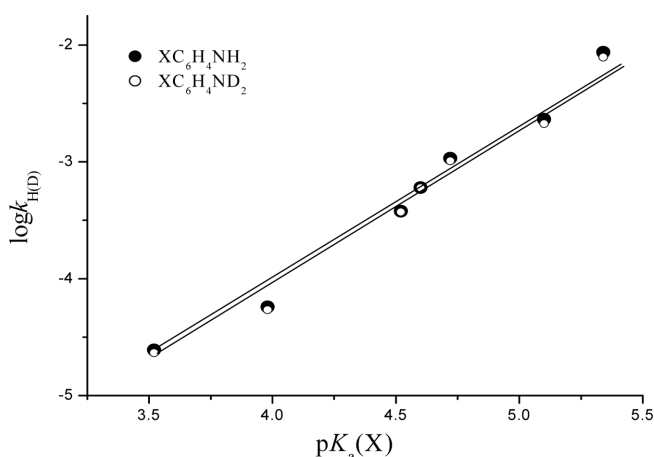


**Figure 1.** The B3LYP/6-311+G(d,p)<sup>5</sup> geometries and NBO charges of **1**,<sup>4d</sup> **2**, **3**,<sup>4a,c</sup> and **4**.<sup>4c</sup> The relative rate ratios are for unsubstituted aniline ( $C_6H_5NH_2$ ).

**Table 2.** The  $k_H$  ( $\times 10^4/\text{M}^{-1}\text{s}^{-1}$ ),  $\rho_X$ ,  $\beta_X$ , and  $k_H/k_D$  Values of the Reactions of  $\text{Ph}_2\text{P(=O)Cl}$  (**1**),  $\text{Ph}_2\text{P(=S)Cl}$  (**2**),  $(\text{PhO})_2\text{P(=O)Cl}$  (**3**), and  $(\text{PhO})_2\text{P(=S)Cl}$  (**4**) with X-Anilines in Acetonitrile at 55.0 °C

Substrate	$k_H^a$	$-\rho_X^b$	$\beta_X^c$	$k_H/k_D$	ref.
<b>1</b>	17.3	4.78 <sup>d</sup> (4.56) <sup>e</sup>	1.69 <sup>d</sup> (1.62) <sup>e</sup>	1.42-1.82	4d
<b>2</b>	6.01	3.97 <sup>d</sup> (3.94) <sup>e</sup>	1.40 <sup>d</sup> (1.40) <sup>e</sup>	1.00-1.10	This work
<b>3</b>	8.91	3.74	1.35	0.71-0.77	4a
<b>4</b>	1.01	3.88	1.36	1.11-1.27	4c

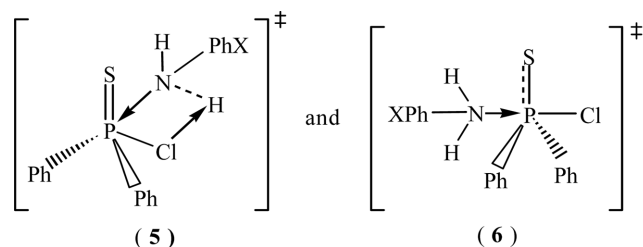
<sup>a</sup>When X = H. <sup>b</sup>The  $\sigma$  values were taken from ref. 10. <sup>c</sup>The  $\text{p}K_a$  values were taken from ref. 11. <sup>d</sup>Calculated from  $k_H$  values. <sup>e</sup>Calculated from  $k_D$  values.

**Figure 2.** Brønsted plots of the anilinolysis of diphenyl thiophosphinic chloride (**2**) with  $\text{XC}_6\text{H}_4\text{NH}_2$  and  $\text{XC}_6\text{H}_4\text{ND}_2$  in acetonitrile at 55.0 °C. The  $\text{p}K_a$  values of  $\text{XC}_6\text{H}_4\text{ND}_2$  are assumed to be the same as those of  $\text{XC}_6\text{H}_4\text{NH}_2$  in water.

justified experimentally and theoretically.<sup>12</sup> The obtained  $\beta_X$  value is larger than those of other phosphoryl and thiophosphoryl reactions in which the reactions proceed through a concerted mechanism ( $\beta_X = 0.2\text{--}0.5$ ).<sup>2b,13</sup> The  $\beta_X$  values of the reactions of (i) 4-nitrophenyl dimethyl phosphinothioate with phenoxides,<sup>2b</sup> (ii) 4-nitrophenyl diphenyl phosphate with phenoxides,<sup>13a</sup> (iii) 4-nitrophenyl diphenyl phosphinate with phenoxides,<sup>13b</sup> (iv) isoquinolino-*N*-phosphonate with pyridines,<sup>13c</sup> and (v) *O,O*-dimethyl *O*-(3-methyl-4-nitrophenyl) phosphorothioate with phenoxides<sup>13d</sup> are 0.47, 0.53, 0.46, 0.15, and 0.49, respectively. The  $\beta_X$  (and  $\beta_X$ ) values of the anilinolysis of **3** and **4** are 1.35 (and 3.74)<sup>4a</sup> and 1.36 (and 3.88),<sup>4c</sup> respectively, somewhat smaller than that of **1**. The especially large  $\rho_X$  and  $\beta_X$  values seem to be characteristic of the anilinolysis of **1-4** in acetonitrile with their Cl leaving group.

In the anilinolysis of **3**, a backside nucleophilic attack concerted mechanism with a late, product-like TS was proposed on the basis of large  $\rho_X$  (and  $\beta_X$ ), large negative cross-interaction constant,<sup>14</sup>  $\rho_{XY} = -1.31$ , and the secondary inverse KIEs,  $k_H/k_D = 0.7\text{--}0.8$ , with deuterated aniline nucleophiles.<sup>4a</sup> In the anilinolysis of **4**, a partial frontside nucleophilic attack concerted mechanism through a hydrogen-bonded four-center type TS was suggested for several reasons, mainly based on the primary KIEs,  $k_H/k_D = 1.1\text{--}1.3$ .<sup>4c</sup> In the anilinolysis of **1**, the greater  $k_H/k_D$  ( $= 1.4\text{--}1.8$ ) values compared to those of **4** ( $k_H/k_D = 1.1\text{--}1.3$ ) were

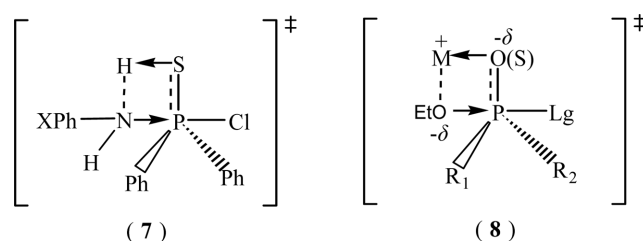
rationalized by the larger proportion of frontside nucleophilic attack compared to that of **4**. In the anilinolysis of **2**, both (i) frontside attack through a hydrogen-bonded four-center type TS (**5**) and (ii) backside attack concerted mechanism through TBP-5C TS (**6**) are suggested for the same reasons as in **1** and **4**.<sup>4a,c</sup>



The observed primary KIEs in **2** would be the sum of (i) the primary normal KIE,  $k_H/k_D > 1$ , because of partial deprotonation of one of the two N-H(D) bonds in TS **5** for a frontside attack, (ii) the secondary inverse KIE,  $k_H/k_D < 1$ , because of steric hindrance that increases the out-of-plane bending vibrational frequencies of the other N-H(D) bond in TS **5** for a frontside attack, (iii) the secondary inverse KIE,  $k_H/k_D < 1$ , because of steric congestion that increases the vibrational frequencies of both of the N-H(D) bonds in TS **6** for a backside attack, (iv) decreased  $k_H/k_D$  value because of the nonlinear and unsymmetrical structure of  $\text{N}\cdots\text{H}(\text{D})\cdots\text{Cl}$  in TS **5**, and finally (v) decreased  $k_H/k_D$  value because of heavy atom (N and Cl) contribution to the reaction-coordinate motion.<sup>15</sup> Thus, the real primary KIE due to the hydrogen bond between the hydrogen of the N-H(D) moiety and the Cl leaving group should be greater than the observed value.

The smaller  $k_H/k_D$  values in **2** compared to those in **1** may be attributed to the smaller proportion of frontside attack in **2** than in **1** or to a lesser degree of bond-formation in **2** than in **1**, assuming the primary KIE is proportional to the degree of bond-formation. Considering the relatively large steric hindrance on the backside attack toward the Cl leaving group due to two phenyl rings in the reactions of **1** and **2** with anilines, a lesser degree of bond-formation in **2** than in **1** is more reasonable, which leads to smaller primary KIEs. This suggestion is consistent with the smaller  $\rho_X$  and  $\beta_X$  values of **2** compared to those of **1**, and with the smaller NBO charge on P in **2** (1.236) than in **1** (1.844) as shown in Figure 1.

Another possible TS structure could be TS **7** where there is a hydrogen bond between the sulfur atom in  $\text{P}=\text{S}$  and the hydrogen of the N-H(D) moiety in aniline. A four-membered TS **8** was proposed in the ethanolysis of the phosphinates, paraxon, and parathion with alkali metal ions by Buncel and his coworkers,<sup>16</sup> and Um and his coworkers.<sup>17</sup>



However, positive charge development on the hydrogen of the N–H moiety in the TS would be much smaller than that of  $M^+$  ions, so hydrogen bond involving the polarizable acceptor P=S, as in TS 7, is not feasible. In addition, the secondary inverse KIE in **3**<sup>4a</sup> cannot be substantiated by TS 7. Moreover, the rate ratio of  $k_{P=S}(2)/k_{P=S}(4) = 6$  cannot be rationalized by the backside attack (TS 7), despite the larger NBO charge on P in **4** (1.661) than in **2** (1.236), since the steric hindrance on the backside attack TS would be larger in **2** than in **4** due to the intervening oxygen atom between the reaction center P atom and the phenyl group in **4**.

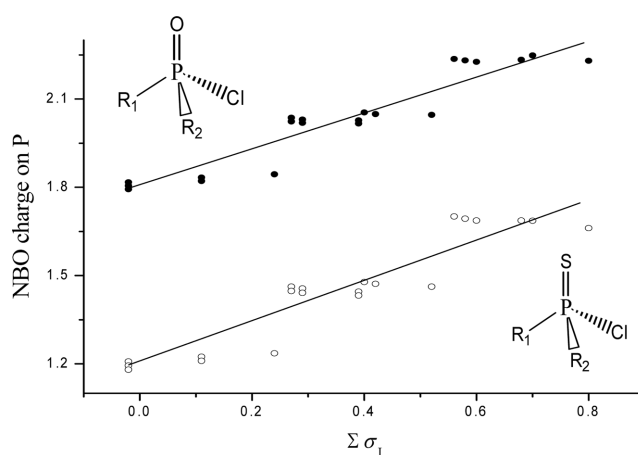
The NBO charges on P of various  $R_1R_2P(=O \text{ or } =S)Cl$  derivatives (42 compounds), calculated at the B3LYP/6-311+G(d,p) level,<sup>5</sup> are summarized in Table 3, and the plots of NBO charges on P against  $\Sigma\sigma_1$  are shown in Figure 3. The slopes for P=O and P=S systems are 0.63 (multiple correlation coefficient,  $r = 0.946$ ) and 0.71 ( $r = 0.936$ ), respectively. The plots show the evident discontinuities between families: *A* [( $R_1O$ )( $R_2O$ )P(=L)Cl; entry no. 1-6], *B* [( $R_1O$ ) $R_2P(=L)Cl$ ; entry no. 7-15], and *C* [ $R_1R_2P(=L)Cl$ ; entry no. 16-21].

The NBO charge on P of P=O system is larger than that of its P=S counterpart due to the larger electronegativity of O compared to that of S. The relative ratio of NBO charges on P for P=O and its P=S counterpart,  $q_{P=O}/q_{P=S}$ , are 1.31-1.34 (family *A*) < 1.39-1.41 (family *B*) < 1.49-1.52 (family *C*). The magnitudes of positive NBO charges on P are  $A > B > C$  with the same  $R_1$  and  $R_2$ , e.g., 2.230 [(PhO)<sub>2</sub>P(=O)Cl] >

**Table 3.** NBO Charges on P, Calculated at the B3LYP/6-311+G(d,p) level,<sup>5</sup> of  $R_1R_2P(=L)Cl$

entry	$R_1$	$R_2$	$\Sigma\sigma_1^a$	$L=O^b$	$L=S^c$
1	PhO	PhO	0.80	2.230 <sup>d</sup>	1.661 <sup>e</sup>
2	PhO	MeO	0.70	2.248	1.686
3	PhO	EtO	0.68	2.233	1.687
4	MeO	MeO	0.60	2.226	1.687
5	MeO	EtO	0.58	2.231	1.693
6	EtO	EtO	0.56	2.236 <sup>f</sup>	1.701 <sup>f</sup>
7	PhO	Ph	0.52	2.043	1.462
8	MeO	Ph	0.42	2.049	1.472
9	EtO	Ph	0.40	2.054	1.478
10	PhO	Et	0.39	2.027	1.445
11	PhO	Me	0.39	2.017	1.432
12	MeO	Et	0.29	2.030	1.456
13	MeO	Me	0.29	2.019	1.441
14	EtO	Et	0.27	2.036	1.462
15	EtO	Me	0.27	2.024	1.447
16	Ph	Ph	0.24	1.844 <sup>g</sup>	1.236 <sup>h</sup>
17	Ph	Et	0.11	1.833	1.224
18	Ph	Me	0.11	1.821	1.210
19	Et	Et	-0.02	1.817	1.208
20	Et	Me	-0.02	1.805	1.194
21	Me	Me	-0.02	1.793	1.180

<sup>a</sup>The  $\sigma_1$  values of PhO, MeO, EtO, Ph, Et, and Me are 0.40, 0.30, 0.28, 0.12, -0.01, and -0.01, respectively, taken from ref. 9. <sup>b</sup>NBO charges on P when L=O. <sup>c</sup>NBO charges on P when L=S. <sup>d</sup>Ref. 4a, c. <sup>e</sup>Ref. 4c. <sup>f</sup>Ref. 4e. <sup>g</sup>Ref. 4d. <sup>h</sup>Ref. 4i.



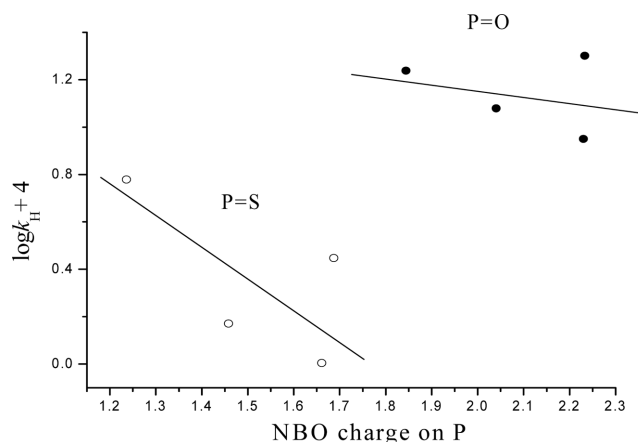
**Figure 3.** The plots of NBO charges on P, calculated at the B3LYP/6-311+G(d,p) level,<sup>5</sup> against  $\Sigma\sigma_1$ .

2.043 [(PhO)PhP(=O)Cl] > 1.844 [Ph<sub>2</sub>P(=O)Cl] and 1.661 [(PhO)<sub>2</sub>P(=S)Cl] > 1.462 [(PhO)PhP(=S)Cl] > 1.236 [Ph<sub>2</sub>P(=S)Cl]. Intervening oxygen atoms between R and P increase the magnitude of positive charge on P, but decrease the relative ratio of positive charges on P,  $q_{P=O}/q_{P=S}$ , for P=O and its P=S counterpart. Figure 4 shows the plots of the second-order rate constant ( $k_H$ ) against NBO charge on P for the anilinolysis of diphenyl chlorophosphate,<sup>4a</sup> 4-chlorophenyl phenyl chlorophosphate,<sup>4b</sup> phenyl ethyl chlorophosphate,<sup>4c</sup> and diphenyl phosphinic chloride,<sup>4d</sup> and their P=S counterparts<sup>4c,e</sup> in acetonitrile at 55.0 °C. Steric effects on the reaction rates and the attacking direction, backside or frontside, are the main factors that lead to bad correlation (even negative slope) between  $k_H$  and NBO charges on P of P=O and P=S systems.

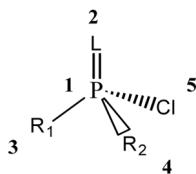
The degree of distortion of  $R_1R_2P(=O \text{ or } =S)Cl$  from the regular tetrahedral structure can be defined as eq. (3),<sup>4c</sup>

$$\Delta\delta = \Sigma |\theta_c - \theta_i| / \theta_i = \Sigma |\theta_c - 109.5| / 109.5 \quad (3)$$

where  $\Delta\delta$  is the degree of distortion,  $\Sigma$  means the sum of all of six bond angles,  $\theta_c$  is the calculated bond angle at the



**Figure 4.** The plots of  $\log k_H$  (in acetonitrile at 55.0 °C) against NBO charges on P for the anilinolysis of diphenyl chlorophosphate,<sup>4a</sup> 4-chlorophenyl phenyl chlorophosphate,<sup>4b</sup> phenyl ethyl chlorophosphate,<sup>4c</sup> and diphenyl phosphinic chloride,<sup>4d</sup> and their P=S counterparts.<sup>4c,e</sup>

**Table 4.** Bond Angles and Degrees of Distortion, Calculated at the B3LYP/6-311+G(d,p) level,<sup>5</sup> of R<sub>1</sub>R<sub>2</sub>P(=L)Cl in the Gas Phase

entry	L	R <sub>1</sub>	R <sub>2</sub>	∠213	∠214	∠215	∠314	∠415	∠315	Δδ
1 O	O	PhO	PhO	118.5	116.7	113.9	100.7	104.8	99.8	0.40 <sup>a</sup>
1 S	S	PhO	PhO	119.4	117.9	115.8	99.4	103.4	97.5	0.48 <sup>a</sup>
2 O	O	PhO	MeO	114.9	118.0	112.9	101.2	103.0	105.2	0.33
2 S	S	PhO	MeO	115.4	119.4	114.6	99.8	101.6	103.6	0.41
3 O	O	PhO	EtO	118.1	116.0	114.1	101.2	104.3	100.9	0.38 <sup>a</sup>
3 S	S	PhO	EtO	119.0	117.4	115.3	99.9	103.4	98.8	0.45 <sup>a</sup>
4 O	O	MeO	MeO	118.3	115.5	113.8	102.1	104.8	100.3	0.37
4 S	S	MeO	MeO	119.1	116.7	115.4	100.7	103.5	98.5	0.44
5 O	O	MeO	EtO	118.1	115.8	113.7	102.3	104.6	100.2	0.37
5 S	S	MeO	EtO	118.9	116.9	115.3	100.9	103.5	98.5	0.44
6 O	O	EtO	EtO	118.3	115.7	113.6	102.4	104.5	100.2	0.37
6 S	S	EtO	EtO	118.9	116.8	115.0	101.4	103.4	98.6	0.43
7 O	O	PhO	Ph	115.9	117.7	111.9	101.8	102.0	105.9	0.33
7 S	S	PhO	Ph	118.4	118.4	113.0	99.8	101.4	103.3	0.41
8 O	O	MeO	Ph	116.5	117.4	111.2	102.6	102.2	105.2	0.32
8 S	S	MeO	Ph	118.5	117.9	112.8	100.8	101.0	103.3	0.40
9 O	O	EtO	Ph	116.3	117.5	111.2	102.8	102.3	105.0	0.32
9 S	S	EtO	Ph	118.2	117.9	112.7	101.1	101.2	103.2	0.40
10 O	O	PhO	Et	117.4	117.3	111.8	100.5	103.0	105.0	0.35
10 S	S	PhO	Et	118.9	118.4	113.4	98.4	102.3	102.7	0.43
11 O	O	PhO	Me	117.2	117.3	112.1	100.8	103.1	104.5	0.35
11 S	S	PhO	Me	118.5	118.5	113.7	99.0	102.3	102.0	0.43
12 O	O	MeO	Et	118.0	116.6	111.4	101.7	103.1	104.2	0.34
12 S	S	MeO	Et	119.1	117.5	113.2	99.8	102.1	102.5	0.41
13 O	O	MeO	Me	117.9	116.6	111.6	101.7	103.3	103.8	0.34
13 S	S	MeO	Me	118.8	117.7	113.5	100.0	102.2	102.0	0.42
14 O	O	EtO	Et	117.7	116.9	111.3	101.9	103.1	104.2	0.34
14 S	S	EtO	Et	118.8	117.7	113.2	100.0	102.2	102.4	0.41
15 O	O	EtO	Me	117.7	116.8	111.5	102.0	103.3	103.7	0.34
15 S	S	EtO	Me	118.5	117.8	113.4	100.4	102.3	101.8	0.41
16 O	O	Ph	Ph	113.4	112.7	113.9	110.0	102.8	103.2	0.23
16 S	S	Ph	Ph	115.3	115.0	113.5	107.4	101.3	102.6	0.30
17 O	O	Ph	Et	115.0	113.7	113.2	108.4	103.3	101.9	0.26
17 S	S	Ph	Et	115.9	115.8	114.4	106.0	102.1	100.6	0.34
18 O	O	Ph	Me	113.7	115.0	113.5	108.6	101.2	103.5	0.26
18 S	S	Ph	Me	116.0	115.3	114.7	106.6	99.9	102.2	0.34
19 O	O	Et	Et	114.8	114.7	113.7	107.6	102.8	101.9	0.28
19 S	S	Et	Et	116.3	116.3	114.8	105.5	100.9	100.9	0.37
20 O	O	Et	Me	115.1	115.2	113.2	107.9	102.3	101.6	0.29
20 S	S	Et	Me	115.8	116.5	115.0	106.0	101.1	100.3	0.36
21 O	O	Me	Me	115.1	115.1	113.5	108.0	101.7	101.7	0.29
21 S	S	Me	Me	115.9	115.9	115.4	106.3	100.5	100.6	0.36

<sup>a</sup>Ref. 4e.

B3LYP/6-311+G(d,p) level<sup>5</sup> and  $\theta_i$  is the ideal bond angle (109.5°) of a regular tetrahedral structure. The  $\Delta\delta$  values of 42 compounds are summarized in Table 4 together with six

bond angles. Due to the larger size and polarizability of P=S sulfur compared to those of P=O oxygen, the distortion of P=S substrates is larger than that of P=O substrates. The increments of the degree of distortion from P=O to P=S counterparts are 1.17-1.21, 1.22-1.27, and 1.23-1.30 times larger for families A, B, and C, respectively. The larger the ligand, the greater the increment of degree of distortion, e.g.,  $\Delta\delta = 0.400$  ( $R_1 = R_2 = \text{PhO}$ ), 0.327 ( $R_1 = \text{PhO}$ ,  $R_2 = \text{Ph}$ ), and 0.228 ( $R_1 = R_2 = \text{Ph}$ ).

### Summary

The reactions of diphenyl thiophosphinic chloride (2) with X-anilines were studied kinetically in acetonitrile at 55.0 °C. Structure-reactivity relationships between diphenyl phosphinic chloride (1), diphenyl chlorophosphate (3), and diphenyl chlorothiophosphate (4), were discussed based on NBO charges and steric effects. The primary normal KIEs involving deuterated aniline (XC<sub>6</sub>H<sub>4</sub>ND<sub>2</sub>) nucleophiles were obtained and were consistent with a partial frontside attack concerted mechanism through a hydrogen-bonded four-center type TS. The smaller magnitudes of  $\rho_X$  and  $\beta_X$  values of 2 compared to those of 1 suggest a lesser degree of bond-formation in the TS. The NBO charge on P and the degree of distortion of 42 R<sub>1</sub>R<sub>2</sub>P(=O or =S)Cl compounds were calculated at the B3LYP/6-311+G(d,p) level. The bad correlation between reaction rates and NBO charges on P was ascribed to steric effects and the attacking direction of the nucleophile.

### Experimental Section

**Materials.** Diphenyl thiophosphinic chloride (min. 95%) 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.<sup>18</sup> Deuterated anilines were synthesized by heating anilines and deuterium oxide (99.9 atom % D) at 90 °C for 72 hours, and after numerous attempts, anilines were deuterated more than 98%, as confirmed by <sup>1</sup>H NMR.

**Kinetics Measurement.** Rates were measured conductometrically as previously described.<sup>4</sup> [Substrate] = 0.001 M and [Nucleophile] = 0.03-0.15 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.** Diphenyl thiophosphinic chloride was reacted with excess anilines (XC<sub>6</sub>H<sub>4</sub>NH<sub>2</sub>; X = 4-CH<sub>3</sub>, H) for more than 15 half-lives at 55.0 °C in acetonitrile, as previously described.<sup>4c</sup> Analytical data of the products gave the following results:

(C<sub>6</sub>H<sub>5</sub>)<sub>2</sub>P(=S)NHC<sub>6</sub>H<sub>4</sub>-4-CH<sub>3</sub>. Light-Brown solid; mp 169-171 °C; IR(nujol mull): 3358 (NH), 3055 (C-H, aromatic), 2955 (CH<sub>3</sub>), 1612, 1516, 1436, 1104 (P-C<sub>6</sub>H<sub>5</sub>), 809 (P=S); <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>)  $\delta$  2.22 (3H, s, CH<sub>3</sub>), 6.79-6.81 (2H, d, *J* = 8.0 Hz), 6.94-6.97 (2H, d, *J* = 12.0 Hz), 7.25-7.54 (6H, m, phenyl), 7.98-8.04 (4H, m,

phenyl), 4.78-4.80 (1H, d,  $J = 6.0$  Hz, NH);  $^{13}\text{C}$  NMR (100 MHz, DMSO- $d_6$ )  $\delta$  118.6-118.8 (CH<sub>3</sub>, d,  $J = 7.5$  Hz), 128.4-138.7 (C=C, aromatic);  $^{31}\text{P}$  NMR (162 MHz, DMSO- $d_6$ )  $\delta$  59.7 (1P, s, P=S);  $m/z$ , 323 (M<sup>+</sup>); Anal. Calcd for C<sub>19</sub>H<sub>18</sub>NPS: C, 70.57; H, 5.61; N, 4.33; S, 9.92. Found: C, 70.57; H, 5.61; N, 4.26; S, 9.77.

(C<sub>6</sub>H<sub>5</sub>)<sub>2</sub>P(=S)NHC<sub>6</sub>H<sub>5</sub>. Fawn solid; mp 159-161 °C; IR (nujol mull): 3124; (NH), 3054 (C-H, aromatic), 1602, 1479, 1437, 1103 (P-C<sub>6</sub>H<sub>5</sub>), 797 (P=S);  $^1\text{H}$  (400 MHz, DMSO- $d_6$ ),  $\delta$  6.89-6.93 (3H, m, phenyl), 7.13-7.17 (2H, m, phenyl), 7.45-7.55 (6H, m, phenyl), 7.98-8.05 (4H, m, phenyl), 4.87-4.89 (1H, d,  $J = 6$  Hz, NH);  $^{13}\text{C}$  NMR (100 MHz, DMSO- $d_6$ )  $\delta$  118.5-141.3 (C=C, aromatic);  $^{31}\text{P}$  NMR (162 MHz, DMSO- $d_6$ )  $\delta$  59.6 (1P, s, P=S);  $m/z$ , 309 (M<sup>+</sup>); Anal. Calcd for C<sub>18</sub>H<sub>16</sub>NPS: C, 69.88; H, 5.21; N, 4.53; S, 10.37. Found: C, 69.81; H, 5.22; N, 4.38; S, 10.15.

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

### References

- (a) Corbridge, D. E. C. *Phosphorus-An Outline of its Chemistry, Biochemistry and Uses*, 5th ed.; Elsevier: Amsterdam, 1995; Chapter 11. (b) Williams, A. *Concerted Organic and Bio-Organic Mechanisms*; CRC Press: Boca Raton, 2000. (c) Hudson, R. F. *Structure and Mechanism on Organophosphorus Chemistry*; Academic Press: New York, 1965.
- (a) Humphry, T.; Forconi, M.; Williams, N. H.; Hengge, A. C. *J. Am. Chem. Soc.* **2004**, *126*, 11864. (b) Onyido, I.; Swierczek, K.; Purcell, J.; Hengge, A. C. *J. Am. Chem. Soc.* **2005**, *127*, 7703. (c) Um, I. H.; Shin, Y. H.; Han, J. Y.; Mishima, M. *J. Org. Chem.* **2006**, *71*, 7715. (d) Skoog, M. T.; Jencks, W. P. *J. Am. Chem. Soc.* **1984**, *106*, 7597. (e) Harger, M. J. P. *J. Chem. Soc., Perkin Trans. 2* **2002**, 489. (f) Hengge, A. C. *Adv. Phys. Org. Chem.* **2005**, *40*, 49. (g) van Bochove, M. A.; Swart, M.; Bickelhaupt, M. *J. Am. Chem. Soc.* **2006**, *128*, 10738.
- (a) Hall, C. R.; Inch, T. D. *Tetrahedron* **1980**, *36*, 2059. (b) Rowell, R.; Gorenstein, D. G. *J. Am. Chem. Soc.* **1981**, *103*, 5894. (c) Inch, T. D.; Lewis, G. J.; Wilkinson, R. G.; Watts, P. *J. Chem. Soc., Chem. Commun.* **1975**, 500. (d) Inch, T. D.; Lewis, G. J. *Carbohydrate Research*, **1975**, *45*, 65. (e) Harrison, J. M.; Inch, T. D.; Lewis, G. J. *J. Chem. Soc., Perkin 1* **1974**, 1053. (f) Stec, W. J.; Okruszek, A.; Lesiak, K.; Uznanski, B.; Michalski, J. *J. Org. Chem.* **1976**, *41*, 22. (g) Hall, C. R.; Inch, T. D. *J. Chem. Soc., Perkin 1* **1979**, 1104. (h) Hall, C. R.; Inch, T. D. *J. Chem. Soc., Perkin 1* **1979**, 1646. (i) Corriu, R. J. P.; Dutheil, J. P.; Lanneau, G. F. *J. Am. Chem. Soc.* **1984**, *106*, 1060. (j) Corriu, R. J. P.; Dutheil, J. P.; Lanneau, G. F.; Leclercq, D. *Tetrahedron Lett.* **1983**, *24*, 4323. (k) Corriu, R. J. P.; Fernandez, J. M.; Guerin, C. *Nouv. J. Chem.* **1984**, *8*, 279. (l) Corriu, R. J. P.; Dutheil, J. P.; Lanneau, G. F.; Ould-Kada, S. *Tetrahedron* **1979**, *35*, 2089.
- Anililindolysis*: (a) Guha, A. K.; Lee, H. W.; Lee, I. *J. Chem. Soc., Perkin Trans. 2* **1999**, 765. (b) Lee, H. W.; Guha, A. K.; Lee, I. *Int. J. Chem. Kinet.* **2002**, *34*, 632. (c) Hoque, M. E. U.; Dey, S.; Guha, A. K.; Kim, C. K.; Lee, B. S.; Lee, H. W. *J. Org. Chem.* **2007**, *72*, 5493. (d) Hoque, M. E. U.; Lee, H. W. *Bull. Korean Chem. Soc.* **2007**, *28*, 936. (e) Hoque, M. E. U.; Dey, N. K.; Kim, C. K.; Lee, B. S.; Lee, H. W. *Org. Biomol. Chem.* **2007**, DOI: 10.1039/B713167D. *Pyridinolysis*: (f) Guha, A. K.; Lee, H. W.; Lee, I. *J. Org. Chem.* **2000**, *65*, 12. (g) Lee, H. W.; Guha, A. K.; Kim, C. K.; Lee, I. *J. Org. Chem.* **2002**, *67*, 2215. (h) Adhikary, K. K.; Lee, H. W.; Lee, I. *Bull. Korean Chem. Soc.* **2003**, *24*, 1135. (i) 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. *Theoretical*: (j) 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**, *112*, 11162.
- Hehre, W. J.; Random, L.; Schleyer, P. V. R.; Pople, J. A. *Ab Initio Molecular Orbital Theory*; Wiley: New York, 1986; Chapter 4.
- (a) Neimysheva, A. A.; Savchik, V.; Ermolaeva, M. V.; Knunyants, I. L. *Bull. Acad. Sci. USSR Div. Chem. Sci. (Engl. Transl.)* **1968**, 2104. (b) Ketelaar, J. A. A.; Gresmann, H. R.; Koopmans, K. *Recl. Trav. Chim. Pays-Bas.* **1952**, *71*, 1253. (c) Chlebowski, J. F.; Coleman, J. E. *J. Biol. Chem.* **1974**, *247*, 7192.
- (a) Cook, R. D.; Farah, S.; Ghawi, L.; Itani, A.; Rahil, J. *Can. J. Chem.* **1986**, *64*, 1630. (b) Bel'skii, V. E.; Bezzubova, N. N.; Akamsin, V. D.; Eliseenkov, V. N.; Rizpolozhenskii, N. I.; Pudevik, A. N. *Dokl. Akad. Nauk. SSSR* **1971**, *197*, 85; Eng Trans PP. 171. (c) Onyido, I.; Swierczek, K.; Purcell, J.; Hengge, A. C. *J. Am. Chem. Soc.* **2005**, *127*, 7703. (d) Douglas, K. T.; Williams, A. *J. Chem. Soc., Perkin Trans. 2* **1976**, 515. (e) Um, I. H.; Akhtar, K.; Shin, Y. H.; Han, J. Y. *J. Org. Chem.* **2007**, *72*, 3823. (f) Cook, R. D.; Daouk, W. A.; Hajj, Kabbani, A.; A. N.; Kurku, A.; Samaha, M.; Shayban, F.; Tanielian, O. V. *Can. J. Chem.* **1986**, *64*, 213.
- (a) Hengge, A. C.; Onyido, I. *Curr. Org. Chem.* **2005**, *9*, 61. (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) Hondal, R. J.; Bruzik, K. S.; Zhao, Z.; Tsai, M. D. *J. Am. Chem. Soc.* **1997**, *119*, 5477.
- Charton, M. *Prog. Phys. Org. Chem.* **1987**, *16*, 287
- Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165.
- Streitwieser, A. Jr.; Heathcock, C. H. *Introduction to Organic Chemistry*, 3rd ed.; Macmillan Publishing Co.: New York, 1989; p 693.
- (a) Ritchie, C. D. In *Solute-Solvent Interactions*; Coetzee, J. F.; Ritchie, C. D., Eds.; Marcel Dekker: New York, 1969; Ch. 4. (b) Coetzee, J. F. *Prog. Phys. Org. Chem.* **1967**, *4*, 54. (c) Spillane, W. J.; Hogan, G.; McGrath, P.; King, J.; Brack, C. *J. Chem. Soc., Perkin Trans. 2* **1996**, 2099. (d) Oh, H. K.; Woo, S. Y.; Shin, C. H.; Park, Y. S.; Lee, I. *J. Org. Chem.* **1997**, *62*, 5780.
- (a) Ba-Saif, S. A.; Waring, M. A.; Williams, A. *J. Am. Chem. Soc.* **1990**, *112*, 8115. (b) Bourne, N.; Chrystiuk, E.; Davis, A. M.; Williams, A. *J. Am. Chem. Soc.* **1988**, *110*, 1890. (c) Bourne, N.; Williams, A. *J. Am. Chem. Soc.* **1984**, *106*, 7591. (d) Omakor, J. E.; Onyido, I.; vanLoon, G. W.; Buncel, E. *J. Chem. Soc., Perkin Trans. 2* **2001**, 324.
- (a) Lee, I. *Chem. Soc. Rev.* **1990**, *19*, 317. (b) Lee, I. *Adv. Phys. Org. Chem.* **1992**, *27*, 57. (c) Lee, I.; Lee, H. W. *Collect. Czech. Chem. Commun.* **1999**, *64*, 1529.
- (a) Lee, I.; Koh, H. J.; Lee, B. S.; Lee, H. W. *J. Chem. Soc., Chem. Commun.* **1991**, 335. (b) Melander, L.; Saunders, Jr. W. H. *Reaction Rates of Isotopic Molecules*; Wiley: New York, 1981. (c) Kaldor, S. B.; Saunders, Jr. W. H. *J. Chem. Phys.* **1978**, *68*, 2509. (d) Swain, C. C.; Pegues, E. E. *J. Am. Chem. Soc.* **1958**, *80*, 812. (e) Kwart, H. *Acc. Chem. Res.* **1982**, *15*, 401. (f) Kwart, H.; Brechbid, M. W.; Acheson, R. M.; Ward, D. C. *J. Am. Chem. Soc.* **1982**, *104*, 4671.
- (a) Onyido, I.; Albright, K.; Buncel, E. *Org. Biomol. Chem.* **2005**, *3*, 1468. (b) Buncel, E.; Albright, K.; Onyido, I. *ibid.* **2004**, *2*, 601.
- Um, I. H.; Jeon, S. E.; Baek, M. H.; Park, H. R. *Chem. Commun.* **2003**, 3016.
- Lee, I.; Lee, H. W.; Sohn, S. C.; Kim, C. H. *Tetrahedron* **1985**, *41*, 2635.