

Kinetics and Mechanism of the Anilinolysis of Dicyclohexyl Phosphinic Chloride in Acetonitrile

Md. Ehtesham Ul Hoque and Hai Whang Lee*

Department of Chemistry, Inha University, Incheon 402-751, Korea. *E-mail: hwlee@inha.ac.kr
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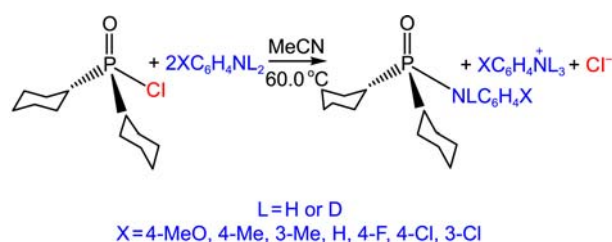
The nucleophilic substitution reactions of dicyclohexyl phosphinic chloride [**3**; cHex₂P(=O)Cl] with substituted anilines (XC₆H₄NH₂) and deuterated anilines (XC₆H₄ND₂) are investigated kinetically in acetonitrile at 60.0 °C. The anilinolysis rate is too slow to be rationalized by the stereoelectronic effects. The rate is contrary to expectations for the electronic influence of the two ligands and exhibits exceptionally great negative deviation from the Taft's eq. The deuterium kinetic isotope effects (DKIEs) involving deuterated anilines invariably change from primary normal ($k_H/k_D > 1$; max $k_H/k_D = 1.10$ with X = 4-MeO) with the strongly basic anilines (X = 4-MeO, 4-Me, 3-Me) to secondary inverse ($k_H/k_D < 1$; min $k_H/k_D = 0.673$ with X = 3-Cl) with the weakly basic anilines (X = H, 4-F, 4-Cl, 3-Cl). A concerted S_N2 mechanism is proposed on the basis of both secondary inverse and primary normal DKIEs. The obtained DKIEs imply that the fraction of a frontside attack increases as the aniline becomes more basic. A hydrogen-bonded, four-center-type transition state is suggested for a frontside attack, while the trigonal bipyramidal pentacoordinate transition state is suggested for a backside attack.

Key Words : Phosphoryl transfer reaction, Anilinolysis, Dicyclohexyl phosphinic chloride, Deuterium kinetic isotope effects

Introduction

Nucleophilic substitution at a phosphoryl (P=O) or thiophosphoryl (P=S) center generally proceeds either through stepwise mechanism (A_N + D_N) with a trigonal bipyramidal pentacoordinate (TBP-5C) intermediate or a concerted S_N2 mechanism (A_ND_N) with a TBP-5C transition state (TS).¹ The deuterium kinetic isotope effects (DKIEs; k_H/k_D) are one of the strong tools to clarify the reaction mechanism. The DKIEs have provided a useful means to determine the TS structures in nucleophilic substitution reactions, and how the reactants, especially through changes in substituents, alter the TS structures.² 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 ($k_H/k_D > 1.0$).³ 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.^{2,3}

Continuing the studies on phosphoryl transfer reactions (anilinolysis,⁴ pyridinolysis,⁵ and theoretical study⁶), the reactions of dicyclohexyl phosphinic chloride [**3**; cHex₂P(=O)Cl] with substituted anilines (XC₆H₄NH₂) and deuterated anilines (XC₆H₄ND₂) are investigated kinetically in acetonitrile at 60.0 ± 0.1 °C (Scheme 1) to gain further information into the phosphoryl transfer reactions, as well as to compare the reactivity, mechanism and DKIEs of the anilinolyses of R₁R₂P(=O)Cl-type substrates where R₁ and



Scheme 1. The studied reaction system.

R₂ are alkyl and/or phenyl: dimethyl [**1**; Me₂P(=O)Cl];⁴ⁱ diethyl [**2**; Et₂P(=O)Cl];⁴ⁱ methyl phenyl [**4**; MePhP(=O)Cl];⁴ⁱ and diphenyl [**5**; Ph₂P(=O)Cl]^{4d} phosphinic chlorides in MeCN. The numbering of the substrates follows the sequence of the summation of the Taft's steric constants⁷ [$\Sigma E_S = E_S(R_1) + E_S(R_2)$] of the two ligands; dimethyl ($\Sigma E_S = 0.00$; **1**), diethyl (−0.14; **2**), dicyclohexyl (−1.58; **3**), methyl phenyl (−2.48; **4**), and diphenyl (−4.96; **5**) phosphinic chlorides. The Taft's steric constant (E_S) is inversely proportional to the size of the ligand since the E_S value of methyl group is defined as null.

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.

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

The k_{H} and k_{D} values are summarized in Table 1, together with the DKIEs ($k_{\text{H}}/k_{\text{D}}$) and the Hammett ρ_{X} and Brønsted β_{X} values. The B3LYP/6-311+G(d,p)⁸ geometry, dihedral angles, and natural bond order (NBO) charges of **3** in the gas phase are shown in Figure 1.⁹ The $\text{p}K_{\text{a}}$ values of the anilines in water are used to obtain the Brønsted β_{X} values in MeCN, and this procedure are justified experimentally and theoretically.¹⁰ The $\text{p}K_{\text{a}}$ and σ values of the deuterated anilines are assumed to be identical to those of the anilines.¹¹ The stronger nucleophile leads to the faster rate as observed in a typical nucleophilic substitution reaction. The magnitudes of the ρ_{X} and β_{X} values of the reactions of **3** with the deuterated anilines are slightly smaller than those with the anilines, suggesting less sensitivity to substituent effects of deuterated

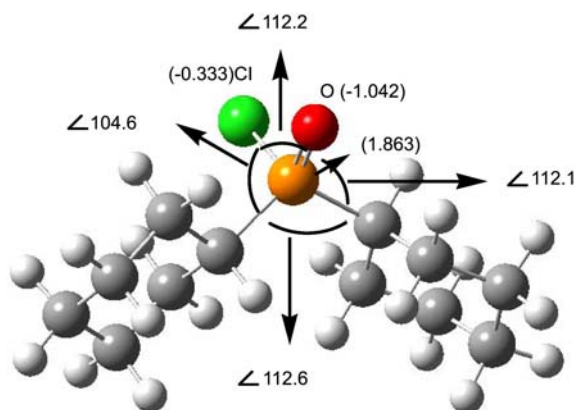


Figure 1. The B3LYP/6-311+G(d,p) geometry of **3** (dicyclohexyl phosphinic chloride) in the gas phase.

Table 1. The second-order rate constants ($k_{\text{H(D)}} \times 10^5/\text{M}^{-1} \text{s}^{-1}$), selectivity parameters^a (ρ_{X} and β_{X}), and deuterium kinetic isotope effects ($k_{\text{H}}/k_{\text{D}}$) for the reactions of **3** (dicyclohexyl phosphinic chloride) with $\text{XC}_6\text{H}_4\text{NH}_2(\text{D}_2)$ in MeCN at 60.0 °C

X	$k_{\text{H}} \times 10^5/\text{M}^{-1} \text{s}^{-1}$	$k_{\text{D}} \times 10^5/\text{M}^{-1} \text{s}^{-1}$	$k_{\text{H}}/k_{\text{D}}$
4-MeO	5.64 ± 0.04^b	5.15 ± 0.04	1.10 ± 0.01^i
4-Me	3.65 ± 0.03	3.48 ± 0.04	1.05 ± 0.01
3-Me	2.11 ± 0.01	2.04 ± 0.02	1.03 ± 0.01
H	1.50 ± 0.01	1.78 ± 0.01	0.843 ± 0.001
4-F	1.48 ± 0.01	1.80 ± 0.02	0.822 ± 0.001
4-Cl	0.616 ± 0.004	0.799 ± 0.003	0.791 ± 0.001
3-Cl	0.334 ± 0.003	0.496 ± 0.005	0.673 ± 0.001
$-\rho_{\text{X(H or D)}}$	$1.90 \pm 0.04^{c,d}$	$1.56 \pm 0.05^{f,g}$	
$\beta_{\text{X(H or D)}}$	$0.67 \pm 0.05^{c,e}$	$0.56 \pm 0.03^{f,h}$	

^aThe σ values were taken from Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* 1991, 91, 165. The $\text{p}K_{\text{a}}$ 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. ^bStandard deviation. ^cCalculated from k_{H} values. ^dCorrelation coefficient, $r = 0.997$. ^e $r = 0.995$. ^fCalculated from k_{D} values. ^g $r = 0.992$. ^h $r = 0.997$. ⁱStandard error $\{= 1/k_{\text{D}}[(\Delta k_{\text{H}})^2 + (k_{\text{H}}/k_{\text{D}})^2 \times (\Delta k_{\text{D}})^2]^{1/2}\}$ from Crumpler, T. B.; Yoh, J. H. *Chemical Computations and Errors*; John Wiley: New York, 1940; p 178.

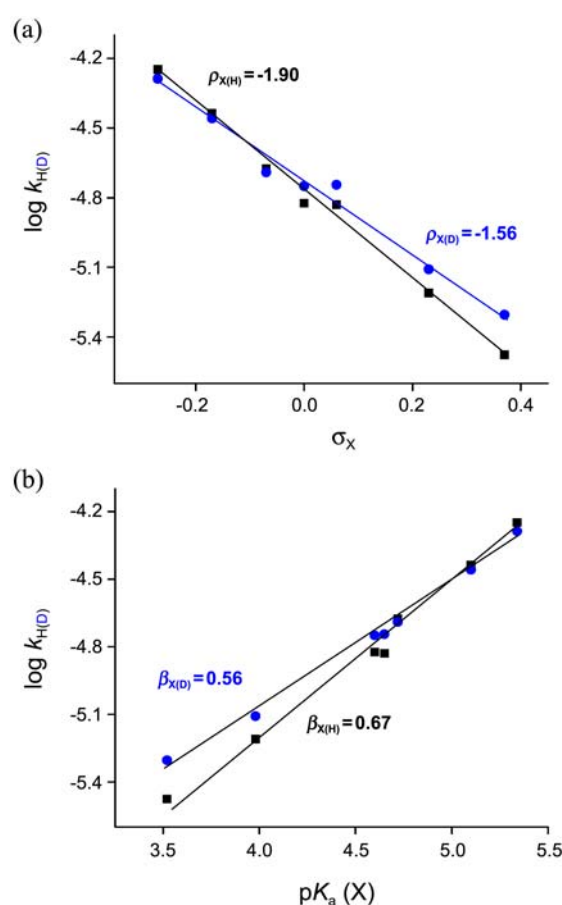


Figure 2. The (a) Hammett ($\log k_{\text{H(D)}} \text{ vs } \sigma_{\text{X}}$) and (b) Brønsted [$\log k_{\text{H(D)}} \text{ vs } \text{p}K_{\text{a}}(\text{X})$] plots of the reactions of **3** (dicyclohexyl phosphinic chloride) with $\text{XC}_6\text{H}_4\text{NH}_2(\text{D}_2)$ in MeCN at 60.0 °C.

anilines compared to anilines (Fig. 2). The same tendency was observed for the anilinoyses of **1**,⁴ⁱ **2**,⁴ⁱ **4**,⁴ⁱ and **5**.^{4d} The DKIEs invariably decrease from a primary normal ($k_{\text{H}}/k_{\text{D}} = 1.10$; max with X = 4-MeO) to a secondary inverse ($k_{\text{H}}/k_{\text{D}} = 0.673$; min with 3-Cl) as substituent X changes from electron-donating to electron-withdrawing, as observed for the anilinoyses of **1**,⁴ⁱ **2**,⁴ⁱ **4**,⁴ⁱ and **5**.^{4d} Until now, the anilinoyses of the three substrates, **3** (this work), dimethyl chlorophosphate [(MeO)₂P(=O)Cl],^{4g} and Y-O-aryl methyl phosphonochloridothioates [(YC₆H₄O)MeP(=S)Cl],^{4k} show both primary and secondary DKIEs among nineteen R₁R₂P(=O or S)Cl-type substrates.^{4a-1}

The second-order rate constants (k_{H}) with unsubstituted aniline (C₆H₅NH₂) at 55.0 °C, summations of the Taft's steric constants [$\Sigma E_{\text{S}} = E_{\text{S}}(\text{R}_1) + E_{\text{S}}(\text{R}_2)$]⁷ and Charton's corrected atomic radii [$\Sigma v_{\text{X}} = v_{\text{X}}(\text{R}_1) + v_{\text{X}}(\text{R}_2)$],¹² NBO charges at the P reaction center [B3LYP/6-311+G(d,p) level of theory],⁸ summations of the inductive effects [$\Sigma \sigma_{\text{I}} = \sigma_{\text{I}}(\text{R}_1) + \sigma_{\text{I}}(\text{R}_2)$],¹³ Brønsted coefficients (β_{X}), and DKIEs ($k_{\text{H}}/k_{\text{D}}$) of the reactions of five phosphinic chlorides with $\text{XC}_6\text{H}_4\text{NH}_2(\text{D}_2)$ in MeCN are summarized in Table 2. The NBO charges at the reaction center P atom are consistent with the summation of the inductive effects ($\Sigma \sigma_{\text{I}}$) of the two ligands, R₁ and R₂, for **1**,⁴ⁱ **2**,⁴ⁱ **4**,⁴ⁱ and **5**^{4d} when excluding **3**. Solely considering

Table 2. Summary of the second-order rate constants ($k_H \times 10^3/M^{-1} s^{-1}$) with $C_6H_5NH_2$ at 55.0 °C, summations of the Taft's steric constants (ΣE_S) and Charton's corrected atomic radii (Σv_x), NBO charges at the P reaction center, summations of the inductive effects ($\Sigma \sigma_i$), Brönsted coefficients (β_X), and DKIEs (k_H/k_D) of the reactions of **1**, **2**, **3**, **4**, and **5** with $XC_6H_4NH_2(D_2)$ in MeCN

Substrate	$k_H \times 10^3$	$-\Sigma E_S$	Σv_x	charge at P	$\Sigma \sigma_i$	$\beta_{X(H)}/\beta_{X(D)}^d$	k_H/k_D	ref
1 ; Me ₂ P(=O)Cl	7,820 ^a	0.00	1.04	1.793	-0.02	1.62/1.56 ^e	0.740-0.945 ^e	4i
2 ; Et ₂ P(=O)Cl	189 ^b	0.14	1.08	1.817	-0.02	0.56/0.52 ^f	0.828-0.974 ^f	4l
3 ; cHex ₂ P(=O)Cl	0.00940 ^c	1.58	1.74	1.863	0.00	0.67/0.56 ^g	0.673-1.10 ^g	this work
4 ; MePhP(=O)Cl	138	2.48	2.18	1.821	0.11	0.88/0.81 ^h	1.62-2.10 ^h	4i
5 ; Ph ₂ P(=O)Cl	1.73	4.96	3.32	1.844	0.24	1.69/1.62 ^h	1.42-1.82 ^h	4d

^aThe value of $k_H = 7,820 \times 10^{-3} M^{-1} s^{-1}$ at 55.0 °C was obtained by extrapolation in the Arrhenius plot ($r = 0.999$) with kinetic data: $k_H = 776, 1,010,$ and $1,610 \times 10^{-3} M^{-1} s^{-1}$ at 0.0, 5.0, and 15.0 °C, respectively, from ref. 4i. ^bThe 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: $k_H = 117, 162,$ and $211 \times 10^{-3} M^{-1} s^{-1}$ at 40.0, 50.0, and 60.0 °C, respectively, from ref. 4l. ^cEmpirical kinetic value. See ref. 14. ^d $\beta_{X(H)}/\beta_{X(D)}$ indicates that the values are calculated from k_H and k_D values, respectively. ^eValues at 15.0 °C. ^fValues at 50.0 °C. ^gValues at 60.0 °C. ^hValues at 55.0 °C.

the magnitudes of the positive charges at the reaction center P atom, the sequence of the anilinolysis rate should be **3** > **5** > **4** > **2** > **1**. However, the observed sequence of the rate, **1** >> **2** > **4** >> **5** >> **3**, is completely contrary to expectations for the electronic influence of the two ligands. It is evident that the magnitude of the positive charge at the reaction center P atom does not play any role to determine the anilinolysis rate of the phosphinic chloride systems.

The second-order rate constants for the reactions of five phosphinic chlorides with unsubstituted aniline ($C_6H_5NH_2$) in MeCN at 55.0 °C give the relative rate ratio of 832,000 (**1**)⁴ⁱ : 20,100 (**2**)^{4l} : 14,700 (**4**)⁴ⁱ : 184 (**5**)^{4d} : 1 (**3**).¹⁴ When **3** is not considered, the sequence of the anilinolysis rates of the phosphinic chlorides, **1** >> **2** > **4** >> **5**, is inversely proportional to the size of the two ligands; Ph,Ph (**5**) > Ph,Me (**4**) > Et,Et (**2**) > Me,Me (**1**). The greater the size of the two ligands, the anilinolysis rate becomes slower, i.e., the relative rates of 4,520 (**1**)⁴ⁱ : 109 (**2**)^{4l} : 80 (**4**)⁴ⁱ : 1 (**5**).^{4d} Figure 3 shows the plots of $\log k_H$ against the summation of the Taft's steric constants and Charton's corrected atomic radii of the two ligands of the reactions of five phosphinic chlorides, **1**, **2**, **3**, **4**, and **5**, with unsubstituted aniline ($C_6H_5NH_2$) in MeCN at 55.0 °C, according to eqs, (a) $\log k_H = \delta \Sigma E_S + C$ and (b) $\log k_H = \nu \Sigma v_x + C$, respectively.

The obtained values of sensitivity coefficients are $\delta = 0.737$ ($r = 0.999$) and $\nu = -1.60$ ($r = 0.999$) from **1**, **4**, and **5**, and $\delta = 0.572$ ($r = 0.895$) and $\nu = -1.25$ ($r = 0.898$) from **1**, **2**, **4**, and **5**. Buncl and his coworkers reported that the second-order rate constants for the ethanolyses of the three phosphinates, 4-nitrophenyl dimethyl ($R_1 = R_2 = Me$), methyl phenyl ($R_1 = Me, R_2 = Ph$), and diphenyl ($R_1 = R_2 = Ph$) phosphinates in $R_1R_2P(=O)OC_6H_4-4-NO_2$ type, gave the relative rates 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 $\delta = 0.478$ ($r = 0.953$) and $\nu = -1.04$ ($r = 0.953$).¹⁵ Williams and his coworkers reported that the second-order rate constants for the phosphate catalyzed hydrolyses of two phosphinates, 4-nitrophenyl dimethyl and diphenyl phosphinates, gave a relative rate of 52 ($k_{HPO_4^{2-}} = 1.06 \times 10^{-2}$) : 1 ($k_{HPO_4^{2-}} = 2.05 \times 10^{-4} M^{-1} s^{-1}$) in 10% dioxane-aqueous 0.1 M NaCl at 25.0 °C, resulting in $\delta = 0.345$ and $\nu = -0.753$.¹⁶ These results suggest that the relative reactivities of the

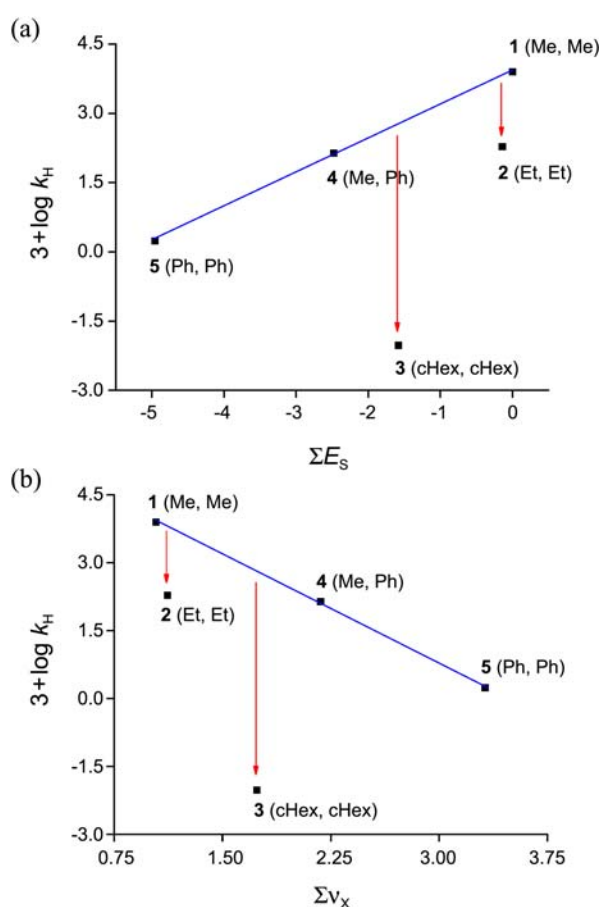


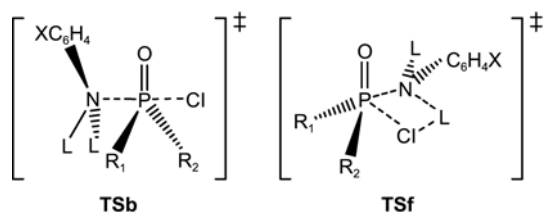
Figure 3. The plots of $\log k_H$ against (a) ΣE_S and (b) Σv_x of the reactions of **1**, **2**, **3**, **4**, and **5** with $C_6H_5NH_2$ in MeCN at 55.0 °C. The literature values of $E_S = 0.00(Me), -0.07(Et), -0.79(cHex),$ and $-2.48(Ph)$,⁷ and $v_x = 0.52(Me), 0.56(Et), 0.87(cHex),$ and $1.66(Ph)$.¹² The two ligands, R_1 and R_2 , are displayed next to the substrate number.

phosphinic chlorides and phosphinates are predominantly dependent upon steric effects over the inductive effects of the ligands, and the anilinolysis rates of the phosphinic chloride systems are much more dependent on the steric effects of the ligands compared to solvolyses of the phosphinate systems.

As seen in Figure 3, the anilinolysis rate of **2** exhibits

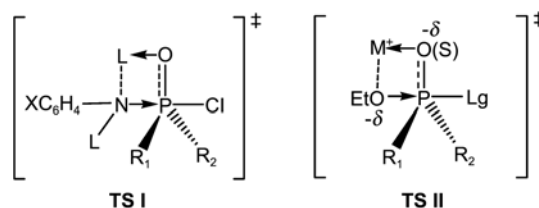
somewhat negative deviation from the slope of $\delta = 0.737$ and $\nu = -1.60$, however, the degree of negative deviation may be qualitatively acceptable. This suggests that the steric effects of the two ethyl ligands in **2** are greater than the reference reaction,⁷ resulting in slower rate than expected one from the ΣE_S and $\Sigma \nu_x$ values. The rate ratio of $k_H(\mathbf{2})/k_H(\mathbf{4}) = 1.4$ implies that the steric effects on the anilinolysis rate of two ethyl ligands is slightly smaller than those of methyl and phenyl ligands. However, the anilinolysis rate of **3** exhibits exceptionally *great* negative deviation from the slope of $\delta = 0.737$ and $\nu = -1.60$. The substrate **3** has not only the greater magnitude of the positive charge at the reaction center P atom compared to **2** and **4** but also smaller size of the two ligands compared to **2** and **4**. This means that the anilinolysis rate of **3** (with two cHex ligands) is too slow to be rationalized by the conventional stereoelectronic effects: 14,700 times slower than that of **2** (with phenyl and methyl ligands), and even 184 times slower than that of **4** (with two phenyl ligands). Furthermore, the exceptional slow rate of the studied reaction system is not attributed to an intrinsic controlled, considering the activation energy of 7.7 (**1**),⁴ⁱ 6.1 (**2**),⁴ⁱ 20.2 (**3**),¹⁵ 10.2 (**4**),⁴ⁱ and 34.4 (**5**)^{4d} kcal/mol. At this point, the authors tentatively suggest that the exceptionally slow rate of the anilinolysis of **3** is attributed to an unexpected steric hindrance of the two cyclohexyl ligands which cannot be predicted by the Taft's ΣE_S and Charton's $\Sigma \nu_x$.

When the anilinolysis proceeds through a stepwise mechanism with a rate-limiting leaving group departure from the intermediate, the secondary normal β -DKIEs ($k_H/k_D = 1.0$ - 1.1)¹⁷ are observed because of the elongation of the N-H(D) bond in the TS.^{2d,18} The relatively large magnitudes of the DKIEs of **4** and **5** ($k_H/k_D > 1.4$) suggest that the DKIEs are not a secondary normal β -type but a primary normal α -type and that the anilinolysis mechanism is not a stepwise with a rate-limiting bond breaking but a concerted S_N2 . The secondary inverse DKIEs of **1** and **2** ($k_H/k_D < 0.97$) also suggest that the anilinolysis mechanism is a concerted S_N2 . Thus, the authors proposed that the anilinolyses of **1** and **2** proceed through a concerted mechanism involving a predominant backside attack TSb on the basis of the secondary inverse DKIEs, whereas the anilinolyses of **4** and **5** proceed through a concerted mechanism involving a predominant frontside attack with a hydrogen-bonded, four-center-type TSf on the basis of the considerably large primary normal DKIEs.



Another plausible TS structure with $k_H/k_D > 1$ could be TS I where there is a hydrogen bond between the oxygen atom in P=O and the hydrogen (deuterium) of the N-H(D)

moiety in aniline. A four-membered TS II was proposed in the ethanolysis of the phosphinates, paraxon, and parathion with alkali metal ions by Bunce¹⁹ and Um.^{1c}



However, positive charge development on the hydrogen (deuterium) of the N-H(D) moiety in the TS I would be much smaller than that on M^+ ions, so that a hydrogen bond involving the acceptor P=O, as in TS I, is not feasible. In addition, the difference between the secondary inverse DKIEs in **1** and **2** and the primary normal DKIE in **4** and **5** cannot be substantiated by TS I. Moreover, the DKIEs, $k_H/k_D = 0.673$ - 1.10 , in **3** cannot be rationalized by TS I at all. So the authors can neglect TS I with $k_H/k_D > 1$.

The DKIEs of five phosphinic chlorides change from secondary inverse with **1** ($k_H/k_D = 0.740$ - 0.945)⁴ⁱ and **2** ($k_H/k_D = 0.828$ - 0.974),⁴ⁱ via *both* secondary inverse and primary normal with **3** ($k_H/k_D = 0.673$ - 1.10), to primary normal with **4** ($k_H/k_D = 1.62$ - 2.10)⁴ⁱ and **5** ($k_H/k_D = 1.42$ - 1.82)^{4d} as the size of the two ligands becomes greater. In **1**, the two small methyl ligands readily enable a backside nucleophilic attack. In **2**, two relatively small ethyl ligands enable a backside nucleophilic attack. The magnitudes of the secondary inverse DKIEs of **2** are slightly greater than those of **1**, indicating less fraction of a backside attack compared to **1**. On the contrary, in **5**, a frontside attack is more favorable than a backside attack due to the large size of the two phenyl ligands. Although the primary normal DKIEs of **4** are greater than those of **5**, there is no doubt that the anilinolyses of both substrates, **4** and **5**, predominantly proceed through a frontside nucleophilic attack. The subtle combination of small methyl and large phenyl ligand gave an interesting result (i.e., greater values of DKIEs compared to **5**), and the value of $k_H/k_D = 2.10$ for the reaction of **4** with 4-methoxy aniline is the largest one observed for the anilinolyses of $R_1R_2P(=O)$ or $S)Cl$ -type substrates.⁴ⁱ

In the present work, the DKIEs invariably decrease from a primary normal ($k_H/k_D > 1$) to a secondary inverse ($k_H/k_D < 1$) as substituent X changes from electron-donating to electron-withdrawing. Herein, the DKIEs of $k_H/k_D = 1.03$ - 1.10 for X = 3-Me, 4-Me and 4-MeO are not the secondary normal β -type but the primary normal α -type since the Hammett and Brønsted plots exhibit linear without break point or region. Thus, the authors propose a concerted S_N2 mechanism on the basis of both secondary inverse and primary normal DKIEs. A hydrogen-bonded, four-center-type TSf is suggested for a frontside attack, while the TBP-5C TSb is suggested for a backside attack. The attacking direction with X = 3-Cl would be predominant backside, and the fraction of a backside attack gradually decreases while the fraction of a frontside attack gradually increases as the

nucleophile becomes stronger: $X = 3\text{-Cl} \rightarrow 4\text{-Cl} \rightarrow 4\text{-F} \rightarrow \text{H} \rightarrow 3\text{-Me} \rightarrow 4\text{-Me} \rightarrow 4\text{-MeO}$. It needs to be stressed that the real primary normal DKIE due to the hydrogen bond between the hydrogen of the N–H(D) moiety and the Cl leaving group is greater than the observed value since the other hydrogen of the N–H(D) moiety yields the secondary inverse DKIE.

As seen in Table 2, the greater the size of the two ligands, the greater steric hindrance occurs, and a frontside nucleophilic attack becomes more favorable, and as a result, the primary normal DKIE becomes greater: greater secondary inverse with **1** (two Me) \rightarrow secondary inverse with **2** (two Et) \rightarrow secondary inverse and primary normal with **3** (two cHex) \rightarrow primary normal with **4** (Me and Ph) and **5** (two Ph). These results indicate that the DKIEs have close relationship with the steric effects of the two ligands on the anilinolysis of the phosphinic chloride system.

The magnitude of the Brønsted coefficient ($\beta_X = 0.67$) of **3** is comparable with that ($\beta_X = 0.56$) of **2** and smaller than that ($\beta_X = 0.88$) of **4**, considerably smaller than those ($\beta_X = 1.62$ and 1.69) of **1** and **5**. There is no relationship between β_X and ΣE_S (and Σv_X). The smaller β_X values of **2** and **3** would suggest earlier TS compared to **1**, **4**, and **5**.

Experimental Section

Materials. Dicyclohexyl phosphinic chloride (more than 98.0%) and MeCN (HPLC-grade; 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.⁴ Deuterated anilines were prepared by heating anilines and deuterium oxide (99.9 atom % D) and one drop of HCl catalyst at 85 °C for 72 hours, and after numerous attempts, anilines were deuterated more than 98%, as confirmed by ¹H NMR.

Kinetic Measurement. Rates were measured conductometrically as previously described.⁴ [Substrate] = 0.003 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 $\pm 3\%$.

Product Analysis. Dicyclohexyl phosphinic chloride was reacted with excess 4-methoxyaniline, for more than 15 half-lives at 60.0 °C in MeCN. The 4-methoxy aniline hydrochloride salt was separated by filtration. Acetonitrile was removed under reduced pressure. The product was isolated by adding ether and insoluble fraction was collected. Analytical and spectroscopic data of the product gave the following results:

(*cyclo*-C₆H₁₁)₂P(=O)NHC₆H₄-4-CH₃O. Light purple solid, mp (159–160) °C; ¹H NMR (400 MHz, CDCl₃) δ 1.21–1.54 (10H, m, cyclohexyl), 1.69–2.22 (12H, m, cyclohexyl), 3.75 (3H, s, CH₃O), 4.15 (1H, d, $J = 12$ Hz, NH), 6.91 (2H, d, $J = 9.2$ Hz, aromatic), 7.07 (2H, d, $J = 8.8$ Hz, aromatic); ¹³C NMR (100 MHz, CDCl₃) δ 25.86, 26.48 (CH, cyclohexyl), 36.57, 37.38 (CH₂, cyclohexyl), 55.53 (CH₃O), 114.67, 116.74, 120.82, 134.81 (C=C, aromatic); ³¹P NMR (162 MHz, CDCl₃) δ 50.25 (1P, s, P=O); m/z , 335 (M⁺).

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References and Notes

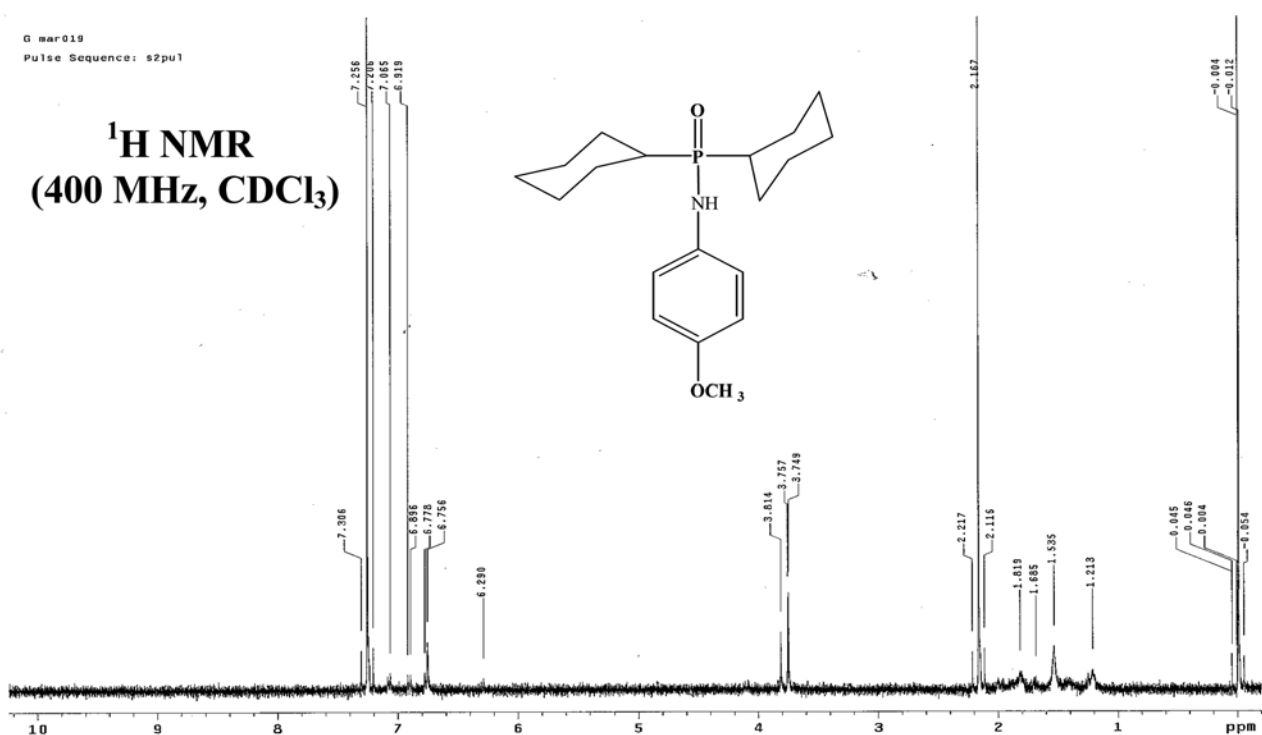
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17. The secondary normal β -type-DKIEs, $k_{\text{H}}/k_{\text{D}} > 1$, involving the rate-limiting leaving group expulsion from the intermediate were obtained: (i) $k_{\text{H}}/k_{\text{D}} = 1.03$ -1.11 for the reactions of phenylacetyl chlorides with deuterated anilines in MeCN (Lee, H. W.; Lee, J. W.; Koh, H. J.; Lee, I. *Bull. Korean Chem. Soc.* **1998**, 19, 642); (ii) $k_{\text{H}}/k_{\text{D}} = 1.04$ -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); and (iii) $k_{\text{H}}/k_{\text{D}} = 1.02$ -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). 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).
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Supplementary Materials

Kinetics and Mechanism of the Anilinolysis of Dicyclohexyl Phosphinic Chloride in Acetonitrile

Md. Ehtesham Ul Hoque and Hai Whang Lee*

Department of Chemistry, Inha University, Incheon 402-751, Korea. *E-mail: hwlee@inha.ac.kr
Received April 8, 2011, Accepted April 26, 2011Figure S1. ^1H NMR spectrum of $(\text{C}_6\text{H}_{11})_2\text{P}(=\text{O})\text{NH}-\text{C}_6\text{H}_4-4-\text{CH}_3\text{O}$.

red mar007
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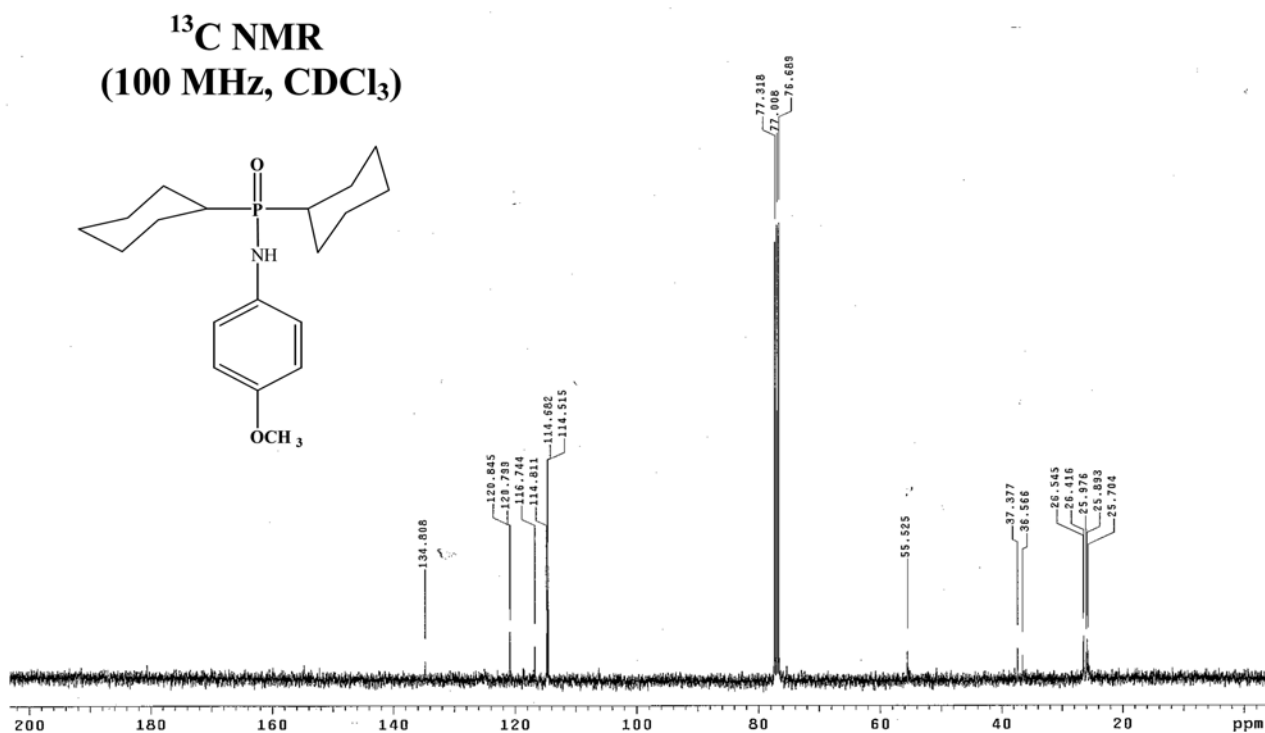


Figure S2. ^{13}C NMR spectrum of $(\text{C}_6\text{H}_{11})_2\text{P}(=\text{O})\text{NH}-\text{C}_6\text{H}_4-4-\text{CH}_3\text{O}$.

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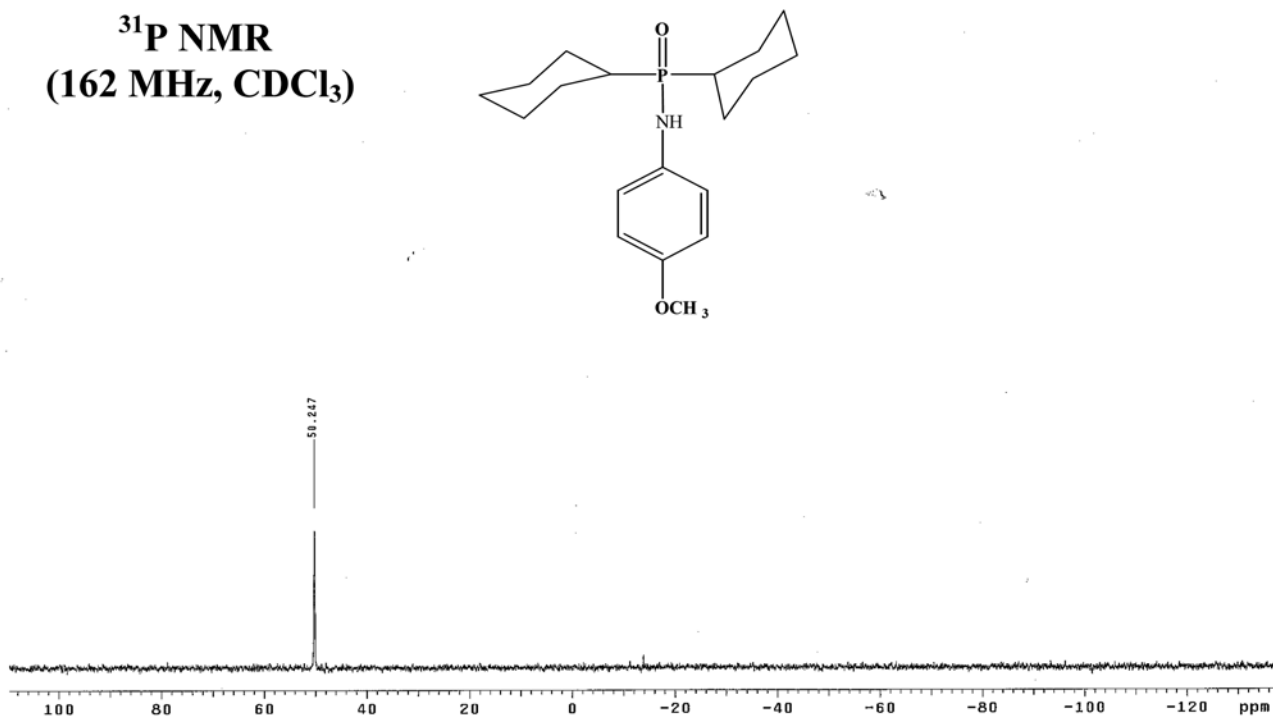


Figure S3. ^{31}P NMR spectrum of $(\text{C}_6\text{H}_{11})_2\text{P}(=\text{O})\text{NH}-\text{C}_6\text{H}_4-4-\text{CH}_3\text{O}$.

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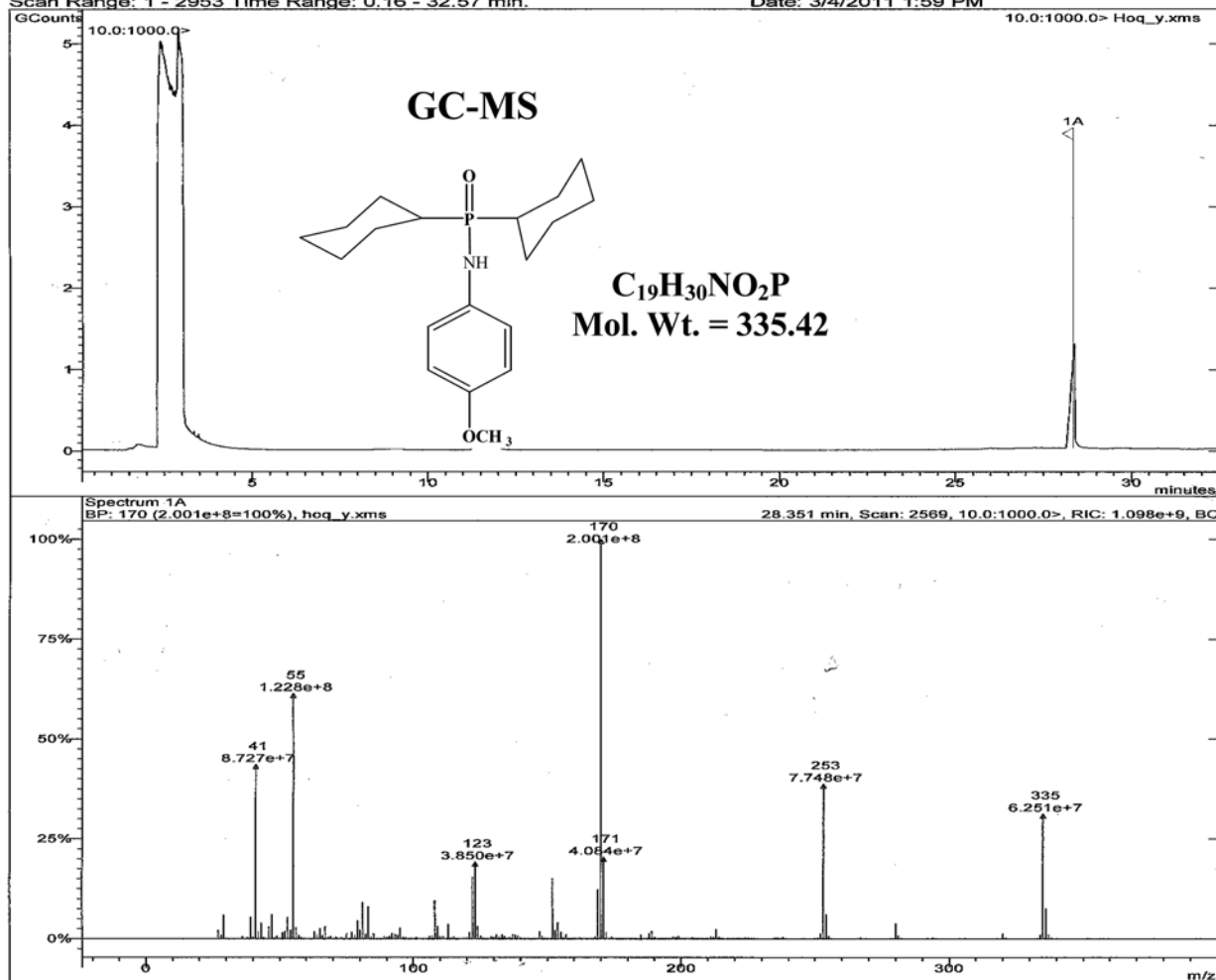
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Date: 3/4/2011 1:59 PM

Figure S4. GC-MS spectrum of $(C_6H_{11})_2P(=O)NH-C_6H_4-4-CH_3O$,