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Kinetics and mechanism of the pyridinolysis of *N*-aryl-*P,P*-diphenyl phosphinic amides in dimethyl sulfoxide

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Kinetic studies for the reactions of Z-*N*-aryl-*P,P*-diphenyl phosphinic amides with X-pyridines have been carried out in dimethyl sulfoxide at 85.0 °C. The two strong π-acceptor substituents, X = 4-Ac and 4-CN in the X-pyridine, exhibit positive deviations from both the Hammett and Brönsted plots. The Hammett plots for substituent Z variations are anomalously biphasic concave upwards with a break point at Z = H, and the sign of ρ_Z changes from *negative* for electron-donating to positive for electron-withdrawing substituents Z in the leaving group. The negative sign of the cross-interaction constants (ρ_{XZ}) for both electron-donating (large magnitude of $\rho_{XZ} = -1.54$) and -withdrawing ($\rho_{XZ} = -0.27$) substituents Z indicates that the reaction proceeds through a concerted mechanism. These results are indicative of frontside and backside nucleophilic attacks at the P reaction center for electron-donating and -withdrawing substituents Z, respectively. The poor leaving group mobility of NHPhZ yields the change of the nucleophilic attacking direction, resulting in biphasic concave upwards Hammett plots for substituent Z variations. Copyright © 2010 John Wiley & Sons, Ltd.

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Keywords: biphasic concave upward free energy relationship; *N*-aryl-*P,P*-diphenyl phosphinic amides; negative sign of ρ_{lg}; phosphoryl transfer reaction; pyridinolysis

INTRODUCTION

Nucleophilic substitution at a P=O center is important in chemistry since the phosphorus chemistry is interesting because of its relevance to biological chemistry and usefulness in synthesis. Two main types of displacement processes are reported regarding the phosphoryl species; either stepwise ($A_N + D_N$) through a trigonal bipyramidal pentacoordinate (TBP-5C) intermediate or a concerted process (A_ND_N).[1,2]

Nonlinear free energy relationships for variation of the nucleophile (X) and/or substrate (Y) and/or leaving group (Z) were observed for the pyridinolyses of Z-aryl bis(4-methoxyphenyl) phosphates,[3] Y-aryl phenyl isothiocyanophosphates,[4] diphenyl thiophosphinic chloride,[5] *O,O*-diphenyl Z-*S*-aryl phosphorothiolates,[6] dimethyl chlorothionophosphate,[7] and diethyl chlorothionophosphate.[7] In contrast, the pyridinolyses of Y-aryl phenyl chlorophosphates,[8] diphenyl phosphinic chloride,[5] Y-*O*-aryl phenyl phosphonochloridothiates,[9] dimethyl chlorophosphate,[7] and diethyl chlorophosphate[7] showed linear free energy correlations. However, the anilinolyses of phosphates and derivatives showed linear free energy correlations[10–19] except Y-*O*-aryl methyl phosphonochloridothioates,[20] As seen, the substituent effects of the nucleophiles and/or substrates and/or leaving groups upon the pyridinolysis mechanism were more surprising than those upon the anilinolysis mechanism.

In this paper, kinetic studies of the reactions of Z-*N*-aryl-*P,P*-diphenyl phosphinic amides with X-pyridines in DMSO at 85.0 °C (Scheme 1) are reported to gain further information into the phosphoryl transfer reactions and the substituent effects of the nucleophiles and leaving groups on the reaction mechanism.

RESULTS AND DISCUSSION

The reactions were carried out under pseudo-first-order conditions with a large excess of pyridine. The observed pseudo-first-order rate constants (k_{obsd}) for all reactions obeyed Eqn (1) with negligible k_0 (= 0) in DMSO.

$$k_{obsd} = k_0 + k_2[XC_5H_4N] \quad (1)$$

The second-order rate constants were determined with at least five pyridine concentrations. The linear plots of Eqn (1) suggest a lack of any base-catalysis or side reactions; the overall reaction is described by Scheme 1.

The second-order rate constants [k_2 ($M^{-1}\,s^{-1}$)] and selectivity parameters (ρ_X, β_X, ρ_Z, and ρ_{XZ}) are summarized in Table 1. The β_X ($= \beta_{nuc}$) values were determined using pK_a values in water; the slopes from the plots of log k_2(DMSO) against $pK_a(H_2O)$. Justification of this procedure has been experimentally and theoretically provided.[21]

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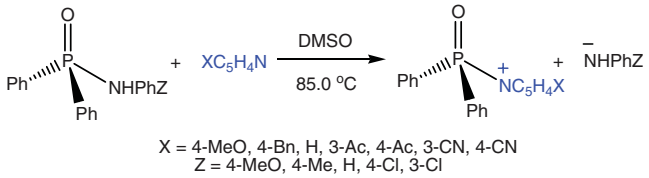


Scheme 1. The reaction system

The Hammett and Brönsted plots for substituent X variations in the nucleophiles show typical trends of nucleophilic substitution reactions, $\rho_X < 0$ and $\beta_X > 0$ (Figs 1 and 2). The two strong π-acceptor substituents, X = 4-Ac and 4-CN in the X-pyridine, exhibit positive deviations from both the Hammett and Brönsted plots (*vide infra*). However, the Hammett plots (Fig. 3) for substituent Z variations in the leaving groups are anomalously biphasic concave upwards with a break point at Z = H ($\sigma_Z = 0$), and as a result, the sign of ρ_Z ($= \rho_{lg}$) changes from *negative* for electron-donating substituents (Z = 4-MeO, 4-Me, H) to positive for electron-withdrawing substituents (Z = H, 4-Cl, 3-Cl). As seen in Fig. 3, the sign of ρ_Z for electron-donating substituents Z is negative, regardless of the nature of the substituent X, electron-donating or -withdrawing.

The anomalous negative sign of ρ_Z implies that the N atom in the leaving group becomes more positively charged in the transition state (TS) than in the ground state (GS: reactants). To rationalize the unusual negative ρ_Z value for electron-donating substituents Z, the TS I involving frontside nucleophilic attack (Scheme 2) is proposed.

When both the leaving group and nucleophile occupy the equatorial positions in a TBP-5C TS I, the π-cloud of the phenyl ring in the 'electron-rich' leaving group interacts strongly with the π-cloud of the pyridine ring in the adjacent equatorial position by through-space interaction. Thus, as a result, the charge of the N atom in the leaving group becomes more positive in the TS than the GS. Considerably large magnitudes of ρ_Z ($= -2.60$ to -4.10) indicate that the electron transfer by through-space interaction from the leaving group to the nucleophile is efficient. As seen in Table 1, the magnitude of the ρ_Z value gradually increases as substituent X of the nucleophile changes from electron-donating ($\rho_Z = -2.60$: weakest through-space interaction when X = 4-MeO) to electron-withdrawing ($\rho_Z = -4.10$: strongest through-space interaction when X = 3-CN). This could be supporting evidence of the proposed TS I. After TS I, the fast intramolecular exchange

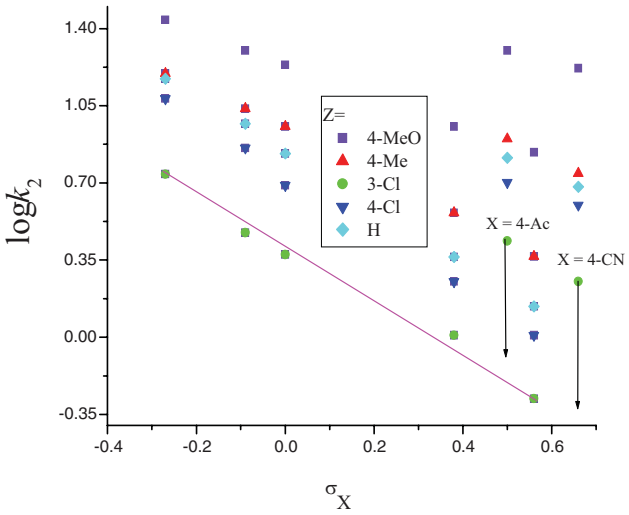


Figure 1. The Hammett plots (log k_2 *vs.* σ_X) of the reactions of Z-*N*-aryl-*P*,*P*-diphenyl phosphinic amides with X-pyridines in DMSO at 85.0 °C

Table 1. Second-order rate constants ($k_2 \times 10^4$, $M^{-1}\,s^{-1}$) and selectivity parameters[a] for the reactions of Z-*N*-aryl-*P*,*P*-diphenyl phosphinic amides with XC_5H_4N in DMSO at 85.0 °C

X\Z	4-MeO	4-Me	H	4-Cl	3-Cl	ρ_Z[b,c]	ρ_Z[d,e]
4-MeO	27.5	15.7	5.49	12.1	14.9	−2.60	1.20
4-Bn	20.0	10.9	2.98	7.23	9.31	−3.09	1.37
H	17.2	9.02	2.37	4.88	6.81	−3.21	1.25
3-Ac	9.02	3.67	1.02	1.79	2.31	−3.48	1.00
4-Ac	20.0	7.94	2.73	5.03	6.51	−3.16	1.03
4-CN	16.6	5.53	1.79	3.98	4.81	−3.50	1.20
3-CN	6.90	2.32	0.526	1.02	1.38	−4.10	1.15
ρ_X[f,g]	0.73	1.01	1.16	1.28	1.25		
β_X[f,h]	0.12	0.17	0.20	0.22	0.21	$\rho_{XZ} = -1.54$[f,i]	$\rho_{XZ} = -0.27$[f,j]

[a] The σ values and the pK_a values were taken from Refs [22–27], respectively.
[b] For Z = 4-MeO, 4-Me and H.
[c] Correlation coefficients, *r*, are better than 0.990.
[d] For Z = H, 4-Cl, and 3-Cl.
[e] $r \geq 0.979$.
[f] The two π-acceptors, 4-Ac and 4-CN, are excluded.
[g] $r \geq 0.996$.
[h] $r \geq 0.986$.
[i] $r = 0.998$.
[j] $r = 0.997$.

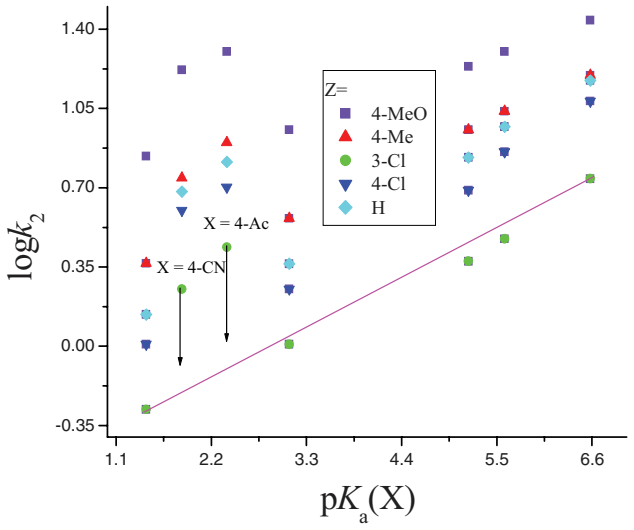


Figure 2. The Brönsted plots [log k_2 *vs.* pK_a(X)] of the reactions of Z-*N*-aryl-*P*,*P*-diphenyl phosphinic amides with X-pyridines in DMSO at 85.0 °C

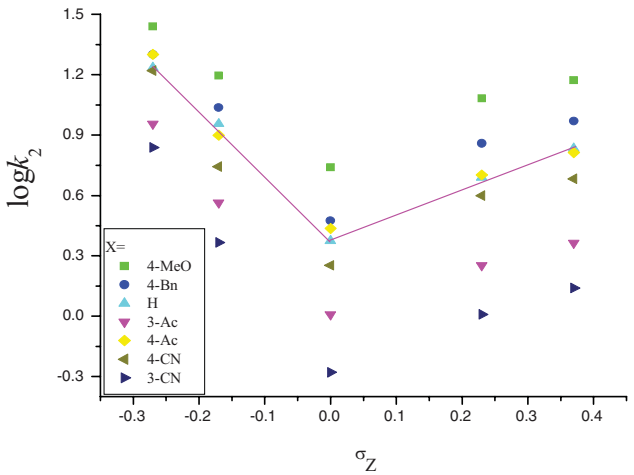
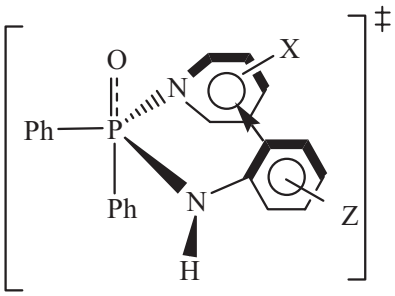
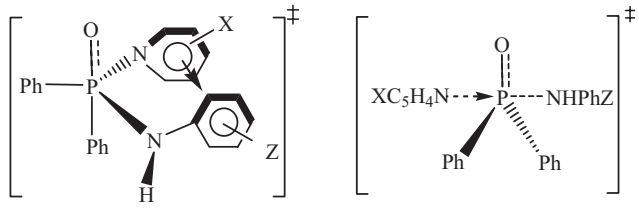


Figure 3. The Hammett plots (log k_2 *vs.* σ_Z) of the reactions of Z-*N*-aryl-*P*,*P*-diphenyl phosphinic amides with X-pyridines in DMSO at 85.0 °C



TS I

Scheme 2. TS I for electron-donating substituents Z



TS II **TS III**

Scheme 3. Two plausible TSs for electron-withdrawing substituents Z

process of the leaving group from the equatorial to the apical position would follow by a Berry-type pseudorotation (or turnstile rotation).[28,29]

When substituent Z of the leaving group is electron-withdrawing, the sign of ρ_Z is positive and in accordance with those expected from a typical nucleophilic substitution reaction. Two plausible TSs, frontside (TS II) and backside nucleophilic attack (TS III), can be proposed as shown in Scheme 3. In the TS II, electron transfer by through-space interaction would occur from the nucleophile to the leaving group, in an opposite direction to that in the TS I. In the TS III, both the nucleophile and leaving group occupy the apical positions in a TBP-5C TS, where substituents X and Z are far apart.

The cross-interaction constants (CICs), ρ_{XZ}, Eqns (2) and (3), are determined, where X and Z represent the substituents in the nucleophile and leaving group, respectively.[30–32]

$$\log(k_{XZ}/k_{HH}) = \rho_X\sigma_X + \rho_Z\sigma_Z + \rho_{XZ}\sigma_X\sigma_Z \quad (2)$$

$$\rho_{XZ} = \partial\rho_X/\partial\sigma_Z = \partial\rho_Z/\partial\sigma_X \quad (3)$$

The sign and magnitude of the CICs have made it possible to correctly interpret the reaction mechanism and degree of tightness of the TS, respectively. In general, the ρ_{XZ} has a negative value (or sometimes a small positive value) in a concerted S_N2 and a stepwise mechanism with a rate-limiting bond formation. However, it has a positive value for a stepwise mechanism with a rate-limiting leaving group departure from the intermediate. The magnitude of ρ_{XZ} is inversely proportional to the distance between the nucleophile and leaving group in the TS.[30–32]

The sign of the CICs, ρ_{XZ}, is negative for both electron-donating and -withdrawing substituent Z (Table 1 and Fig. 4), indicating that the reaction proceeds through a concerted mechanism. However, the magnitude of ρ_{XZ} (= −1.54) for electron-donating substituents Z is much greater than that (ρ_{XZ} = −0.27) for electron-withdrawing. The unusual large negative ρ_{XZ} (= −1.54) for the electron-donating substituents Z implies that the nucleophile and leaving group are in close enough proximity to interact strongly. This is in agreement with the proposed TS I involving a frontside nucleophilic attack. The large magnitudes of the ρ_{XZ} values ($\rho_{XZ} \geq |-0.4|$)[33] were obtained due to the frontside nucleophilic attack as follows: (i) the reactions of aryl bis(4-methoxyphenyl) phosphates with the weakly basic pyridines in MeCN (ρ_{XZ} = −1.98);[3] (ii) the anilinolysis of anilino thioethers in MeOH (ρ_{XZ} = −1.70);[34] (iii) the anilinolysis of both 2- and 3-thiopheneethyl arenesulfonates in MeCN (ρ_{XZ} = −0.50);[35] (iv) the anilinolysis of cumyl arenesulfonates in MeCN (ρ_{XZ} = −0.75);[36] (v) the anilinolysis of 1-phenylethyl arenesulfonates in MeOH (ρ_{XZ} = −0.56);[37] (vi) the anilinolysis of 2-phenylethyl arenesulfonates in MeOH (ρ_{XZ} = −0.45);[38] (vii) the benzylaminolysis of Z-aryl cyclopropanecarboxylates in MeCN (ρ_{XZ} =

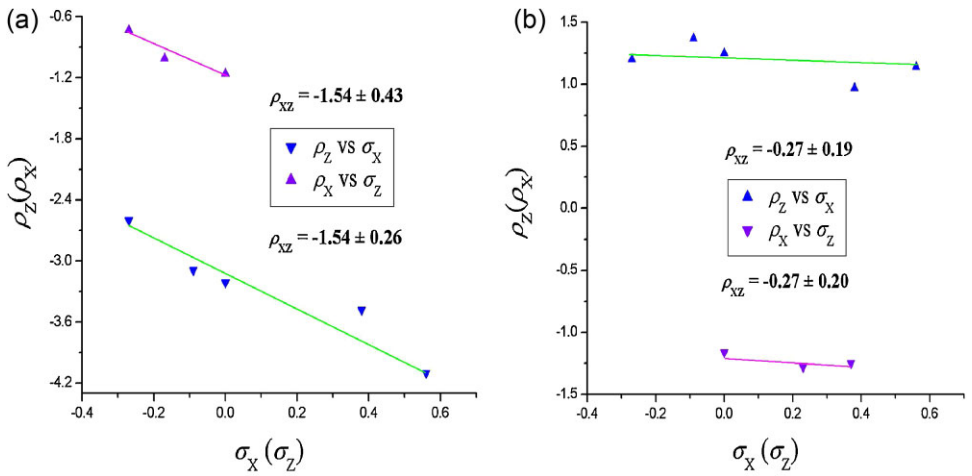


Figure 4. Determination of ρ_{XZ} ($= \partial\rho_Z/\partial\sigma_X = \partial\rho_X/\partial\sigma_Z$) of the reactions of Z-*N*-aryl-*P*,*P*-diphenyl phosphinic amides with X-pyridines in DMSO at 85.0 °C. The obtained values by multiple regression are: (a) $\rho_{XZ} = -1.54 \pm 0.24$ for electron-donating substituents Z = 4-MeO, 4-Me, H; (b) $\rho_{XZ} = -0.27 \pm 0.21$ for electron-withdrawing substituents Z = H, 4-Cl, 3-Cl

+1.06);[39] (viii) the benzylaminolysis of Z-aryl 2-furoates in MeCN ($\rho_{XZ} = +1.19$);[40] (ix) the benzylaminolysis of Z-thiophenyl acetates in MeCN ($\rho_{XZ} = +0.90$).[41]

In contrast, the small negative ρ_{XZ} ($= -0.27$) for electron-withdrawing substituent Z indicates that the nucleophile and leaving group are far apart due to backside nucleophilic attack.[42] Thus, the TS II can be safely ruled out for electron-withdrawing substituent Z. It is the proposal of the authors that the reaction proceeds through TS III involving backside nucleophilic attack in which both the nucleophile and leaving group occupy the apical positions. Considerably smaller magnitudes of ρ_Z ($= 1.00 - 1.37$) for electron-withdrawing substituent Z than those ($\rho_Z = -2.60$ to -4.10) for electron-donating substituent Z could be further supporting evidence of TS III for electron-withdrawing substituent Z. If the TS II is involved in the reaction path, the magnitude of the positive ρ_Z value would be great since the negative charge on the N atom of the leaving group becomes greater.

In general, the nonlinear free energy correlation of a concave upward plot is diagnostic of a change in the reaction mechanism where the reaction path is changed depending on the substituents, while nonlinear free energy correlation of the concave downward plot is diagnostic of a rate-limiting step change from bond breaking with less basic nucleophiles to bond formation with more basic nucleophiles.[43–52] In the present work, the nonlinear free energy correlation of a biphasic concave upward plot for substituent Z variations in the leaving groups is due to a change in the attacking direction of the nucleophile from a backside (TS III) for electron-withdrawing Z to a frontside attack (TS I) for electron-donating substituent Z in the leaving group.

The two strong π-acceptor *para*-substituents, X = 4-Ac and 4-CN in X-pyridines, exhibit positive deviations from both the Hammett (Fig. 1) and Brönsted plots (Fig. 2) for substituent X variations in the nucleophiles (*vide supra*). This behavior indicates that the two π-acceptor substituents yield exalted reactivity. Since both positive deviations are exhibited regardless of the nature of the substituent Z in the leaving group, electron-donating or -withdrawing, the reason for such exalted reactivity should be rationalized in two ways for TS I and III, respectively.

Firstly, in the case of the TS I for electron-donating substituent Z, the pyridine ring becomes π-electron-rich due to the through-space interaction with the adjacent electron-rich phenyl ring. Thus, the TS I can be effectively stabilized by the two strong π-acceptor substituents (X = 4-Ac and 4-CN) more than expected from their σ_X [and pK_a(X)] values. As a result, the two strong π-acceptor substituents yield exalted reactivity and exhibit positive deviations from the Hammett (and Brönsted) plot.

Secondly, in the case of the TS III for electron-withdrawing substituent Z, the exalted reactivity (or enhanced nucleophilicity) of the strong π-acceptor groups would be owing to the weak π-donor effects.[27,53–56] The Hammett σ_p values of the π-acceptor substituents represent the inductive and π-electron-withdrawing effects. However, the experimental pK_a value only represents the inductive effect of X, since protonation/deprotonation takes place at the σ lone pair on N which is orthogonal to the ring π-system.[27] As a result, the protonation/deprotonation does not disturb the ring π-system, but the positive charge center in the conjugate acid, naturally, attracts π-electrons inductively without through-conjugation between the σ-lone pair and the π-acceptor *para*-substituent. Thus, the pK_a values of π-acceptor substituents correctly reflect the substituent effects when the N atom of pyridine becomes positively charged in the TS, since the determination of pK_a involves a positive charge on N (azonium type).

The two π-acceptor substituents exhibited positive deviations from the Hammett plots, while no deviations from the Brönsted plots, for the pyridinolyses of methyl chloroformates in MeCN[27] and water,[57,58] benzenesulfonyl chlorides in MeOH,[59] benzyl bromides in DMSO,[60] and phenacyl bromides in MeCN.[61] This indicated that the N atom of pyridine becomes positively charged in the TS. In the pyridinolysis of Y-aryl phenyl chlorophosphates, the two π-acceptor substituents did not exhibit deviations from either the Hammett or Brönsted plots.[8] No positive deviations for the π-acceptor in both plots were rationalized by the early TS with little positive charge development on the N atom of pyridine. The early TS, in which the extent of both the bond formation and leaving group departure is small, was supported by the small CIC, $\rho_{XY} = -0.15$.[62] In the present work, the two strong π-acceptor substituents exhibit positive deviations from both the Hammett (Fig. 1) and Brönsted plots (Fig. 2) for substituent X variations in the nucleophiles. This indicates that

the degree of positive charge development on the N atom of pyridine is substantial in the TS III.

The second-order rate constants of the pyridinolysis (with unsubstituted pyridine: C_5H_5N) of diphenyl phosphinic chloride in MeCN at 35.0 °C[5] and *N*-phenyl-*P,P*-diphenyl phosphinic amide in DMSO at 85.0 °C are $k_2 = 5.46 \times 10^{-4}$ and $2.37 \times 10^{-4}\,M^{-1}\,s^{-1}$, respectively. The difference between the two substrates, $Ph_2P(=O)Cl$ and $Ph_2P(=O)NHPh$, is the leaving group. Taking into account the differences of solvent polarity and reaction temperature between the two reactions; MeCN (dielectric constant: $\varepsilon_r = 35.94$) *versus* DMSO ($\varepsilon_r = 46.45$) and 35.0 *versus* 85.0 °C, respectively, the leaving group mobility of NHPh is very poor compared to Cl. This poor leaving group mobility of NHPh leads to the late TS III, in which the extent of bond formation and leaving group departure is great, and as a result, the positive charge development on the N atom in the pyridine nucleophile is substantial.

When the substituent Z in the leaving group changes from electron-withdrawing to -donating, the leaving group mobility becomes poor. This results in the change of the nucleophilic attacking direction from backside to frontside. For electron-donating substituent Z, thus, the reaction proceeds through the TS I involving a frontside nucleophilic attack as discussed earlier, and the Hammett plots for substituent Z variations in the leaving groups exhibit biphasic concave upwards with a break point at Z = H. It is surprising substituent effects of the leaving group even to yield the *anomalous large negative* ρ_Z ($= -2.60$ to -4.10).

CONCLUSIONS

A concerted S_N2 mechanism for the pyridinolysis of *N*-aryl-*P,P*-diphenyl phosphinic amides in DMSO at 85.0 °C is proposed on the basis of the negative cross-interaction constants, ρ_{XZ}. The Hammett plots for substituent Z variations in the leaving groups are biphasic concave upwards with a break point at Z = H. A frontside nucleophilic attack is proposed based on the considerably large magnitude of ρ_{XZ} ($= -1.54$) for the electron-donating substituent Z of the leaving group. In contrast, a backside nucleophilic attack is proposed based on the small magnitude of ρ_{XZ} ($= -0.27$) for the electron-withdrawing substituent Z. The two strong π-acceptor substituents, X = 4-Ac and 4-CN in the X-pyridine, exhibit positive deviations from both the Hammett and Brönsted plots. Both positive deviations are rationalized by TS stabilization for electron-donating substituent Z and weak π-donor effect of the two π-acceptor substituents for electron-withdrawing substituent Z. The biphasic concave upward Hammett plots for substituent Z variations in the leaving groups and anomalous large negative ρ_Z are due to the poor leaving group mobility of NHPhZ.

EXPERIMENTAL

Materials

Z-*N*-Aryl-*P,P*-diphenyl phosphinic amides were prepared by reacting diphenyl phosphinic chloride with Z-anilines for 5 h in methylene chloride at room temperature. The Z-anilinium chloride salt was filtered out. The remaining product was treated with ether and water for workup. The product mixture was treated with ether and dilute hydrochloric acid to remove excess anilines as Z-anilinium chloride salt. The remaining product was then dried over anhydrous magnesium sulfate. The product was isolated by evaporating the solvent under reduced pressure after filtration. The GR grade dimethyl sulfoxide was dried over molecular sieves and used after three distillations under reduced pressure prior to use. The GR grade X-pyridines were used without further purification. The analytical and spectroscopic data of substrates are summarized in supporting information.

Kinetic procedure

Rates were measured conductometrically[3] in dimethyl sulfoxide at 85.0 °C. The conductivity bridge used in this work was a self-made computer automated A/D converter conductivity bridge. Pseudo-first-order rate constants (k_{obsd}) were measured by curve fitting analysis in an origin program with a large excess of pyridine, [Z-*N*-aryl-*P,P*-diphenyl phosphinic amides] $\approx 3 \times 10^{-3}$ M and [X-pyridine] = 0.1 − 0.3 M. The k_2 values in Table 1 are the average of more than three runs and were reproducible to within ±3%.

Product analysis

The *N*-(4-Chlorophenyl)-*P,P*-diphenyl phosphinic amide was reacted with excess 4-methoxy pyridine for more than 15 half lives at 85.0 °C in DMSO. The solvent was evaporated under reduced pressure. The solid product was washed several times with ether to remove excess pyridine. The analytical and spectroscopic data of product are summarized in supporting information.

Acknowledgements

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REFERENCES

[1] R. F. Hudson, *Structure and Mechanism in Organophosphorus Chemistry*, Chapter 3, Academic Press, London, **1965**.
[2] A. Williams, *Concerted Organic and Bio-organic Mechanisms*, Chapter 6, CRS Press, Boca Raton, **2000**.
[3] H. W. Lee, A. K. Guha, C. K. Kim, I. Lee, *J. Org. Chem.* **2002**, *67*, 2215–2222.
[4] K. K. Adhikary, H. W. Lee, I. Lee, *Bull. Korean Chem. Soc.* **2003**, *24*, 1135–1140.
[5] M. E. U. Hoque, N. K. Dey, A. K. Guha, C. K. Kim, B. S. Lee, H. W. Lee, *Bull. Korean Chem. Soc.* **2007**, *28*, 1797–1802.
[6] K. K. Adhikary, B. J. Lumbiny, C. K. Kim, H. W. Lee, *Bull. Korean Chem. Soc.* **2008**, *29*, 851–855.
[7] N. K. Dey, M. E. U. Hoque, C. K. Kim, H. W. Lee, *J. Phys. Org. Chem. DOI: 10.1002/poc.1709*.
[8] A. K. Guha, H. W. Lee, I. Lee, *J. Org. Chem.* **2000**, *65*, 12–15.
[9] B. J. Lumbiny, K. K. Adhikary, B. S. Lee, H. W. Lee, *Bull. Korean Chem. Soc.* **2008**, *29*, 1769–1773.
[10] A. K. Guha, H. W. Lee, I. Lee, *J. Chem. Soc., Perkin Trans. 2*, **1999**, 765.
[11] H. W. Lee, A. K. Guha, I. Lee, *Int. J. Chem. Kinet.* **2002**, *34*, 632–637.
[12] M. E. U. Hoque, S. Dey, A. K. Guha, C. K. Kim, B. S. Lee, H. W. Lee, *J. Org. Chem.* **2007**, *72*, 5493–5499.
[13] M. E. U. Hoque, H. W. Lee, *Bull. Korean Chem. Soc.* **2007**, *28*, 936–940.
[14] N. K. Dey, I. S. Han, H. W. Lee, *Bull. Korean Chem. Soc.* **2007**, *28*, 2003–2008.
[15] M. E. U. Hoque, N. K. Dey, C. K. Kim, B. S. Lee, H. W. Lee, *Org. Biomol. Chem.* **2007**, *5*, 3944–3950.
[16] N. K. Dey, M. E. U. Hoque, C. K. Kim, B. S. Lee, H. W. Lee, *J. Phys. Org. Chem.* **2008**, *21*, 544–548.
[17] B. J. Lumbiny, H. W. Lee, *Bull. Korean Chem. Soc.* **2008**, *29*, 2065–2068.

[18] N. K. Dey, M. E. U. Hoque, C. K. Kim, B. S. Lee, H. W. Lee, *J. Phys. Org. Chem.* **2009**, *22*, 425–430.
[19] N. K. Dey, C. K. Kim, H. W. Lee, *Bull. Korean Chem. Soc.* **2009**, *30*, 975–978.
[20] M. E. U. Hoque, A. K. Guha, C. K. Kim, B. S. Lee, H. W. Lee, *Org. Biomol. Chem.* **2009**, *7*, 2919–2925.
[21] I. Lee, S. W. Hong, H. J. Koh, Y. Lee, B. S. Lee, H. W. Lee, *J. Org. Chem.* **2001**, *66*, 8549–8555.
[22] C. Hansch, A. Leo, R. W. Taft, *Chem. Rev.* **1991**, *91*, 165–195.
[23] A. Albert, E. P. Serjeant, *The Determination of Ionization Constants*, 3rd edn, Chapman and Hall, New York, **1984**, pp. 154–155.
[24] J. A. Dean, *Handbook of Organic Chemistry*, Chapter 8, McGraw-Hill, New York, **1987**.
[25] A. Fischer, W. J. Galloway, J. Vaughan, *J. Chem. Soc.* **1964**, 3591–3596.
[26] H. J. Koh, K. L. Han, I. Lee, *J. Org. Chem.* **1999**, *64*, 4783–4789.
[27] H. J. Koh, K. L. Han, H. W. Lee, I. Lee, *J. Org. Chem.* **1998**, *63*, 9834–9839. Herein, the authors showed that substituent 4-CN in pyridine has strong para π-acceptor ability.
[28] R. S. Berry, *J. Chem. Phys.* **1960**, *32*, 933–938.
[29] I. Ugi, D. Marquarding, H. Klusacek, P. Gillespie, F. Ramirez, *Acc. Chem. Res.* **1971**, *4*, 288–296.
[30] I. Lee, *Chem. Soc. Rev.* **1990**, *9*, 317–333.
[31] I. Lee, *Adv. Phys. Org. Chem.* **1992**, *27*, 57–117.
[32] I. Lee, H. W. Lee, *Collect. Czech. Chem. Commun.* **1999**, *64*, 1529–1550.
[33] The ρ_{XZ} values greater than ~0.4 ($|\rho_{XZ}| \geq 0.4$) suggest that the reactions proceed predominantly by the frontside nucleophilic attack S_N2 pathways.
[34] H. K. Oh, J. H. Yang, H. W. Lee, I. Lee, *New J. Chem.* **2000**, *24*, 213–219.
[35] H. K. Oh, J. H. Yun, I. H. Cho, I. Lee, *Bull. Korean Chem. Soc.* **1997**, *18*, 390–394.
[36] H. J. Koh, H. W. Lee, I. Lee, *J. Chem., Soc., Perkin Trans.* **1994**, *2*, 125–129.
[37] I. Lee, H. Y. Kim, H. K. Kang, H. W. Lee, *J. Org. Chem.* **1988**, *53*, 2678–2683.
[38] I. Lee, Y. H. Choi, H. W. Lee, *J. Chem. Soc., Perkin Trans.* **1988**, *2*, 1537–1540.
[39] H. J. Koh, C. H. Shin, H. W. Lee, I. Lee, *J. Chem., Soc., Perkin Trans.* **1998**, *2*, 1329–1332.
[40] H. J. Koh, J. W. Lee, H. W. Lee, I. Lee, *New J. Chem.* **1997**, *21*, 447–451.
[41] H. K. Oh, J. H. Yang, H. W. Lee, I. Lee, *Bull. Korean Chem. Soc.* **1999**, *21*, 1418–1420.
[42] The ρ_{XZ} values for backside nucleophilic attack S_N2 pathways are generally in the range of −0.1 to −0.3.
[43] Ref. 2, Chapter 7.
[44] A. Ruff, I. G. Csizmadia, *Organic Reactions Equilibria, Kinetics and Mechanism*, Chapter 7, Elsevier, Amsterdam, Netherlands, **1994**.
[45] H. K. Oh, M. H. Ku, H. W. Lee, I. Lee, *J. Org. Chem.* **2002**, *67*, 3874–3877.
[46] H. K. Oh, M. H. Ku, H. W. Lee, I. Lee, *J. Org. Chem.* **2002**, *67*, 8995–8998.
[47] H. K. Oh, J. M. Lee, H. W. Lee, I. Lee, *Int. J. Chem. Kinet.* **2004**, *36*, 434–440.
[48] H. K. Oh, J. E. Park, H. W. Lee, *Bull. Korean Chem. Soc.* **2004**, *25*, 1041–1045.
[49] E. A. Castro, P. M. Angel, D. Arellano, J. G. Santos, *J. Org. Chem.* **2001**, *66*, 6571–6575.
[50] E. A. Castro, P. Pavez, J. G. Santos, *J. Org. Chem.* **2002**, *67*, 4494–4497.
[51] E. A. Castro, M. Aliaga, P. Campodonico, J. G. Santos, *J. Org. Chem.* **2002**, *67*, 8911–8916.
[52] E. Humeres, N. A. Debacher, M. M. D. Sierra, J. D. Franco, A. Shutz, *J. Org. Chem.* **1998**, *63*, 1598–1603.
[53] D. A. Dixon, P. A. Charlier, P. G. Gassman, *J. Am. Chem. Soc.* **1980**, *102*, 3957–3959.
[54] M. N. Paddon-Row, C. Santiago, K. N. Houk, *J. Am. Chem. Soc.* **1980**, *102*, 6561–6563.
[55] G. A. Olah, M. Arvanaghi, G. K. Surya Prakash, *J. Am. Chem. Soc.* **1982**, *104*, 1628–1631.
[56] V. V. Krishnamurthy, G. K. Surya Prakash, P. S. Iyer, G. A. Olah, *J. Am. Chem. Soc.* **1986**, *108*, 1575–1579.
[57] P. M. Bond, E. A. Castro, R. B. Moodie, *J. Chem., Soc., Perkin Trans.* **1976**, *2*, 68–72.
[58] D. Palling, W. P. Jencks, *J. Am. Chem. Soc.* **1984**, *106*, 4869–4876.
[59] S. W. Hong, H. J. Koh, I. Lee, *J. Phys. Org. Chem.* **1999**, *12*, 425–429.
[60] S. W. Hong, H. J. Koh, H. W. Lee, I. Lee, *Bull. Korean Chem. Soc.* **1999**, *20*, 1172–1176.
[61] H. J. Koh, K. L. Han, H. W. Lee, I. Lee, *J. Org. Chem.* **2000**, *65*, 4706–4711.
[62] The magnitude of $\rho_{XY} = -0.15$ is the smallest one that the authors have obtained for the phosphoryl transfer reactions. In general, the magnitude of ρ_{XY} is greater than that of ρ_{XZ}, since the distance between the nucleophile and substrate is closer than the distance between the nucleophile and leaving group for backside nucleophilic attack S_N2 pathways.

