

# Studies on Organophosphorus Compounds 61 Substituent Effects in Organophosphorus Esters

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## ABSTRACT

Examination of several model organophosphorus compounds, bicyclic phosphates (**1**), *p*-substituted phenylphosphonates (**2**), and acidic alkylphosphonates (**3**) reveals that the polar substituent effect in organophosphorus esters parallels that of carbon compounds. No significant variation in polar effects of different alkyl groups with up to 10 carbon atoms is observed. As demonstrated by us, the commonly used Kabachnik polar constant  $\sigma_\phi$  for alkyl groups of organophosphorus compounds reflects the steric effect associated with steric hindrance to solvation of acidic anions. Therefore, a set of solvation steric parameters  $E_s^p$  has been calculated from  $pK_a$  values of organophosphorus acids. This parameter can be applied to describe the structural effect on dissociation of organic acids and, after suitable modification, may reflect the steric effect of alkyl groups in hydrolytic reactions of organophosphorus esters.

## INTRODUCTION

The classic nuclear polar parameters of substituents of organic compounds were introduced by Hammett as  $\sigma_p$  and  $\sigma_m$  in 1937 [1]. Later on, Taft [2] suggested a new set of polar parameters,  $\sigma^*$ , to account for the polar effect of alkyl groups on the rate of hydrolysis of carboxylic esters in addition to steric parameters,  $E_s$ . The polar effect of sub-

stituents can be divided into field ( $\sigma_F$ ), inductive ( $\sigma_I$ ), resonance ( $\sigma_R$ ), and polarization ( $\sigma_a$ ) effects [3]. The steric effect of substituents is usually characterized by Taft's  $E_s$  [2] or Charton's  $v$  [4], although the latter is correlated linearly with the former [5]. In structure-reactivity studies of organophosphorus compounds, it is often found that these parameters cannot give satisfactory results. Based on the  $pK_a$  values of a series of acidic phosphorus esters, Kabachnik proposed a set of specific polar parameters ( $\sigma_\phi$ ) for substituents of organophosphorus compounds [6]. As an extension of the Kabachnik treatment, we have used  $\sigma^p$  to describe polar effects for long chain alkyl and alkoxy groups with carbon numbers up to 12 [7]. It also works well in QSAR studies in metal extraction [7]. However, Charton has pointed out that  $\sigma_\phi$  can be expressed as a function of both  $\sigma_I$  and  $\sigma_R$  [8].

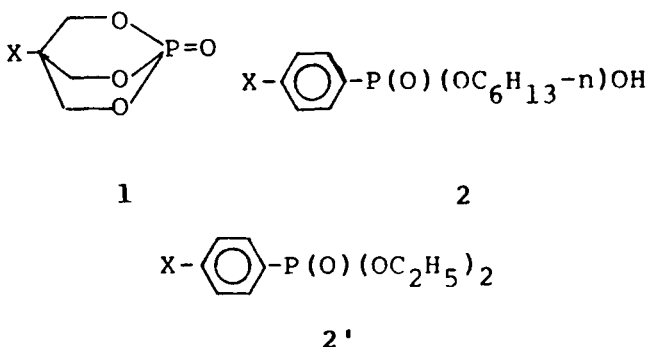
In hydrolytic reactions of organophosphorus compounds, the transition states are often pentacoordinate. The steric effect is, therefore, quite different from that of carboxylic esters which have a planar transition state. QSAR results cannot be accounted for by  $E_s$  and  $v$ . Therefore, Charton revised  $v$  and proposed a small set of new steric parameters  $v'$  [9] to account for the steric effect of substituents in pentacoordinate transition states of phosphorus compounds. Recently, we have developed a series of steric parameters to account for different reactions [10–13]. We have shown that the steric effect of a given substituent group has different contributions in different specific reactions or specific conformations of metal complexes.

As far as  $\sigma_\phi$  or  $\sigma^p$  is concerned, the  $pK_a$  value is influenced not only by the polar but also by the steric effect. Therefore, the change of the  $pK_a$  value cannot be taken as a measurement of the polar ef-

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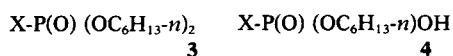
Dedicated to Professor Dr. L. Horner on the occasion of his seventieth birthday.

fect. For example, from Kabachnik's  $\sigma_\phi$  scale, the difference between  $\text{CH}_3$  and  $t\text{-C}_4\text{H}_9$  is 0.58, while the difference between  $\text{CH}_3$  and  $n\text{-C}_4\text{H}_9\text{O}$  is 0.52. According to the  $\Delta\sigma_\phi$ , the difference of the polar effect between  $\text{CH}_3$  and  $t\text{-C}_4\text{H}_9$  is larger than that between  $\text{CH}_3$  and  $n\text{-C}_4\text{H}_9\text{O}$ , which is inconsistent with general observations. Maybe some steric effect is included in  $\sigma_\phi$  or  $\sigma^p$ . In order to understand the nature of polar effects of substituents, particularly the alkyl groups, in organophosphorus compounds, several types of organophosphorus compounds have been designed as models, namely, 4-substituted-2,6,7-trioxa-1-phospha-bicyclo-[2,2,2]octane-1-oxides (**1**), monohexyl *p*-substituted phenylphosphonates (**2**), diethyl *p*-substituted phenylphosphonates (**2'**), dihexyl alkylphosphonates (**3**), and alkylphosphonate monohexyl esters (**4**). The substituents X in compounds **1**, **2**, and **2'** are remote from the phosphoryl group or phosphoryl hydroxyl group. However, in compounds **3** and **4** substituents X are directly connected to the phosphorus atom and are located very close to the phosphoryl oxygen or phosphoryl hydroxyl group. The steric contribution of these substituents to the reaction center is remarkable, and compounds **3** and **4** may be regarded as models for the evaluation of the steric effects of substituents. By comparison of the structure-activity relationships of compounds **1**–**4**, we can have a clear picture of polar and steric effects of substituents in organophosphorus compounds.



X	$\text{C}_2\text{H}_5$	$\text{C}_3\text{H}_7$	$i\text{-C}_3\text{H}_7$	$s\text{-C}_4\text{H}_9$	$s\text{-C}_5\text{H}_{11}$	$t\text{-C}_4\text{H}_9$
No.	<b>1a</b>	<b>1b</b>	<b>1c</b>	<b>1d</b>	<b>1e</b>	<b>1f</b>
X	$\text{CH}_3\text{O}$	$\text{C}_2\text{H}_5\text{O}$	Cl	$\text{CO}_2\text{C}_2\text{H}_5$	COOH	$\text{NO}_2$
No.	<b>1g</b>	<b>1h</b>	<b>1i</b>	<b>1j</b>	<b>1k</b>	<b>1l</b>
X	$\text{CH}_2\text{OH}$	$\text{C}(\text{CH}_3)_2\text{OH}$	$\text{CH}_3\text{CH}=\text{CH}$	$\text{CH}_2=\text{C}(\text{CH}_3)_2$		
No.	<b>1m</b>	<b>1n</b>	<b>1o</b>	<b>1p</b>		

X	H	$\text{CH}_3$	$\text{C}_2\text{H}_5$	$i\text{-C}_3\text{H}_7$	$n\text{-C}_4\text{H}_9$	$i\text{-C}_4\text{H}_9$
No.	<b>2a</b>	<b>2b</b>	<b>2c</b>	<b>2d</b>	<b>2e</b>	<b>2f</b>
X	$t\text{-C}_4\text{H}_9$	$n\text{-C}_8\text{H}_{17}$	$\text{CH}_3\text{O}$	$(\text{CH}_3)_2\text{N}$	Cl	$\text{COOC}_4\text{H}_9$
No.	<b>2g</b>	<b>2h</b>	<b>2i</b>	<b>2j</b>	<b>2k</b>	<b>2l</b>



X	$\text{CH}_3$	$n\text{-C}_3\text{H}_7$	$i\text{-C}_3\text{H}_7$	$n\text{-C}_4\text{H}_9$	$i\text{-C}_4\text{H}_9$	$s\text{-C}_4\text{H}_9$
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No.	<b>3a</b>	<b>3b</b>	<b>3c</b>	<b>3d</b>	<b>3e</b>	<b>3f</b>
	<b>4a</b>	<b>4b</b>	<b>4c</b>	<b>4d</b>	<b>4e</b>	<b>4f</b>
X	$t\text{-C}_4\text{H}_9$	$n\text{-C}_5\text{H}_{11}$	$i\text{-C}_5\text{H}_{11}$	$n\text{-C}_8\text{H}_{17}$	$i\text{-C}_8\text{H}_{17}$	$s\text{-C}_8\text{H}_{17}$
No.	<b>3g</b>	<b>3h</b>	<b>3i</b>	<b>3j</b>	<b>3k</b>	<b>3l</b>
	<b>4g</b>	<b>4h</b>	<b>4i</b>	<b>4j</b>	<b>4k</b>	<b>4l</b>

## RESULTS AND DISCUSSION

### Polar Effect of Substituents in Organophosphorus Esters

The polar effects of substituents X in compounds **1** can be estimated from the change of the basicity or charge density of the phosphoryl oxygen with structural variation of X. In principle, the basicity of the phosphoryl oxygen can be measured from the change of IR frequencies of the hydroxyl group ( $\nu_{\text{OH}}$ ) or the change of  $^1\text{H}$  NMR chemical shift of the hydroxyl group ( $\delta_{\text{OH}}$ ) in associated and dissociated states with alcohol or phenol. However,  $\nu$  is usually too small to reflect correctly the structural effect, and  $\delta_{\text{OH}}$  is effected by the presence of traces of water in the system.  $^{31}\text{P}$  NMR spectroscopy is more easily controlled. On the other hand,  $^{31}\text{P}$  NMR chemical shifts move downfield in protic solvents in comparison with aprotic solvents. In addition, the stronger the intermolecular hydrogen bonding between the phosphoryl oxygen and a given protic solvent, the more downfield is the  $^{31}\text{P}$  NMR chemical shift [14]. Therefore, the difference of the  $^{31}\text{P}$  NMR chemical shifts in methanol and in acetone ( $\Delta\delta^{31}\text{P}$ ) can be used to measure the basicity of the phosphoryl oxygen:

$$\Delta\delta^{31}\text{P} = \delta^{31}\text{P}(\text{MeOH}) - \delta^{31}\text{P}(\text{acetone}) \quad (1)$$

The results in Table 1 show that the larger the electron-withdrawing ability of the substituent, the smaller is the  $\Delta\delta^{31}\text{P}$  value. Meanwhile, the weaker hydrogen bonding between the phosphoryl oxygen and solvent leads to an upfield shift in the  $\delta^{31}\text{P}$  NMR resonance, and therefore, the  $\Delta\delta^{31}\text{P}$  becomes smaller.

On the other hand, the charge density ( $q_0$ ) of the phosphoryl oxygen which was calculated by MNDO from the most stable conformations of compounds **1**, established by the MM2(85) program, may be linearly correlated with  $\Delta\delta^{31}\text{P}$  (see Figure 1), and the polar

$$\Delta\delta^{31}\text{P} = -16.6 - 33.0 q_0$$

$$n = 12, r = -0.974 \quad (2)$$

parameters  $\sigma_7$  are also linearly associated with  $\Delta\delta^{31}\text{P}$  (see Figure 2).

It can be concluded that  $\Delta\delta^{31}\text{P}$  directly reflects the change of the electron density of the phosphoryl oxygen and, therefore, the polar effect of the substituents, including the field and induced effects in compounds **1**.

The data in Table 1 also show that  $\Delta\delta^{31}\text{P}$  does not change much for various alkyl groups. In other

TABLE 1 Substituent Effects on  $\delta^{31}\text{P}$  Values of Compounds 1

No.	X	$\delta^{31}\text{P}$		$\Delta\delta^{31}\text{P}$	$\Delta\Delta\delta^{31}\text{P}$	$q_0$	$\sigma_I$
		MeOH	Acetone				
1a	C <sub>2</sub> H <sub>5</sub>	-6.14	-8.58	2.44	0.0	-0.5776	-0.01
1b	C <sub>3</sub> H <sub>7</sub>	-6.21	-8.70	2.49	0.0	-0.5776	-0.01
1c	<i>i</i> -C <sub>3</sub> H <sub>7</sub>	-5.77	-8.24	2.47	0.0	-0.5783	-0.01
1d	<i>s</i> -C <sub>4</sub> H <sub>9</sub>	-5.80	-8.29	2.49	0.0	-0.5783	-0.01
1e	<i>s</i> -C <sub>5</sub> H <sub>11</sub>	-5.68	-8.14	2.46	0.0	-0.5784	-0.01
1f	<i>t</i> -C <sub>4</sub> H <sub>9</sub>	-4.99	-7.44	2.45	0.0	-0.5787	-0.01
1g	CH <sub>3</sub> O	-7.39	-9.58	2.19	0.28	-0.5716	0.30
1h	C <sub>2</sub> H <sub>5</sub> O	-7.39	-9.60	2.21	0.26	-0.5726	0.30
1i	Cl	-9.61	-11.70	2.09	0.38	-0.5654	0.47
1j	CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	-6.88	-9.07	2.19	0.28	-0.5721	0.30
1k	CO <sub>2</sub> H	-6.68	-8.97	2.29	0.18	-0.5700	0.30
1l	NO <sub>2</sub>	-8.19	-9.93	1.74	0.73	-0.5570	0.67
1m	CH <sub>2</sub> OH	-5.94	-8.17	2.23	0.24		
1n	C(CH <sub>3</sub> ) <sub>2</sub> OH	-4.79	-7.36	2.57	-0.11		
1o	CH <sub>3</sub> CH=CH	-6.29	-8.66	2.37	0.10		0.11
1p		-8.65					

$^{31}\text{P}$  NMR chemical shift in  $\delta$ .

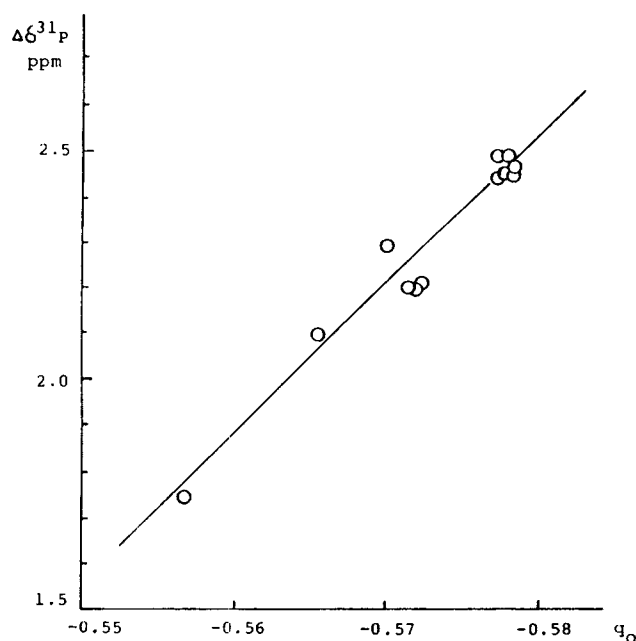


FIGURE 1 Plot of  $q_0$  vs.  $\Delta\delta^{31}\text{P}$  for four-substituted Bicyclic Phosphates (1)

words, the difference in the polar effect among alkyl groups is very small. If the average of  $\Delta\delta^{31}\text{P}(\text{R})$  is taken as a reference, the relative polar effect can be expressed by  $\Delta\Delta\delta^{31}\text{P}$ :

$$\Delta\Delta\delta^{31}\text{P} = \Delta\delta^{31}\text{P}(\text{R}) - \Delta\delta^{31}\text{P}(\text{X}) \quad (3)$$

$\Delta\Delta\delta^{31}\text{P}$  has a magnitude very similar to that of  $\sigma_I$

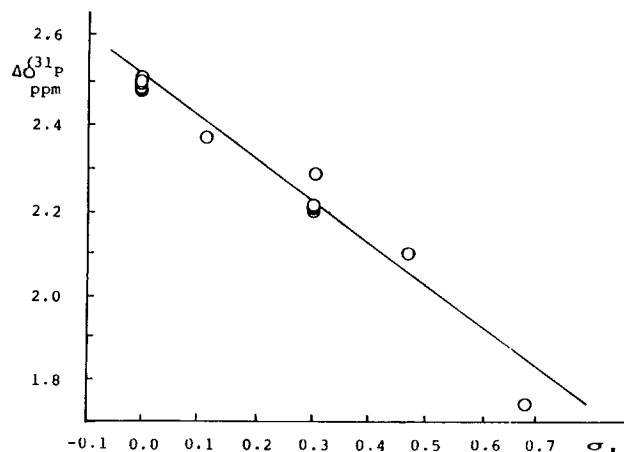


FIGURE 2 Relationship between  $\sigma_I$  and  $\Delta\delta^{31}\text{P}$  for Compounds 1

used in carbon chemistry and linearly correlates with  $\sigma_I$ .

$$\Delta\Delta\delta^{31}\text{P} = -0.004 + 0.949 \sigma_I \quad (4)$$

$n = 13, r = 0.978$

Figure 2 shows that the substituent carboxyl group gives rise to a negative deviation, while the deviation for a nitro group is positive. This is because the hydrogen bonding between the carboxyl group and solvent makes the electron-withdrawing ability of the carboxyl group weaker, while that between the nitro group and the solvent increases the electron-withdrawing ability of the nitro group.

It can be concluded from the above discussion that the polar effect predominantly results from the field and inductive effects of substituents from which the steric influence has been eliminated and is similar to that of  $\sigma_I$  used in carbon chemistry. Finally, the polar effect of various alkyl groups is small, and no significant difference can be found among these groups.

In compounds **2**, the polar effects of substituents are transferred to the active center through the resonance effect of the benzene ring. The  $^{31}\text{P}$  chemical shift in various solvents and  $\text{p}K_a$ 's of compounds **2** are listed in Table 2. Both the  $^{31}\text{P}$  chemical shift and  $\text{p}K_a$  values linearly correlate with Hammett's  $\sigma_p$ :

$$^{31}\text{P}(\text{MeOH}) = 16.9 - 4.26 \sigma_p$$

$$n = 11, r = 0.984 \quad (5)$$

$$^{31}\text{P}(\text{acetone}) = 17.8 - 4.94 \sigma_p$$

$$n = 11, r = 0.985 \quad (6)$$

$$\text{p}K_a = 3.40 - 0.82 \sigma_p$$

$$n = 11, r = 0.981 \quad (7)$$

The similar results for compound **2'** are also observed (see Table 2). The interactions between the phosphoryl hydroxyl group and solvent make the difference of  $\delta^{31}\text{P}$  in methanol and acetone smaller and produce larger experimental errors. However,  $\Delta\delta^{31}\text{P}$  still parallels  $\sigma_p$  values with a correlation coefficient of 0.968. These results indicate that *p*-alkylphenylphosphonic acids are also similar to each other, as expected.

The results with compounds **1** and **2** indicate that the  $\Delta\delta^{31}\text{P}$ ,  $\Delta\Delta\delta^{31}\text{P}$ , or  $\text{p}K_a$  values for the alkyl group substituents are not significantly different. This means that the polar effects (whether through field, inductive, and/or resonance) of all alkyl groups, without appreciable steric effect, are small and no major differences can be found.

### Steric Effects of Alkyl Groups in Organophosphorus Esters

As above, when the basicity or charge density of the phosphoryl oxygen decreases,  $\Delta\delta^{31}\text{P}$  becomes small. However, this relationship is not observed for compounds **3**, in which the substituents are directly connected with the phosphorus atom.  $\Delta\delta^{31}\text{P}$  values for compounds **3** in methanol and carbon tetrachloride are given in Table 3. Although a linear relationship exists between  $\Delta\delta^{31}\text{P}$  and  $\sigma^*$  or  $\sigma_\phi$  (see Table 3), the direction of change of  $\Delta\delta^{31}\text{P}$  is not consistent with the electron-releasing ability of the various alkyl groups. For example, the  $\Delta\delta^{31}\text{P}$  of dihexyl methylphosphonate is the largest, and those of dihexyl *s*-alkylphosphonates are the smallest. Hence, the methyl group has a larger electron-releasing ability than the secondary alkyl groups, and those of *n*-alkyl groups are larger than those of branched groups. This is inconsistent with general trends in organic chemistry. Therefore, the  $\Delta\delta^{31}\text{P}$  values of compounds **3** are not determined by the polar effects of the alkyl group.

The difference in  $\Delta\delta^{31}\text{P}$  between methyl and isopropyl groups in compounds **3** is 1.2 ppm, while that in compounds **2** is 0.13 ppm and that in compounds **1** only 0.05 ppm. Therefore, the size of  $\Delta\delta^{31}\text{P}$  and the abnormal change in its direction for compounds **3** is not controlled by electronic but rather by steric effects. This is because the alkyl groups are directly bonded to the phosphorus atom in compounds **3**, and the solvation of the phosphoryl oxygen will be hindered by the steric effects of the alkyl groups. Hydrogen bonding between the phosphoryl oxygen and a protic solvent will become weaker with an increase in the size of the alkyl groups, and  $\Delta\delta^{31}\text{P}$  will become smaller. This interpretation is consistent with experimental observations. Therefore,  $\Delta\delta^{31}\text{P}$  in compounds **3** reflects the steric effect on the solvation of phosphorus esters resulting from the alkyl groups. This steric ef-

TABLE 2 Substituent Effects on  $\delta^{31}\text{P}$  and  $\text{p}K_a$  Values for Compounds **2**

No.	X	$\sigma^p$	$\delta^{31}\text{P}(2)$		$\Delta\delta^{31}\text{P}$	$\text{p}K_a$	$\delta^{31}\text{P}(2')$	
			MeOH	Acetone			MeOH	Acetone
<b>2a</b>	H	0.00	17.70	16.95	0.65	3.43	18.63	17.19
<b>2b</b>	CH <sub>3</sub>	-0.17	18.66	17.70	0.96	3.52	19.41	17.81
<b>2c</b>	C <sub>2</sub> H <sub>5</sub>	-0.15	18.70	17.70	1.00	3.55	19.36	17.75
<b>2d</b>	<i>i</i> -C <sub>2</sub> H <sub>7</sub>	-0.15	18.53	17.58	0.95	3.53	19.29	17.60
<b>2e</b>	<i>n</i> -C <sub>4</sub> H <sub>9</sub>	-0.16	18.73	17.70	1.03	3.53	19.39	17.68
<b>2f</b>	<i>i</i> -C <sub>4</sub> H <sub>9</sub>	-0.13	18.73	17.70	0.97	3.55		
<b>2g</b>	<i>t</i> -C <sub>4</sub> H <sub>9</sub>	-0.20	18.63	17.63	1.00	3.54	19.29	17.63
<b>2h</b>	<i>n</i> -C <sub>8</sub> H <sub>17</sub>	-0.16	18.70	17.63	1.07	3.53		
<b>2i</b>	CH <sub>3</sub> O	-0.27	19.09	18.01	1.07	3.60	19.80	18.00
<b>2j</b>	(CH <sub>3</sub> ) <sub>2</sub> N	-0.83	21.65	20.22	1.43	4.05	22.31	20.02
<b>2k</b>	Cl	-0.23	16.22	15.49	0.73	3.12	17.51	15.83

TABLE 3 Substituent Effect on  $\Delta\delta^{31}\text{P}$  Values for Compound 3

No.	X	$\delta^{31}\text{P}$		$\Delta\delta^{31}\text{P}$	Y				
		MeOH	$\text{CCl}_4$		$\nu$	$E_s$	$\sigma_\phi$	$\sigma$	
3a	$\text{CH}_3$	31.50	28.66	2.8	0.52	0.0	-0.96	0.00	
3b	$\text{C}_3\text{H}_7$	32.64	30.60	2.0	0.68	-0.36	-1.18	-0.12	
3c	<i>i</i> - $\text{C}_3\text{H}_7$	35.45	33.81	1.6	0.76	-0.47	-1.30	-0.19	
3d	<i>n</i> - $\text{C}_4\text{H}_9$	32.93	30.94	2.0	0.68	-0.39	-1.22	-0.13	
3e	<i>i</i> - $\text{C}_4\text{H}_9$	31.79	30.13	1.7	0.98	-0.93	-1.30	-0.12	
3f	<i>s</i> - $\text{C}_4\text{H}_9$	34.76	33.28	1.5	1.02		-1.36	-0.21	
3g	<i>n</i> - $\text{C}_5\text{H}_{11}$	33.16	31.21	2.0	0.68	-1.40	-1.21	-0.61	
3h	<i>i</i> - $\text{C}_5\text{H}_{11}$	33.22	31.30	1.9	0.68	-0.35	-1.27	-0.16	
3i	<i>n</i> - $\text{C}_8\text{H}_{17}$	32.91	31.04	1.9	0.68	-0.33	-1.11	-0.17	
3j	<i>i</i> - $\text{C}_8\text{H}_{17}$	32.71	31.01	1.7					
3k	<i>s</i> - $\text{C}_8\text{H}_{17}$	34.89	33.50	1.4					
$\Delta\delta^{31}\text{P} = a + bY$					<i>r</i>	-0.80	0.77	0.92	0.91
					<i>a</i>	3.33	2.43	5.42	2.72
					<i>b</i>	-1.89	1.09	2.87	5.61
					<i>n</i>	9	8	9	9

$^{31}\text{P}$  NMR chemical shift in  $\delta$ .

fect is different from that produced in the hydrolysis reactions of carboxylic esters. The steric effect in the latter comes mainly from the energy contribution to the transition state, not only from solvation. Therefore, the case of  $\Delta\delta^{31}\text{P}$  herein is not parallel to either  $E_s$  or  $\nu$ . The correlation coefficient between  $\Delta\delta^{31}\text{P}$  and either  $E_s$  or  $\nu$  is less than 0.8 (Table 3).

The  $\text{p}K_a$  values of alkylphosphonic monohexyl esters (4), prepared from compounds 3, were determined, and a very good linear correlation between  $\Delta\delta^{31}\text{P}$  of 3 and  $\text{p}K_a$  of 4 is observed:

$$\text{p}K_a = 5.31 - 0.53 \Delta\delta^{31}\text{P} \quad (8)$$

$n = 11, r = 0.988$

The  $\Delta\text{p}K_a$  for compounds 4 is much larger than that observed in compounds 2. For example, the  $\Delta\text{p}K_a$  between methyl and tertiary butyl groups in 4 is 0.86, while in 2, it is only 0.03. This indicates that the substituent effect of the alkyl groups in 4 mainly comes from steric effects on solvation. Branching of the alkyl groups hinders solvation of the acidic anion and leads to an increase in the dissociation free energy of the acids; hence, the  $\text{p}K_a$  values increase. These results are consistent with the observations in 1 and 2.

From the above discussion, it can be seen that either  $\sigma_\phi$  or  $\sigma^p$ , based on the  $\text{p}K_a$  measurement of organophosphorus acids, does not represent the polar effect of substituents at all. For alkyl groups,  $\sigma_\phi$   $\sigma^p$  mainly represents the steric effect. However, for *n*-alkyl and *n*-alkoxyl groups,  $\sigma_\phi$  or  $\sigma^p$  reflects their relative polar effects.

Based on the above discussion, the steric effects of alkyl groups can be estimated from the  $\text{p}K_a$  values of alkylphosphonic acid monohexyl esters.

If the  $\text{p}K_a$  value of methylphosphonic acid monohexyl ester (4a) is taken as a reference, the  $\Delta\text{p}K_a$  gives the relative steric hindrance to solvation of acid dissociation:

$$\Delta\text{p}K_a = \text{p}K_a(\text{R}) - \text{p}K_a(\text{Me}) \quad (9)$$

In order to make the magnitude of  $\text{p}K_a$  correspond to either the  $E_s$  or  $\nu$  scale, 0.5 is taken as the origin point for the methyl group. In this way, a set of steric parameters (represented by the symbol  $E_s^p$ ) can be obtained:

$$E_{s,\text{R}}^p = \Delta\text{p}K_a + 0.5 \quad (10)$$

For alkoxy groups, due to a lack of systematic data, we have followed Charton's treatment [15]. Considering the influence of oxygen in alkoxy groups on solvation,  $E_{s,\text{RO}}^p$  is calculated from Equation 11:

$$E_{s,\text{RO}}^p = 0.96 E_{s,\text{R}}^p - 0.1 \quad (11)$$

A series of  $E_{s,\text{R}}^p$  and  $E_{s,\text{RO}}^p$  values calculated from Equations 10 and 11 are listed in Table 4. For a phenyl group, according to the general treatment of the polar effect which corresponds to a decrease of 0.32 in  $\text{p}K_a$  value, the  $E_{s,\text{Ph}}^p$  calculated from Equation 12 is 0.4.

$$E_{s,\text{Ph}}^p = \Delta\text{p}K_{a,\text{Ph}} - (-0.32) + 0.5 = 0.4 \quad (12)$$

In conclusion, the proposed parameter  $E_s^p$  is different from Taft's  $E_s$  and Charton's  $\nu$ . It basically reflects the solvation steric effect in the dissociation of organophosphorus acids and thus can be applied as an empirical structural parameter to describe the chemical processes in which such effects play a predominant role.

TABLE 4 Influence of Substituent Steric Parameters on  $pK_a$  Value of Compounds 4

No.	R	$pK_a$	$\Delta pK_a$	$E_{s,R}^p$	$E_{s,RO}^p$	$\nu_R$	$\nu_{RO}$	$E_{s,R}$	$E_{s,RO}$
4a	CH <sub>3</sub>	3.85	0.0	0.50	0.38	0.52	0.36	-1.24	-0.55
4b	C <sub>3</sub> H <sub>7</sub>	4.20	0.35	0.85	0.72	0.68	0.56	-1.60	-0.55
4c	<i>i</i> -C <sub>3</sub> H <sub>7</sub>	4.47	0.62	1.12	0.98	0.76	0.75	-1.71	-0.55
4d	<i>n</i> -C <sub>4</sub> H <sub>9</sub>	4.26	0.41	0.91	0.77	0.68	0.58	—	-0.55
4e	<i>i</i> -C <sub>4</sub> H <sub>9</sub>	4.40	0.55	1.05	0.91	0.98	0.62	—	-0.55
4f	<i>s</i> -C <sub>4</sub> H <sub>9</sub>	4.52	0.63	1.17	1.02	1.02	0.86	-2.37	-0.55
4g	<i>t</i> -C <sub>4</sub> H <sub>9</sub>	4.71	0.86	1.36	1.21	1.24	1.22	-2.78	—
4h	<i>n</i> -C <sub>5</sub> H <sub>11</sub>	4.26	0.41	0.91	0.77	0.68	—	—	—
4i	<i>i</i> -C <sub>5</sub> H <sub>11</sub>	4.27	0.42	0.92	0.78	0.68	—	—	—
4j	<i>n</i> -C <sub>8</sub> H <sub>17</sub>	4.25	0.40	0.90	0.76	0.68	—	—	—
4k	<i>i</i> -C <sub>8</sub> H <sub>17</sub>	4.45	0.60	1.10	0.96	1.01	0.76	—	—
4l	<i>s</i> -C <sub>8</sub> H <sub>17</sub>	4.60	0.75	1.25	1.05	1.05	0.92	—	—
4m	C <sub>2</sub> H <sub>5</sub>	4.10	0.25	0.75	0.62	0.56	0.48	-1.31	-0.55
4n	cyc-C <sub>6</sub> H <sub>11</sub>	4.42	0.57	1.07	0.93	0.87	—	-1.01	—
4o	C <sub>6</sub> H <sub>5</sub>	3.43	-0.42	0.40	0.28	0.57	—	—	—

### Applications of Empirical Parameters

**Dissociation Reactions of Acidic Organophosphorus Esters.** The  $pK_a$  values of acidic organophosphorus esters are influenced by the solvation involving the hydronium cation and the acidic anion. The hydronium ion is the same for all the acidic organophosphorus esters. Therefore, the difference of  $pK_a$  values mainly comes from the polar effects and the solvation steric effects of acidic anions. Thus, the  $pK_a$  values of acidic organophosphorus esters can be described by means of  $E_s^p$  and  $\sigma_1$ . The  $pK_a$  values of 36 acidic organophosphorus esters have been reported in this article, and  $pK_a$  values of 35 acidic organophosphorus esters which were previously obtained in our laboratory [7] have been analyzed with Equation 13:

$$pK_a = C + \rho \Sigma \sigma_1 + \delta \Sigma E_s^p$$

$$C = 3.78, \rho = -3.10, \delta = 0.80$$

$$r = 0.987, S = 0.089, n = 71$$

$$t_c = 44.73, t_\rho = -26.97, t_\delta = 23.81 \quad (13)$$

where  $r$  = correlation coefficient,  $S$  = RMS error,  $n$  = points and  $t_c, t_\rho, t_\delta$  are the T-tests for each term, respectively. The difference between the calculated and the observed  $pK_a$  values is, in general, less than 0.1 units (see Table 5). In order to check the reliability of Equation 13, several organophosphorus acids with very high steric hindrance were prepared. Their calculated and observed  $pK_a$  values are listed in Table 6. The results show that the calculated values from Equation 13 are consistent with observed values.

**Steric Effects of Dialkyl Alkylphosphonates in Alkaline Hydrolysis Reactions.** In general, the steric effects of alkyl groups on hydrolytic reaction rate

constants of alkylphosphonates can be estimated from the energy difference ( $\Delta E$  or  $\Delta \Delta E$ ) between the substrate and its transition state. This can be calculated by molecular mechanics methods [12,13]. Although the physical meanings of  $\Delta \Delta E$  and  $E_s^p$  may be quite different, the contribution of the substituent steric effect in hydrolytic reactions closely parallels that in solvation. Therefore,  $E_s^p$  may also be used in correlation analysis with the rate constant  $k$  of hydrolytic reactions of organophosphorus esters. For example, the rate constants of hydrolysis of six- or seven-membered cyclic alkylphosphonate esters correlate linearly with  $E_s^p$  with correlation coefficients greater than 0.95 (Table 7), with the exception of entries 3 and 5 which have huge and bulky alkyl groups. Hence,  $E_s^p$  is not suitable for highly hindered groups. Regression analysis using  $E_s^p$  for *n*-alkyl groups usually provides better results than that with  $\Delta \Delta E$ . It is highly probable that the  $E_s^p$  term embraces entropy effects. It is also found that no correlation exists between  $E_s^p$  and  $\Delta \Delta E$  if the structures of the alkyl and alkoxy groups vary, since  $E_s^p$  does not reflect the steric effect of substituents in hydrolytic reactions of phosphorus-based esters. For example, the regression analysis involving  $\log k$  [16] and  $E_s^p$  in dialkyl alkyl phosphonates provides poor correlation coefficients ( $r = 0.90-0.92$ ) (Table 8). In comparison of  $E_s^p$  with  $\Delta \Delta E$ , it is observed that the increasing trend of  $\Delta \Delta E$  with the bulk of the alkyl groups is significantly larger than that of  $E_s^p$ . For alkoxy groups, the increasing trend of  $\Delta \Delta E$  is less pronounced than that of  $E_s^p$  (Table 9). This is well demonstrated by the differences between *s*-butyl, *i*-propyl, and *i*-butoxy groups. This situation encourages us to modify the  $E_s^p$  values of the mentioned groups from 1.25, 1.15, and 0.91 to 1.40, 1.30, and 0.81, respectively. As a result of this modifi-

**TABLE 5**  $pK_a$  Values and Substituent Parameters for Acidic Organophosphorus Esters  $(C_6H_{17})_2CHO[X(Y)P(O)OH]$ 

No.	X	Y	$pK_a$	$\Sigma\sigma_i$	$\Sigma E_s^P$	$\Delta pK_a^*$
1	CH <sub>3</sub>	<i>n</i> -C <sub>6</sub> H <sub>13</sub> O	3.85	0.29	1.26	-0.036
2	C <sub>3</sub> H <sub>7</sub>	<i>n</i> -C <sub>6</sub> H <sub>13</sub> O	4.20	0.29	1.61	-0.035
3	<i>i</i> -C <sub>3</sub> H <sub>7</sub>	<i>n</i> -C <sub>6</sub> H <sub>13</sub> O	4.47	0.29	1.88	0.089
4	<i>n</i> -C <sub>4</sub> H <sub>9</sub>	<i>n</i> -C <sub>6</sub> H <sub>13</sub> O	4.26	0.29	1.67	0.047
5	<i>i</i> -C <sub>4</sub> H <sub>9</sub>	<i>n</i> -C <sub>6</sub> H <sub>13</sub> O	4.40	0.29	1.71	0.155
6	<i>s</i> -C <sub>4</sub> H <sub>9</sub>	<i>n</i> -C <sub>6</sub> H <sub>13</sub> O	4.48	0.29	1.93	0.060
7	<i>t</i> -C <sub>4</sub> H <sub>9</sub>	<i>n</i> -C <sub>6</sub> H <sub>13</sub> O	4.70	0.29	2.12	0.138
8	<i>n</i> -C <sub>5</sub> H <sub>11</sub>	<i>n</i> -C <sub>6</sub> H <sub>13</sub> O	4.26	0.29	1.67	0.047
9	<i>i</i> -C <sub>5</sub> H <sub>11</sub>	<i>n</i> -C <sub>6</sub> H <sub>13</sub> O	4.27	0.29	1.68	0.049
10	<i>n</i> -C <sub>6</sub> H <sub>17</sub>	<i>n</i> -C <sub>6</sub> H <sub>13</sub> O	4.25	0.29	1.66	0.045
11	<i>i</i> -C <sub>6</sub> H <sub>17</sub>	<i>n</i> -C <sub>6</sub> H <sub>13</sub> O	4.45	0.29	1.86	0.085
12	<i>n</i> -C <sub>6</sub> H <sub>17</sub>	<i>n</i> -C <sub>6</sub> H <sub>13</sub> O	4.60	0.29	2.01	0.116
13	<i>n</i> -C <sub>6</sub> H <sub>17</sub>	<i>n</i> -C <sub>6</sub> H <sub>17</sub> O	4.21	0.29	1.66	0.005
14	<i>n</i> -C <sub>6</sub> H <sub>17</sub>	<i>i</i> -C <sub>6</sub> H <sub>17</sub> O	4.31	0.29	1.86	-0.055
15	<i>n</i> -C <sub>6</sub> H <sub>17</sub>	<i>s</i> -C <sub>6</sub> H <sub>17</sub> O	4.54	0.29	1.95	0.104
16	<i>i</i> -C <sub>6</sub> H <sub>17</sub>	<i>n</i> -C <sub>6</sub> H <sub>17</sub> O	4.33	0.29	1.86	-0.035
17	<i>i</i> -C <sub>6</sub> H <sub>17</sub>	<i>i</i> -C <sub>6</sub> H <sub>17</sub> O	4.50	0.29	2.06	-0.024
18	<i>n</i> -C <sub>6</sub> H <sub>17</sub>	<i>s</i> -C <sub>6</sub> H <sub>17</sub> O	4.65	0.29	2.15	-0.014
19	<i>s</i> -C <sub>6</sub> H <sub>17</sub>	<i>n</i> -C <sub>6</sub> H <sub>17</sub> O	4.50	0.29	2.01	0.016
20	<i>s</i> -C <sub>6</sub> H <sub>17</sub>	<i>i</i> -C <sub>6</sub> H <sub>17</sub> O	4.55	0.29	2.21	-0.094
21	<i>s</i> -C <sub>6</sub> H <sub>17</sub>	<i>s</i> -C <sub>6</sub> H <sub>17</sub> O	4.80	0.29	2.30	0.084
22	<i>n</i> -C <sub>6</sub> H <sub>17</sub>	<i>n</i> -C <sub>4</sub> H <sub>9</sub> O	4.20	0.29	1.67	-0.013
23	<i>n</i> -C <sub>6</sub> H <sub>17</sub>	<i>i</i> -C <sub>4</sub> H <sub>9</sub> O	4.30	0.29	1.81	-0.025
24	<i>n</i> -C <sub>6</sub> H <sub>17</sub>	<i>s</i> -C <sub>4</sub> H <sub>9</sub> O	4.50	0.29	1.92	0.088
25	<i>i</i> -C <sub>6</sub> H <sub>17</sub>	<i>n</i> -C <sub>4</sub> H <sub>9</sub> O	4.30	0.29	1.87	-0.073
26	<i>i</i> -C <sub>6</sub> H <sub>17</sub>	<i>i</i> -C <sub>4</sub> H <sub>9</sub> O	4.40	0.29	2.01	-0.084
27	<i>i</i> -C <sub>6</sub> H <sub>17</sub>	<i>s</i> -C <sub>4</sub> H <sub>9</sub> O	4.60	0.29	2.12	0.028
28	<i>s</i> -C <sub>6</sub> H <sub>17</sub>	<i>n</i> -C <sub>4</sub> H <sub>9</sub> O	4.31	0.29	2.02	-0.182
29	<i>s</i> -C <sub>6</sub> H <sub>17</sub>	<i>i</i> -C <sub>4</sub> H <sub>9</sub> O	4.55	0.29	2.16	-0.054
30	<i>s</i> -C <sub>6</sub> H <sub>17</sub>	<i>s</i> -C <sub>4</sub> H <sub>9</sub> O	4.71	0.29	2.34	0.042
31	<i>i</i> -C <sub>6</sub> H <sub>17</sub>	<i>i</i> -C <sub>6</sub> H <sub>13</sub> O	4.40	0.29	2.06	-0.124
32	<i>n</i> -C <sub>6</sub> H <sub>17</sub>	<i>i</i> -C <sub>6</sub> H <sub>13</sub> O	4.30	0.29	1.86	-0.065
33	<i>i</i> -C <sub>3</sub> H <sub>7</sub>	<i>i</i> -C <sub>12</sub> H <sub>25</sub> O	4.40	0.29	1.88	0.011
34	<i>i</i> -C <sub>3</sub> H <sub>7</sub>	<i>s</i> -C <sub>13</sub> H <sub>27</sub> O	4.65	0.29	2.37	-0.122
35	<i>i</i> -C <sub>3</sub> H <sub>7</sub>	<i>s</i> - <i>s</i> -C <sub>13</sub> H <sub>27</sub> O	4.85	0.29	2.48	-0.093
36	<i>i</i> -C <sub>3</sub> H <sub>7</sub>	<i>i</i> -C <sub>14</sub> H <sub>29</sub> O	4.48	0.29	2.09	-0.068
37	<i>i</i> -C <sub>3</sub> H <sub>7</sub>	<i>n</i> -C <sub>6</sub> H <sub>17</sub> O	4.40	0.29	1.88	0.019
38	<i>i</i> -C <sub>3</sub> H <sub>7</sub>	<i>i</i> -C <sub>6</sub> H <sub>17</sub> O	4.47	0.29	2.08	-0.070
39	<i>i</i> -C <sub>3</sub> H <sub>7</sub>	<i>s</i> -C <sub>6</sub> H <sub>17</sub> O	4.66	0.29	2.17	0.048
40	CH <sub>3</sub>	<i>s</i> -C <sub>6</sub> H <sub>17</sub> O	4.10	0.29	1.75	-0.177
41	CH <sub>3</sub>	<i>i</i> -C <sub>6</sub> H <sub>17</sub> O	3.95	0.29	1.60	-0.207
42	CH <sub>3</sub>	<i>i</i> -C <sub>16</sub> H <sub>33</sub> O	3.98	0.29	1.48	-0.081
43	CH <sub>3</sub>	(C <sub>7</sub> H <sub>15</sub> ) <sub>2</sub> CHO	4.20	0.29	1.75	-0.077
44	CH <sub>3</sub>	(C <sub>6</sub> H <sub>13</sub> ) <sub>2</sub> CHO	4.20	0.29	1.75	-0.077
45	CH <sub>3</sub>	(C <sub>8</sub> H <sub>17</sub> ) <sub>2</sub> CHO	4.20	0.29	1.75	-0.077
46	CH <sub>3</sub>	<i>i</i> -C <sub>14</sub> H <sub>29</sub> O	3.98	0.29	1.48	-0.081
47	CH <sub>3</sub>	<i>i</i> -C <sub>16</sub> H <sub>33</sub> O	3.95	0.29	1.48	-0.111
48	<i>n</i> -C <sub>6</sub> H <sub>17</sub>	<i>n</i> -C <sub>6</sub> H <sub>17</sub>	5.30	-0.02	1.80	0.022
49	<i>i</i> -C <sub>6</sub> H <sub>17</sub>	<i>i</i> -C <sub>6</sub> H <sub>17</sub>	5.45	-0.02	2.20	0.147
50	<i>s</i> -C <sub>6</sub> H <sub>17</sub>	<i>s</i> -C <sub>6</sub> H <sub>17</sub>	5.85	-0.02	2.50	0.014
51	<i>n</i> -C <sub>6</sub> H <sub>17</sub> O	<i>n</i> -C <sub>6</sub> H <sub>17</sub> O	3.05	0.60	1.52	-0.082
52	<i>i</i> -C <sub>6</sub> H <sub>17</sub> O	<i>i</i> -C <sub>6</sub> H <sub>17</sub> O	3.35	0.60	1.92	-0.102
53	<i>s</i> -C <sub>6</sub> H <sub>17</sub> O	<i>s</i> -C <sub>6</sub> H <sub>17</sub> O	3.75	0.60	2.10	0.155
54	cyc-C <sub>6</sub> H <sub>11</sub>	<i>n</i> -C <sub>6</sub> H <sub>17</sub> O	4.40	0.29	1.83	0.059
55	cyc-C <sub>6</sub> H <sub>11</sub>	<i>i</i> -C <sub>6</sub> H <sub>17</sub> O	4.55	0.29	2.03	0.050
56	cyc-C <sub>6</sub> H <sub>11</sub>	<i>s</i> -C <sub>6</sub> H <sub>17</sub> O	4.75	0.29	2.12	0.178
57	C <sub>6</sub> H <sub>5</sub>	<i>n</i> -C <sub>6</sub> H <sub>17</sub> O	3.43	0.42	1.30	-0.085
58	C <sub>6</sub> H <sub>5</sub>	<i>i</i> -C <sub>6</sub> H <sub>17</sub> O	3.53	0.42	1.50	-0.144
59	C <sub>6</sub> H <sub>5</sub>	<i>s</i> -C <sub>6</sub> H <sub>17</sub> O	3.70	0.42	1.65	-0.094

**TABLE 5** Continued

No.	X	Y	$pK_a$	$\Sigma\sigma_i$	$\Sigma E_s^P$	$\Delta pK_a^*$
60	<i>o</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	<i>n</i> -C <sub>6</sub> H <sub>17</sub> O	3.60	0.41	1.20	0.134
61	<i>o</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	<i>i</i> -C <sub>6</sub> H <sub>17</sub> O	3.68	0.41	1.41	0.096
62	C <sub>6</sub> H <sub>5</sub>	<i>n</i> -C <sub>6</sub> H <sub>13</sub> O	3.43	0.42	1.16	0.027
63	<i>p</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	<i>n</i> -C <sub>6</sub> H <sub>13</sub> O	3.51	0.40	1.16	0.045
64	<i>p</i> -C <sub>2</sub> H <sub>5</sub> C <sub>6</sub> H <sub>4</sub>	<i>n</i> -C <sub>6</sub> H <sub>13</sub> O	3.54	0.40	1.16	0.075
65	<i>p</i> - <i>i</i> -C <sub>3</sub> H <sub>7</sub> C <sub>6</sub> H <sub>4</sub>	<i>n</i> -C <sub>6</sub> H <sub>13</sub> O	3.53	0.40	1.16	0.065
66	<i>p</i> -C <sub>4</sub> H <sub>9</sub> C <sub>6</sub> H <sub>4</sub>	<i>n</i> -C <sub>6</sub> H <sub>13</sub> O	3.53	0.40	1.16	0.065
67	<i>p</i> - <i>i</i> -C <sub>4</sub> H <sub>9</sub> C <sub>6</sub> H <sub>4</sub>	<i>n</i> -C <sub>6</sub> H <sub>13</sub> O	3.53	0.40	1.16	0.065
68	<i>p</i> - <i>t</i> -C <sub>4</sub> H <sub>9</sub> C <sub>6</sub> H <sub>4</sub>	<i>n</i> -C <sub>6</sub> H <sub>13</sub> O	3.54	0.40	1.16	0.075
69	<i>t</i> -C <sub>4</sub> H <sub>9</sub>	<i>t</i> -C <sub>4</sub> H <sub>9</sub>	6.09	-0.02	2.72	0.070
70	<i>t</i> -C <sub>5</sub> H <sub>11</sub>	<i>t</i> -C <sub>5</sub> H <sub>11</sub>	6.26	-0.02	2.72	0.188

\* $\Delta pK_a = pK_a(\text{obs}) - pK_a(\text{calc})$ **TABLE 6** Calculated and Observed  $pK_a$  Values for Some Organophosphorus Acids with Highly Hindered Groups [XYP(O)OH]

No.	X	Y	$\Sigma\sigma_i$	$\Sigma E_s^P$	$pK_{a\text{obs}}$	$pK_{a\text{calc}}$
5a	<i>t</i> -C <sub>4</sub> H <sub>9</sub>	<i>t</i> -C <sub>4</sub> H <sub>9</sub>	-0.02	2.72	6.09	6.02
5b	<i>t</i> -C <sub>5</sub> H <sub>11</sub>	<i>t</i> -C <sub>5</sub> H <sub>11</sub>	-0.02	2.80	6.20	6.08
4m	<i>t</i> -C <sub>4</sub> H <sub>9</sub>	<i>n</i> -C <sub>4</sub> H <sub>9</sub> O	0.29	2.13	4.62	4.59

**TABLE 7** Correlation Analysis of  $\log k$  with  $E_s^P$ 

$$\log k = a + b \Delta\Delta E \quad (1)$$

$$\log k = a' + b'E_s^P \quad (2)$$

Compound	$\log k$ of various series						
	1	2	3	4	5	6	7
CH <sub>3</sub>	2.27	2.68					
C <sub>2</sub> H <sub>5</sub>	1.60	1.78			1.34	1.58	1.86
<i>n</i> -C <sub>3</sub> H <sub>7</sub>	1.38	1.66	2.05		1.17	1.41	1.67
<i>n</i> -C <sub>4</sub> H <sub>9</sub>	1.13	1.36	1.76		1.02	1.30	1.51
<i>n</i> -C <sub>6</sub> H <sub>13</sub>	1.19	1.37	1.86		0.94	1.20	1.51
<i>n</i> -C <sub>6</sub> H <sub>17</sub>		1.29	1.73	2.83	0.88	1.19	1.45
<i>n</i> -C <sub>12</sub> H <sub>25</sub>		1.15	1.56	1.88			
<i>i</i> -C <sub>4</sub> H <sub>9</sub>		1.23	1.63	1.95	0.69	0.97	1.21
<i>i</i> -C <sub>3</sub> H <sub>7</sub>		0.20	0.64	0.99			0.53
<i>s</i> -C <sub>4</sub> H <sub>9</sub>		0.05	0.48	0.82			0.19
<i>r</i> (1)	0.976	0.936	0.963	0.985	0.681	0.716	0.971
<i>r</i> (2)	0.998	0.953	0.920	0.870	0.954	0.965	0.964
<i>r'</i> (2)*	0.998	0.980	0.964	0.953	0.957	0.970	0.997

\**r'* (2) is the correlation coefficient with modified  $E_s^P$  (see text).

**TABLE 8** Regression Analysis of  $\log k$  of Dialkyl Alkyl Phosphonates  $[\text{RP}(\text{O})(\text{OR}')_2]$  with  $E_s^P$ 

R	R'	$E_s^P$	$\log k$				
			1	2	3	4	5
<i>n</i> -C <sub>8</sub> H <sub>17</sub>	<i>n</i> -C <sub>4</sub> H <sub>9</sub> O	2.44	2.05	1.99	1.89	1.83	1.75
<i>n</i> -C <sub>8</sub> H <sub>17</sub>	<i>i</i> -C <sub>4</sub> H <sub>9</sub> O	2.72	1.91	1.77	1.73	1.64	1.54
<i>i</i> -C <sub>8</sub> H <sub>17</sub>	<i>n</i> -C <sub>4</sub> H <sub>9</sub> O	2.64	1.61	1.53	1.41	1.35	1.23
<i>i</i> -C <sub>8</sub> H <sub>17</sub>	<i>i</i> -C <sub>4</sub> H <sub>9</sub> O	2.92	1.49	1.41	1.29	1.20	1.05
<i>i</i> -C <sub>8</sub> H <sub>17</sub>	<i>i</i> -C <sub>6</sub> H <sub>13</sub> O	2.94	1.00	0.95	0.92	0.76	0.64
<i>s</i> -C <sub>8</sub> H <sub>17</sub>	<i>i</i> -C <sub>4</sub> H <sub>9</sub> O	3.47	0.74	0.73	0.62	0.50	0.51
<i>i</i> -C <sub>6</sub> H <sub>13</sub>	<i>i</i> -C <sub>6</sub> H <sub>13</sub> O	2.91	1.19	1.06	1.03	0.92	0.78
<i>i</i> -C <sub>4</sub> H <sub>9</sub>	<i>i</i> -C <sub>8</sub> H <sub>17</sub> O	2.97	0.87	0.79	0.71	0.69	0.55
	<i>r</i>		0.901	0.913	0.908	0.917	0.922
	<i>r</i> (modified $E_s^P$ )		0.996	0.998	0.997	0.998	0.995

cation, significant improvement in correlation analysis ( $r > 0.99$ ) was achieved (Table 8).

In conclusion, it should be emphasized that appropriate modification of the  $E_s^P$  parameters seems necessary if it is used for reactions other than the hydrogen ionization process.

## CALCULATIONS AND EXPERIMENTS

### Calculations

Molecular mechanics calculations employed Allinger's MM2 force field [17]. The most stable conformation, optimized by the MM2(85) program, was used as input structural data for quantum chemical calculations without minimization by Dewar's MNDO method [18]. The parameters of phosphorus compounds for molecular mechanics calculations were taken from Reference [19].

Molecular mechanics and quantum chemical calculations, as well as multiple regression analyses, were performed on the VAX-780 computer.

### Apparatus

The <sup>31</sup>P NMR spectra were recorded on a JEOL FX-90Q spectrometer, operating at 36.19 MHz, of 0.5 M samples in acetone, methanol, or carbon tetrachloride; 85% H<sub>3</sub>PO<sub>4</sub> was used as an external ref-

**TABLE 9**  $\Delta\Delta E_R$  and  $E_s^P$  for Some Alkyl and Alkoxy Groups

R	$\Delta\Delta E_R$	$\Delta\Delta E_{RO}$	$E_{s,R}^P$	$E_{s,RO}^P$
CH <sub>3</sub>	0.0	0.0	0.50	0.38
C <sub>2</sub> H <sub>5</sub>	0.23	0.0	0.75	0.62
<i>n</i> -C <sub>3</sub> H <sub>7</sub>	0.22	—	0.85	0.72
<i>i</i> -C <sub>3</sub> H <sub>7</sub>	1.76	0.41	1.12	0.98
<i>n</i> -C <sub>4</sub> H <sub>9</sub>	0.22	0.0	0.91	0.77
<i>i</i> -C <sub>4</sub> H <sub>9</sub>	0.64	0.0	1.05	0.91
<i>s</i> -C <sub>4</sub> H <sub>9</sub>	1.85	0.47	1.17	1.02

erence at 25°C. IR spectra of films were recorded on a Shimadzu IR-400 spectrometer. MS were taken on a Finnigan-4021 spectrometer.

The  $pK_a$  values were determined on a METROHM 636-Titroprocessor. The samples were dissolved in 75% alcohol-water, and different amounts of samples were taken not to be larger than 0.1 mmol, which produces an error in the  $pK_a$  value within 0.02–0.03 unit.

### Synthesis of Compounds

*Synthesis of Compounds 1 and 2 will be Reported Elsewhere. Synthesis of Compounds 3.* Usually, compounds **3** were synthesized by the reaction of sodium dihexyl phosphite with an alkyl bromide.

*The General Procedure.* 0.22 mole sodium was added to 150 mL of dry xylene, then 0.22 mole dihexylphosphite was added dropwise with stirring. The mixture was refluxed until the sodium disappeared and was then cooled to room temperature. The alkyl bromide (0.22 mole) was added to the reaction mixture, which was refluxed for 15 hours. After cooling, the mixture was washed by water (4 × 400 mL), separated, the organic phase dried over Na<sub>2</sub>SO<sub>4</sub>, and the solvent removed under reduced pressure. The product was isolated by distillation (see Table 10 for bp of products **3**). Yields were within 70–80%. Compounds **3** were identified by elemental analysis, <sup>31</sup>P NMR, IR, and MS spectra.

*Synthesis of Compounds 4.* Compounds **4** were synthesized by the alkaline hydrolysis of the corresponding dihexyl alkylphosphonates (**3**), except for *t*-butylphosphonic acid monohexyl ester (**4g**) which was prepared by the reaction of *t*-butylphosphonyl dichloride with sodium hexanonate in the presence of a PTC catalyst.

*The General Procedure for the Preparation of 4.* A mixture of 0.1 mole of compound **3** and 80 mL 6N aqueous NaOH solution was refluxed for 15–24 hours. (If the *P*-alkyl group is secondary, addition of a quarternary ammonium salt or a crown ether is usually required). After cooling, the mixture was extracted with ether to remove the neutral impurities. It was then acidified with 6N HCl. The organic phase was collected. The aqueous phase was extracted with petroleum ether. The combined organic phase was washed with water until no chloride ion could be detected. It was separated, dried, and the solvent and other low boiling impurities were removed by evaporation under reduced pressure. Compound **4** was obtained and identified by elemental analysis, <sup>31</sup>P NMR, IR, and MS spectra. The purity of each compound **4** was determined by titration with sodium hydroxide solution. Yields ranged from 81 to 95%.

*t*-Butylphosphonate Monohexyl Ester (**4g**). Sodium (3.5 g) was added to 100 mL of dry benzene.



TABLE 10 Compounds 3 Prepared

No.	bp C/mmHg	Yield %	No.	bp C/mmHg	Yield %
3a	112-4/0.2	71	3g	140-2/0.3	73
3b	138-42/1.0	74	3h	138-42/0.4	72
3c	162-8/0.3	70	3i	162-4/0.3	77
3d	144-5/0.3	78	3j	159-60/0.2	78
3e	122-3/0.03	72	3k	—	69
3f	136-8/0.4	69			

Hexanol (10.2 g, 0.1 mole) was added dropwise to the sodium-benzene mixture with stirring. The reaction mixture was heated at 50°C for 2 hours and then cooled to room temperature. After removal of the excess sodium, the mixture was added dropwise to *t*-butylphosphonyl dichloride (17.5 g, 0.1 mole) in 50 mL of benzene and refluxed for 25 hours. After cooling, filtration, and removal of solvent, 60 ml 6N NaOH and 1.8 g BzNEt<sub>3</sub>Cl were added to the reaction mixture. The reaction was continued for 42 hours at reflux with stirring. After cooling, the reaction mixture was neutralized to pH = 10 with 6N HCl and extracted with ether (2 × 50 mL). The aqueous phase was acidified with 6N HCl to pH 1 and extracted with ether (3 × 50 mL). The combined ether layer was washed with 1% NaHCO<sub>3</sub> (50 mL) and water until no chloride was detected. The organic layer was dried. After removal of ether 5 g product (4g) was obtained; yield 23%. It was identified by IR, <sup>31</sup>P NMR, and elemental analysis.

*Di-t-butylphosphinic acid (5a)*. *t*-C<sub>4</sub>H<sub>9</sub>MgCl (0.4 mol) in 250 mL ether was added dropwise to PCl<sub>3</sub> (24.7 g, 0.18 mole) in 150 mL ether with stirring. After completion of the addition, 100 mL of water was added at such a rate that the reaction solution boiled gently. The reaction mixture separated into three layers. The upper layer was washed with water (2 × 50 mL) and 100 mL of 2N NaOH solution. Evaporation of the solvent from the organic layer gave a solid (S). The aqueous phases (the middle and bottom layers) were extracted with isobutyl alcohol (2 × 100 mL). The isobutyl alcohol extracts were combined with solid S. It was then oxidized with 40 mL of 30% H<sub>2</sub>O<sub>2</sub> for 20 minutes. The reaction mixture was refluxed for 8.5 hours. The organic phase was washed with 100 mL of water several times. These aqueous extracts and the water layer of the reaction mixture were ex-

tracted with 100 mL of isobutyl alcohol. The isobutyl alcohol extracts were combined, and the solvent was removed under reduced pressure. In this way, 10 g of crude 5a was obtained. It was recrystallized from *n*-heptane; 6 g of white crystalline 5a was obtained. Yield 20%, purity 99.7%. Anal. Calcd.: C, 53.92; H, 10.72; P, 17.24. Found: C, 53.52; H, 10.80; P, 17.19. δ<sup>31</sup>P, 66.86.

*Di-t-pentylphosphinic acid (5b)* was prepared as above. Yield 7%, purity 99.9%. Anal. Calcd.: C, 58.22; H, 11.24; P, 15.02. Found: C, 58.41; H, 11.56; P, 14.67. δ<sup>31</sup>P, 67.59.

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