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STUDIES ON ORGANOPHOSPHORUS COMPOUNDS XXXII. A MOLECULAR MECHANICS STUDY OF THE HYDROLYTIC REACTION OF ALKYLPHOSPHONATES AND ALKYLPHOSPHONYL CHLORIDES

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ABSTRACT

The alkaline hydrolysis of several alkylphosphonates and alkylphosphonyl chlorides has been investigated by molecular mechanics calculations (MM2, 1985 version). The difference of the steric energies (ΔE) between tetracoordinate substrate and pentacoordinate transition state of phosphorus compounds represents the activation energy ($\Delta E^{\neq}$) in hydrolysis. The change of ΔE for various alkyl groups relative to methyl group ($\Delta\Delta E_R$) is suggested as a measure of the steric effect of substituents. Thus the correlation analysis involving log k and $\Delta\Delta E_R$ of the branched alkyl group gives good results and it is reasonable to anticipate that analogous treatment using $\Delta\Delta E_R$ for the straight chain alkyl group is not satisfactory owing to the minor contribution of steric effect of the latter. However, the multiple regression analysis of log k with $\Delta\Delta E_R$ and Taft's σ^* provides very good results. As shown by us, for the hydrolytic reactions studied, the proposed $\Delta\Delta E_R$ is much better than Taft's E_s and Charton's ν, the commonly used well-known steric parameters in the chemistry of carbon compounds.

The hydrolytic reaction of alkylphosphonates and alkylphosphonyl chlorides has been the subject of many previous investigations.[1–6] In QSAR studies Charton suggested using ν[7,8] and/or ν'[9] as steric parameters of alkyl groups in correlation with the rate constants (log k) of the hydrolytic reaction. Unfortunately, the results were not very satisfactory. More recently, a kinetic study of alkaline hydrolysis of 2-alkyl-2-oxo-1,3,2-dioxaphosphorinanes and -phosphepanes was reported by us.[10] The results showed a significant difference in hydrolytic behavior between phosphonates and carboxylic esters. The commonly used structural parameters E_s, ν, ν', and σ^* provided, as a rule, not very satisfactory results with phosphorus compounds. In order to evaluate the substituent effect on the hydrolytic process of alkylphosphonates and alkylphosphonyl chlorides, molecular mechanics calculations (Allinger's 1977 force field, MM2, 1985 version)[11] were used to investigate the contribution of the steric effect of the alkyl group in these compounds. The molecular mechanics calculations have been used to study the steric effect in the hydrloytic reactions of carboxylic esters,[12,13] tosylates[14,15] and other reactions.[14,16] The energy difference between a substrate and its transition state was used to measure the steric effect of substituents. Our results also indicate that the difference of energy

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between the tetracoordinated and pentacoordinated species presents a good measure of the steric effect of the substituents in phosphorus compounds.

MOLECULAR MECHANICS CALCULATIONS OF PENTACOORDINATE PHOSPHORUS COMPOUNDS

Holmes[17] modified MM1 (Allinger's 1973 force field) for calculating the pentacoordinate phosphorus compounds. In order to account for the stability difference between the trigonal bipyramid (TP) and square pyramid (SP) conformations, the 1,3 bond electron-pair repulsion for the atoms bonded to the pentacoordinate phosphorus atom was introduced, and this 1,3 repulsion energy $E^{1,3}_{AB}$ was calculated by means of van der Waals interaction:

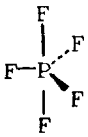
$$E_{AB} = D\,[a \exp(-bP^*) - c\,(P^*)^6]^{1,3} \tag{1}$$

a, b, and c are general constants. D is a constant which is used to balance the contribution of each enery term, usually in the region of 0·05–0·2.

$$P^* = (r_{VDW,A} + r_{VDW,B})/r^* \tag{2}$$

$r_{VDW,A}$ and $r_{VDW,B}$ represent van der Waals radius of atom A and B respectively. r^* is the modified distance between A and B (see below).

According to the structural data of pentacoordinate phosphorus compounds, the bond angles between equatorial bonds which possess different polarity are derived from 120° in trigonal bipyramid, such as in PF_5 (**1**), $\angle F_{eq}PF_{eq} = 120°$, while in PHF_4 (**2**), $\angle F_{eq}PF_{eq} = 112°$, $\angle HPF_{eq} = 124°$, in PF_4CH_3 (**3**), $\angle CPF_{eq} = 122·2°$, $\angle F_{eq}PF_{eq} = 115·6°$, in $PF_3(CH_3)_2$ (**4**), $\angle CPC = 124°$, $\angle CPF_{eq} = 118°$. These data demonstrate that the smaller the electronegativity of the atom bonded to phosphorus will shorten the distance of the bond electron-pair to the P atom. Consequently as the bond electron-pair repulsion increases, the bond angles become larger than 120°. In order to account for this effect, Holmes[17] introduced modified bond lengths for different P—X bonds which were used to calculate the distance (r^* in equation (2)) between two atoms which are directly connected to the P atom. With this treatment, the structure of the pentacoordinate phosphorus compounds were well reproduced. In a similar manner, we modified MM2 for calculating the pentacoordinate phosphorus compound, without revision of the distance r^* and modified the van der Waals radius of the atom bonded to P atom by equation (3).



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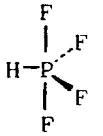

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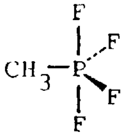

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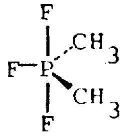

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$$P^* = (r_{1,3,A} + r_{1,3,B})/r_{AB} \tag{3}$$

$r_{1,3}$ is usually larger than the van der Waals radius which is used for the calculation of 1,4 or greater van der Waals interactions. It seems that the smaller electronegativity of the atom bonded to P tends to markedly increase the 1,3 van der Waals radius.

With this treatment the structure of the pentacoordinate phosphorus compounds also can be reproduced well (see Appendix). The $r_{1,3}$ values of several atoms are listed in Table 1.

Table 1. $r_{1,3}$ of several atoms

atom	H	C	O	N	F
$r_{1,3}$ (Å)	2·15	3·53	2·20	2·43	1·72
r^* (Å)	1·50	1·90	1·74	1·82	1·65

*r is the van der Waals radius which is used for calculating 1,4 and greater van der Waals interaction energies.

The other calculation parameters are listed in Table 2. It should be mentioned that the torsional barrier parameters can not be estimated exactly due to insufficient experimental data. Holmes also did not give the general torsional parameters. However, there are two ways to treat these parameters; either the torsional parameters of dihedral angles X_1—X_2—P^V—X_3 were replaced by that of X_1—X_2—P^{IV}—X_3, or the torsional parameters are taken as zero. Such treatment is usually adopted in molecular mechanics calculations of metal complexes.[18,19] According to our results, by using these two methods, there is not a large difference in the reproduced structures of the pentacoordinate phosphorus compounds. The bond moments of P—X bonds were not concerned in the calculations owing to the insufficiency of the experimental data. For acyclic pentacoordinate phosphorus compounds,

Table 2. Force field parameters used for pentacoordinated phosphorus compounds

Torsional parameters	Torsional constants (kcal/mol)			Angle	Angle bending	
Dihedral angle	v_1	v_2	v_3		θ. (deg)	k (mdyn deg^{-1})
C—C—N—P	−0·200	0·730	0·800	H—O—P	0·350	112·000
H—C—N—P	0·000	0·000	0·500	C—N—P	0·630	117·000
C_{sp^2}—C_{sp^2}—O—P	3·530	2·300	−3·500	L_p—N—P	0·500	109·200
H—C—O—P	0·000	0·000	0·530	C_{sp^2}—O—P	0·770	110·800
C—C—O—P	0·000	0·000	0·467	C—O—P	0·770	108·000
H—C—C—P	0·000	0·000	0·267	Lp—O—P	0·350	105·160
C—C—C—P	0·200	0·000	0·593	C_{sp^2}—C_{sp^2}—P	0·550	121·400
C—C—C—P*	0·200	0·270	1·533	C—C—P	0·450	109·470
H—C_{sp^2}—C_{sp^2}—P	0·000	15·000	0·000	C—C—P*	0·340	109·470
C_{sp^2}—C_{sp^2}—C_{sp^2}—P	−0·270	15·000	0·000	C—P—C*	1·500	86·600
				H—C—P	0·360	109·400

Bond	Bond stretching		
	k (mdyn.A^{-1})	l_a	l_{eq}
H—P	6·0	1·48	1·44
C—P	4·00	1·790	1·729
C_{sp^2}—P	4·00	1·790	1·719
N—P	3·50	1·677	1·610
O—P	4·00	1·650	1·590
F—P	5·45	1·600	1·535

*These parameters are for a four-membered ring.

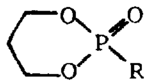
the minimum point can be reached more easily when the torsional parameters containing the P^V—X bond rotation are taken as zero. Therefore, we took this treatment in our calculations.

As shown in the Appendix, the D value in equation (1) can not be kept as a constant for different compounds. But in our case, there is only a variation in alkyl groups with identical types of compound, and the D value was taken as a constant with the value of 0·05.

THE MODEL OF THE TRANSITION STATE AND THE CALCULATION OF $\Delta\Delta E_R$

There are many conformations available for phosphonates and their transition states. For each compound and its transition state the most stable conformation and its energy was selected to compare with the others. In the alkaline hydrolytic reaction of phosphonate the transition state is usually considered to be a trigonal bipyramidal pentacoordinate species such as for 2-alkyl-2-oxo-1,3,2-dioxaphosphorinanes (**5**):

(1)



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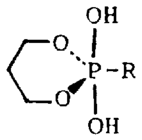

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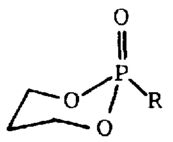
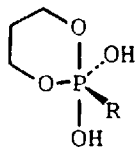


5a



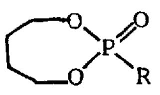
6a

The most stable conformation of **5** is the chair form with an equatorial alkyl group (**5a**). For the corresponding pentacoordinate transition state (**6**) the most stable conformation is the twist chair form with the one axial *endo*-cyclic P—O bond, one equatorial *endo*-cyclic P—O bond, and the alkyl group in equatorial position (**6a**). On the basis of the assumption that the attack of OH^- on the P atom to form the pentacoordinate trigonal bipyramid is the rate determining step in the hydrolytic reaction, the difference of the steric energy (ΔE) between **5a** and **6a** can be used as a measure of the activation energy of the alkaline hydrolytic reaction of **5**: $\Delta E = E_{6a} - E_{5a}$. When R = CH_3 is taken as a reference, $\Delta\Delta E_R$ can be derived from the equation

$$\Delta\Delta E = \Delta E_R - \Delta E_{CH_3}$$

Therefore, the $\Delta\Delta E_R$ can be regarded as a measure of the steric effect of alkyl groups on the hydrolytic reaction.

Similarly, for the hydrolytic reaction of 2 alkyl-2-oxo-1,3,2-dioxaphosphepane (**7**):



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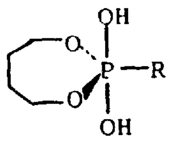

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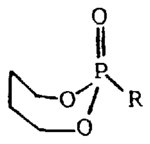
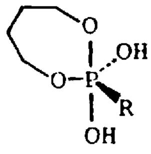
(2)



7a

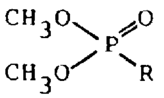


8a

The most stable conformation of **7** is the twist boat (**7a**) with R in the equatorial position. The ΔE_R and $\Delta\Delta E_R$ can be obtained from the steric energy of **7a** and **8a**:

$$\Delta E = E_{8a} - E_{7a}, \qquad \Delta\Delta E_R = \Delta E_R - \Delta E_{CH_3}.$$

For dialkyl alkylphosphonates (**9**), in order to find the most stable conformation, the lower homologue of the series, dimethyl methylphosphonate, was taken as a model, and the most stable conformation of alkylphosphonates with a large alkyl group can thus be estimated by substitution of CH_3 with other alkyl groups. The most stable conformation of **9** possesses two RO groups *gauche* to P═O (**9a**) and the most stable conformation of its pentacoordinated species has two OH groups in axial position in the trigonal bipyramid (**10a**). From the steric energies of **9a** and **10a** the ΔE_R and $\Delta\Delta E_R$ of reaction (3) can be evaluated.



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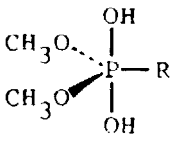

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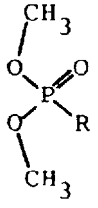
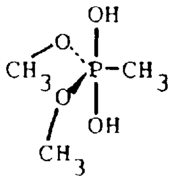
(3)

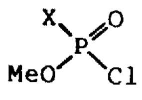
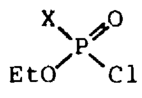
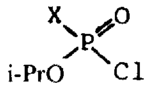


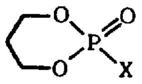
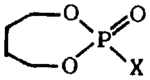
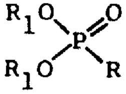
9a



10a

Table 3. Log k and $\Delta\Delta E_R$ of phosphonates and phosphonyl chlorides (energy unit: kcal/mol)

Compounds	No	X	Me	Et	*n*-Pr	*n*-Bu	i-Pr
		$\Delta\Delta E$	0·00 (0·00	0·290 0·201	0·241 0·185	0·215 0·166	0·928 1·292)
	1	log k	2·13	1·78	1·71	1·56	0·395
	2	log k	2·30	1·92	1·92	1·76	0·622
	3	log k	2·57	2·13	2·13	2·00	0·816
	4	log k	2·67	2·29	2·27	2·17	0·986
		X	Me	Et	*n*-Pr	*i*-Bu	i-Pr
		$\Delta\Delta E$	0·00 (0·00	0·283 0·233	0·239 0·219	0·560 0·258	1·020 1·584)
	5	log k	1·91	1·48	1·41	1·24	
	6	log k	2·14	1·72	1·62		0·248
	7	log k	2·37	1·88	1·84	1·59	0·489
	8	log k	2·53	2·06	2·00	1·79	0·782
		X	Me	Et	*n*-Pr	i-Pr	
		$\Delta\Delta E$	0·00 (0·00	0·238 0·379	0·371 0·393	1·740 1·305)	
	9	log k	2·29	1·83	1·75	0·581	

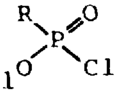
		X	Me	Et	*n*-Pr	*n*-Bu	*n*-Hx	*n*-Oct	*n*-Dod	i-Bu	i-Pr	s-Bu
		ΔΔ*E*	0·00	0·329	0·300	0·252	0·231	0·292	0·237	0·496	1·53	1·91
	10	log *k*	2·27	1·60	1·38	1·13	1·19					
	11	log *k*		1·78	1·66	1·36	1·37	1·29	1·15	1·23	0·201	0·0492
	12	log *k*			2·05	1·76	1·86	1·73	1·56	1·63	0·638	0·479
	13	log *k*						2·03	1·88	1·95	0·985	0·822
		X	Et	*n*-Pr	*n*-Bu	*n*-Hx	*n*-Oct	i-Bu	i-Pr	s-Pent		
		ΔΔ*E*	0·00	0·00	0·00	0·00	0·00	0·400	1·20	1·26		
	14	log *k*	1·34	1·17	1·02	0·942	0·880	0·692				
	15	log *k*	1·58	1·41	1·30	1·20	1·19	0·970				
	16	log *k*	1·86	1·67	1·62	1·51	1·45	1·21	0·528	0·188		
				R = Me		Et		*n*-Pr		i-Pr		
			R_1 = Me	Et	i-Pr	Me	Et	i-Pr	i-Pr	Et	i-Pr	
	17	ΔΔ*E*	0·00	0·031	2·810	0·741	0·805	3·76	3·72	0·739	3·75	
		log *k*	2·37	1·26	0·317	2·16	0·973	−1·06	−2·30	0·312	−1·82	

*The values in parentheses are calculated from OH model instead of Cl.

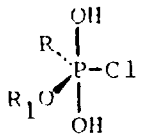
**Me = CH_3, Et = C_2H_5, *n*-Pr = C_3H_7, i-Pr = i-C_3H_7, *n*-Bu = *n*-C_4H_9, i-Bu = i-C_4H_9, s-Bu = S-C_4H_9, s-Pent = s-C_5H_{11}, *n*-Hx = *n*-C_6H_{13}, *n*-Oct = *n*-C_8H_{17}, *n*-Dod = *n*-$C_{12}H_{25}$.

Since there are no data available for the bond angle and torsional parameters for the chlorine atom bonded to phosphorus, we use CH_3 or OH instead of Cl in tetracoordinated alkylphosphonyl chloride (**11**) and the corresponding pentacoordinated species for the convenience of calculation. Obviously, this is an empirical approximation treatment which meets the basic requirements. From the steric energies of the most stable conformation of **11a** and **12a**, the ΔE_R and $\Delta\Delta E_R$ of reaction (4) can be derived.

(4)



11



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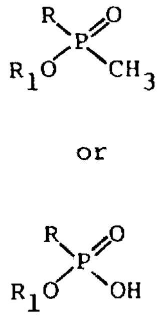
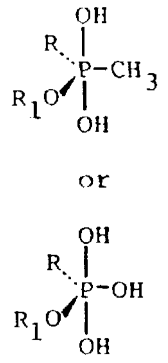


11a



12a

RESULTS AND DISCUSSION

The $\Delta\Delta E_R$ of reactions (1–4) are listed in Table 3 together with rate constant k in alkaline hydrolysis.

From Table 3, it seems that the $\Delta\Delta E_R$ value has an increment from CH_3 to C_2H_5, but it kept nearly constant or even decreased very smoothly on further increase of the length of the alkyl chains. However, the $\Delta\Delta E_R$ are dramatically increased with increasing the bulkiness of the alkyl groups.

The linear regression analysis of log k with $\Delta\Delta E_R$ (see equation (4)) showed that if the data set contains the alkyl groups with branched chains, the correlation coefficients are very good

$$\log k = s\ \Delta\Delta E_R + h \ldots \qquad (4)$$

(11 sets in Table 4), or good (sets 5, 11, 17 in Table 4); if there are no branched chains in the alkyl groups, the correlations are poor (sets 10, 14, 15 in Table 4). This indicates that the steric effect is one of the predominating factors controlling the hydrolytic process of alkyl phosphonates and phosphonyl chlorides with branched alkyl groups. On the other band, for straight alkyl chain compounds, even from normal octyl to dodecyl groups, the variation of

Table 4. Linear regression analysis of log k with $\Delta\Delta E_R$ in equation (4)

No	s	h	r	n	CL%	No	s	h	r	n	CL%
1	−1·85	2·13	0·983	5	99	7	−1·77	2·38	0·984	5	99
	(−1·24	2·01	0·979	5)	99		(−1·06	2·12	0·965	5)	99
2	−1·80	2·30	0·987	5	99	8	−1·63	2·52	0·981	5	99
	(−1·20	2·15	0·981	5)	99		(−0·975	2·28	0·962	5)	99
3	−1·82	2·53	0·990	5	99·9	9	−0·919	2·33	0·989	4	95
	(−1·24	2·39	0·980)	5	99		(−1·31	2·29	0·999	4)	99·9
4	−1·81	2·68	0·991	5	99·9	10	−2·71	2·12	0·769	5	<90
	(−1·21	2·52	0·986	5)	99	11	−0·925	1·69	0·936	9	99·9
5	−1·16	1·82	0·935	5	95	12	−0·826	2·00	0·963	8	99·9
	(−1·94	1·85	0·815	4)	<90	13	−0·727	2·17	0·985	5	99·9
6	−1·85	2·15	0·996	4	99	14	−0·946	1·07	0·681	6	95
	(−1·12	2·19	0·990	4)	99	15	−0·915	1·34	0·716	6	<90
						16	−1·03	1·62	0·971	8	99·9
						17	−0·903	1·89	0·902	9	99·9

rate constant cannot be neglected. It is therefore reasonable to conclude that the $\Delta\Delta E_R$ proposed by us, is very specific to steric effect of the substituent. In the meantime, the hydrolytic rate constants for straight chain compounds are governed chiefly by polar or solvation effects rather than steric influence of the substituent.

In 1978 Charton[7] reported the linear regression analysis of log k with v and v′ parameters for sets 1–9 in Table 3, but it was unsuccessful for all of the sets. We carried out the linear regression analysis of log k with v and v′ for sets 10–16 (see Table 5). The correlation coefficients are not so good as those for $\Delta\Delta E_R$.

In order to account for the steric effect and the polar, solvation or other effects on the hydrolytic reactions (1–4), multiple regression of log k with $\Delta\Delta E_R$ and Taft's σ^* was introduced.

$$\log k = \delta\Delta\Delta E_R + \rho\sigma^* + C \qquad (5)$$

The regression results from equation (5) are listed in Table 6. All the correlation coefficients exceed 0·97. The t-tests, t_δ and t_ρ values, indicate that they make different contributions to log k for each set. For sets 10, 14, 15 (R—straight chain alkyl), the weight of σ^* is almost the same or even greater than that of $\Delta\Delta E_R$. For the other sets, however, $\Delta\Delta E_R$ makes a much greater

Table 5. Linear regression analysis of log k with v or v′

No	s	h(v)	r	s	h(v′)	r	n
10	−4·62	4·44	0·896	−13·8	7·01	0·957	5
11	−3·11	3·46	0·718	−5·08	3·51	0·934	9
12	−2·99	3·78	0·654	−4·98	3·88	0·925	8
13	−2·07	3·24	0·509	−4·57	3·97	0·876	5
14	−1·41	2·02	0·868	−3·17	2·39	0·818	6
15	−1·34	2·24	0·902	−3·02	2·59	0·849	6
16	−2·81	3·39	0·753	−5·13	3·76	0·974	8

Table 6. Multiple regression analysis with equation (5)

No	ρ	s	c	s_ρ	s_s	s_c	t_ρ	t_s	t_c	r	n	R
1	1·22	−1·65	2·20	2·34	0·460	0·163	0·520	−3·58	13·5	0·9834	5	0·107
	(2·68	−0·96	2·16	1·06	0·140	0·091	2·52	−6·86	23·7	0·9950	5	0·0590)
2	0·97	−1·63	2·35	1·98	0·390	0·138	0·490	−4·19	17·1	0·9872	5	0·0909
	(2·49	−0·943	2·32	0·884	0·117	0·0756	2·82	−8·09	30·7	0·9963	5	0·0490)
3	0·676	−1·71	2·56	1·84	0·362	0·128	0·368	−4·72	20·0	0·9892	5	0·0844
	(2·84	−0·947	2·58	0·637	0·0840	0·0545	4·46	−11·3	47·4	0·9982	5	0·0353)
4	0·715	−1·69	2·72	1·72	0·338	0·120	0·417	−5·00	22·7	0·9905	5	0·0788
	(2·32	−0·969	2·68	0·570	0·0751	0·0487	4·08	−12·9	55·1	0·9985	5	0·0315)
5	3·31	−0·454	1·91	0·582	0·146	0·0301	5·68	−3·11	63·6	0·9960	4	0·0152
	(5·45	0·294	1·92	6·39	3·08	0·0980	0·853	0·0956	19·6	0·9798	4	0·0493)
6	0·378	−1·79	2·16	2·20	6·39	0·125	0·171	−4·59	17·2	0·9852	4	0·0637
	(2·60	−0·885	2·15	0·723	0·0779	0·0521	3·60	−11·4	41·2	0·9993	4	0·0263)
7	1·10	−1·59	2·42	2·93	0·515	0·165	0·376	−3·09	14·7	0·9852	5	0·107
	(4·27	−0·586	2·39	1·20	0·108	0·102	3·57	−5·41	23·5	0·9946	5	0·0652
8	1·39	−1·50	2·58	2·69	0·473	0·152	0·558	−2·94	17·0	0·9854	5	0·0986
	(3·99	−0·636	2·55	1·05	0·113	0·0865	3·79	−5·63	29·4	0·9954	5	0·0555)
9	2·69	−0·687	2·29	0·542	0·0541	0·365	4·95	−12·7	62·6	0·9996	4	0·0183
	(0·0579	−2·30	2·30	0·873	0·123	0·0434	0·0662	−10·6	58·9	0·9994	4	0·0219)
10	7·34	−0·0209	2·26	2·07	0·966	0·156	3·54	−0·0216	14·5	0·9710	5	0·0985
11	7·98	−0·536	2·65	1·96	0·110	0·252	4·06	−4·88	10·5	0·9819	9	0·107
12	5·13	−0·629	2·67	2·68	0·129	0·360	1·92	−4·86	7·44	0·9785	8	0·112
13	3·91	−0·595	2·72	2·74	0·113	0·389	1·43	−5·26	7·00	0·9924	5	0·0639
14	6·65	−1·08	1·95	1·11	0·164	0·150	6·00	−6·57	13·1	0·9792	6	0·0420
15	5·86	−1·03	2·12	0·904	0·134	0·122	6·48	−7·70	17·3	0·9836	6	0·0343
16	4·92	−0·765	2·26	1·59	0·109	0·210	3·10	−7·05	10·8	0·9902	8	0·0773

*The values in parentheses are calculated from $\Delta\Delta E_R$ with OH instead of Cl.

Table 7. Results of correlation analyses with equation (6)

No	ρ	s	c	S_ρ	S_s	S_c	t_ρ	t_s	t_c	r	n	R
1	8·28	0·0177	2·43	6·92	2·28	2·80	1·20	0·00776	0·866	0·869	5	0·292
2	8·61	−0·225	2·29	6·72	2·21	2·72	−1·28	−0·102	0·842	0·867	5	0·283
3	8·79	−0·281	2·44	6·94	2·29	2·81	−1·27	−0·123	0·868	0·861	5	0·293
4	8·68	−0·256	2·62	6·83	2·25	2·77	−1·27	−0·114	0·948	0·863	5	0·289
5	3·99	0·174	2·12	0·404	0·0550	0·0704	−9·88	3·16	30·2	0·9982	4	0·0149
6	7·69	0·721	3·27	9·08	3·14	3·83	−0·848	0·230	0·853	0·9119	4	0·292
7	9·93	−0·197	2·37	3·61	0·666	0·916	−2·75	−0·296	2·59	0·9150	5	0·252
8	9·24	−0·177	2·53	3·18	0·587	0·808	−2·90	−0·301	3·13	0·9229	5	0·223
9	7·38	0·501	3·09	7·11	2·46	3·00	−1·04	0·203	1·03	0·9320	4	0·228
10	5·49	0·815	3·26	1·24	0·425	0·531	−4·42	1·92	6·15	0·9898	5	0·0585
11	12·85	0·503	3·92	2·79	0·308	0·486	−4·61	1·63	8·06	0·9364	9	0·199
12	13·3	0·641	4·69	3·20	0·341	0·642	−4·17	1·88	7·29	0·9260	8	0·205
13	14·9	0·506	4·99	4·69	0·433	1·05	−3·17	1·17	4·77	0·9309	5	0·190
14	5·07	0·625	2·70	0·778	0·0661	0·144	−6·52	9·46	18·8	0·9897	6	0·0297
15	4·36	0·596	2·83	0·580	0·0493	0·107	−7·51	12·1	26·32	0·9932	6	0·0222
16	10·5	0·684	4·00	2·59	0·286	0·444	−4·04	2·39	9·01	0·9488	8	0·175

contribution than σ^*. In multiple regression analysis involving Taft's E_s and σ^* (equation (6))

$$\log k = \delta E_s + \rho\sigma^* + C \tag{6}$$

the correlation coefficients were poor in most cases (Table 7). If the v was substituted for E_s as a steric parameter in equation (6) no radical improvement was found. It indicates that the steric parameters, E_s, derived from the hydrolytic reaction of carboxylic esters are not suitable for alkylphosphonates. It may be due to the different transition states of the alkaline hydrolysis of phosphonates and carboxylates. The alkaline hydrolysis of alkylphosphonates proceeds from a tetracoordinated substrate through pentacoordinate transition states to products. However, alkaline hydrolysis of a carboxylate takes place from a planar tricoordinate substrate to the final product through a tetracoordinate transition state. Therefore, the steric effect of alkyl groups in phosphonates is significantly larger than that in carboxylic esters. The γ-hydrogen six-number effect on the rate constant in the hydrolysis of carboxylic esters is demonstrated by acceleration of the rate of hydrolysis of isopropyl carboxylate in comparison with that of isobutyl carboxylate. In constrast to the hydrolytic behavior of carboxylates, the rate constant of isobutylphosphonate is larger than that of isopropylphosphonate (see Table 3). Therefore, Taft's E_s value of iso-C_4H_9 group is larger than that of iso-C_3H_7 group, but in the $\Delta\Delta E_R$ scale for phosphonates, the iso-C_4H_9 group is smaller than that of iso-C_3H_7 group.

Another problem is concerning the signs of the δ and ρ in equation (6). It is in contradiction to experimental data that the σ^* has a negative effect on k value, which E_s has a positive effect on k value in several sets (see Table 7). However, no such problem appears for equation (5). It indicates that the molecular mechanics calculations reflect the steric effect more correctly than Taft's E_s in the hydrolysis of phosphonates.

If E_s was replaced by v in equation (6), the correlations are not improved. However, substituting E_s by v' in equation (6), the correlation coefficient became better. Unfortunately, only limited numbers of v′ parameter are available.

Finally, it should be pointed out that our molecular mechanics calculations contain the following approximations: the torsional parameters containing P—X rotation for the pentacoordinate transition state were not concerned, the oxygen anion O^- was replaced by the OH group, the solvation effect was not included, ... However, this study indicates that the molecular mechanics calculations are useful for the study of the steric effect of substituents, especially the alkyl groups, in the hydrolytic reaction of phosphonates.

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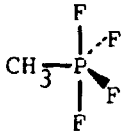
APPENDIX



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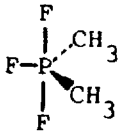
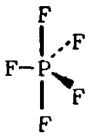


D = 0·125

P—F$_{ax}$	1·619	(1·612)
P—F$_{eq}$	1·536	(1·543)
P—C$_{eq}$	1·800	(1·780)
F$_{ax}$—P—F$_{ax}$	176.1	(176·4)
F$_{ax}$—P—F$_{eq}$	88·92	(--)
F$_{ax}$—P—C$_{eq}$	92·07	(91·80)
F$_{eq}$—P—F$_{eq}$	113.9	(115·6)
F$_{eq}$—P—C$_{eq}$	123·0	(122·2)

P—F$_{ax}$	1·627	(1·643)
P—F$_{eq}$	1·549	(1·533)
P—-1C$_{eq}$	1·800	(1·798)
F$_{ax}$—P—F$_{ax}$	175·2	(177·8)
F$_{ax}$—P—F$_{eq}$	91·10	(91·00)
F$_{ax}$—P—F$_{eq}$	87·60	(88·90)
C$_{eq}$—P—C$_{eq}$	123·6	(124·0)
C$_{eq}$—P—F$_{eq}$	118·2	(118·0)



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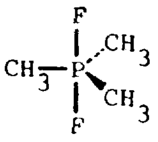


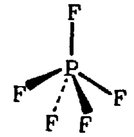
D = 0·125

P—F$_{ax}$	1·513	(1·514)
P—F$_{eq}$	1·534	(1·534)

P—F$_{ax}$	1·638	(1·685)
P—C$_{eq}$	1·813	(1·810)
C$_{eq}$—P—C$_{eq}$	120·0	(--)
C$_{eq}$—P—F$_{ax}$	90·00	(--)
F$_{ax}$—P—F$_{ax}$	179·0	(--)

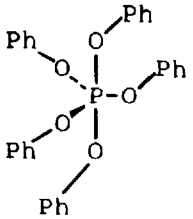
D = 0·150

P—F_{ax}	1·613	(1·594)
P—F_{eq}	1·543	(1·550)
P—H	1·454	(1·36*)
F_{ax}—P—F_{ax}	179·0	(--)
F_{ax}—P—H	90·51	(90·00)
F_{ax}—P—F_{eq}	89·70	(--)
H_{eq}—P—F_{eq}	121·15	(124·0)
F_{eq}—P—F_{eq}	117·70	(112·0)



$D = 0·300$

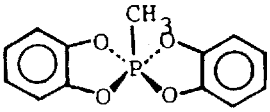
P—F_{ap}	1·513	(1·514)
P—F_{bas}	1·562	(1·561)
F_{ap}—P—F_{bas}	103·34	(101·3)
cis—F_{bas}—P—F_{bas}	86·95	(87·8)
trans—F_{bas}—P—F_{bas}	153·32	(157·3)



$D = 0·05$

	1	2			1	2	
P—O_2	1·701	1·702	(1·662)	P—O_3	1·604	1·591	(1·602)
P—O_4	1·607	1·617	(1·596)	P—O_5	1·590	1·600	(1·600)
P—O_6	1·692	1·686	(1·663)				
O_2—P—O_3	90·67	90·27	(88·21)	O_2—P—O_5	89·92	88·69	(91·62)
O_2—P—O_4	89·80	90·42	(92·08)	O_2—P—O_6	179·43	178·47	(176·57)
O_3—P—O_4	122·28	124·35	(125·51)	O_3—P—O_5	117·60	117·15	(118·27)
O_3—P—O_6	88·80	89·13	(88·99)	O_4—P—O_5	120·04	118·49	(116·19)
O_4—P—O_6	90·68	91·07	(87·93)	O_5—P—O_6	90·11	90·32	(91·44)

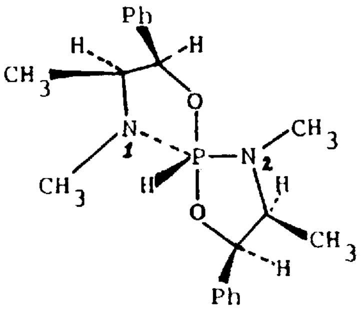
*1, P O V_1, V_2, $V_3 = 0$ 2, P O V_1, V_2, $V_3 = 0$



$D = 0·05$

	1	2			1	2	
P—C_2	1·763	1·763	(1·777)	P—O_1	1·672	1·672	(1·670)
P—O_2	1·672	1·673	(1·670)	P—O_3	1·673	1·671	(--)
P—O_4	1·676	1·676	(--)				
O_1—P—O_2	90·12	89·90	(90·20)	O_1—P—O_3	85·20	85·20	(82·80)
O_1—P—O_4	155·66	154·70	(156·90)	O_2—P—O_3	155.50	154·80	(148·10)
O_1—P—C_3	111·5	111·3	(111·7)	O_1—C_3—C_1	111·4	111·4	(112·0)

*1, P X V_1, V_2, $V_3 = 0$ 2, P X V_1, V_2, $V_3 = 0$



$D = 0{\cdot}10$

P—O	1·696	(1·700)	P—N	1·699	(1·690)
P—H	1·457	(--)	O—P—O	176·5	(176·6)
O—P—N_1	90·40	(89·20)	O—P—N_2	90·60	(92·40)
N_1—P—N_2	126·9	(123·3)	C—C—O	103·0	(103·2)
C—C—N	101·4	(100·3)	P—O—C	111·1	(111·9)
P—N—C	112·6	(115·4)			

*The values in parentheses are experimental data.