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SOLVATION AND METAL ION EFFECTS ON STRUCTURE AND REACTIVITY OF PHOSPHORYL COMPOUNDS. 1. β-SUBSTITUTED ALKYLPHOSPHONIC ESTERS

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NMR spectroscopic and conformational analyses were performed for three β-substituted β-phenylethylphosphonic esters, $PhCHXCH_2PO_3Me_2$ (X = OH, OMe, Cl) in five solvents and in acetone containing sodium and magnesium salts. Strong attractive interactions between the phosphoryl group and the oxygen-containing substituent X were demonstrated, and were shown to involve intramolecular hydrogen bonding, donor–acceptor $O \rightarrow P$ effect and the chelation of a metal ion. These effects led to marked selectivity in the population of individual conformations of the phosphonates. The analogous intramolecular effects were found to be much weaker in the corresponding carboxylic ester systems.

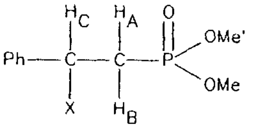
INTRODUCTION

Electronic effects of the dialkoxyphosphoryl, $P(O)(OR)_2$, group are strong and comparable to those of the alkoxycarbonyl group (for the PO_3Et_2 group $\sigma_I = 0{\cdot}06$,[1] $0{\cdot}21$;[2] $\sigma_R^0 = 0{\cdot}16$,[1] $0{\cdot}17$.[2] For the CO_2Et group the corresponding constants are $0{\cdot}30$ and $0{\cdot}18$, respectively[3]). It is therefore expected that the PO_3R_2 group can interact strongly with its environment via dipole–dipole, dipole–ion or hydrogen-bonding mechanisms. The ability of phosphoryl compounds to form complexes with metal ions found wide applications in catalytic polymerization processes and extractions.[4] Interactions of nucleotides with some metal ions have major roles in biochemical systems; for example, Mg^{2+} binds to the β- and γ-phosphate in ATP, but does not interact with the adenine ring.[5] Recently, Buncel and co-workers reported that the nature of the cation has a profound effect on the rate of the nucleophilic displacement at the phosphoryl centre by the ethoxide[6] and the phenoxide[7] ions, thus indicating important interactions between the metal ion and the phosphoryl substrate in the transition state. We have observed that alkali metal ions induce significant differential shielding of diastereotopic groups in the racemic dimethyl 2-chloropentylphosphonate, $PrCHClCH_2PO_3Me_2$, the effect decreasing in the order $Li^+ > Na^+ > K^+$.[8] In this study we investigated solvent and metal ion effects on the solution structure of dimethyl esters of 2-substituted 2-phenylethylphosphonic acids, $PhCHXCH_2PO_3Me_2$ (**1**), in order to determine conformational preferences of these compounds, to provide an insight into the nature of their interactions with metal ions and to compare system **1** with the analogous carboxylic derivatives, $PhCHXCH_2CO_2R$ (**2**). As before,[8] the study was mainly achieved by the analysis of the ^1H (supported by ^{31}P) NMR parameters.

RESULTS AND DISCUSSION

Substrates

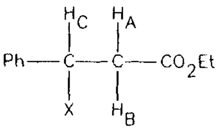
Three phosphonic esters, **1a–c**, and two carboxylic esters, **2a** and **b**, were synthesized and used as models in the NMR spectroscopic studies.



1a, X = OH

1b, X = OMe

1c, X = Cl



2a, X = OH

2b, X = OMe

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$$\mathrm{ME{-}PO_3Me_2} \xrightarrow{\text{(i), (ii)}} \underset{\mathbf{3}}{\mathrm{PhC(O)CH_2PO_3Me_2}} \xrightarrow{\text{(iii)}} \mathbf{1a}$$

(i) BuLi, CuI; (ii) PhC(O)Cl; (iii) NaBH$_4$

Scheme 1

Alcohol **1a** was prepared from dimethyl methylphosphonate and benzoyl chloride,[9] followed by the slightly modified method[10] for the reduction of the ketophosphonate **3** (Scheme 1).

Substrate **1b** was prepared from **1a** by treatment with sodium hydride, followed by iodomethane,[11] and **1c** was obtained in the reaction of **1a** with CCl$_4$ in the presence of triphenylphosphine.[12] Hydroxy ester **2a** was prepared from ethyl acetate and benzoyl chloride in a manner analogous to that for the preparation of **1a**, but different literature procedures were applied for the condensation[13] and reduction[14] steps. Finally, **2b** was obtained by methylation of **2a** with iodomethane in the presence of silver oxide.[15]

NMR spectra

The assignment of the ^{1}H and ^{31}P NMR spectra of all substrates was straightforward. Extended (^{1}H, ^{31}P) couplings were observed in the ^{1}H NMR spectra of **1**. The protons H$_A$, H$_B$ and H$_C$, together with the phosphorus atom of **1**, give rise to ABMX spin systems. The ^{1}H chemical shifts and the geminal (^2J) and vicinal (^3J) proton–proton coupling constants were obtained from a complete ABM sub-spectral analysis[16] of the ^{1}H NMR spectra. Protons H$_A$ and H$_B$ in these ABMX spin systems normally gave rise to sixteen line patterns, except in a few cases where deceptively simple ABMX spin systems were observed. The protons H$_A$, H$_B$ and H$_C$ in **2** gave rise to an ABM spin system and were analysed as such.

Conformational analysis

Three stable staggered conformations (X$_1$, X$_2$, X$_3$, or their enantiomeric forms) are obtained when the C(1)—C(2) bond in **1** or **2** is rotated.

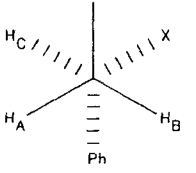
The observed vicinal proton–proton coupling constants are related to the populations (χ_1, χ_2, χ_3) and the vicinal coupling constants of the individual rotamers in the following way:

$$^3J(\mathrm{AC}) = \chi_1{}^3J_g(\mathrm{X}_1) + \chi_2{}^3J_t(\mathrm{X}_2) + \chi_3{}^3J_{g'}(\mathrm{X}_3)$$
$$^3J(\mathrm{BC}) = \chi_1{}^3J_t(\mathrm{X}_1) + \chi_2{}^3J_g(\mathrm{X}_2) + \chi_3{}^3J_{g'}(\mathrm{X}_3)$$

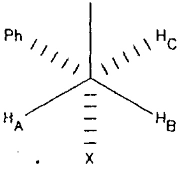
where ^3J_g and ^3J_t refer to the vicinal coupling constants between *gauche* protons (dihedral angle ≈ 60°) and *trans* protons (dihedral angle ≈ 180°), respectively. According to the Karplus equation, ^3J_g should be 'small' and ^3J_t 'large'. Calculating the individual vicinal coupling constants according to the approach of Haasnoot *et al.*[17] and using the reported group electronegativities[18] allowed the estimation of the population of the conformations of compounds **1** and **2** in different solvents and with different metal ions.

Solvent effects

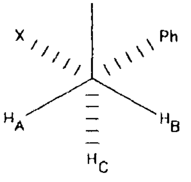
Selected NMR data for substrates **1** and **2** obtained in five solvents covering wide range of polarity ($E_T = 32{\cdot}5$–$45{\cdot}0$[19]) are given in Tables 1 and 2. Considering that environmental effects on ^{31}P chemical shifts are generally small,[20] the observed variations in δ_P values for **1a–c** are relatively large, with the chemical shift difference $\Delta\delta_P\{\Delta\delta_P = \delta_P[(CD_3)_2SO] - \delta_P[CCl_4]\}$ increasing from 2·1 to 4·8 and 5·3 for **1a**, **1b** and **1c**, respectively. The last value is comparable to $\Delta\delta_P = 6{\cdot}3$ ppm reported for triphenylphosphine oxide in the same solvents, and used to develop an empirical solvent polarity parameter.[21] As the population of the different roamers in **1c** (see below), which showed the biggest $\Delta\delta_P$, does not change much with solvents, the observed increase in $\Delta\delta_P$ within the series **1a–c** probably arises from varying degree of intramolecular interactions between substituent X and the phosphoryl group, diminishing the involvement of the latter in the solute–solvent interactions. ^{1}H NMR chemical shifts of hydrogens H$_A$, H$_B$ and H$_C$ (substrates **1** and **2**), and also of the P(OMe)(OMe′) groups (substrates **1**), are also subject to solvent effects, the average variation in δ_H being 0·21 ppm for the hydrogen of the ethylphosphonic skeleton and 0·33 ppm for the ester groups.



X$_1$



X$_2$



X$_3$

Z = PO$_3$ME$_2$ (**1**); CO$_2$Et (**2**) X = OH (**1a**, **2a**). OMe (**1b**, **2b**); Cl (**1c**)

Table 1. Solvent effects on chemical shifts of selected nuclei in compounds **1** and **2**[a]

		δ (ppm)				
Substrate	Nucleus	CCl_4	C_6D_6	$CDCl_3$	$(CD_3)_2CO$	$(CD_3)_2SO$
1a	^{31}P	34·13	32·58	32·26	32·58	32·03
1b		31·88	30·57	31·07	31·23	35·37
1c		28·54	27·25	27·60	28·05	32·52
1a	H_A, H_B	2·03	2·03	2·19	2·17	2·13
		2·12	2·16	2·29	2·24	2·22
1b		1·96	2·03	2·12	2·09	2·14
		2·20	2·34	2·36	2·32	2·35
1c		2·55	2·44	2·65	2·77	2·84
		2·64	2·59	2·75	2·77	2·84
2a		2·55	2·46	2·68	2·62	2·60
		2·61	2·61	2·26	2·69	2·60
2b		2·41	2·49	2·58	2·55	2·60
		2·68	2·85	2·81	2·72	2·72
1a	H_C	5·01	5·26	5·13	5·03	4·87
1b		4·46	4·63	4·56	4·51	4·45
1c		5·17	5·32	5·25	5·32	5·33
2a		5·00	5·06	5·12	5·11	4·95
2b		4·53	4·70	4·64	4·61	4·51
1a	Me, Me′	3·61	3·28	3·72	3·62	3·51
		3·64	3·35	3·75	3·67	3·60
1b		3·50	3·29	3·62	3·55	3·49
		3·66	3·49	3·73	3·67	3·60
1c		3·59	3·30	3·51	3·63	3·58
		3·69	3·46	3·66	3·72	3·67

[a] Substrate concentration = 0·20 M. Chemical shifts and coupling constants were unaffected by *concentration changes in the range 0·05–0·50* M.

Table 2. Solvent effects on selected values of proton–proton coupling constants (Hz) in compounds **1** and **2**

Substrate	Coupling constant	CCl_4	C_6D_6	$CDCl_3$	$(CD_3)_2CO$	$(CD_3)_2SO$
1a	$^2J(AB)$	15·4	15·3	15·3	15·3	15·3
1b		15·3	15·6	15·4	15·3	15·5
1c		15·4	15·4	15·5	–[a]	–[a]
2a		16·2	16·0	16·2	15·2	–[a]
2b		15·4	15·4	15·3	15·3	15·2
1a	$^3J(AC)$,	3·3	2·8	2·9	4·2	4·5
	$^3J(BC)$	9·8	9·9	10·1	9·2	8·6
1b		4·6	4·7	4·6	5·0	5·2
		8·8	8·9	9·0	8·8	8·6
1c		6·8	7·0	7·1	7·6[b]	7·4[b]
		9·1	7·8	7·6		
2a		5·1	3·7	4·3	5·5	6·8[b]
		7·8	9·1	8·3	8·1	
2b		5·0	4·7	4·8	5·0	5·2
		8·8	9·0	9·1	8·9	8·8

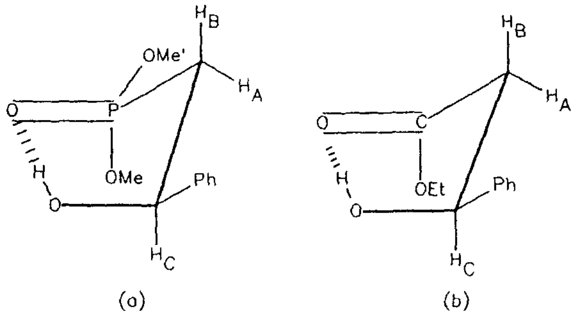
[a] Not measurable; $\delta_A = \delta_B$.

[b] Average value for J_{AC}, J_{BC}.

The diastereotopic protons (or groups of protons), i.e. the geminal protons (H_A, H_B), and the methyl groups Me, Me′, are highly non-equivalent in all structures and solvents studied. Only in exceptional cases (**1c** in acetone and DMSO, and **2a** in DMSO) did we find $\delta_H(A) = \delta_H(B)$, hence we were unable to measure the individual vicinal coupling constants. As far as the coupling constants are concerned (Table 2), the geminal (H_A, H_B) [$^2J(AB)$] constants are, in agreement with the general observation on solvent effects on ^2J values,[22] approximately unchanged. The vicinal (H_A, H_C) [$^3J(AC)$] and (H_B, H_C) [$^3J(BC)$] coupling constants, on the other hand, vary significantly, the change of ^3J with solvent varying from substrate to substrate. This solvent-induced differential effect indicate restrictions of the conformational freedom of a solute's molecules and offers a probe for the conformational analysis of systems **1** and **2**. The variations in the ^3J values within a given series of solvents are greatest for the hydroxy substrates (**1a** and **2a**), suggesting that for these compounds the nature of the solvent has strongest effect on the distribution of the individual conformations. The populations of the individual rotamers in the different solvents calculated from the observed vicinal coupling constants as outlined above are given in Table 3. The data in Table 3 enabled us to draw the following conclusions.

For all compounds, except **1c** (X = Cl), conformation X_1 represents the most favourable orientation of substituents around the C(1)—C(2) bond. This preference reflects two structural features present in X_1: the release of the unfavourable steric Z–Ph interactions, and the attractive interactions between groups Z and X (X = OH, OMe). In **1c**, $X_1 \approx X_2$, indicating the absence of any stabilizing Z–X(PO_3Me_2–Cl) interactions, and the approximately equal magnitude of the repulsion between Z–X and Z–Ph groups. The Z–X attraction in alcohols **1a** and **2a** results, of course, from the intramolecular hydrogen bonding involving the 2-OH group and the phosphoryl or carbonyl function (Figure 1). This specific interaction is strong enough to introduce some relative stability to the conformation X_3 (*ca* 12% for **1a** and **2a**, vs 1–6% for the remaining substrates), despite the unfavourable location of groups Z and Ph. The observed greatest stability of X_1 remains in excellent agreement with earlier reports on the intramolecular hydrogen bonding in 2-hydroxy-2,3- disubstituted carboxylic acids and esters[23] and substituted β-hydroxysulphoxides.[24]

It is interesting that for **1a**, on moving from non-hydrogen-bonding solvents (CCl_4, C_6D_6, $CDCl_3$) to hydrogen-bonding acceptors (acetone-d_6, DMSO-d_6), the population of the rotamer X_1 does not decrease too much (from *ca* 82% to 64–70%). The observed decrease in the population of X_1 results from the competitive involvement of the solvent in the intermolecular hydrogen bonding with the phosphoryl group. However, earlier spectroscopic studies of hydrogen bonding carried out by Gramstad and Becker[25] and by Russian workers[26] demonstrated stronger hydrogen-bonding acceptor properties of the phosphoryl group relative to the carbonyl or sulphoxide acceptors. As a consequence of this, intramolecular P=O···H—O bonding in **1a** prevails also in the acetone or DMSO solutions. For the carboxylic hydroxy ester **2a**, in agreement with the weaker donor ability of carbonyl substrates, the contribution of the rotamer X_1 is lower than that for **1a** and in a strongly hydrogen-bonding solvent (DMSO) it is X_2



(a) (b)

Figure 1. Intramolecular hydrogen bonding in conformation X_1: (a) **1a**; (b) **2a**

Table 3. Solvent effects on the conformational behaviour of phosphonates **1** and carboxylates **2** (population of rotamers, %)

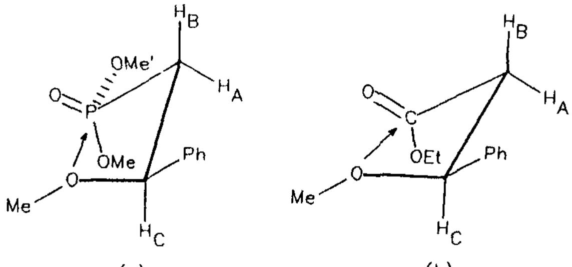
	1a			1b			1c			2a			2b		
Solvent[a]	X_1	X_2	X_3	X_1	X_2	X_3	X_1	X_2	X_3	X_1	X_2	X_3	X_1	X_2	X_3
A	80	9	11	66	25	9	42	46	12	56	34	10	68	30	2
B	82	3	15	67	26	7	51	47	2	75	13	12	71	26	3
C	83	5	12	69	25	6	49	48	3	65	19	16	72	28	0
D	70	20	10	65	30	5	49	51	0	58	34	8	68	30	2
E	64	22	14	63	32	5	46	52	2	41	49	10	67	33	0

[a] A = CCl_4; B = C_6D_6; C = $CDCl_3$; D = $(CD_3)_2CO$; E = $(CD_3)SO$.

which represents the major conformation of the compound.

When **1a** was converted into its methyl ether **1b**, the population of X_1 decreased, but it still remained the highest, and was approximately constant (66 ± 2%) over the whole range of solvents. Similar behaviour was observed for cyclic[27] and acyclic[24b,27] 2-hydroxy- and 2-alkoxysulphoxides in which a strong preference exists for the *gauche* orientation of the 2-oxy group with respect to the sulphinyl substituent. This behaviour was interpreted in terms of the stabilizing $n(p) \rightarrow d$ donation of the oxygen non-bonding electrons to one of the vacant 3d orbitals of sulphur, the one which is not involved in the sulphinyl group bonding, and has a proper spatial orientation for such interactions. We propose to extend that model to phosphonic systems by postulating similar $n(p) \rightarrow d$ donor–acceptor interactions involving the 2-OR group and the phosphoryl centre [Figure 2(a)]. The four-membered PCCO oxaphosphetane ring represents a common four-centre cyclic intermediate in the Wittig and Wittig-related reactions,[28] the reaction's driving force being the formation of a strong phosphorus—oxygen bond. In specific cases, such as in the addition of ylide $Ph_3P{=}C{=}PPh_3$ to hexafluoroacetone,[29] the oxaphosphetane product could be isolated and its crystal structure determined. The four-membered ring was found to be planar with the P—C, C—O and P—O bond distances of 1·76, 1·39 and 2·01 Å, respectively.

In a recent structural study of the 2-hydroxyalkylphosphonates formed in the addition of allylic phosphonates to aldehydes,[30] we found that both in solution and in the solid state the molecules adopt a conformation identical with that shown in Figure 2(a). In the solid state, although the P=O and the OH groups are involved in the intermolecular hydrogen bonding, the hydroxyl oxygen is clearly in a 'short contact' with phosphorus atom, the respective P—C, C—O and P ··· O bond distances being 1·82–1·84, 1·38–1·40 and 2·95–3·00 Å respectively. For the 2-chloro derivative, **1c**, the situation is different; X_1 does not represent a major conformation, indicating that the donation of the non-bonding electrons from chlorine to the phosphoryl centre is much weaker. Interestingly for the carboxylic system **2**, the rotamer X_1 is more populated by the ether (**2b**) than by the free alcohol (**2a**). This change in the conformational preferences can be explained by weaker intramolecular hydrogen bonding in **2a** relative to the donor–acceptor interactions between the 2-oxygen atom and the carbonyl carbon [Figure 2(b)].



(a) (b)

Figure 2. Oxygen–phosphoryl and oxygen–carbonyl interactions in conformation X_1: (a) **1b**; (b) **2b**

Metal ion effects

Table 4 shows the effects of NaI and $Mg(ClO_4)_2$ on the selected NMR data of substrates **1** and **2** in acetone-d_6 solutions. The choice of a counterion resulted from solubility considerations; the nature of the anion had no measurable effect on the NMR spectra. The general effect of metal ions is a low-field shift of the signals of hydrogen atoms in the substrates (including those not shown in Table 4). This effect is not due to the change in the bulk properties of the medium; we have shown before for the pentylphosphonic derivative[8] that the change in the ^1H chemical shifts on addition of metal ions decreases with increase in the distance between a given hydrogen and the phosphoryl group. It is therefore the donor–acceptor interaction between the latter group and the metal ion that is responsible for the observed deshielding effects. These effects are, however, substrate dependent; the deshielding is generally much greater for compounds **1** than for **2**, indicating stronger complexation of Na^+ and Mg^{2+} by the phosphoryl group than by the carbonyl group. We were more interested in specific effects of metal ions on the diastereomeric methylene group CH_AH_B, as they should provide information on how these ions modify the distribution of the conformers relative to the ion-free acetone medium. It can be seen from Table 4 that whereas these effects on the CH_AH_B group in the hydroxy- and methoxyalkylphosphonates are fairly strong, they are negligible for substrates **1c** and **2**. The population of rotamers in acetone-d_6, and in acetone-d_6 containing sodium and magnesium salts, are given in Table 5. It is obvious that for the hydroxyphosphonate **1a** and, to a lesser extent, for its methoxy analogue **1b**, metal ions increase the population of the rotamer X_1, mostly at the expense of X_2, that is, favour even more the *gauche* orientation of the PO_3Me_2 and OH (OMe) groups. For **1c**, **2a** and **2b**, the conformational preferences are virtually insensitive to the addition of salts. The observed effect can be taken as evidence for the chelation of a metal ion by the two oxygen atoms in the 1,5-position of the (OPCCO) moiety of **1a** and **1b** (Figure 3).

In a recent study on the stereochemistry of phosphate–Lewis acid interactions, Alexander *et al.*[31] demonstrated that the $R_2PO_2^-$ ions form unidentate structures, with the preferred *syn*, but out-of-plane,

Table 4. Effects of metal ions on selected NMR data for **1** and **2** (acetone-d_6, 30 °C)

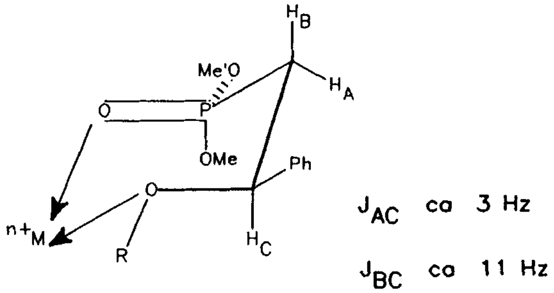
Substrate	Nucleus (parameter)	Salt[a]				
		None	NaI (1)	NaI (2)	NaI (3)	$Mg(ClO_4)_2$
1a	^{31}P (δ_P)	32·58	33·23	33·47	33·63	32·43
1b		31·23	32·03	32·32	32·48	30·94
1c		28·05	28·89	29·14	29·27	28·12
1a	H_A, H_B (δ_H)	2·17	2·27	2·31	2·33	2·47
		2·24	2·50	2·60	2·66	2·65
1b		2·09	2·19	2·22	2·23	2·33
		2·32	2·43	2·49	2·53	2·55
1c		2·77	2·84	2·88	2·88	2·88
		2·77	2·89	2·93	2·97	2·95
2a		2·62	2·67	2·70	2·73	2·66
		2·69	2·77	2·83	2·87	2·73
2b		2·55	2·57		2·60	2·58
		2·72	2·73		2·75	2·74
1a	H_C, COMe (δ_H)	5·03	5·20	5·24	5·29	5·27
1b		4·51	4·63	4·68	4·71	4·62
		3·17	3·20	3·22	3·23	3·19
1c		5·32	5·45	5·50	5·33	5·41
2a		5·11	5·15	5·19	5·21	5·14
2b		4·61	4·62		4·65	4·62
		3·15	3·17		3·18	3·17
1a	Me, Me′ (δ_H)	3·62	3·71	3·73	3·74	3·86
		3·67	3·76	3·80	3·83	3·94
1b		3·55	3·66	3·70	3·73	3·79
		3·67	3·73	3·75	3·76	3·79
1c		3·63	3·70	3·72	3·74	3·63
		3·72	3·79	3·81	3·82	3·79
1a	H_A/H_C, H_B/H_C (J_{AC}, J_{BC})	4·2	3·7	3·6	3·5	3·2
		9·2	9·8	9·9	9·9	10·6
1b		5·0	4·5	4·4	4·3	4·1
		8·8	9·1	9·3	9·4	9·5
1c		7·6	7·4	7·3	7·1	7·3
		7·6	7·4	7·4	7·5	7·3
2a		5·5	5·1	5·2	5·1	5·3
		8·1	8·4	8·3	8·3	8·2
2b		5·0	5·0		5·0	5·0
		8·9	8·8		8·7	8·9

[a] Salt/substrate molar ratio is given in parentheses.

Table 5. Effects of metal ions on the conformational behaviour of phosphonates **1** and carboxylates **2** (population of rotamers, %)

	1a			1b			1c			2a			2b		
Medium[a]	X_1	X_2	X_3	X_1	X_2	X_3	X_1	X_2	X_3	X_1	X_2	X_3	X_1	X_2	X_3
A	70	20	10	65	30	5	49	51	0	58	34	8	68	30	2
B_1	78	15	7	70	24	6	46	52	2	63	30	7	68	30	2
B_2	79	14	7	71	24	5	47	50	3	62	31	7	68	30	2
B_3	73	23	4	48	48	4	62	30	8	68	30	2	68	30	2
C	88	10	2	74	19	7	46	50	4	61	32	7	68	30	2

[a] A = acetone-d_6; B_1, B_2, B_3 = acetone-d_6 + NaI with [NaI]/[substrate] = 1, 2 and 3, respectively; C = acetone-d_6 + $Mg(ClO_4)_2$ with [$Mg(ClO_4)_2$]/[substrate] = 2.



in acetone + $MgClO_4$	population %
R = H	88
R = Me	74

Figure 3. Chelation of metal ions by **1a** (R = H) and **1b** (R = Me)

orientation of a metal ion with respect to the PO_2 group. This geometry is, in fact, present in the structure shown in Figure 3, with respect to the metal ion, and the P=O and the P—OMe (axial) groups. Since the carboxylate group typically prefers a *syn*, but in-plane, interaction with a metal ion,[32] this may be a reason for the much weaker chelating ability of the carboxylic derivatives **2**, and hence the lack of increase in the population of X_1 on the addition of a salt. Energetically favourable chelation of a metal ion by a 1,5-system of two oxygen atoms (OPOCO) was proposed as an explanation for the catalytic effect of Mg^{2+} in the phosphoryl transfer from pyridine to the acetate ion.[33]

In conclusion, we have demonstrated that in the β-hydroxy- or β-methoxyphosphonic systems, the $P(O)(OMe)_2$ and the OH (or OMe) groups attract each other, resulting in their *gauche* orientation in the most populated conformer, in both non-polar and polar aprotic solvents. The attraction is achieved via the intramolecular hydrogen bonding, or via the donor–acceptor electronic interactions between the β-oxygen atom and the phosphoryl centre. In the presence of ions such as Na^+ or Mg^{2+}, the attraction is increased by the involvement of the phosphoryl group, and the β-OR group (R = H, Me) in chelation of the metal ion, thus limiting even more the conformational freedom of the molecule. It is perhaps relevant to note that the 1,5-chelation of Na^+ by two phosphoryl groups in bis(diphenylphosphinyl)methane is responsible for the formation of one of the few crystalline sodium complexes of phosphoryl compounds.[34]

EXPERIMENTAL

General. Solvents and commercially available substrates were purified by conventional methods. Melting points were determined on a Gallenkamp apparatus and are uncorrected. The salts were dried in an oven at 120 °C and stored in a desiccator over P_4O_{10} immediately before use. Preparation of the solutions containing the salts was carried out in a dry atmosphere in a glove-box. NMR spectra were recorded on a Bruker AC 300 MHz spectrometer at a probe temperature 30 °C. Chemical shifts are given in δ (ppm) relative to tetramethylsilane as an internal standard (^1H) or 85% H_3PO_4 as an external standard (^{31}P). The following solvents were used for NMR spectra analysis: tetrachloromethane (BDH, AnalaR) containing 10% (v/v) cyclohexane-d_{12} (Aldrich, 99·5 atom% D), dried over molecular sieves; benzene-d_6, (Uvasol, Merck); chloroform-d_1 (Uvasol, Merck), dried over molecular sieves; acetone-d_6 (Aldrich, 99.5 atom% D), dried over molecular sieves; and dimethyl-d_6 sulphoxide (Uvasol, Merck). The concentration of substrates was 0·20 M

Dimethyl 2-hydroxy-2-phenylethylphosphonate (1a). The β-ketophosphonate precursor **3** was synthesized according to the previously described procedure;[9] no further purification was necessary (80%). ^1H NMR, δ 3·65 (d, 2H, J = 22·6 Hz), 3·78 (d, 6H, J = 11·2 Hz), 7·30–7·70 (m, 5H); ^{31}P NMR, δ 23·40. Compound **3** was reduced following a modified version of the literature procedure.[10] The reaction was carried out in ethanol (not methanol, as described) and for the extraction of the product chloroform was used instead of diethyl ether. Compound **1a** was obtained as a white solid which was recrystallized from THF–hexane (1 : 1) to give colourless crystals, m.p. 56·1–56·5 °C (61%). ^1H NMR, δ 2·19 (ddd, 1H, J = 18·4, 15·3, 10·1 Hz), 2·29 (ddd, 1H, J = 15·4, 15·3, 2·9 Hz), 3·72 (d, 3H, J = 11·0 Hz), 3·75 (d, 3H, J = 10·9 Hz), 3·74 (broad s, 1H), 5·13 (dd, 1H, J = 10·1, 2·9 Hz), 7·25–7·41 (m, 5H); ^{31}P NMR, δ 32·26; MS, *m/z* 230 (M^+, 17%), 124 (100), 106 (35), 110 (34), 120 (35).

Dimethyl 2-methoxy-2-phenylethylphosphonate (1b). Compound **1a** was methylated by treatment with sodium hydride, followed by iodomethane;[11] a virtually pure compound was obtained (45%). ^1H NMR, δ 2·12 (ddd, 1H, J = 18·1, 15·4, 4·6 Hz), 2·36 (ddd, 1H, J = 16·8, 15·4, 9·0 Hz), 3·23 (s, 3H), 3·62 (d, 3H, J = 10·8 Hz), 3·73 (d, 3H, J = 10·8 Hz), 4·56 (ddd, 1H, J = 9·0, 8·9, 4·6 Hz), 7·30–7·39 (m, 5H); ^{31}P NMR, δ 31·70; MS, *m/z* 244 (M^+, <1%), 121 (100), 167 (19), 109 (35), 91 (64), 77 (60), 65 (20).

Dimethyl 2-chloro-2-phenylethylphosphonate (1c). Substrate **1a** was treated with CCl_4 in the presence of Ph_3P as described.[12] A prolonged reaction time (20 h vs 8 h recommended[12]) was necessary to obtain complete conversion to the desired product which was further purified by column chromatography [benzene–ethyl acetate (1 :1)] (46%). ^1H NMR, δ 2·65 (ddd, 1H, J = 18·2, 15·5, 7·6 Hz), 2·75 (ddd, 1H, J = 18·1, 15·5, 7·1 Hz), 3·51 (d, 3H, J = 11·0 Hz), 3.66 (d, 3H, J = 11·1 Hz), 7.32–7.51 (m, 5H), ^{31}P NMR; δ 27·60; MS, m/z 248 (M^+, <1%), 121 (17), 77 (24), 66 (100).

Ethyl 3-hydroxy-3-phenylpropionate (2a). The intermediate ethyl 3-oxo-3-phenylpropionate (**3**) was prepared as reported previously.[13] It was purified by column chromatography [benzene–ethyl acetate (9 : 1)] (73%). ^{1}H NMR, δ 1·22 (t, 3H, J = 7·1 Hz), 3·96 (s, 2H), 4.15 (q, 2H, J = 7·1 Hz), 7,10–7·91 (m, 5H). Compound **3** was reduced according to the literature procedure,[14] but with the reaction time shortened from 18 to 2 h. Purified by column chromatography [benzene–ethyl acetate (9 :1) containing 5% of ethylamine] or by bulb-to-bulb distillation (oven temperature 180 °C/0·1 Torr) (70%). ^{1}H NMR, δ 1·21 (t, 3H, J = 7·2 Hz), 2·67 (m, 2H), 4·13 (q, 2H, J = 7·2 Hz), 5·08 (dd, 1H, J = 8·3, 4·3 Hz), 7·21–7·36 (m, 5H); MS, m/z 194 (M^+, 18%), 107 (100).

Ethyl 3-methoxy-3-phenylpropionate (2b). Substrate **2a** was methylated with iodomethane in the presence of dry silver oxide. The literature procedure,[15] applied to the ethylation of ethyl 2-hydroxy-2-phenylpropionate, recommended refluxing the reaction mixture for 4 h. We found by following the reaction progress by TLC that a minimum time of 35 h of reflux was necessary to achieve complete conversion and to obtain virtually pure product (85%). ^{1}H NMR (acetone-d_6), δ 1·17 (t, 3H, J = 7·1 Hz), 2·55 (dd, 1H, J = 15·3, 5·0 Hz), 2·72 (dd, 1H, J = 15·3, 8·9 Hz), 3·15 (s, 3H), 4·06 (q, 2H, J = 7·1 Hz), 4·61 (dd, 1H, J = 8·9, 5·0 Hz), 7·27–7·39 (m, 5H).

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