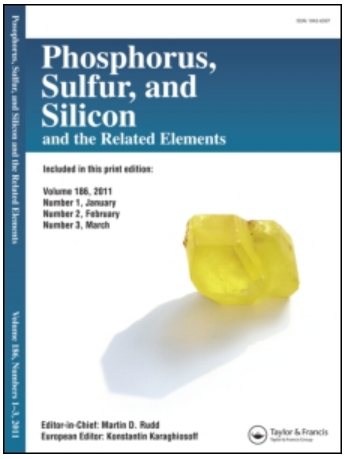

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CHEMICAL SHIFT NON-EQUIVALENCE IN THE NMR SPECTROSCOPY OF DIALKYL α-HYDROXYBENZYL- AND DIALKYL α-METHOXYBENZYLPHOSPHONATES AND THE CRYSTAL STRUCTURE OF DIMETHYL α-CHLOROMETHYL-α-HYDROXYBENZYLPHOSPHONATE

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Single crystal X-ray diffraction of dimethyl α-chloromethyl-α-hydroxybenzylphosphonate shows the compound to exist as hydrogen-bonded dimers in the solid state. In solution, ^{1}H and ^{13}C nmr spectroscopy reveal chemical shift non-equivalence of the corresponding nuclei in the two alkoxy groups of dialkyl α-hydroxybenzyl- and dialkyl α-methoxybenzylphosphonates, an effect that is attributed primarily to the presence of the chiral α-carbon atom, although restriction of rotation about the P—C_α bond by intermolecular hydrogen-bonding may also be a factor in the α-hydroxy compounds. Chemical shift non-equivalence of the α-halogenomethyl protons in dimethyl α-halogenomethyl-α-hydroxybenzylphosphonates is significantly greater for the chloro- than for the bromo-compound.

Key words: X-ray crystal structure; nmr spectroscopy; chemical shift non-equivalence; α-hydroxyphosphonates; α-methoxyphosphonates.

Organophosphorus esters are widely used in industry,[1] agriculture,[2] and organic synthesis.[3] It is well known that their proton nmr spectra may be complex, not only because of coupling to phosphorus but also because of the chemical shift non-equivalence of diastereotopic groups or atoms that are in the proximity of a chiral or prochiral phosphorus atom. The latter effect has been discussed in detail for the α-methylene protons of a range of ethyl esters (**1**).[4] While studying a series of dialkyl α-hydroxybenzylphosphonates (**2**; R = Me or Et, R^3 = CH_2Cl or CH_2Br, R^4 = H), we also observed chemical shift non-equivalence of the corresponding nuclei within each of the two alkoxy groups and suggested an explanation based on restricted rotation of the phosphorus-carbon bond due to intramolecular hy-

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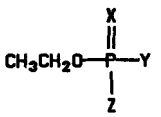
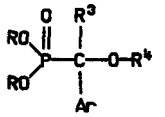
drogen-bonding between the hydroxyl and phosphoryl groups.[5] Infrared spectroscopy of a range of α-hydroxy phosphoryl compounds in the solid state and in solution (in carbon disulphide) had previously indicated the presence of both inter- and intra-molecular hydrogen bonding as general features of compounds of this type.[6] In order to obtain more specific information on the possibilities for hydrogen bonding in α-hydroxyphosphonates, we have determined the structure of dimethyl α-chloromethyl-α-hydroxybenzylphosphonate (**3**) by single crystal X-ray diffraction. In the solid state the compound exists as hydrogen-bonded dimers, with strong hydrogen bonds of 1.74 Å between the α-hydroxy protons and the phosphoryl oxygen atoms of the respective monomers (Figure 1). There is no evidence for intramolecular hydrogen-bonding between the hydroxyl and phosphoryl groups in the solid state [O(1) · · · H(4) interatomic distance = 2.95 Å] and the calculated minimum distance in the free molecule (2.15 Å), assuming a planar configuration for the relevant atoms and using the bond lengths and bond angles determined in the present studies, shows that any such interaction in solution must be relatively weak. In each dimeric unit, one molecule of (*R*)-configuration is associated with one of (*S*)-configuration. Bond angles at phosphorus are approximately tetrahedral, although those involving O(1) (112.8–115.1°) are significantly larger than the other angles at phosphorus (102.3–106.4°), in accord with the relative shortness of the P=O bond (1.463 Å) and a corresponding increase in the relative steric effect of the phosphoryl oxygen atom.

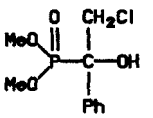
It is reasonable to suppose that strong intermolecular hydrogen bonding of a similar type will be present in other α-hydroxyphosphonates and that it will persist in solvents of low polarity. Dialkyl α-hydroxyphosphonates (**4**; R = Et, R^1 = H, R^2 = H, Me, Pr^n, Pr^i, Ph, PhCH=CH; R = Et, R^1 = Me, R^2 = Me) have previously been reported to exist as dimers in benzene or carbon tetrachloride at the boiling point.[7] A dimeric structure (Figure 1) will restrict rotation about the P—C_α bond, even if intramolecular hydrogen-bonding is absent. Restricted rotation, however, is not now thought to be the principal origin of the observed chemical shift non-equivalence of the two alkoxy groups.[8] ^{1}H and ^{13}C nmr data for a number of dimethyl α-hydroxy- and dimethyl α-methoxybenzylphosphonates are given in



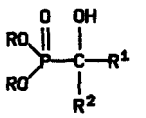
(1)



(2)



(3)



(4)

Table I and it is significant that a similar degree of chemical shift non-equivalence is seen in both types of compound, although neither intra- nor inter-molecular hydrogen-bonding can occur in the α-methoxy derivatives. The predominant effect is therefore thought to be the chirality of the phosphorus-bonded α-carbon atom.

The ethyl groups of diethyl α-hydroxybenzylphosphonates (**2**; R = Et, R^3 = CH_2Cl or CH_2Br, R^4 = H) also exhibit chemical shift non-equivalence.[5] The ^1H nmr signals of the terminal methyl groups are separated by a maximum of 0.1–0.15 ppm although in several cases they are indistinguishable at 60 MHz. In addition, the methylene protons within each ethoxy group are diastereotopic because of their proximity to the prochiral phosphorus atom.[4] These factors, together with coupling to the adjacent methyl group and to phosphorus, give rise to highly complex multiplets centered at ca. 4.0 ppm due to the overlap of signals from two spin systems, each approximating to ABM_3X; and this region is further complicated by overlap of the CH_2Cl or CH_2Br multiplet. We have examined the ^1H nmr spectra of a wide range of diethyl α-hydroxybenzylphosphonates (**2**, R = Et, R^3 = R^4 = H) in which the methylene signals of the ethoxy groups are not subject to overlap by signals due to other groups[9] but in no case was full resolution achieved (250 MHz). In the most favourable cases (**2**; R = Et, R^3 = H, R^4 = H, Ar = mesityl or *o*-anisyl) a maximum of ca. 38 lines were observed, compared to the 64 theoretically possible.

The methylene protons of the chloromethyl group (CH_2Cl) in dimethyl α-hydroxy-α-chloromethylbenzylphosphonate (**3**) give rise to an ABX spectrum, the

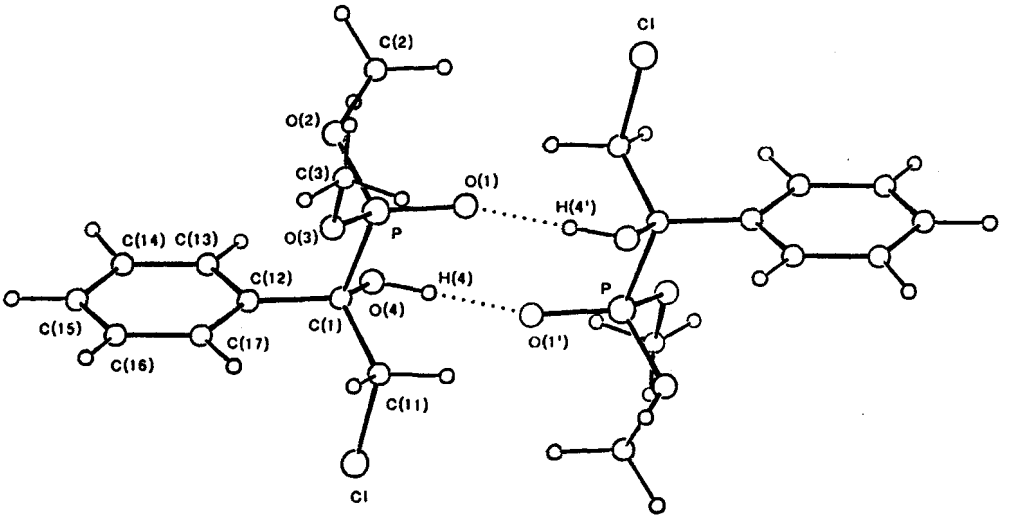


FIGURE 1 Structure of dimethyl α-chloromethyl-α-hydroxybenzylphosphonate (**3**). Selected bond lengths (Å): P—O(1) 1.463(3), P—O(3) 1.552(4), O(2)—C(2) 1.417(7), C(1)—C(11) 1.516(5), C(1)—O(4) 1.413(5), C(12)—C(13) 1.383(6), C(13)—C(14) 1.379(6), C(15)—C(16) 1.377(9), P—O(2) 1.545(3), P—C(1) 1.840(4), O(3)—C(3) 1.442(8), C(1)—C(12) 1.520(5), C(11)—C(1) 1.777(5), C(12)—C(17) 1.388(6), C(14)—C(15) 1.354(8), C(16)—C(17) 1.384(7), O(4)—H(4) 0.944(2). Selected bond angles (°): O(2)—P—O(1) 114.6(2), O(3)—P—O(2) 104.4(2), C(1)—P—O(2) 106.4(2), O(3)—P—O(1) 115.1(2), C(1)—P—O(1) 112.8(2), C(1)—P—O(3) 102.3(2), P—C(1)—O(4) 105.1(2), C(1)—O(4)—H(4) 115.6(3).

TABLE I

Nmr data for diastereotopic methyl ester groups (R) in dimethyl α-hydroxy- and dimethyl α-methoxybenzylphosphonates (2)[a]

R	R^3	R^4	Ar	δ_H/ppm (J_{POCH}/Hz)		δ_C/ppm (J_{POC}/Hz)	
Me	CH_2Cl	H	Ph	3.54 (10.5)	3.77 (10.5)	54.3 (7.4)	54.5 (7.4)
Me	CH_2Br	H	Ph	3.57 (10.4)	3.77 (10.5)	54.2 (6.7)	54.5 (6.7)
Me	H	H	Ph	3.66 (10.7)	3.69 (10.3)	53.6 (7.3)	53.9 (6.7)
Me	H	Me	Ph	3.66 (10.7)	3.71 (10.7)	53.6 (6.7)	53.7 (6.7)
Me	H	Me	C_6H_4Cl-*p*	3.70 (10.7)	3.73 (10.7)	53.6 (6.3)	53.8 (7.3)

[a] Recorded in $CDCl_3$ at 80 MHz.

AB subspectrum of which is fully resolved at 250 MHz. Since the phosphorus nucleus (X) is further coupled to anisochronous methyl groups, the fully coupled X-spectrum is too complex to allow discrimination between alternative parameter sets obtained by analysis of the AB subspectrum. Instead, determination of the spectrum at higher field (500 MHz) provided the basis[10] for choosing the parameters: $\delta_{H(A)}$ 4.26, $\delta_{H(B)}$ 4.18 ppm, $^2J_{H(A)H(B)}$ 11.8, $^3J_{H(A)P}$ 4.5, $^3J_{H(B)P}$ 9.5 Hz. Surprisingly, the protons of the CH_2Br group in the corresponding bromo compound (**2**; R = Me, R^3 = CH_2Br, R^4 = H, Ar = Ph) show almost no evidence of chemical shift non-equivalence. At 80 MHz a simple doublet (due to phosphorus coupling) is seen (δ_H 4.13, J_{PH} 5.9 Hz), while at 250 or 500 MHz, only the slightest sign of further resolution can be observed.

EXPERIMENTAL

α-Hydroxybenzylphosphonates[5,11] were prepared as described,[5] and α-methoxybenzylphosphonates by methylation of the corresponding hydroxy compounds with dimethyl sulphate under conditions of phase-transfer catalysis.[12] A suitable crystal of dimethyl α-chloromethyl-α-hydroxybenzylphosphonate for X-ray diffraction measurements was obtained by recrystallization from dichloromethane. X-ray diffraction data were collected with Mo—K_α radiation (λ = 0.71069 Å). Refinement using 1305 reflections with $I/\sigma(I) > 3.0$ gave R = 0.0496. Nmr spectra were obtained using Bruker WP 80 and Bruker AM 250 spectrometers. Chemical shifts (^{1}H and ^{13}C) are given relative to TMS.

Crystal data. (**3**), $C_{10}H_{14}ClO_4P$, M = 264.54, monoclinic, space group $P2_1/c$, a = 8.663(2), b = 18.476(5), c = 8.399(2) Å, β = 108.51(4)°, V = 1274.78 Å^3, Z = 4, $F(000)$ = 552, μ = 3.66 cm^{-1}. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre.

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8. No firm conclusions can be drawn from the fact that chemical shifts and $^3J_{PH}$ coupling constants for the methoxy protons in 3 showed no change over the temperature range 300–333 K in $CDCl_3$, since it is probable that α-hydroxyphosphonates retain a dimeric structure at elevated temperatures (cf. Reference 7). The small changes observed in the chemical shift and coupling constant of the hydroxyl proton over the same temperature range (from δ_H 3.56, $^3J_{PH}$ 14.1 at 300 K to δ_H 3.29, $^3J_{PH}$ 14.3 at 333 K) may be indicative of slight dissociation into monomers as the temperature is increased, but the preservation of phosphorus-proton coupling suggests that exchange between such species is slow on an nmr timescale.
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