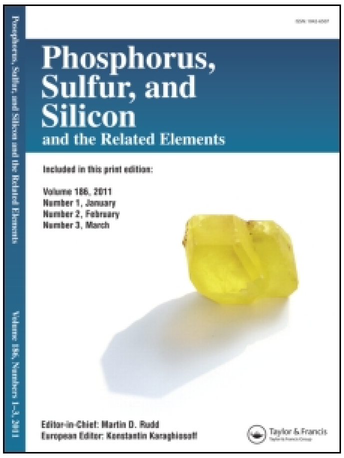

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1,2-DIHYDROXY-ETHANE-1,2-DIPHOSPHONIC ACID DERIVATIVES: STEREOCHEMICAL INVESTIGATIONS BY NMR METHODS

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1,2-DIHYDROXY-ETHANE-1,2-DIPHOSPHONIC ACID DERIVATIVES: STEREOCHEMICAL INVESTIGATIONS BY NMR METHODS

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A variety of NMR spectroscopic methods has been used to investigate the stereochemistry of a series of derivatives of 1,2-dihydroxy-ethane-1,2-diphosphonic acid, a structural analogue of tartaric acid. These derivatives are prepared by diastereospecific reactions of P(O)H compounds with glyoxal. ^{1}H, ^{13}C, and ^{31}P spectra using single and double resonance techniques have been measured for eight typical derivatives **1–8**.

In the case of the tetramethyl ester both diastereomers **2a** and **2b** were available, and they have been distinguished by measurement of coupling constants $^3J_{PP}$ and $^3J_{HH}$ as well as by measuring the proton decoupled ^{31}P NMR spectrum in the presence of a chiral additive, L(+)-dibenzoyltartaric acid.

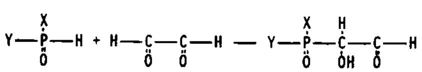
Both meso and racemic forms **2a** and **2b** have the two phosphonic acid groups in an anti-periplanar arrangement, as do all the other derivatives **1**, **3–8** we have studied.

Key words: 1,2-Dihydroxy-ethane-1,2-diphosphonic acid; stereochemistry; NMR.

INTRODUCTION

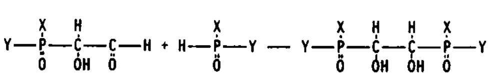
In preceding publications one of us (J.M.)[1] described the synthesis of a novel series of 1,2-dihydroxy-ethane-1,2-diphosphorus derivatives, which are accessible by the reaction of P(O)H compounds with glyoxal:

(1)



$$Y-\overset{X}{\underset{O}{P}}-H + H-\underset{O}{C}-\underset{O}{C}-H \longrightarrow Y-\overset{X}{\underset{O}{P}}-\overset{H}{\underset{OH}{C}}-\underset{O}{C}-H$$

(2)



$$Y-\overset{X}{\underset{O}{P}}-\overset{H}{\underset{OH}{C}}-\underset{O}{C}-H + H-\overset{X}{\underset{O}{P}}-Y \longrightarrow Y-\overset{X}{\underset{O}{P}}-\overset{H}{\underset{OH}{C}}-\overset{H}{\underset{OH}{C}}-\overset{X}{\underset{O}{P}}-Y$$

2 - 8

COMPOUND:	1	2	3	4	5	6	7	8
X = Y	OH	OMe	OEt	OiPr	OnBu	OBzl	OcHx	Et

For X = Y = alkoxy novel tetraalkyl esters of 1,2-dihydroxyethane-1,2-diphosphonic acid **2–7** results which may be cleaved by conventional methods to the parent acid **1**.

An analogous procedure with X = Y = alkyl leads to the corresponding 1,2-dihydroxy-ethane-1,2-diphosphine dioxide structures e.g. **8**.

These novel compounds are formal analogues of the well known tartaric acid, having two centres of asymmetry, at carbon atoms C_1 and C_2, and prochiral phosphorus centres. Consequently two different diastereomeric forms are expected as shown in Figure 1:

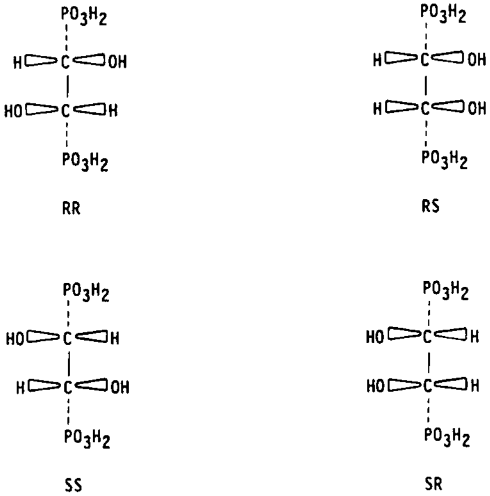


FIGURE 1 The two diastereomers (meso and dl) of the acid **1**. (Similarly related structures **2–7**).

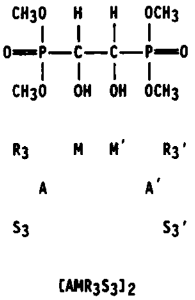
Even more complex are products resulting from addition of alkylphosphonous acid alkyl esters to glyoxal with X ≠ Y, X = alkoxy and Y = alkyl, having four centres of asymmetry and thus giving rise to five pairs of C- and P-epimeric stereoisomers.[1]

Here we report on the first two classes of organophosphorus derivatives, compounds **1–8**. In the initial preparative studies only elementary ^1H and $^{31}P\{^1H\}$ NMR spectra were reported.[1] These confirmed the general structures proposed for compounds **1–8** and showed that in almost all cases only one diastereomer was present in the products obtained after recrystallisation. But unfortunately—from the NMR point of view—the tetramethylester of 1,2-dihydroxy-ethane-diphosphonic acid, **2**, could be obtained as a mixture of diastereomers, although, as with the other compounds, recrystallisation of this mixed product yielded a single diastereomer.

The standard approach to an understanding of the stereochemistry of compounds **1–8** is the evaluation of the vicinal coupling constants $^3J_{HH}$, $^3J_{PP}$, and $^3J_{PH}$, since Karplus-type relationships are well established for similar model systems.[2]

These coupling constants cannot be extracted from the basic ^1H spectra because of their second-order character (see Figure 2-a) and the $^{31}P\{^1H\}$ spectra simply consist of singlets. The spin systems are of the complex $[AXR_nS_n]_2$ type closely related to the $[AR_tX_n]_2$ systems which have been described elsewhere.[3]

For example, the spin system of the methyl ester **2** is



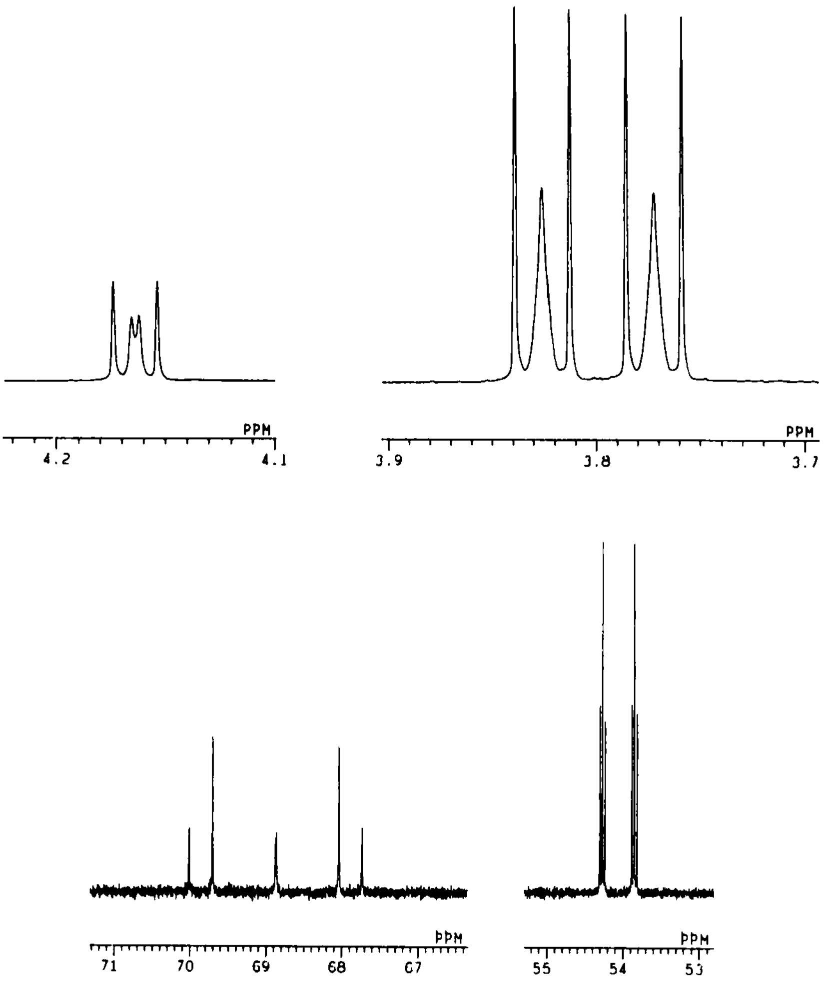


FIGURE 2 NMR spectra of **2a**, dissolved in CD_3OD. a) above: 400 MHz ^1H spectrum. b) below: 100.5 MHz ^{13}C spectrum. c) next page: 161.7 MHz ^{31}P spectrum, showing the ^{13}C satellites.

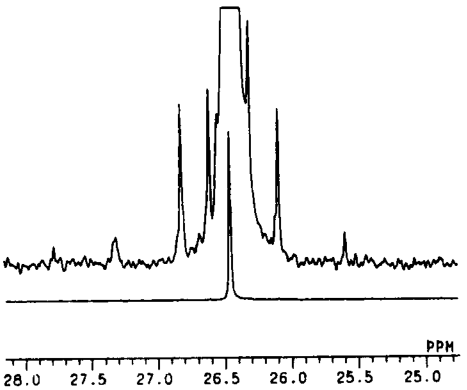
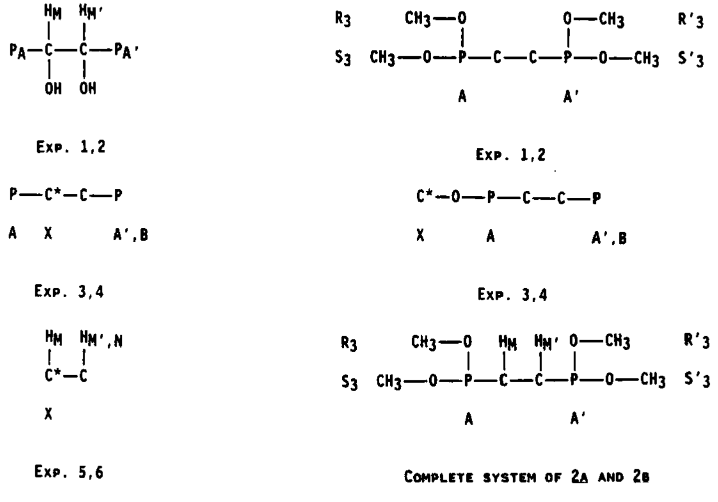


FIGURE 2 *Continued*

In the present studies further complications occur due to the problem known as deceptive simplicity, caused by the relatively large value of $^3J_{PP}$. This deceptive simplicity prevents the determination from the normal ^1H or ^{31}P spectra of the coupling constants $^3J_{PP}$ and $^3J_{HH}$, which are excellent guides to the stereochemistry of the compounds inspected here. We were interested in finding suitable

TABLE I

Double Resonance Experiments leading to stereospecific coupling constants. a) selective decoupling of protons. b) Complete decoupling of protons. c) Observation of ^{13}C-satellites in ^{31}P-decoupled ^1H spectrum. d) Rapid intermolecular exchange of —COH protons removes them from the molecular spin systems. e) Definition of Spin Systems



Experiment	Parameters available	Residual Spin Systems[d,e]
1. $^1H\{^1H\}$ sel.[a] 2. $^{31}P\{^1H\}$ sel.[a]	J_{PP} J_{HH} J_{PH}	$[AM]_2$, $[AR_nS_n]_2$
3. $^{13}C\{^1H\}$ com.[b] 4. $^{31}P\{^1H\}$ com.[b]	J_{PP} J_{PC}	AA'X, ABX
5. $^1H\{^{31}P\}^{13}C$ sat.[c] 6. $^{13}C\{^{31}P\}$ dec.	J_{HH} J_{CH}	MM'X, MNX

ways of determining these parameters and Table 1 shows the experiments that can in principle supply them. It will be noticed that most of these experiments rely on the removal of chemical equivalence by the presence of ^{13}C nuclei at unique sites in the molecule. We have therefore carried out a series of careful measurements of the ^{13}C NMR spectra and of the ^{13}C satellite signals in the ^1H and ^{31}P spectra of compounds **1–8**, including both diastereomers of the tetramethyl ester **2**. Typical spectra of one of the diastereomers are shown in Figure 2. We have thus been able to obtain significant parameters which were not available from previous studies,[1] since these only involved basic ^1H and $^{31}P\{^1H\}$ NMR spectra.

RESULTS AND DISCUSSION

The $^{13}C\{^1H\}$ spectra of the derivatives **1–8** show coupling to the phosphorus nuclei, which results in second-order spectra of the AA′X type, since the two phosphorus nuclei have effectively the same chemical shift but different couplings to the ^{13}C nucleus. The small isotope shift, caused by the presence of a ^{13}C nucleus next to one of the ^{31}P nuclei, leading to an ABX system, can normally be ignored. The AA′X system, which is a special case of the more general ABX spin system, has been widely used in practical spectroscopy and is the subject of some misunderstandings in the literature.[4] This problem has recently been completely described in two independent studies of our groups.[5,6]

In compounds **1–8**, where $^3J_{PP}$ is moderately large, we observe typically either three or five line patterns symmetrically spaced about ν_C; only at 100 MHz do we observe six line patterns due to a small splitting of the central line of the five line patterns because of the isotope shift mentioned above. Small values of J_{PC} give rise to the three line spectra, while large values yield the characteristic five line patterns. The former case is observed for the carbons of the ester groups, which are typically two or more bonds removed from the phosphorus nuclei, e.g. in C—O—P—C—C—C—P units of **2–7**. Five line spectra are obtained for carbons directly bonded to phosphorus, typically the carbons from the ethane skeleton in P—C—C—P units.

In either case it is easy to extract the parameter N_{PC}, which is defined as the sum of the two phosphorus carbon coupling constants, $J_{PC} + J_{P'C}$. N_{PC} is equal to the separation of the two lines with intensities summing up to 50% of the total intensity in either three or five line patterns. In five line patterns the separation of the other pair of lines is 4D, which is equal to $(L_{PC}^2 + 4J_{PP}^2)^{1/2}$, where L_{PC} is the difference of the two phosphorus carbon coupling constants, $J_{PC} - J_{P'C}$.

The general appearance of an AA′X spectrum is governed by 3 coupling constants J_{AX}, $J_{A'X}$, and $J_{AA'}$. As shown in References 5–7 it is impossible to determine all three parameters solely from experimental frequencies in five line patterns of X-nuclei, in our case the carbon region. Where J_{AX} (J_{PC}) is large enough, it is easiest to measure $J_{AA'}$ from the A spectrum, which in this case is the ^{13}C satellite part of the proton decoupled ^{31}P spectrum (see Figure 2-c). The satellites take the form of two ab subspectra, from which all three coupling constants are easily obtained, if all eight lines can be observed. Because of the

TABLE II

^{1}H, ^{13}C, and ^{31}P NMR data for P—CH—CH—P systems in **1–8** [$X_2P(O)$—CH(OH)—CH(OH)—$P(O)X_2$]. a) obscured by other signals; b) determined from the $^1H\{^{31}P\}$ spectrum

Compound	X	Solvent	δ_H	δ_P	δ_C	N_{PH}	N_{PC}	4D	L_{PC}	$^1J_{PC}$	$^2J_{P'C}$	$^3J_{PP}$
1	OH	D_2O	4.14	20.3br	68.74	4.9	159.0	179.2	153.5	+156.3	+2.8	46.2
2a	OMe	D_2O	4.28	26.6	69.37	7.1	166.0	222.6	163.6	+164.8	+1.2	75.2
		CD_3OD	4.17	26.2	68.77	8.2	166.4	228.9	163.8	+165.1	+1.3	79.8
2b	OMe	CD_3OD	4.35	24.9	68.69	6.2	163.9	235.5	168.9	+166.3	−2.4	83.4
3	OEt	CD_3OD	^{a}	24.3	67.78	^{a}	167.3	227.9	164.7	+166.0	+1.3	78.8
		$CDCl_3$	4.25^b	23.4	67.80	^{a}	163.9	222.9	162.0	+163.0	+1.0	76.6
4	OiPr	CD_3OD	4.03	22.7	69.27	7.6	168.4	231.8				
		$CDCl_3$		20.7	67.74		164.5	231.6	165.5	+165.0	−0.5	80.6
5	OnBu	CD_3OD	^{a}	24.2	69.09	^{a}	167.3	227.9	163.7	+165.5	+1.8	79.3
6	OBz	CD_3OD	4.22	25.3	68.19	8.5	164.1	213.9				
7	Ocyclo	CD_3OD	4.05	21.3	69.48	7.8	168.2	230.7				
8	Et	CD_3OD	4.30	60.3	68.54	9.0	78.5	102.5	78.9	+78.7	−0.2	32.7

large values of ${}^3J_{PP}$ found in the compounds studied, the outer lines of the ab subspectra are often too weak to be observed, especially if the compound is poorly soluble. In such cases the relationship $J_{PP} = 2D - S_i$ is used, where 4D is the separation measured in the ${}^{13}C$ spectrum (see above) and S_i is the separation of the inner lines of the ab subspectra observed in the ${}^{31}P$ spectrum (${}^{13}C$ satellites). To complete the analysis of the AA'X spin system a value for L_{PC} is required. It is easily calculated from the relationship $4D = (L_{PC}^2 + 4J_{PP}^2)^{1/2}$.

For the ester derivatives **2–7** values of ca. 80 Hz were found for ${}^3J_{PP}$ (see Table 2), whereas for **1** (the free acid) and **8** (a diphosphine dioxide) considerably lower values were measured. The values of ${}^3J_{PP}$ obtained, and the other parameters of the AA'X spin systems observed for the P—C—C—P backbones, are presented in Table 2. An alternative method of analysing an AA'X spectrum is to use the intensities of the 5 line ${}^{13}C\{{}^1H\}$ spectrum.[5,6] This procedure is required when no ${}^{13}C$ satellites can be observed in the ${}^{31}P\{{}^1H\}$ spectrum, but is generally less accurate than the method described above.

Where only a three line ${}^{13}C\{{}^1H\}$ spectrum is observed it is only possible to determine N_{PC}, but for the carbons in the ester groups of derivatives **2–7** it is generally valid to assume that J_{PC} (a five or more bond coupling) is zero, so that $N_{PC} = J_{PC}$. This assumption has been used to determine the values of J_{PC} for the carbons of the ester groupings given in Table 3. The large values of ${}^3J_{PP}$ observed for the esters **2–7** are a good indication that the two phosphonate groups are arranged in an anti-periplanar configuration across the ethane bridge in the dominant rotamer, corresponding to the structures of Figure 3-a or 3-d:

This follows from the Karplus type relationships established for ${}^3J_{PP}$ in polyphosphonic acids.[2] The smaller value observed for the free acid, **1**, indicates appreciable contributions from forms 3-b, 3-c, if the compound has the dl structure, or 3-e, 3-f if it has the meso structure. However the data does not allow us to distinguish between meso (Figure 3-d) or dl (Figure 3-a) isomers.

This distinction can be made in two ways. The first is by a determination of ${}^3J_{HH}$, which is expected from the Karplus relationship valid in phosphonic acid derivatives[2] to be much larger in the meso structure (Figure 3-d, anti-periplanar configuration of the two protons) than in the dl structure (Figure 3-a, gauche configuration).

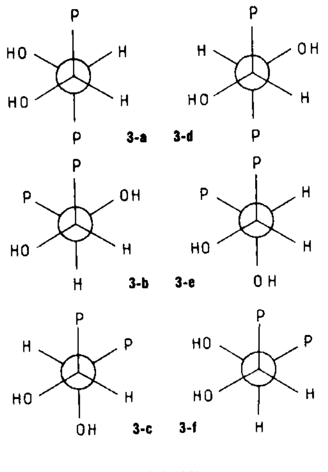
In the case of the free acid **1**, where ${}^3J_{PP}$ is smaller, and the spin system is of the simpler $[AX]_2$ type because there are no couplings to ester protons, ${}^3J_{HH}$ can be determined from the positions of the weak outer lines in the ${}^1H$ spectrum. The value found, 7.5 Hz (see Table 4), is indicative that the structure is not totally one with an anti-periplanar arrangement of the protons (e.g. 3-c or 3-d), but has contributions from other structures of Figure 3. In this case a distinction between dl (3-a to 3-c) and meso (3-d to 3-f) structures is not possible.

In the other cases (**2** to **8**) the weak outer lines in the ${}^1H$ spectra of the CH groups cannot be observed. In such situations the normal method of determining J_{HH} is the use of the ${}^{13}C$ satellites of the ${}^1H$ spectrum, since the presence of the single ${}^{13}C$ nucleus removes the chemical equivalence of the two protons. The $[AMR_3S_3]_2$ spin system of the tetramethyl ester **2a** becomes $ABMNQ_3R_3S_3T_3X$ upon inclusion of the ${}^{13}C$ nucleus (X), and the H—H coupling constant, J_{MN}, should be easily measurable. The large value of J_{PP} (J_{AB}) however still causes

TABLE III

^{13}C data for X groups in **2–8**. [$X_2P(O)—CH(OH)—CH(OH)—P(O)X_2$]

Compound	X	Solvent	carbon atom	δ_C	N_{PC}
2a	OMe	D_2O	C_1	56.75	7.1
				57.09	7.1
3	OEt	$CDCl_3$	C_1	63.17	6.4
				63.84	6.9
			C_2	16.5	5.6
				16.4	5.7
4	OiPr	CD_3OD	C_1	72.69	7.0
				72.95	7.0
			C_2	24.15	~5
				24.60	~5
5	OnBu	CD_3OD	C_1	67.57	7.3
				68.01	6.5
			C_2	33.72	5.5
				33.83	5.5
			C_3	19.80	
			C_4	13.98	
6	OBzl	$(CD_3)_2SO$	C	66.55	5.5
				66.98	5.9
7	OcHx	CD_3OD	C_1	77.54	7.4
				77.83	7.4
			$C_{2,6}$	34.51	
				35.08	
			$C_{3,5}$	24.56	
				24.62	
			C_4	26.36	
8	Et	CD_3OD	C_1	18.41	62.7
				19.90	65.8
			C_2	5.72	4.4
				5.88	4.4



$P = -P(O)(OR)_2$

FIGURE 3 Hypothetical rotameric forms (Newman projections of the two diastereomers of **2a**. a, b, c) Rotamers of the RR stereoisomer. d, e, f) Rotamers of the meso (RS) stereoisomer.

second order effects, and the observed satellites of the CH signals of **2a** (Figure 4-a, 400 MHz) are not easily interpreted. They are more easily understood in the ^{31}P decoupled ^{1}H spectrum, which was kindly measured for us at 360 MHz by Dr. I. Sadler of Edinburgh University. Only the high-frequency satellites of the CH signals are clearly visible in the spectrum, the low-frequency satellites being partially obscured by other signals, but the coupling constant $^{3}J_{HH}$ can easily be measured. The value observed, 10.3 Hz, is consistent with an anti-periplanar arrangement of the two hydrogen atoms, and hence with the meso structure of the compound in the rotameric form of Figure 3-d.

Once J_{HH} had been obtained, it became easier to simulate the spectrum with phosphorus coupling (Figure 4-a). We at first thought that the spin system $[AM]_2X$ would afford a sufficiently close approximation to the true spin system, since there is no coupling of the CH protons to the protons of the methyl groups. From the simulations of this simpler spin system (Figure 4-b) it is however apparent that four of the observed lines are broadened. This is due to the second-order behaviour of the two phosphorus nuclei (A and B) being modified by their coupling to the protons of the methyl groups. Since the full $[AMR_3S_3]_2X$ spin system, including the four different methyl groups, was too large for our computers, we simulated the $abmnr_4s_4$ sub-spectrum of the closely similar $[AMR_4]_2X$ system. This approximation is justified, since J_{AR} and J_{AS} have almost identical numerical values. The result of this simulation (Figure 4-c) clearly shows the broadening of four of the expected eight lines, and gives good agreement with the experimental spectrum (Figure 4-a). A further advantage of this successful simulation of the ^{13}C satellites in the ^{31}P coupled spectrum is that it also gives the values of $^{3}J_{PH}$ and $^{2}J_{PH}$, whereas only their sum is available from the deceptively simple ^{1}H spectrum of the ^{12}C isotopomer presented in Figure 2-a. The values obtained were 11.7 and 3.5 Hz, of opposite sign, though the analysis cannot say which is which.

By analogy with other polyphosphonic acid derivatives,[2] however, it is possible to assign a value of -11.7 Hz to $^{2}J_{PH}$ and a value of $+3.5$ Hz to $^{3}J_{PH}$. These values confirm the stereochemistry of the structures given in Figure 3-d.

Further confirmations for the assignment of the meso structure to the single diastereomer **2a** studied previously (sample 2-A)[1] were available from our measurements on a second sample which contained both diastereomers **2a** and **2b** (sample 2-B). While sample 2-A, dissolved in dmso-d_6, showed a ^{31}P{^{1}H} NMR singlet with $\delta_P = 26.2$ ppm, two signals were detected for sample 2-B in CD_3OD at 26.2 and 24.9 ppm, with an intensity ratio of ca. 1:2. In the 400 MHz ^{1}H spectrum of this mixed sample 2-B the ^{13}C satellites of the CH signal of **2a** were completely obscured, since the CH signal of the second diastereomer **2b** appears accurately at the position of the high-frequency satellites from **2a**. However the high-frequency satellites of **2b** could be observed, as shown in Figure 5, and gave a value of 1.6 Hz for $^{3}J_{HH}$, as expected for a structure according to Figure 3-a. The analysis of this spectrum also provided values for $^{2}J_{PH}$ and $^{3}J_{PH}$ of -11.2 and $+5.0$ Hz respectively.

The complete ^{1}H data for **1**, **2a**, and **2b**, including values of J_{CH} for **2a** and **2b** is presented in Table 4. Using the values in this table, together with the values of $^{3}J_{PP}$, the ^{1}H spectra of the ^{12}C isotopomers of **2a** and **2b** were simulated as

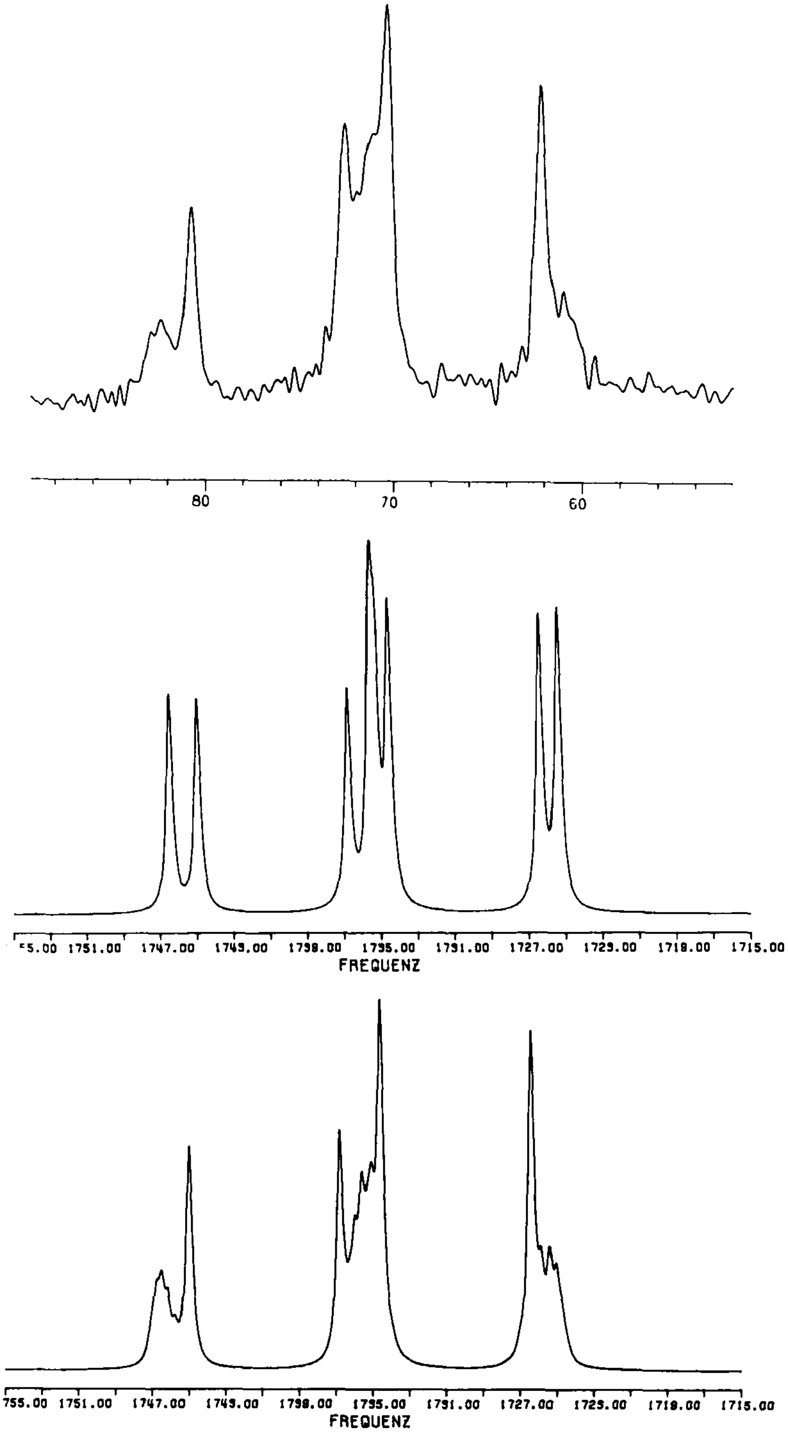


FIGURE 4 ^1H NMR spectra of the ^{13}C satellites of the CH signal of **2a** in CD_3OD (high frequency part). a) 400 MHz spectrum (^{31}P coupled). b) Simulation of (a): high-frequency mn-part of an abmn sub-spectrum of the $[AM]_2X$ system. c) Simulation of (a): high-frequency mn-part of an $abmnr_4r'_4$ sub-spectrum of the $[AMR_4]_2X$ approximation.

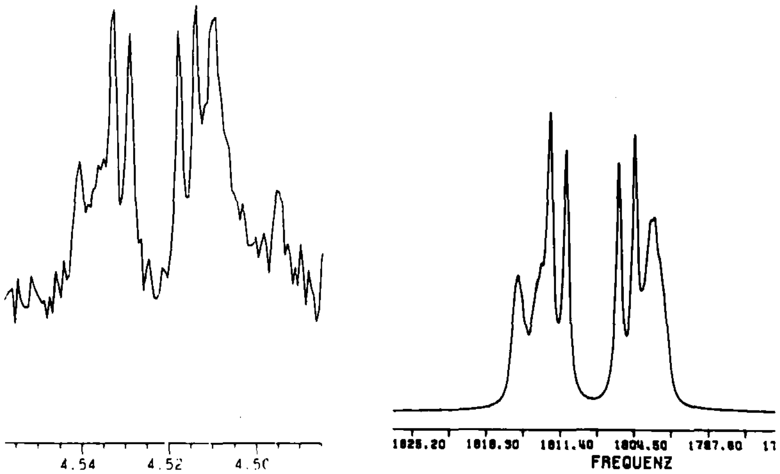


FIGURE 5 400 MHz ^1H spectrum of the ^{13}C satellites of the CH signal of **2b**, high frequency part. a) experimental spectrum (in CD_3OD). b) Simulation of (a): high-frequency mn-part of an $abmn_4r'_4$ sub-spectrum of the $[AMR_4]_2X$ approximation.

TABLE IV

Complete ^1H data for compounds **1**, **2a**, and **2b**. a) These protons have been included in the $[AMR_3S_3]_2$ spin system as species M. b) Measured in D_2O at 200 MHz. c) Measured in CD_3OD at 400 MHz. d) Measured in $CDCl_3$ at 200 MHz. e) These two proton species, H and H', are included in the $[AMR_3S_3]_2$ spin system as species R_3 and S_3. f) $^3J_{PH}$ is assumed to be equal to N_{PH}, the separation of the sharp doublet observed in the signal of these protons. g) These protons undergo rapid intermolecular exchange, so are not involved in the spin system. h) Not distinguishable from solvent protons.

CH protons[a]	**1**[b]	**2a**[c]	**2a**[d]	**2b**[c]	**2b**[d]
δ_H	4.14	4.17	4.30	4.35	4.49
$^3J_{HH}$	7.5	+10.4		+1.6	
N_{PH}	−13.0	8.2	7.0	6.2	7.4
$^2J_{PH}$	+8.1	−11.7		−11.2	
$^3J_{PH}$		+3.5		+5.0	
$^1J_{CH}$		+142.5		+137.2	
$^2J_{CH}$		+6.3		+6.0	
OCH_3 protons[e]					
δ_H		3.77	3.82	3.82	3.835
$\delta_{H'}$		3.81	3.85	3.84	3.842
$^3J_{PH}$[f]		10.7	10.7	10.5	10.7
$^3J_{PH'}$[f]		10.5	10.6	10.6	10.5
OH protons[g]					
δ_H	h	4.95	4.78	4.95	4.78

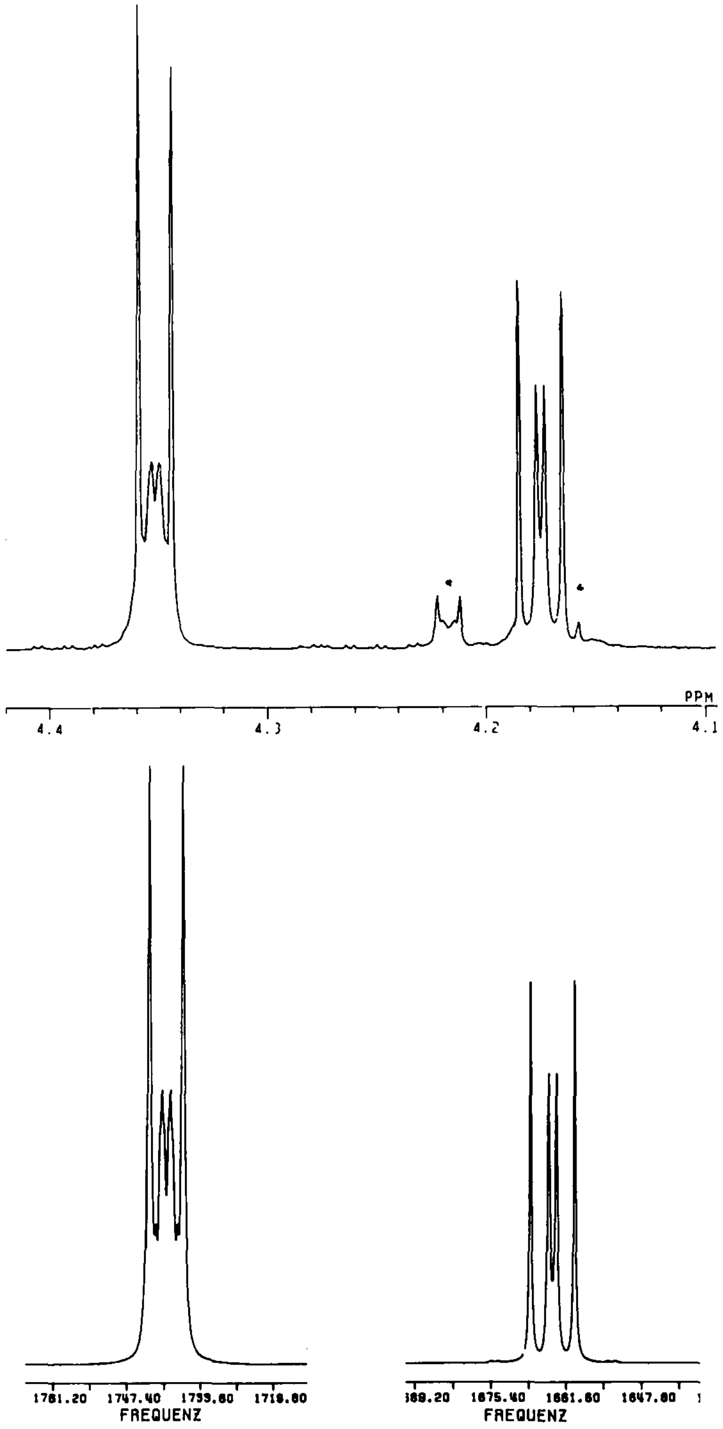


FIGURE 6 400 MHz NMR spectrum of a mixture of **2a** and **2b**, CH region (M-parts of $[AMR_3S_2]_2$ systems) a) experimental spectrum (in CD_3OD). Signals marked * are due to impurities. b) Simulation for the M-part of the $[AMR_4]_2$ approximation.

M-parts of $[AMR_4]_2$ spin systems. This approximation to the M-part of a true $[AMR_3S_3]_2$ spin system was the largest spin system we could simulate, and the approximation is justified since J_{AR} and J_{AS} have practically identical numerical values. The results of the simulations are presented in Figure 6-b, along with the spectrum of the mixture of **2a** and **2b** measured at 400 MHz in CD_3OD (Figure 6-a). An alternative approach to the identification of **2a** and **2b** uses optically active media as described by Albrand and Robert.[8]

We found that L(+)-dibenzoyltartaric acid, which was used by Brunner and Pieronczyk[9] to separate the two enantiomers of NORPHOS-dioxide, produced sufficiently large enantiospecific shifts in the $^{31}P\{^1H\}$ spectra of **2a** and **2b** to allow the distinction between meso and racemic isomers to be made.

In the isomers having RR or SS configurations at C_1 and C_2 both phosphorus nuclei are shifted in the same direction by the optically active medium, so that for each of these enantiomers an A_2 spectrum is still observed, with slightly different chemical shifts for the two enantiomers. For the meso isomer however, having RS or identical SR configuration, the two phosphorus nuclei in each molecule are shifted by different amounts. This effect results in an AB spectrum with $\Delta\nu_{AB}$ being of the same order as the shift difference observed between RR and SS enantiomers. The relatively large P—P coupling, in combination with a small value of $\Delta\delta_P$ gives rise to a deceptively simple singlet for a strongly coupled AB system.

Sample 2-B was mixed with L(+)-dibenzoyltartaric acid in a molar ratio of 1:0.6 and dissolved in CH_3OH/CD_3OD with a concentration of 10%. The proton decoupled 161.7 MHz ^{31}P NMR spectrum of this solution (Figure 7) clearly shows the splitting of the signal for **2b** at 24.9 ppm $\Delta\delta_P = 1.8$ Hz corresponding to 0.011 ppm), whereas no splitting is observed for **2a**, the signal at 26.4 ppm. This

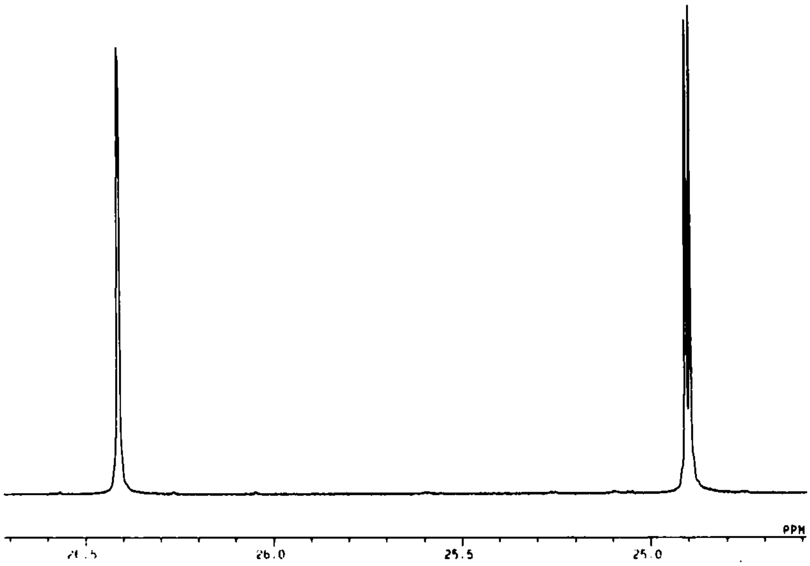


FIGURE 7 161.7 MHz $^{31}P\{^1H\}$ NMR spectrum of sample 2-A (a mixture of **2a** and **2b**) in CD_3OD/CH_3OH in the presence of L(+)-dibenzoyltartaric acid.

result again confirms that **2a** is the meso stereoisomer while **2b** is a racemic mixture of d and l stereoisomers.

EXPERIMENTAL

Compounds **1–8** were prepared by previously described methods.[1] All NMR spectra were measured by the Fourier transform technique using the solvents specified in the text and Tables. Solutions were made up to concentrations about 10%. JEOL FX90Q, FX200, and GX400 spectrometers were used at Bristol, a BRUKER AM200 NMR spectrometer at Düsseldorf, and a BRUKER WM360 spectrometer at Edinburgh for one $^1H\{^{31}P\}$ spectrum.

References: ^1H and ^{13}C: non-aqueous solutions int. TMS, aqueous solutions: trimethylsilylgroup of $(CH_3)_3SiCH_2CH_2CH_2SO_3Na$; ^{31}P: virtual standard ext. H_3PO_4 85%. Chemical shift values are given in ppm, coupling constants in Hz.

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