Structural Study of Fosfomycin [(−)-*cis*-1,2-Epoxypropylphosphonic Acid] Salts and Related Compounds

Carlos von Carstenn-Lichterfelde and Matilde Fernández-Ibañez
Instituto de Farmacología Española, Méndez Alvaro 57, Madrid 7, Spain
Enrique Gálvez-Ruano *
Departamento de Química Orgánica, Universidad de Alcalá de Henares, Alcalá de Henares, Madrid, Spain
Juana Bellanato
Instituto de Optica, C.S.I.C., Madrid, Spain

Disodium, calcium, and (+)-α-phenethylammonium salts of fosfomycin, the sodium salt of the monomethyl ester, and the dimethyl ester of fosfomycin have been studied by ^1H, ^{13}C, and ^{31}P n.m.r., i.r., and Raman spectroscopy. From the n.m.r. study it can be deduced that the steric factors are mainly responsible for the molecular arrangement of these compounds in solution. Taking into account the rigidity of the oxiran ring, the n.m.r. results have been correlated with *X*-ray data for the (+)-α-phenethylammonium salt of fosfomycin and sodium methyl (−)-*cis*-1,2-epoxypropylphosphonate. I.r. and Raman data confirm the known structure of fosfomycin derivatives deduced from the routes for their synthesis. Moreover these data suggest the existence of rotational isomerism in the dimethyl ester of fosfomycin.

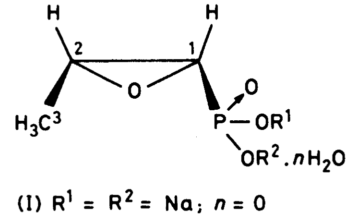
Fosfomycin,[1,2] (−)-*cis*-1,2-epoxypropylphosphonic acid, is a broad spectrum antibiotic, which inhibits the first step of bacterial cell wall biosynthesis.[3] Christensen *et al.*[4] determined its chemical structure by synthesis. Subsequently several routes have been reported to afford 1,2-epoxypropylphosphonates.[5-7] In this work a structural analysis of the disodium salt (I), the (+)-α-phenethylammonium salt (II), the monoanionic methyl ester (III), and the dimethyl ester (IV) of fosfomycin is reported with the aid of ^1H, ^{13}C, and ^{31}P n.m.r., i.r., and Raman spectroscopy. Some other vibrational spectroscopic data for calcium (VI) and disilver (V) salts are also included and discussed. This study elucidates the contribution of the steric factors of the dianionic, monoanionic, and neutral phosphonate groups on the valence angles at C(1) and C(2).

Experimental

Substances.—The following compounds were prepared by procedures given in the literature, and their properties were in agreement with those reported: disodium[8] and (+)-α-phenethylammonium salt of (−)-*cis*-1,2-epoxypropylphosphonic acid,[5] sodium methyl (−)-*cis*-1,2-epoxypropylphosphonate,[9] dimethyl (−)-*cis*-1,2-epoxypropylphosphonate,[9] and disilver[10] and calcium[8] salts of (−)-*cis*-1,2-epoxypropylphosphonic acid.

Instruments.—^1H N.m.r. spectra were recorded at 90 MHz with a Varian E.M. 390 spectrometer or at 250 MHz with a Bruker WP 250 SY instrument. ^{13}C N.m.r. spectra were determined at 22.6 MHz with a Bruker HX-90-E spectrometer. ^{31}P N.m.r. spectra were recorded at 22.2 MHz with a Varian FT-80A instrument or at 101 MHz with a Bruker WP 250 SY apparatus.

I.r. spectra were obtained on a Perkin-Elmer 457 spectrophotometer. Indene and polystyrene were used for instrument calibration. Samples were studied in KBr pellets or as Nujol mulls. Spectra in water, deuterium oxide, carbon tetrachloride, and deuteriated chloroform of some compounds were also recorded. Raman spectra were measured using powdered samples with a Ramanor U 1000 (5145 Å) spectrometer.



(I) $R^1 = R^2 = Na$; $n = 0$
(II) $R^1 = H$, $R^2 = H_3\overset{+}{N}-CH(CH_3)C_6H_5$; $n = 1$
(III) $R^1 = CH_3$, $R^2 = Na$; $n = 0$
(IV) $R^1 = R^2 = CH_3$; $n = 0$
(V) $R^1 = R^2 = Ag$; $n = 0$
(VI) R^1, $R^2 = Ca$; $n = 1$

Table 1. ^1H N.m.r. chemical shifts and coupling constants (*J*/Hz) of compounds (I)—(IV)

		δ					*J*/Hz						
Compd.	Solvent	H-1	H-2	H-3	H-4	H-5	$J_{H_1-H_2}$	$J_{H_2-H_3}$	J_{H_1-P}	J_{H_2-P}	J_{H_3-P}	J_{H_4-P}	J_{H_5-P}
(I)	D_2O [a,c]	2.70	3.13	1.34			5.15	5.55	18.58	5.5	0.7		
	CD_3OD [b,d]	2.76	3.06	1.51			5.00	5.00	17.00				
(II)	D_2O [b,c]	2.76	3.16	1.35			5.00	5.00	21.00	5.0			
	CD_3OD [b,d]	2.67	3.12	1.52			5.00	5.40	21.00	5.0			
(III)	CD_3OD [a,d]	2.81	3.17	1.52	3.62		4.76	5.50	22.80	5.5	0.7	10.4	
(IV)	$CDCl_3$ [a,d]	2.84	3.18	1.46	3.70	3.72	4.50	5.50	27.70	6.5	0.8	10.8	10.8
	CD_3OD [b,d]	2.94	3.12	1.46	3.70	3.70	4.00	6.00	27.00			9.0	9.0

[a] At 250 MHz. [b] At 90 MHz. [c] Sodium 4,4-dimethyl-4-silapentane-1-sulphonate as internal reference. [d] Me_4Si as internal reference.

Table 2. ^{13}C N.m.r. chemical shifts and coupling constants (J/Hz) of compounds (I)—(IV)

Compd.	Solvent	δ (p.p.m.) C-1	C-2	C-3	C-4	C-5
(I)	D_2O [a]	57.60	57.30	16.32		
(II)	D_2O [a]	55.44	56.80	15.93		
	CD_3OD [a]	53.85	54.54	14.73		
(III)	CD_3OD [a]	52.95	54.32	15.04	52.52	
(IV)	$CDCl_3$ [a]	49.00	52.89	13.72	52.70	52.40

Compd.	Solvent	J/Hz $J_{C_1-H_1}$	$J_{C_1-H_2}$	$J_{C_1-H_3}$	$J_{C_2-H_2}$	$J_{C_2-H_1}$	$J_{C_2-H_3}$	$J_{C_3-H_3}$	$J_{C_3-H_2}$	$J_{C_4^*-H_4}$	$J_{C_5^*-H_5}$	J_{C_1-P}	J_{C_2-P}	$J_{C_4^*-P}$	$J_{C_5^*-P}$
(I)	D_2O [a]	159	~1	2.5	172			127	6			175	1.5		
(II)	D_2O [a]	166		~3.0	178			127	6			186			
	CD_3OD [a]	161	~2	~2.5			~6	127	5.8			189	1.9		
(III)	CD_3OD [a]	162	2	2	163	2		127	6	139		189	2.0	6	
(IV)	$CDCl_3$ [a]	170	2	4	170			128	6	149	150	205	2.0	9	9

[a] At 22.6 MHz.

* Methoxy-groups.

Results and Discussion

(1) *N.m.r. Spectra.*—The chemical shifts and coupling constants of compounds (I)—(IV) are listed in Tables 1—3.

(i) ^1H *Chemical shifts.* The 1-H signals in (I)—(IV) are similar to those reported for fosfomycin [4] and some esters of 1,2-epoxyphosphonic acid.[7] The 1-H signals are to higher field than the 2-H signals in (I)—(IV). This effect is contrary to that expected from the electron-attracting effect of the phosphoryl group, and may be a consequence of the anisotropic shielding effect exerted by the phosphoryl group.[4] The δ values for 2-H increase from (I) to (IV) in agreement with the electron-attracting effect of the phosphoryl group.

A magnetic non-equivalence between the protons of the methoxy-groups is observed in (IV), in the solvents studied. This result is probably due to the molecular asymmetry and conformational non-equivalence of these groups.

(ii) ^{13}C *Chemical shifts.* The C-2 signals in (I)—(IV) are shifted to lower field than those for 1,2-epoxypropane and 2,3-epoxybutane.[11] This fact is attributed to the β-deshielding effect of the phosphoryl groups. The sequence δC-2(I) < δC-2(II) < δC-2(III) < δC-2(IV) is explained by the increasing electron-attracting effect of the phosphoryl group in (I)—(IV).

In compounds (II)—(IV) the C-1 signals are to higher field than those for C-2. In (I)—(IV) the δ values for C-1 follow the sequence δC-1(I) > δC-1(II) > δC-1(III) > δC-1(IV). These facts are attributed to the increasing geminal steric effect exerted by the phosphoryl group on H-1. Similar effects have been described in phosphonate [12] and oxiran systems.[13]

The sequence δC-3(I) > δC-3(II) > δC-3(III) > δC-3(IV) is consistent with the increased shielding γ-*cis* steric effect exerted by the phosphoryl groups.

(iii) *Coupling constants.* Taking into consideration the rigid structure of the oxiran ring, we have extrapolated *X*-ray data of compounds (II) and (III) for the interpretation of the n.m.r. results in the series (I)—(IV).[14,15] The $^3J_{1,2}$ values in (I)—(IV) suggest that the H(1)-C(1)-C(2)-H(2) dihedral angles are very similar. It can be assumed that this angle is *ca.* 9° for (I) and (IV) as was found by *X*-ray measurements for (II) and (III) (Table 4).

The sequence $J_{C_1-H_1}(I) < J_{C_1-H_1}(II) \simeq J_{C_1-H_1}(III) < J_{C_1-H_1}(IV)$ is attributed mainly to: (a) the increasing electron-attracting character of the phosphoryl groups, and consequently an increase in the Fermi contact term from (I) to (IV), and (b) the increasing *s*-character of the C(1)–H(1) bond which is related to the H(1)–C(1)–P angle which increases with the size of the phosphoryl group from (I) to (IV).

In compounds (I) and (II) $J_{C_2-H_2} - J_{C_1-H_1} \simeq 12.5$ Hz is mainly attributed to a greater *s*-character of the C(2)–H(2) bond than that of C(1)–H(1), since the H(2)–C(2)–C(3) angle is greater than the H(1)–C(1)–P angle (Table 4). However, in compounds (III) and (IV) $J_{C_2-H_2} - J_{C_1-H_1}$ is close to zero as a consequence of the similarity of the related angles.

The Figure shows a linear relationship between $^1J_{C_1-P}$ and $^2J_{P-H_1}$. From these results it can be assumed that these coupling constants depend on the same factors. In the present case, one of these factors is the increasing H(1)–C(1)–P angle and hence the increasing *s*-character of the C(1)–P and C(1)–H(1) bonds in (I)—(IV).[16,17]

(2) *I.r. Spectra.*—Owing to the recent interest in epoxyphosphonates we have registered the i.r. spectra of compounds (I)—(VI). These spectra provide additional information about the structure of the compounds in the solid state and in solution. The main i.r. frequencies and the band assignments are listed in Table 5. Some Raman data are also included.

Epoxide ring bands. The assignment of epoxide bands is based on that of the literature for ethylene and propylene oxides [18-21] and 1 : 2 disubstituted epoxides.[21,22]

The low frequency of the symmetric ring deformation vibration (756—720 cm^{-1}) which is sensitive to structure modifications should be noted. Moreover, this vibration appears split in some cases, and the corresponding bands are stronger in the Raman than in the i.r. The asymmetric ring deformation vibration at *ca.* 850 cm^{-1} also appears split in some compounds.

As in the case of other compounds having a 1 : 2 disubstituted epoxide group the spectra of (I)—(VI) show one or two weak bands in the 3 000 cm^{-1} i.r. region which are assigned to epoxymethine C–H stretching vibrations.

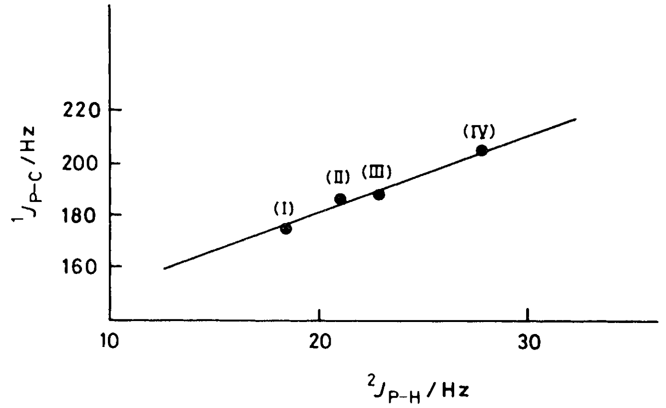
Regarding the CH_3 torsion mode, in propylene oxide it has been assigned to the very weak Raman band at 277 cm^{-1}.[21] In the present compounds an i.r. weak band has also been detected at 305—283 cm^{-1}, and a Raman band at approximately the same frequency as in the i.r. (see Table 5). Moreover, the frequency of the torsion mode is higher in compound (VI) suggesting lower ' mobility ' in this case as can be also deduced from the ^1H n.m.r. spectra in the solid state.[23] The data for (I) and (III) also suggest that the methyl group in these compounds

Table 3. ^{31}P N.m.r. chemical shifts and coupling constants (J/Hz) of compounds (I)—(IV)

Compound	Solvent	δ (p.p.m.)	J/Hz $J_{H_1\text{–}P}$	$J_{H_2\text{–}P}$	$J_{H_3\text{–}P}$	$J_{H_4\text{–}P}$
(I)	D_2O [a]	−11.70	18.6	5.8		
	D_2O [b]	−10.20	18.0	5.4	0.6	
(II)	CD_3OD [a]	−36.79	22.3	5.7		
(III)	CD_3OD [a]	−14.60				
	D_2O [b]	−15.56	23.4	6.1	0.7	10.4
(IV)	$CDCl_3$ [a]	−22.14				

[a] At 22.2 MHz. [b] At 101 MHz.

Calibration was by measurement of the ^{31}P n.m.r. spectrum of $P(OMe)_3$ under the same conditions. The ^{31}P chemical shifts are quoted with respect to 85% by taking the chemical shift of $P(OMe)_3$ with respect to 85% H_3PO_4 as −141.0 p.p.m.



Relationship between $^1J_{C_1\ P}$ and $^2J_{P\text{–}H_1}$

has less steric hindrance than in the previous case, and this agrees with the ^1H n.m.r. spectra in the solid state.

$PO_n{}^{n-1}$ *groups*. Thomas and Chittenden[24] discuss the several possibilities given in the literature to explain the main factors which influence the frequencies of the absorption bands assigned to the P=O and $P\text{–}O^-$ vibrations. From their results they conclude that the number of negative charges on the anion is the main influence which decides the region in which the bands associated with the phosphorus anion are found and that the P–O bond order plays a major role in determining the vibration frequency. However, as we will see later, other factors must be also taken into consideration, specially in the solid state, such as crystal-structure environment, hydrogen-bonded water, *etc.*

$PO_3{}^{2-}$ *anion*. Characteristic i.r. and Raman bands of the $PO_3{}^{2-}$ group for compounds (I), (V), and (VI) and the proposed assignments are given in Table 5. The bands associated with the $PO_3{}^{2-}$ anion in inorganic salts have been reported as occurring in the 1 150—1 000 cm^{-1} region. This anion is characterized by two bands, the higher frequency (asymmetric) band being strong, and the lower frequency (symmetric) band much weaker in intensity. Both bands in the three compounds studied appear in the expected range in the solid state and the intensity ratio in the Raman spectrum is the opposite of that in the i.r. Furthermore, as often occurs in phosphonic acid salts, the asymmetric bands appear as doublets in the i.r. spectra of (I) and (V) and the nature of the cation influences the frequency of the bands. Compound (I) was also studied in water solution and the observed frequency shifts are attributed to hydrogen bonding of the P–O bonds with the solvent. As this compound is very hygroscopic, its KBr spectrum is similar to the spectrum of an aqueous solution.

Table 4. Main angles (°) of compounds (II)[14] and (III)[15]

	(II)	(III) *
H(1)–C(1)–P	106.8	110.4
H(2)–C(2)–C(3)	127.0	102.9
H(1)–C(1)–C(2)–H(2)	9.0	9.25

* Mean value of the two molecules in the asymmetric unit.

From compound (V) only one i.r. spectrum in the Nujol mull was recorded, this spectrum showing striking differences with that of (I). The changes observed for the $PO_3{}^{2-}$ frequencies are mainly caused by the presence of different cations, in agreement with literature data.[24]

The i.r. and Raman spectra of (VI) show also significant variations compared with the corresponding spectra of (I) and the bonding of the P–O bonds with the water molecules in (VI) must be responsible for some of the observed changes.

$PO_2{}^-$ *anion*. Compound (II) containing this anion shows two characteristic strong bands attributed to the asymmetric and symmetric stretching vibrations. The complexity of the asymmetric PO_2 band in this compound is attributed to the existence of different types of hydrogen bonding involving both water molecules and NH groups, as has been demonstrated by *X*-ray data.[14]

According to the literature the P–O–(H) vibration appears as a strong i.r. band at 913 cm^{-1} (medium in Raman).

In compound (III) it could be assumed that the negative charge is mainly localized on one of the P–O bonds, while the second P–O bond has a 'partial' double bond character. However, some authors consider that the ionized $PO_2{}^-$ group exists in sodium salts of aminophosphonic acid monoesters;[25,26] that is in substantial agreement with *X*-ray data which reveal bond distances of P–O(1) 1.497(3); P–O(2) 1.482(3), and P′–O′(1) 1.488(3); P′–O′(2) 1.494(3) Å, for the two crystallographic independent molecules present in the unit cell.[15] In any case it is expected that both P–O vibrations are coupled, producing two absorption bands due to the asymmetric and symmetric stretching modes as in compound (II) (see Table 5). These bands are within the overall frequency regions of 1 323—1 092 and 1 156—990 cm^{-1} found for the $PO_2{}^-$ anion in numerous phosphorus compounds.[27] Furthermore, the existence of two independent molecules per asymmetric unit justifies the splitting of bands observed in some regions.

P=O *and* P–O–C *groups*. Data for the diester (IV) are given in Table 5. The phosphoryl stretching frequency falls within the ranges previously reported in the literature for related compounds.[27] Thomas and Chittenden[24] discuss the origin of the presence of two apparent phosphoryl absorption bands which frequently appear in the i.r. spectrum, as also happens in (IV). Some earlier authors concluded either that the doublet arises from two conformers or that one

Table 5. I.r. and Raman frequencies (cm^{-1}) of compounds (I)—(VI)

		P=O, P–O, C–O(P), and PO_n^{n-1} frequencies								Epoxide ring frequencies						
Compd.	Medium	ν(P=O)	$\nu_a(PO_2^-)$	$\nu_s(PO_2^-)$	$\nu_a(PO_3^{2-})$	$\nu_s(PO_3^{2-})$	ν[C–O(P)]	ν[P–O(H)] or ν[P–O(C)]	δ(P=O)	ν(C–H) (Ring)	$\delta(CH_3)$	Ring breathing	Ring deformation		Ring-CH_3 bending	τ CH_3
(I)	Nujol				1 125s[a] 1 096vs	1 008m				3 010	1 414w	1 270w 1 260w	860w 849w	725sh 720m	396w 360w	283vw
	Solid (Raman)				1 125vw	1 007vs				3 015vw 3 007vw	1 413w	1 268w 1 258w	857w 848w	725vs 719m	395w 355w	287vw
	H_2O				1 090sh 1 075vs	981m				*b*	1 413w	1 270w	843w			
	H_2O (Raman)				1 085sh 1 070vw	983vs, p				*b*	1 420m, p	1 270vs	850s	742vs 717s, p	397 362	
(II)	KBr		1 166vs 1 160vs 1 152vs 1 144vs 1 135vs	1 053vs				913vs	563s	3 015 3 000	1 414m	1 262w	848s	722w	385m	295w
	Solid (Raman)		1 163m	1 043m				914m	565vw	3 015sh 3 003vw	1 416w	1 260vs	848s	725vs	389w	298vw
	H_2O		1 180s	1 070vs							1 415m	1 265m				
(III)	Nujol		1 222vs	1 093s 1 087s				1 050s	568s[c]	3 020w 3 002w	1 415m 1 408sh	1 268sh 1 259m	858m 848s	754w	392w 351vw	290vw
	Solid (Raman)		1 224vw	1 096vs				1 055w	564vw[c] 540vw[c]	3 003m	1 414vw	1 268vw 1 259w	857w 848vw	753s	395m 356w	295vw
	H_2O		1 200vs	1 071vs				1 048s		*b*	1 411m	1 262w				
	H_2O (Raman)		1 210vw	1 072vs				1 050sh		*b*	1 412w	1 264m	845w	745m 719m	390vw 356vw	
(IV)	Liquid	1 267s 1 253s					1 183m	1 054vs 1 030vs	563m	3 005w	1 413m		852m	756m	380w 342vw	283sh
	$CDCl_3$	1 267m 1 252m					1 189w	1 063s 1 053s 1 040vs	563m	3 015vw 3 000vw	1 413w	1 240sh	852w	*b*		
	CCl_4	1 272s 1 253m					1 189w	1 063s 1 053sh 1 038vs	563m	3 015vw 2 985vw	1 414w	1 238sh	854w	*b*		
(V)	Nujol				1 058vs 1 040sh	1 008m				*b*	1 413w 1 408sh	1 261w 1 253w	849w 831w	720w	395vw 360vw	290vw
(VI)	KBr				1 095vs	1 017m				3 000w	1 423w 1 419sh	1 262vw	851m	734w 722w	400w 354m	305w
	Solid (Raman)				1 095vw	1 022s				3 028vw 2 992w	1 422vw	1 260w	848m	735w 724m	399vw 355w	323vw

[a] Abbreviations: s, strong; m, medium; w, weak; v, very; sh, shoulder; p, polarized. [b] Obscured by the medium. [c] $\delta(P\cdots O)$.

component of the doublet has its origin in a vibration not connected with the phosphoryl bond. It has also been remarked in the literature that the P–O–C bond gives rise to two characteristic frequencies, ν(P–O) modified by the O–C bond and ν(O–C) modified by the phosphorus atom. Taking into consideration the frequency limits given in the literature for these two vibrations we assign the bands in the 1 070—1 030 cm^{-1} region (two in the liquid, three in solution) to the ν(P–O) vibration and the band at 1 189—1 183 cm^{-1} to the ν(C–O). The intensity ratio of the bands appearing in the 1 070—1 030 cm^{-1} and in the 1 270—1 250 cm^{-1} region changes with the medium and this fact suggests that in the present compound the band multiplicity most probably originates from rotational isomerism.

The O–H *frequencies*. The spectrum of compound (II) shows characteristic broad absorptions between 2 500 and 1 700 cm^{-1} which are typical of hydrogen bonded P(O)OH groups. Other absorptions at 3 165 and 1 628 cm^{-1} are attributed to ν(O–H) and δ(H–O–H) modes of the strongly bonded water molecules, respectively. The absorptions at 790 and 650 cm^{-1} are assigned to water libration modes.

In the case of compound (VI) the hydration water molecule gives rise to two bands at 3 485 and 3 170 cm^{-1}. These bands are assigned to ν(O–H) of two O–H groups which are involved in different hydrogen bonds. The low frequency of the latter band indicates strong hydrogen bonding and agrees with the high frequency of the δ(H_2O) mode (1 670 cm^{-1}). Moreover, the strong bands at 797 and 651 cm^{-1} are assigned to librational modes.

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References

1 D. Hendlin, E. O. Stapley, M. Jackson, H. Wallick, H. Miller, F. J. Wolf, T. W. Miller, L. Chaiet, F. M. Kahan, E. L. Folk, H. B. Woodruff, J. M. Mata, S. Hernández, and S. Mochales, *Science*, 1969, **166**, 122.
2 J. M. Mata, A. Rodríguez, and A. Gallego, *Drugs of Today*, 1974, **10**, Suppl., 169.
3 F. M. Kahan, J. S. Kahan, P. J. Cassidy, and H. Kropp, *Ann. N.Y. Acad. Sci.*, 1974, **235**, 364.
4 B. G. Christensen, W. J. Leanza, T. R. Beattie, and A. A. Patchett, *Science*, 1969, **166**, 123.
5 E. J. Glamkowski, G. Gal, R. Purick, A. J. Davidson, and H. Sletzinger, *J. Org. Chem.*, 1970, **35**, 3510.
6 M. Sekine, K. Okimoto, K. Yamada, and M. Hata, *J. Org. Chem.*, 1981, **46**, 2097.
7 B. Springs and P. Haake, *J. Org. Chem.*, 1976, **41**, 1165.
8 U.S.P. 728 059.
9 U.S.P. 849 206.
10 U.S.P. 848 206.
11 E. L. Eliel and K. M. Pietrusiewicz in 'Topics in Carbon-13 NMR Spectroscopy,' ed. G. C. Levy, Wiley, New York, 1979, vol. 3, p. 174.
12 G. W. Buchanan and J. H. Bowen, *Can. J. Chem.*, 1977, **55**, 604.
13 D. R. Paulson, F. Y. N. Tang, G. F. Morán, A. S. Murray, B. P. Pelka, and E. M. Vázquez, *J. Org. Chem.*, 1975, **40**, 184.
14 A. Perales and S. García Blanco, *Acta Crystallogr.*, 1978, **B34**, 238.
15 A. Perales, J. Fayos, M. Martínez-Ripoll, C. von Carstenn-Lichterfelde, and M. Fernández-Ibañez, personal communication.
16 R. M. Lequan, M. J. Pouet, and M. P. Simonnin, *J. Chem. Soc., Chem. Commun.*, 1974, 475.
17 R. M. Lequan, M. J. Pouet, and M. P. Simonnin, *Org. Magn. Reson.*, 1975, **7**, 392.
18 R. C. Lord and B. Nolin, *J. Chem. Phys.*, 1956, **24**, 656.
19 O. Ballaus and J. Wagner, *Z. Phys. Chem.*, 1939, **B45**, 272.
20 H. B. Henbest, G. D. Meakins, B. Nicholls, and K. J. Taylor, *J. Chem. Soc.*, 1957, 1459.
21 M. C. Tobin, *Spectrochim. Acta*, 1960, **16**, 1108.
22 J. Bomstein, *Anal. Chem.*, 1958, **30**, 544.
23 J. Sanz, C. von Carstenn-Lichterfelde, M. Fernández, E. Gálvez, and J. Bellanato, unpublished results.
24 L. C. Thomas and R. A. Chittenden, *Spectrochim. Acta*, 1970, **26A**, 781.
25 V. Jagodić and Lj. Tusek, *Croat. Chem. Acta*, 1972, **44**, 445.
26 V. Jagodić, *Croat. Chem. Acta*, 1977, **49**, 127.
27 L. J. Bellamy and L. Beecher, *J. Chem. Soc.*, 1952, 475.

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