Cyclic Organophosphorus Compounds. Part XI.[1] Stereoisomeric Aralkyl Phosphonates of the 1,3,2-Dioxaphosphorinan Series

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New, configurationally isomeric phosphonates of the 5,5-disubstituted 2-oxo-1,3,2-dioxaphosphorinan series have been prepared. Variable-temperature studies and ABX analyses of the ^{1}H n.m.r. spectra suggest that they are conformationally mobile systems.

FROM a stereochemical point of view, cyclic phosphonates are of interest since they can be prepared by a stereospecific route involving interaction of cage-like phosphites and suitable organic halides. Thus, 2,6,7-trioxa-1-phosphabicyclo[2,2,2]octanes react with alkyl and aralkyl halides yielding 2-alkyl(aralkyl)-*cis*-5-alkyl-5-halogenomethyl-2-oxo-1,3,2-dioxaphosphorinans, while both *cis*- and *trans*-stereoisomers may be obtained by reaction between a diol and a phosphonic dichloride in the presence or absence of pyridine.[2,3] The related stereospecific formation of phosphoramidates from *N*-chloroamines has also been reported[4,5] and the reaction has been further extended to non-symmetrical cage phosphites.[6]

Following our observations on the ^{1}H n.m.r. spectra of 5,5-dimethyl- and related 1,3,2-dioxaphosph(v)orinans[7] and our correlations involving related phosphoramidates,[5] we have now prepared some new 5-methyl-5-halogenomethyldioxaphosph(v)orinans. In all cases, we obtained only two stereoisomeric forms of a given phosphonate, possessing non-identical groups at C-5.

cis- and *trans*-Benzyl and α-phenylethyl phosphonates were obtained by the two procedures just outlined, *viz.* from 4-methyl-2,6,7-trioxa-1-phosphabicyclo[2,2,2]octane (II) with benzyl or α-phenylethyl chloride, and from the phosphonic dichloride with 2-chloromethyl-2-methylpropane-1,3-diol. The very low yield of the *cis*-benzyl phosphonate by the former process was surprising in view of the much higher reactivity of the ethyl bicyclic phosphite (I) towards the same halide, already experienced by us and other workers.[2] Low yields of the α-phenylethyl phosphonate in the Arbuzov reaction were probably the result of extensive thermal decomposition of the halide.

The methyl bicyclic phosphite was, however, very reactive towards both bromo- and chloro-triphenylmethane. *cis*-5-Chloromethyl-5-methyl-2-oxo-2-triphenylmethyl-1,3,2-dioxaphosphorinan has been described elsewhere[3] but we were unable to obtain the

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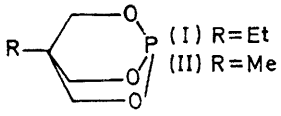
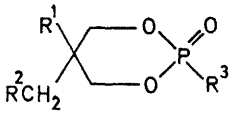
[2] W. S. Wadsworth and W. D. Emmons, *J. Amer. Chem. Soc.*, 1962, **84**, 610.
[3] J. G. Verkade, T. J. Hutteman, M. K. Fung, and R. W. King, *Inorg. Chem.*, 1965, **4**, 83.
[4] W. S. Wadsworth, *J. Org. Chem.*, 1967, **32**, 1603.
[5] R. S. Edmundson and E. W. Mitchell, *J. Chem. Soc.* (*C*), 1968, 3033.
[6] R. S. Edmundson and E. W. Mitchell, *Chem. Comm.*, 1966, 482.
[7] R. S. Edmundson and E. W. Mitchell, *J. Chem. Soc.* (*C*), 1968, 2091.

corresponding *trans*-form from triphenylmethylphosphonic dichloride.

In order to observe any magnetic shielding effects caused by the benzene rings of the aralkyl groups, a suitably similar but nonaromatic analogue was required. Previously, a comparison was made between 2-benzyl-5,5-dimethyl-2-oxo-1,3,2-dioxaphosphorinan and the corresponding 2-methyl ester.[7] In the present case, 2-bromomethyl-2-methylpropane-1,3-diol reacted with methylphosphonic dichloride to give an inseparable mixture of products; under similar conditions, benzylphosphonic dichloride gave a mixture of *cis*- and *trans*-benzyl phosphonates (XI) readily separable into pure isomeric forms. Further, reaction between the cage phosphite (II) and chloro- or bromo-methane would be experimentally inconvenient [(II) did not react with boiling iodomethane].





	R^1	R^2	R^3
(III)	Et	Cl	CH_2Ph
(IV)	Et	Cl	CHMePh
(V)	Me	Cl	CH_2Ph
(VI)	Me	Cl	CHMePh
(VII)	Me	Cl	CPh_3
(VIII)	Me	Br	CPh_3
(IX)	$ClCH_2$	Cl	CH_2Ph
(X)	Me	TsO	CH_2Ph
(XI)	Me	Br	CH_2Ph
(XII)	Me	TsO	Me
(XIII)	Me	Br	Me
(XIV)	Me	Cl	cyclo-C_6H_{11}
(XV)	Me	Cl	CCl_3
(XVI)	Me	Cl	NC_5H_{10}
(XVII)	Me	H	CH_2Ph
(XVIII)	Me	H	CHMePh
(XIX)	Me	H	CPh_3
(XX)	Me	H	Me

cis- and *trans*-5-Bromomethyl-2,5-dimethyl-2-oxo-1,3,2-dioxaphosphorinan were finally obtained by reaction between the 5-*p*-tolylsulphonyloxymethyldioxaphosphorinan and lithium bromide. The convenience of this procedure was demonstrated with the analogous benzyl phosphonates. *cis*-2-Benzyl-5-methyl-2-oxo-5-*p*-tolylsulphonyloxymethyl-1,3,2-dioxaphosphorinan has previously been prepared from the bicyclic phosphite (II) and benzyl toluene-*p*-sulphonate.[3] *cis* and *trans*-Forms of the cyclic tosyl ester (X) have now been obtained from 2-methyl-2-*p*-tolylsulphonyloxymethylpropane-1,3-diol; when heated with lithium bromide in 2-ethoxyethanol or dimethylformamide each is converted into the chromatographically pure 5-bromomethyl ester (XI) of corresponding configuration.

The preparation of *cis*-2,5-dimethyl-5-*p*-tolylsulphonyloxymethyl-2-oxo-1,3,2-dioxaphosphorinan from (II) and methyl toluene-*p*-sulphonate was only moderately successful, and the separation of the esters (XII) proved more difficult: each configurational isomer, when treated with lithium bromide, gave a single product to which the corresponding configuration was assigned.

Attempted reductions of *cis*- and *trans*-2-benzyl-5-chloromethyl-5-methyl-2-oxo-1,3,2-dioxaphosphorinan with lithium aluminium hydride were unsuccessful, as was that of the former stereoisomer with tributyltin hydride. However, the latter hydride and *cis*-2-benzyl-5-bromomethyl-5-methyl-2-oxo-1,3,2-dioxaphosphorinan gave 13% of the corresponding 5,5-dimethyl ester (XVII): the *trans*-form gave only 3% of the same product under similar conditions. In each case the major product probably contained P(O)CHSn units, and the results do not necessarily prove identity of conformation at phosphorus in the 5-bromomethyl esters.

EXPERIMENTAL

Light petroleum refers to the fraction b.p. 60—80° unless otherwise specified. Evaporations were carried out at 55° *in vacuo*. G.l.c. was carried out on columns (3 ft.) of 20% silicone E 301 on 40—60 mesh brick. Preparative column chromatography employed (A) silica gel (100—200 mesh) or (B) silica gel (Merck; for t.l.c.) with the solvent systems (C) benzene with increasing amounts of ether, and (D) ethyl methyl ketone–hexane (1 : 1). T.l.c. employed silica gel (B) with solvent systems (D) or (E) benzene–acetic acid–hexane (1 : 1 : 2). Spots were located with an ethanolic iodine spray.

I.r. spectra were recorded for films or potassium bromide discs with a Perkin-Elmer 237 instrument: the use of a Perkin-Elmer 521 instrument is recorded separately. ^1H

TABLE 1

T.l.c. of cyclic phosphonates

Solvent:	(D)		(E)	
	cis	*trans*	*cis*	*trans*
(V)	0·55	0·3	0·5	0·5
(VI)	0·45	0·25	0·7	0·75
(VII)	0·85		0·9	
(VIII)	0·85		0·95	
(X)	0·4	0·25	0·35	0·4
(XI)	0·5	0·3	0·55	0·7
(XII)	0·15	0·15	0·15	0·15
(XIII)	0·35	0·25	0·45	0·2
(XVII)	0·35		0·55	
(XVIII)	0·35		0·7	
(XIX)	0·7		0·95	

Pairs of isomers [with or without analogues (XVII)—(XIX)] were run on the same plates.

N.m.r. spectra were measured with a Varian A60 spectrometer for solutions containing 100—150 mg. per ml. in benzene or deuteriochloroform with tetramethylsilane as internal standard. Compounds so examined were of analytical purity and chromatographically homogeneous. Variable temperature results were obtained with a Varian V-6040 probe.

cis-2-*Benzyl*-5-*chloromethyl*-5-*ethyl*-2-*oxo*-1,3,2-*dioxaphosphorinan*.—This (84%) had m.p. 114—115° (from carbon tetrachloride) (lit.,[2] 118°), $\nu_{max.}$ 1271 cm.$^{-1}$ (P=O).

cis-5-*Chloromethyl*-5-*ethyl*-2-*oxo*-2-α-*phenylethyl*-1,3,2-*dioxaphosphorinan*.— 4-Ethyl-2,6,7-trioxa-1-phosphabicyclo-[2,2,2]octane (16·0 g.) and α-phenylethyl chloride (16·0 g.) were heated together at 160—170° (bath) for 20 hr. The cooled residue was extracted with light petroleum and then with ethanol. The ethanol was evaporated off and the residual crude ester was chromatographed on silica gel (A) in solvent (C). The *cyclic ester* (1·6 g., 5%) had m.p. 122—123° (from carbon tetrachloride), $\nu_{max.}$ 1272 cm.$^{-1}$ (P=O) (Found: C, 55·75; H, 6·9; P, 10·25. $C_{14}H_{20}ClO_3P$ requires C, 55·5; H, 6·6; P, 10·25%).

5-*Chloromethyl*-5-*methyl*-2-*oxo*-2-α-*phenylethyl*-1,3,2-*dioxaphosphorinan*.—(*a*) A mixture of 4-methyl-2,6,7-trioxa-1-phosphabicyclo[2,2,2]octane (7·4 g.) and α-phenylethyl chloride (7·8 g.) was heated at 150—160° (bath) for 6 hr. The viscous liquid was extracted first with light petroleum and then with ethanol, and the latter extract was evaporated. Chromatography of the residue (11 g.) on silica gel (A) with solvent (C) gave the cis-*ester* (3·1 g., 22%), m.p. 168° (from benzene–light petroleum), $\nu_{max.}$ 1258 (P=O), 1058, and 1017 (POC) cm.$^{-1}$ (Found: C, 54·25; H, 6·1; P, 10·8. $C_{13}H_{18}ClO_3P$ requires C, 54·05; H, 6·25; P, 10·75%).

(*b*) A mixture of α-phenylethylphosphonic dichloride [7] (7·5 g.), 2-chloromethyl-2-methylpropane-1,3-diol (4·6 g.) and pyridine (6·0 g.) in benzene (50 ml.) was heated under reflux for 7 hr. The solution was worked up in the usual way [5,7] to give a mixture of *cis*- and *trans*-isomers (13 g.). Addition of ether to a solution of the mixed isomers in benzene yielded the cis-*ester* (3·0 g.). The mother liquors were evaporated and the residue was chromatographed on silica gel (A) with solvent (C) giving the trans-*ester* (3·6 g.), m.p. 101° (from carbon tetrachloride–light petroleum), $\nu_{max.}$ 1272 (P=O), 1052, and 1012 (POC) cm.$^{-1}$ (Found: C, 54·1; H, 6·25; P, 10·85%).

2-*Benzyl*-5-*chloromethyl*-5-*methyl*-2-*oxo*-1,3,2-*dioxaphosphorinan*.—(*a*) A mixture of the methyl bicyclic phosphite (3·0 g.) and benzyl chloride (2·5 g.) was heated at 170° (bath) for 14 hr. and chromatographed on silica gel (A) with solvent (C), giving the cis-*ester* (0·5 g., 9%), m.p. 156·5—157° (from carbon tetrachloride), $\nu_{max.}$ 1258 (P=O), 1054, and 1017 (POC) cm.$^{-1}$ (Found: C, 52·2; H, 5·9; P, 11·35. $C_{12}H_{16}ClO_3P$ requires C, 52·45; H, 5·9; P, 11·25%).

(*b*) A mixture of the isomers obtained from benzylphosphonic dichloride [5·3 g.; prepared (71%) from diethyl benzylphosphonate and phosphorus pentachloride; b.p. 110—114°/0·7 mm. (lit.,[8] b.p. 130°/2 mm.)], 2-chloromethyl-2-methylpropane-1,3-diol (3·45 g.), and pyridine (4·0 g.) was taken up in hot chloroform–benzene, which when cooled deposited the *cis*-stereoisomer (2·0 g.). The mother liquors were evaporated and the residue was chromatographed on silica gel (A) with solvent (C) to give the trans-*ester* (1·65 g.), m.p. 110—111° (from benzene–light petroleum), $\nu_{max.}$ 1266 (P=O), 1051, and 1007 (POC) cm.$^{-1}$ (Found: C, 51·8; H, 5·9; P, 11·3%).

2-*Benzyl*-5-*bromomethyl*-5-*methyl*-2-*oxo*-1,3,2-*dioxaphosphorinan*.—(*a*) Reaction between methyl bicyclic phosphite (5·2 g.) and benzyl bromide (6·0 g.) at 140—160° (bath) for 17 hr. gave the cis-*ester* (1·3 g., 17%), m.p. 170—171° (from carbon tetrachloride), $\nu_{max.}$ 1256 (P=O), 1052, and 1016 (POC) cm.$^{-1}$ (Found: C, 45·5; H, 4·85; P, 9·7. $C_{12}H_{16}BrO_3P$ requires C, 45·15; H, 5·05; P, 9·7%).

(*b*) The mixture of isomers prepared from benzylphosphonic dichloride (4·2 g.), 2-bromomethyl-2-methylpropane-1,3-diol (3·6 g.), and pyridine (3·2 g.) was crystallised from benzene to give the cis-*ester* (0·9 g.). The mother liquors were evaporated and the residue was chromatographed on silica gel (B) with solvent (D) to give the trans-*ester* (0·85 g.), m.p. 122—123° (from cyclohexane), $\nu_{max.}$ 1289 (P=O), 1046, and 1010 (POC) cm.$^{-1}$ (Found: C, 45·0; H, 5·25; P, 9·5%).

Reaction between 2-*Benzyl*-5-*bromomethyl*-5-*methyl*-2-*oxo*-1,3,2-*dioxaphosphorinan and Tributyltin Hydride*.—(*a*) The *cis*-ester (319 mg.) and tributyltin hydride (0·5 g.) were heated together at 160—170° (bath) for 6 hr. The cooled mixture was extracted with boiling cyclohexane; the cooled extract deposited 2-benzyl-5,5-dimethyl-2-oxo-1,3,2-dioxaphosphorinan (31 mg., 13%), identified by m.p., mixed m.p., and i.r. spectrum.

(*b*) In the same way, the *trans*-ester yielded the same 5,5-dimethyl ester (7 mg., *ca.* 3%).

2-*Methyl*-2-p-*tolylsulphonyloxymethylpropane*-1,3-*diol*.— Toluene-*p*-sulphonyl chloride (190 g.) was added in portions to a solution of 1,1,1-tris(hydroxymethyl)ethane (120 g.) in pyridine (80 g.), with the temperature maintained at *ca.* 80—90°. Heating was continued for 0·5 hr. after the addition was complete. Water (2 vols.) was added, and the mixture was extracted with ethyl acetate. Evaporation of the dried extract gave the *diol* (95 g.), m.p. 93—95° (from benzene), $\nu_{max.}$ 3240 (OH) and 1172 (SO_2) cm.$^{-1}$ (Found: C, 52·9; H, 6·85. $C_{12}H_{18}SO_5$ requires C, 52·5; H, 6·6%).

2-*Benzyl*-5-*methyl*-2-*oxo*-5-p-*tolylsulphonyloxymethyl*-1,3,2-*dioxaphosphorinan*.—A solution of 2-methyl-2-*p*-tolylsulphonyloxymethylpropane-1,3-diol (13·6 g.) and pyridine (7·9 g.) in benzene (25 ml.) was added to benzylphosphonic dichloride (10·0 g.) in benzene (50 ml.). The mixture was heated under reflux for 1·5 hr. and worked up in the usual way to give a mixture of stereoisomers as an oil (16 g.). Crystallisation of this from methanol gave *cis*-2-benzyl-5-methyl-2-oxo-5-*p*-tolylsulphonyloxymethyl-1,3,2-dioxaphosphorinan (2·8 g.), m.p. 169—169·5° (from methanol) (lit.,[3] 171°), $\nu_{max.}$ 1262 (P=O) and 1172 (SO_2) cm.$^{-1}$ (Found: C, 55·3; H, 5·75; P, 7·65. Calc. for $C_{19}H_{23}O_6PS$: C, 55·6; H, 5·65; P, 7·55%). Evaporation of the mother liquors and chromatography of the residue on silica gel (B) with solvent (C) gave more *cis*-ester (4·4 g.), followed by the trans-*stereoisomer* (2·6 g.), m.p. 103—104° (from benzene–light petroleum), $\nu_{max.}$ 1282 (P=O) and 1178 (SO_2) cm.$^{-1}$ (Found: C, 55·0; H, 5·75; P, 7·85%).

Reaction between 2-*Benzyl*-5-*methyl*-2-*oxo*-5-p-*tolylsulphonyloxymethyl*-1,3,2-*dioxaphosphorinan and Lithium Bromide*.—(*a*) The *cis*-dioxaphosphorinan (1·05 g.) in 2-ethoxyethanol (20 ml.) was heated under reflux with lithium bromide monohydrate (0·5 g.) for 4 hr. The solution was poured into water; chromatographically pure *cis*-2-benzyl-5-bromomethyl-5-methyl-2-oxo-1,3,2-dioxaphosphorinan (0·50 g., 94%) separated and was identified by m.p., mixed m.p., and i.r. spectrum.

(*b*) In the same way, the *trans*-tosylate (128 mg.) gave chromatographically pure *trans*-2-benzyl-5-bromomethyl-5-methyl-2-oxo-1,3,2-dioxaphosphorinan (12 mg., 17%).

Action of Heat on 2-*Benzyl*-5-*bromomethyl*-5-*methyl*-2-*oxo*-1,3,2-*dioxaphosphorinan*.—*cis*- and *trans*-2-Benzyl-5-bromomethyl-5-methyl-2-oxophosphorinan were heated at 160—180° (bath) for 3 hr. T.l.c. of the products showed that no interconversion had taken place; this was confirmed by m.p. and mixed m.p.

2-*Benzyl*-5,5-*bischloromethyl*-2-*oxo*-1,3,2-*dioxaphosphorinan*.—Prepared from 2,2-bischloromethylpropane-1,3-diol (3·45 g.), benzylphosphonic dichloride (4·1 g.), and pyridine

[8] A. M. Kinnear and E. H. Perrin, *J. Chem. Soc.*, 1952, 3437.

(3·2 g.) in benzene, the compound (45%) had m.p. 125·5—127° (from benzene) (lit.,[2] 124—125°), $\nu_{max.}$ 1264 (P=O), 1073, and 1003 (POC) cm.$^{-1}$ (Found: C, 46·4; H, 5·0; P, 10·25. Calc. for $C_{12}H_{15}Cl_2O_3P$: C, 46·7; H, 4·9; P, 10·0%).

2,5-*Dimethyl*-2-*oxo*-5-p-*tolylsulphonyloxymethyl*-1,3,2-*dioxaphosphorinan*.—(*a*) A mixture of methyl bicyclic phosphite (14·8 g.) and methyl toluene-*p*-sulphonate (18·6 g.) was heated for 5 hr. at 50—70°, 5 hr. at 90—110°, and 13 hr. at 150—160°. The odour of the phosphite was still discernible. The mixture was extracted with light petroleum, and the gummy, phosphite-free residue was chromatographed on silica gel (B) with chloroform to give cis-2,5-*dimethyl*-2-*oxo*-5-p-*tolylsulphonyloxymethyl*-1,3,2-*dioxaphosphorinan* (2·15 g., 6·5%), m.p. 109—109·5° (from ethyl acetate–light petroleum), $\nu_{max.}$ 1268 (P=O), 1174 (SO_2), 1070, and 1020 (POC) cm.$^{-1}$ (Found: C, 47·2; H, 5·8; P, 9·2. $C_{18}H_{19}O_6PS$ requires C, 46·7; H, 5·7; P, 9·25%). Rapid heating of the initial mixture caused violent reaction and decomposition.

(*b*) A solution of methylphosphonic dichloride (2·7 g.) in benzene (10 ml.) was added in portions to 2-methyl-2-*p*-tolylsulphonyloxymethylpropane-1,3-diol (5·5 g.) and pyridine (3·2 g.) in benzene (15 ml.). The solution was heated for 1 hr. and worked up in the usual way. The resultant oil (8·2 g.) was chromatographed on silica gel (B) with solvent (C) giving the *cis*-ester (1·7 g.), m.p. 108—110°. Elution with chloroform then gave the trans-p-*tolylsulphonyldioxaphosphorinan* (1·6 g.), m.p. 131—132° (from ethyl acetate–light petroleum) $\nu_{max.}$ 1267 (P=O), 1170 (SO_2), 1068, and 1016 (POC) cm.$^{-1}$ (Found: C, 46·8; H, 5·65; P, 8·9%).

5-*Bromomethyl*-2,5-*dimethyl*-2-*oxo*-1,3,2-*dioxaphosphorinan*.—(*a*) *cis*-2,5-Dimethyl-2-oxo-5-*p*-tolylsulphonyloxymethyl-1,3,2-dioxaphosphorinan (335 mg.) and lithium bromide monohydrate (164 mg.) in dimethylformamide (5 ml.) were heated under reflux for 4 hr.; the solution was evaporated *in vacuo* and the residue was taken up in chloroform and washed with water. Evaporation of the organic solvent gave chromatographically pure cis-5-*bromomethyl ester* (160 mg., 65%), m.p. 92—94° (from ether), $\nu_{max.}$ 1256 (P=O), 1085, and 1010 (POC) cm.$^{-1}$ (Found: C, 29·75; H, 5·15. $C_6H_{12}BrO_3P$ requires C, 29·65; H, 5·0%).

(*b*) By the same procedure the trans-*tosylate* (323 mg.) gave chromatographically pure trans-5-*bromomethyl ester* (130 mg., 55%), m.p. 99—99·5° (from ether), $\nu_{max.}$ 1258 (P=O) 1085, 1046, and 1010 (POC) cm.$^{-1}$ (Found: C, 30·2; H, 4·7; P, 12·45. $C_6H_{12}BrO_3P$ requires P, 12·45%).

cis-5-*Chloromethyl*-5-*methyl*-2-*oxo*-2-*triphenylmethyl*-1,3,2-*dioxaphosphorinan*.—This had m.p. 190—191° (from acetone) (lit.,[3] 201°), $\nu_{max.}$ 1234 (P=O), 1038, and 1007 (POC) cm.$^{-1}$.

cis-5-*Bromomethyl*-5-*methyl*-2-*oxo*-2-*triphenylmethyl*-1,3,2-*dioxaphosphorinan*.—A mixture of methyl bicyclic phosphite (1·5 g.) and bromotriphenylmethane (3·2 g.) was heated at 170—180° (bath) for 1 hr., yielding the desired *ester* (2·8 g.), m.p. 217° (from ethanol), $\nu_{max.}$ 1232 (P=O), 1038, and 1002 (POC) cm.$^{-1}$ (Found: C, 61·3; H, 5·1; P, 6·6%. $C_{24}H_{24}BrO_3P$ requires C, 61·15; H, 5·1; P, 6·6%).

5-*Chloromethyl*-2-*cyclohexyl*-5-*methyl*-2-*oxo*-1,3,2-*dioxaphosphorinan*.— 2-Chloromethyl-2-methylpropane-1,3-diol, cyclohexylphosphonic dichloride, and pyridine in benzene gave *isomer* (1) m.p. 162·5—163·5 (from benzene), $\nu_{max.}$ 1253 (P=O) cm.$^{-1}$ (Found: C, 49·75; H, 7·8. $C_{11}H_{20}ClO_3P$ requires C, 49·5; H, 7·55%). Concentration of the benzene mother liquors then gave *isomer* (2), m.p. 134—135° (from ethyl acetate–light petroleum), $\nu_{max.}$ 1252 (P=O) cm.$^{-1}$ (Found: C, 49·7; H, 7·6%).

5-*Chloromethyl*-5-*methyl*-2-*oxo*-2-*trichloromethyl*-1,3,2-*dioxaphosphorinan*.—Reaction of 2-chloromethyl-2-methyl-1,3-propane-diol, trichloromethylphosphonic dichloride, and pyridine in benzene gave *isomer* (1), m.p. 172—173° (from benzene), $\nu_{max.}$ 1288 (P=O), 1054, and 1004 (POC) cm.$^{-1}$ (Found: C, 23·9; H, 3·05; P, 10·45. $C_6H_9Cl_4O_3P$ requires C, 23·9; H, 2·9; P, 10·3%). The mother liquors were evaporated and the residue was chromatographed on silica gel (A) with solvent (C) to give *isomer* (2), m.p. 155—156° (from benzene–light petroleum), $\nu_{max.}$ 1283 (P=O), 1054, and 1012 (POC) cm.$^{-1}$ (Found: C, 24·3; H, 3·0; P, 10·6%).

Spectroscopy of the Acyclic Esters.—(*a*) Diethyl methylphosphonate: $J_{PO\cdot CH}$ ±8·7 Hz in $CDCl_3$;[9] (*b*) diethyl benzylphosphonate; found $J_{PO\cdot CH}$ ±7·25 Hz in $CDCl_3$ (lit.,[10] 8·2 Hz); (*c*) diethyl triphenylmethylphosphonate, m.p. 113—114° (from benzene–light petroleum); $J_{PO\cdot CH}$ ±7·2 Hz in $CDCl_3$.

RESULTS AND DISCUSSION

All of the compounds described show the features expected[11] for the assigned chemical structures. Of particular interest are the chemical shifts for the methyl and halogenomethyl groups, and the patterns produced by the methylene protons of the 1,3,2-dioxaphosphorinan ring. The *cis*-stereoisomers of the 5-chloromethyl-5-methyl compounds (V)—(VII) gave particularly satisfactory spectra in which the ring axial protons are indicated by four broad peaks and the equatorial protons by four higher-field triplets; a detailed analysis of these spectra has been given.[11] Unfortunately the *trans*-stereoisomers of compounds (V) and (VI) [that of compound (VII) was not available] gave spectra which were unsuitable for more detailed analysis, without decoupling. *cis*- and *trans*-Stereoisomers of compounds (X)—(XIII) in both chloroform and benzene also gave spectra suitable for detailed analysis. The data are listed in Table 2.

The use of benzene instead of chloroform produces some marked changes in the spectra at room temperature, particularly in the chemical shifts of methyl and halogenomethyl groups at C-5, but the effects are less marked on the tosyloxy-protons and on the spin–spin coupling between phosphorus and side-chain methylene and methine protons. In some cases, *e.g.* (IX), (X), and *cis*-(XIII), a greater resolution of the phosphorus-ring methylene resonances was obtained.

For *gem*-5-dimethyl-1,3,2-dioxaphosphorinans, $\Delta\delta$ (defined as chemical shift in deuteriochloroform *minus* that in benzene) is greater for the equatorial methyl than for the axial methyl.[7] For the aralkyl phosphonates (V) and (VI), $\Delta\delta$ is greater for the halogenomethyl group than for the methyl group in the *cis*-isomers, whereas the reverse is true for the *trans*-isomers; in other cases where lack of solubility prevented measurements [*e.g.* for *cis*-(XI)] or where the *trans*-isomers was not available [*e.g.* (VII) and (VIII)], the results do not suggest a

[9] J. L. Burdett and L. L. Burger, *Canad. J. Chem.*, **1966**, **44**, 111.

[10] T. H. Siddall, tert., and C. A. Prohaska, *J. Amer. Chem. Soc.*, 1962, **84**, 3467.

[11] K. D. Bartle, R. S. Edmundson, and D. W. Jones, *Tetrahedron*, 1967, **23**, 1701.

TABLE 2

^{1}H N.m.r. data for 5,5-disubstituted 2-oxo-1,3-dioxaphosphorinans

Compound	Config.	Solvent	Chemical shifts (p.p.m.) 5-CH_3	Δδ	R^{2}CH_2	Δδ	R^3	4- and 6-CH_2 δ$_A$	δ$_B$	Coupling constants (Hz) $\|^2J_{PH}\|_A$	$\|^3J_{PH}\|^{ax}$	$\Sigma\|^3J_{PH}\|$	$\|^2J_{HH}\|$
(IV)	*cis*	$CDCl_3$			3·57		1·70			18			
						0·52							
		PhH			3·05		1·60	3·2—4·3		18·5			
(V)	*cis*	$CDCl_3$	0·82(0·9)		3·57(1·2)		3·33	4·32	3·78	21	12·0	11·0	23·0	11·6
				0·42		0·62								
		PhH [a]	0·40		2·95		2·95	3·0—4·1		21				
	trans [b]	$CDCl_3$	0·86(1·0)		3·10(1·0)		3·22	3·5—4·5		21				
				0·59		0·26								
		PhH	0·27		2·84		2·98	3·2—4·2		21				
(VI)	*cis*	$CDCl_3$	0·87(0·8)		3·56(0·9)		1·53	2·9—4·3		18·5				
				0·41		0·65								
		PhH [c]	0·46		2·91		1·52	3·0—4·1		18·5				
	trans	$CDCl_3$	0·84(1·2)		3·10(1·3)		1·65	3·2—4·4		18·5				
				0·62		0·19								
		PhH	0·22(1·0)		2·91(1·0)		1·53	3·2—4·4		18·5				
(VII)	*cis*	$CDCl_3$	0·79(1·0)		3·68(1·2)			4·33	3·42		6·8	14·9	21·7	11·3
				0·35		0·56								
		PhH [c]	0·44(1·1)		3·12(1·0)			3·98 *	3·00 * [c]					
(VIII)	*cis*	$CDCl_3$	0·82(1·0)		3·50			4·35 *	3·44 *					
				0·40		0·62								
		PhH [d]	0·42(1·3)		2·88			4·02 *	3·04 * [d]					
(IX)	*cis*	$CDCl_3$			3·45		3·30	4·3	3·7	21·4				
					3·22			4·6	4·2					
		PhH [e]			2·95		3·02	4·0	3·6	21·2				12·0
					2·97			4·3	3·9					
(X)	*cis*	$CDCl_3$ [f]	0·77(1·1)		3·93		3·25	4·18	3·71	21	13·0	10·4	23·4	11·6
				0·36		0·26								
		PhH [g]	0·41		3·67									
	trans	$CDCl_3$ [h]	0·79(1·1)		3·76		3·16	4·33	3·94	22	12·1	11·5	23·6	11·4
				0·54		0·01								
		PhH [i]	0·25		3·75		2·92	3·98	3·48	21·9	3·85	18·75	22·6	11·6
(XI)	*cis*	$CDCl_3$	0·84		3·42		3·30	4·22	3·88	21·2	11·6	10·0	21·6	11·4
		PhH [g]												
	trans	$CDCl_3$	0·85(1·0)		2·92		3·27	4·37	3·97	21·8	3·2	19·4	22·6	11·3
				0·61		0·21								
		PhH	0·24(1·0)		2·71		2·98	4·06	3·52	21·9	3·6	19·25	22·85	11·4
(XII)	*cis*	$CDCl_3$ [j]	1·05(0·9)		4·05		1·56	4·21	3·85	16·8	14·45	8·95	23·4	11·4
				0·44		0·21								
		PhH [k]	0·61(1·0)		3·84		1·09	3·71	3·47	16·7	11·8	11·8	23·6	11·5
	trans	$CDCl_3$ [l]	1·03(1·0)		4·05		1·56	4·23	3·88	17·1	11·7	8·9	20·6	11·6
				0·34		0·13								
		PhH [m]	0·69(1·0)		3·92		1·23	3·3—4·2		16·8				
(XIII)	*cis*	$CDCl_3$	0·98(1·1)		3·63		1·60	4·33	4·08	17·9	4·65	18·9	23·55	11·5
				0·59		0·46								
		PhH	0·39		3·17		1·10	4·08	3·58	17·7	4·55	18·25	22·8	11·4
	trans	$CDCl_3$	1·13(1·1)		3·53		1·60	4·36	3·98	17·2	14·5	8·7	23·2	11·6
				0·55		0·58								
		PhH	0·58		2·95		1·10	3·93	3·39	16·7	13·3	9·3	22·6	11·4
(XIV)	Isomer (1)	$CDCl_3$	1·21		3·56		1·1—2·2	3·3—4·5						
				0·44		0·77								
		PhH [e]	0·77		2·79		0·8—2·2	3·0—4·3						
	Isomer (2)	$CDCl_3$	0·87(1·3)		3·71		1·0—2·3	3·5—4·6						
				0·52		0·3								
		PhH [e]	0·35(1·0)		3·41		0·7—2·2	3·3—4·2						
(XV)	Isomer (1)	$CDCl_3$	1·04		3·88			4·3—4·8 [o]						
				0·80		0·56								
		PhH [n]	0·24		3·32			4—3·7 [p]						
	Isomer (2)	$CDCl_3$	1·41		3·57			4·15—4·9						
				0·63		0·81								
		PhH [n]	0·78		2·76			4·05—4·25	3·5—3·9					

[a] Containing 20% (v/v) $CDCl_3$; for benzene containing 30% [$^2H_6$]Me_2SO, δ_{Me} 0·67, δ_{ClCH_2} 3·48, δ_{CH_2Ph} 3·20 p.p.m., $^2J_{PH}$ 20·5 Hz. [b] In PhBr, δ_{Me} 0·52, δ_{CH_2Cl} 2·98, δ_{CH_2Ph} 3·10 p.p.m. In [$^2H_6$]Me_2CO, the corresponding values are 0·94, 3·43, and 3·31 p.p.m. [c] Containing 20% (v/v) $CDCl_3$. [d] Containing 10% (v/v) $CDCl_3$; too insoluble in 1 : 1 benzene–chloroform for other measurements. In PhBr, δ_{Me} 0·55, δ_{CH_2Br} 3·15, δ_{CH_A} 4·06, δ_{CH_B} 3·13 p.p.m. [e] Containing 30% $CDCl_3$ (v/v). [f] δ_{ArCH_3} 2·42 p.p.m. [g] Compound too insoluble even in 1 : 1 benzene–chloroform. [h] δ_{ArCH_3} 2·45 p.p.m. [i] δ_{ArCH_3} 1·92 p.p.m. [j] δ_{ArCH_3} 2·47 p.p.m. [k] Containing 20% (v/v) $CDCl_3$; δ_{ArCH_3} 2·04 p.p.m. [l] δ_{ArCH_3} 2·47 p.p.m. [m] Containing 50% (v/v) $CDCl_3$; δ_{ArCH_3} 2·17 p.p.m. [n] Containing 10% (v/v) $CDCl_3$. [o] Intense peak (2H) at 4·70 p.p.m. [p] Intense peak (2H) at 3·94 p.p.m.

* Visual inspection of spectrum (*i.e.* not calculated from ABX analysis).

contrary behaviour. The same behaviour has previously been observed for *cis*-2-chloro-5-chloromethyl-5-methyl-2-oxo-1,3,2-dioxaphosphorinan (configuration known by analogy [12]) and the stereoisomeric 5-halogenomethyl-5-methyl-2-oxo-2-piperidino-1,3,2-dioxaphosphorinans (XVI);[5] $\Delta\delta$ is here greater for the methyl than for the halogenomethyl when the latter is (predominantly) axially situated, the reverse being true for (predominantly) equatorially sited halogenomethyl. Moreover, stereoisomeric pairs of cyclohexyl- (XIV) and trichloromethyl- (XV) phosphonates show the same behaviour, although configurations have not been assigned by chemical means. The contrary holds for the methyl phosphonates (XIII), while for those compounds [(X) and (XII)] possessing an aromatic ring in the C-5 position $\Delta\delta$ is greater for the methyl than for the substituted methyl group irrespective of configuration.

The data presented show the following additional features:

(i) Changes in solvent or substitution at C-5 produces little variation in $|^2J_{PH}|$ for the side-chains at phosphorus.

(ii) No variation in $|^2J_{HH}|$ for the phosphorus-ring methylene protons. The value quoted elsewhere [3] for a monocyclic 1,3,2-dioxaphosph(v)orinan is in keeping with our averaged value, 11·5 Hz, irrespective of solvent. Conformational equilibria would be expected to have little, if any, effect on this value.

(iii) No significant alteration in C-5 methyl line width with variation in solvent or substitution at C-5 or at phosphorus.

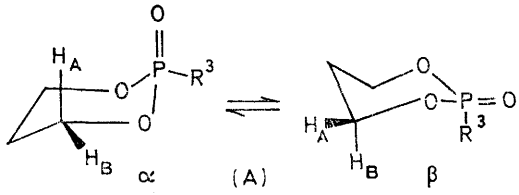
(iv) For the aralkyl phosphonates (IV)—(VIII) and (XI) in chloroform solution, there is very little variation of the chemical shift of the C-5 methyl with change of aralkyl group for a given solvent. On the other hand, the chemical shift of the halogenomethyl group (*ca.* 3·1 for the *trans*- and *ca.* 3·6 p.p.m. for the *cis*-forms, with bromomethyl lying *ca.* 0·2 p.p.m. upfield from chloromethyl) appears to be characteristic of configuration. For the same compounds in benzene solution, the chemical shift of the methyl group (*ca.* 0·45 for the *cis*- and *ca.* 0·25 p.p.m. for the *trans*-form) appears to characterise configuration.

(v) $|J_{PO\cdot CH_A}| + |J_{PO\cdot CH_B}|$ is approximately constant.

Arguments applied previously to the C-5 *gem*-dimethyl series based on a consideration of chemical shift data were essentially (*a*) that the triphenylmethyl group in the axial position was sterically unacceptable, (*b*) that the benzyl and phenylethyl groups show the same shielding behaviour as does the triphenylmethyl group, and hence (*c*) that the benzyl and phenylethyl phosphonates also possess equatorial aralkyl groups.[7] It is reasonable therefore to suppose that for the present series the more stable, major, conformer possesses equatorial aralkyl groups. The triphenylmethyl group should then exhibit a greater shielding of the equatorial methylene protons [relative to the axial protons, and relative to the methylene protons of (XIII)], which is indeed observed. Comparison of (XIII) with (XI) shows the effect of a single aromatic ring in the substituent at phosphorus; equatorial methylene protons are shielded to a greater extent (0·2 p.p.m.) than are the axial protons (0·11 p.p.m.), while the values for three aromatic rings are 0·0 p.p.m. (axial protons) and 0·64 p.p.m. (equatorial protons). In the case of the triphenylmethyl phosphonates, while the distances between the two ring-proton positions and the centre of a benzene ring are not greatly different, the angles presented by the plane of the rings are, if symmetrical geometry is assumed. Thus, the *trans*-forms of the aralkyl phosphonates should possess (predominatly) axial halogenomethyl groups, which should be shielded relative to those of the *cis*-isomers; this is so for compounds (V), (VI), and (X).

Variable temperature studies on the ^1H n.m.r. spectra were hampered by the low solubility of many of the potentially most interesting compounds. Compounds which have been examined include (comments refer to the ring methylene region of the spectrum): (*a*) (V), no variation from −30 to 100° in chloroform and bromobenzene, but some variation between −30 and −70° in deuterioacetone; (*b*) (VII), no variation between 0 and −60° in deuterioacetone–deuteriochloroform (1 : 1); (*c*) (VIII), no variation between 30 and 100° in bromobenzene; (*d*) *trans*-(X), no variation in deuterioacetone between 30 and −70°; (*e*) *cis*- and *trans*-(XIII), marked variation between 30 and −70° in deuteriochloroform or deuterioacetone. In all cases variation of temperature produced a slight change in positions of methyl resonances. The low temperature variation of the methylene patterns for (V) and (XIII) are illustrated in Figures 1 and 2, respectively and demonstrate the conformational mobility of the phosphorus-containing ring in these compounds.[13] In other cases conformational mobility may be real but not apparent because of overwhelming shielding effects of aromatic substituents at C-5 or at phosphorus.

The second method of approach is based on a treatment of spin–spin coupling constants. On the basis of general theory [14] it can be shown that for the conformational equilibrium (A) the time-averaged coupling con-



stants $\langle {}^3J_{PH}\rangle$ can be defined by equations (1) and (2).

$$\langle {}^3J_{PH_A}\rangle = N({}^3J_{PH_A})_\alpha + (1-N)({}^3J_{PH_A})_\beta \quad (1)$$

$$\langle {}^3J_{PH_B}\rangle = N({}^3J_{PH_B})_\alpha + (1-N)({}^3J_{PH_B})_\beta \quad (2)$$

and hence

$$\langle {}^3J_{PH_A} + {}^3J_{PH_B}\rangle = N({}^3J_{PH_A} + {}^3J_{PH_B})_\alpha + (1-N)({}^3J_{PH_A} + {}^3J_{PH_B})_\beta \quad (3)$$

[12] T. A. Beineke, *Chem. Comm.*, 1966, 860.
[13] R. S. Edmundson, *Tetrahedron Letters*, 1969, 1905.
[14] W. A. Thomas, *Annual Rev. N.M.R. Spectroscopy*, 1968, **1**, 43.

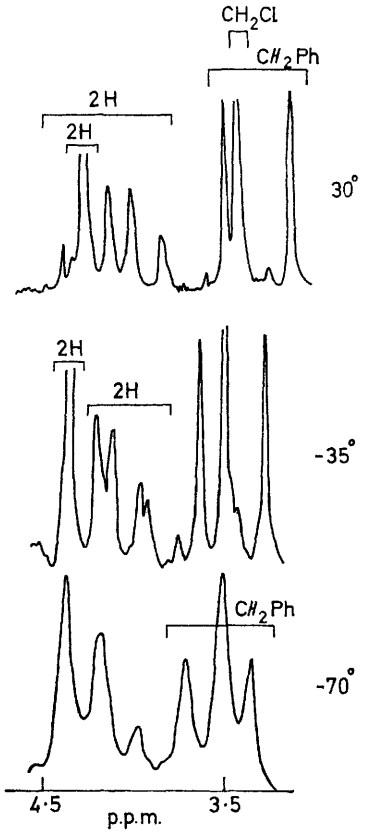


FIGURE 1 ^{1}H N.m.r. spectrum of *trans*-2-benzyl-5-chloromethyl-5-methyl-2-oxo-1,3,2-dioxaphosphorinan in $CDCl_3$–$(CD_3)_2CO$ (1 : 1)

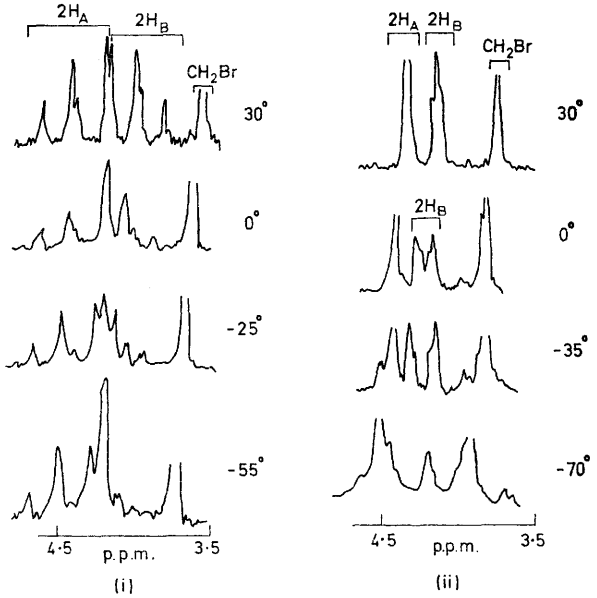


FIGURE 2 ^{1}H N.m.r. spectrum of *trans*-5-bromomethyl-2,5-dimethyl-2-oxo-1,3,2-dioxaphosphorinan (i) in $CDCl_3$ and (ii) in $(CD_3)CO$

In addition, with consideration of the rotameric forms of an acyclic P–O–C–H system, the time-averaged coupling constant can be defined by

$$\langle {}^3J_{PH}\rangle = (2/3)(J_G + J_{G'}) + (1/3)(J_T + J_{T'}) \quad (4)$$

which if free rotation is completely possible, simplifies to

$$\langle {}^3J_{PH}\rangle = (2/3)J_G + (1/3)J_T \quad (5)$$

where G and T represent *gauche* and *trans* situations.

Similarly, if for the cyclic system $J_G = J_{G'}$ and $J_T = J_{T'}$ then it follows that

$${}^3J_{PH_A} = J_G = 3\langle {}^3J_{PH}\rangle - ({}^3J_{PH_A} + {}^3J_{PH_B}) \quad (6)$$

$${}^3J_{PH_B} = J_T = 2({}^3J_{PH_A}{}^3J_{PH_B}) - 3\langle {}^3J_{PH}\rangle \quad (7)$$

In order to evaluate J_G and J_T, and hence N, the proportion of a given conformer, values of $\langle {}^3J_{PH}\rangle$ have been noted for diethyl phosphoryl compounds (see Experimental section). Values thus calculated for the percentage composition (major conformer) of the compounds studied are given in Table 3, in which values

TABLE 3

Conformational composition of cyclic phosphonates in chloroform solution; % of major conformer; values of J_T in parentheses

R^2		R^3		
		Me	CH_2Ph	CPh_3
Cl	*cis*		52 (24·25)	70 (21·8)
	trans			
Br	*cis*	88 (21·0)	55 (21·45)	*ca.* 70
	trans	67 (20·3)	83 (23·45)	
TsO	*cis*	65 (20·7)	55 (25·05)	
	trans	65 (15·1)	50 (25·45)	

for J_T are also included; these may be compared with the 20 Hz recorded elsewhere for this situation [15] in rigid systems. Some justification for this treatment appears to be given by the constancy of $J_{PO\cdot CH_A} + J_{PO\cdot CH_B}$. The average for twenty-one phosphonates described here and elsewhere [11] is 22·4 Hz. The value of *ca.* 30 Hz reported for 1-phenyltrimethylene phosphate [16] (assumed to be conformationally rigid) suggests a difference caused by the benzene ring or by the pattern of ring substitution.

That the conformational preference for the triphenylmethyl group is only moderate is surprising; it may be a reflection of the lack of substituents at positions 1 and 3 coupled with the flattening and broadening at the phosphorus end of the dioxaphosphorinan ring as found for related compounds.[12,17] In this respect the conformational immobility of compounds (VII) and (VIII), as judged from temperature variation studies on the n.m.r. spectra, may be apparent rather than real.

In general, coupling constants for chloroform solutions are similar to those for benzene solutions, but the 5-*p*-tolylsulphonyloxy derivatives appear to be exceptions. Values for the stereoisomers of (X) and (XII) could not be obtained because of poor solubility. The values quoted suggest pronounced changes in the conformational equilibria with changes of solvent, and this may be associated with the formation of the benzene–substrate

[15] J. G. Verkade and R. W. King, *Inorg. Chem.*, 1962, **4**, 948.
[16] M. Tsuboi, F. Kuriyagawa, K. Matsuo, and Y. Kyogoku, *Bull. Chem. Soc. Japan*, 1967, **40**, 1813.
[17] H. J. Geise, *Rec. Trav. chim.*, 1967, **86**, 362.

complexes. Percentages of the major conformer for benzene solutions of (X) and (XII) are 83 and 50 respectively.

Coupling constant data suggest explanations for certain anomalies arising from the chemical shift data. From the latter, we have suggested the probable equatorial preference for the aralkyl group, but comparisons of (A) *cis*-(XI) with *cis*-(XIII), and (B) *trans*-(XI) with *trans*-(XIII) are of interest. Thus for (A) the aromatic ring preferentially shields the C-5 methyl group (thought to be axial) by 0·21 p.p.m. (the effect for the bromomethyl group is 0·16 p.p.m.) while for (B) where the preferential shielding of the bromomethyl groups would be expected, the reverse obtains, *viz.* 0·25 p.p.m. in contrast to 0·28 p.p.m. for the methyl group. Coupling constant data suggest that in fact a comparison is being made between situations in which the differences in conformational equilibria are apparently sufficient to override shielding effects due to the benzene ring of substituents at phosphorus.

Wadsworth and Emmons concluded that *cis*- and *trans*-stereoisomers of 5-alkyl-5-chloromethyl-2-oxo-1,3,2-dioxaphosphorinans differ at C-5 rather than at phosphorus on the grounds that $\nu_{max.}$ (P=O) was identical (1260 cm.$^{-1}$ for benzyl phosphonates) for the members of the stereoisomeric pair. Table 4 lists spectral data for the esters (V) and (XVII); other compounds provide similar data. Phosphoryl absorption for the *cis*-form is identical with that for the *gem*-dimethyl analogue; in solution the absorption moves to longer wavelengths. In the case of the *trans*-form little variation is observed.

TABLE 4

I.r. data $\nu_{max.}$ in cm.$^{-1}$ for 2-benzyl-5-chloromethyl-5-methyl-2-oxo-1,3,2-dioxaphosphorinan (V) *

Solvent:	P=O		P–O–C			
			cis		*trans*	
	cis	*trans*				
(KBr disc	1258	1266	1017	1054	1007	1051
$CHCl_3$	1265	1257	1008	1057	1002	1049
Me_2CO	1280	1269	1008	1055	1003	1050
MeCN	1277	1268	1006	1050	1001	1048
C_5H_5N	1280	1266	1007	1053	1000	1046

* Measured with a Perkin-Elmer 521 spectrometer. The corresponding values for the C-5 *gem*-dimethyl ester (XVII) are 1258, 1010, and 1057 cm.$^{-1}$ (KBr disc).

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