this residue afforded a fraction, bp 32–70° (1.2 mm). Vapor-phase chromatography of this material showed five components; the third component eluted was collected in a series of preparative experiments. The material exhibited an infrared band at 1750 cm^{-1} and a parent ion in the mass spectrum at m/e 186 (yield 1–2%). The olefin appeared to be quite acid sensitive.

Variable-temperature pmr spectra were recorded with a Varian Associates HA-100 spectrometer using samples that were approximately 10% olefin and 5% TMS (v/v) in trichlorofluoromethane. For fluorine spectroscopy the operating frequency was 94.6 MHz. A capillary of ethyl trifluoroacetate was used to provide a lock signal for the fluorine experiments. Samples were degassed and sealed under vacuum. Sample temperatures were estimated by replacing the sample tube with another tube containing solvent and a copper–constantan thermocouple which was connected to a Digitec Model 504 digital thermometer. Sample temperatures are believed to be accurate to ±1°.

Theoretical spectra were generated using an IBM 360/75 computer and a version of the two-site AB exchange program previously described.[5] The rate constants derived by visually fitting theoretical spectra to experimental spectra are believed to be accurate to better than 10%.

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Structural Implications of Nuclear Magnetic Resonance Studies on 1-R-1-Phospha-2,6-dioxacyclohexanes

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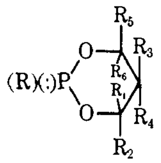
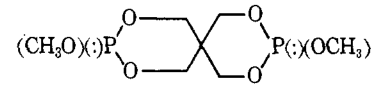
Abstract: ^1H and ^{31}P nmr spectra of 15 1-R-1-phospha-2,6-dioxacyclohexanes have been examined, in which R = OCH_3, $OC(CH_3)_3$, SC_6H_5, C_6H_5, F, Cl and Br. Two methyl substituents were present in the ring at C_3 and C_5 or at C_4. Spectra of several 4-methyl-4-chloromethyl systems were also studied as well as 3,9-dimethoxy-2,4,8,10-tetraoxa-3,9-diphosphaspiro[5.5]undecane. The bulk of the nmr evidence is consistent with the presence of one very dominant chair conformer. The question of the stereochemistry at phosphorus in these systems is examined in the light of present evidence. An intermolecular halide exchange mechanism is proposed to account for the broadening of the ^1H nmr lines with increasing temperature of several of the 1-chloro and 1-bromo derivatives. The order of the 1-R exchange rates appears to be OCH_3 < F < Cl < Br.

The syntheses of many 1-R-1-phospha-2,6-dioxacyclohexanes have been reported in the last 20 years,[3-6] but attempts to study the stereochemistry of these systems have not been made until recently.[7-19] Although a few of the stereochemical investigations have been reviewed,[20] we briefly summarize here previous conclusions pertinent to the new results we describe in this paper. The rings of I; IIIa,b; IVa,b; VII; VIIIa,b; IXa,b; Xa; XIIa,b; XIIIa,b; XIV; XV; XVII; XIXa; XXa; XXIIa; XXIIIa,b; and XXVI, shown in Table I, were assigned chair conformations on the basis of their ^1H nmr spectra.[9,12-15,17,18] In two cases, IIIb[15] and VIIIb,[9] rapid equilibria between two chair conformers have been postulated, but in all of the others one conformer has been concluded to be very dominant under the conditions of observation. Conflicting stereochemistries at phosphorus have been deduced for several of the above derivatives. An axial R, equatorial electron lone-pair stereochemistry has been assigned for IIIa;[15] VIIIa;[10] IXa,b;[18] XXIIIa,b;[14] and the dominant conformer of VIIIb.[10] In contrast, an equatorial R, axial lone-pair stereochemistry has been assigned for VII;[12] Xa;[13] IVa,b;[14] XIIa,b;[14] and the dominant conformer of IIIb at −30°.[15]



I–XXVII
XXIX, XXXI



XXVIII

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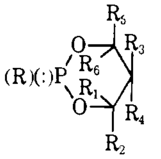
Table I. 1-R-1-Phospha-2,6-dioxacyclohexanes



Compound[a]	R	R_1	R_2	R_3	R_4	R_5	R_6
I	OC_6H_5	H	H	CH_3	CH_3	H	H
II	$OC(CH_3)_3$	H	H	CH_3	CH_3	H	H
IIIa,b	OC_2H_5	CH_3	H	H	H	H	H
IVa,b	OC_2H_5	H	H	CH_3	$CH(CH_3)(OCH_3)$	H	H
Va,b	OCH_3	CH_3	H	H	H	H	H
VIa,b	OCH_3	H	H	CH_3	H	H	H
VII	OCH_3	H	H	CH_3	CH_3	H	H
VIIIa,b	OCH_3	H	H	$C(CH_3)_3$	H	H	H
IXa,b	OCH_3	H	H	CH_2Cl	CH_3	H	H
Xa,b	OCH_3	CH_3	H	H	H	CH_3	H
XI	OCH_3	CH_3	H	H	H	H	CH_3
XIIa,b	OCH_3	H	H	CH_3	$CH(CH_3)(OCH_3)$	H	H
XIIIa,b	OCH_3	H	H	CH_3	NO_2	H	H
XIV	$N(CH_3)_2$	H	H	CH_3	CH_3	H	H
XV	F	H	H	CH_3	CH_3	H	H
XVIa,b	F	H	H	CH_2Cl	CH_3	H	H
XVII	Cl	H	H	CH_3	CH_3	H	H
XVIIIa,b	Cl	H	H	CH_2Cl	CH_3	H	H
XIXa	Cl	H	H	$C(CH_3)_3$	H	H	H
XXa	Cl	CH_3	H	H	H	CH_3	H
XXI	Cl	CH_3	H	H	H	H	CH_3
XXIIa	Cl	CH_3	H	H	H	H	H
XXIIIa,b	Cl	H	H	CH_3	$CH(CH_3)(OCH_3)$	H	H
XXIV	Br	H	H	CH_3	CH_3	H	H
XXVa,b	Br	H	H	CH_2Cl	CH_3	H	H
XXVI	C_6H_5	H	H	CH_3	CH_3	H	H
XXVII	SC_6H_5	H	H	CH_3	CH_3	H	H
XXIX	OCH_3	H	H	H	H	H	H
XXXI	Cl	H	H	H	H	H	H

[a] a and b are geometrical isomers. Isomer a is thermodynamically more stable at room temperature.

Herein, results of the analyses[21] of the ^1H nmr spectra of 15 1-R-1-phospha-2,6-dioxacyclohexanes and 3,9-dimethoxy-3,9-diphospha-2,4,8,10-tetraoxaspiro[5.5]undecane (XXVIII) are interpreted in terms of possible conformations of the rings as well as dispositions of the exocyclic substituents. Particular attention is drawn to the presently available evidence surrounding the controversial stereochemistry at phosphorus. Selected examples from the above systems were examined at several concentrations and temperatures and in more than one solvent. Broadening and coalescence of ^1H nmr spectral lines of several 1-bromo and 1-chloro derivatives are also described, and a mechanism accounting for these and related observations is proposed.

Experimental Section

All solvents were reagent grade and were stored over Linde 3A molecular sieves. All spectra were obtained on samples in spinning 5-mm o.d. precision glass tubes. ^{31}P spectra were obtained at 24.3 MHz on samples at 27.5° with a Varian HR 60 spectrometer operating at 14,100 G. The ^{31}P chemical shifts were obtained either directly from the ^{31}P spectra or from the ^1H spectra (modified Varian HR 60[22]) by the INDOR method and are listed in parts per million (ppm) relative to the chemical shift of 85% phosphoric acid contained in a concentric capillary in the nmr tube. A positive shift is taken to occur at an applied magnetic field greater than that of the standard. Spectra for which $^1H(^{31}P)$ or $^1H(^1H)$ decoupling experiments are reported were obtained on samples at 27.5° at 60 MHz with a Varian HR 60 spectrometer operating at 14,100 G. All other ^1H spectra were obtained with a Varian A 60 spectrometer operating at 14,100 G or a Varian HA 100 spectrometer operating at 23,500 G on samples at 40 and 30°, respectively, unless specified otherwise. All ^1H line positions (δ) are given in parts per million relative to internal tetramethylsilane (TMS) unless stated otherwise. ^{19}F spectra were obtained on the HR-60 spectrometer using $CFCl_3$ as the internal standard.

All reactions in which compounds containing a phosphorus–halogen bond were involved as well as the accompanying isolation and purification steps were carried out under a dry nitrogen atmosphere. Special care was taken to exclude moisture from nonequilibrium mixtures of geometrical isomers. The main criteria of purity of the compounds were constancy of distillation temperature or melting point, proper integration of ^1H nmr resonances, and/or absence of unaccountable ^1H nmr resonances. The ^1H nmr spectra of monocyclic trivalent phosphorus derivatives containing the methoxyl group almost always contain an extra doublet at slightly lower field than the main methoxyl doublet. Distillation in several instances with a 16-in. platinum spinning band column did not eliminate the impurity. Trimethyl phosphite, arising from rearrangement during distillation, is a likely contaminant and would account for no more than 3% of the distillate. A tertiary base such as pyridine or triethylamine was used in many of the preparations as a hydrogen chloride or bromide acceptor. Pyridine is not recommended because its hydrochloride is relatively difficult to separate from the desired product by distillation. Ratios of geometrical isomers were determined by comparing the areas of nonoverlapping ^1H nmr resonances with the aid of a Varian A-60 integrator or planimeter. ^1H nmr spectral descriptions are included in this section if they have not appeared in the literature or in another paper.[21]

2-Chloromethyl-2-methyl-1,3-propanediol. A mixture of 120 g of 2-methyl-2-hydroxymethyl-1,3-propanediol (1 mol), 86 g of diethyl ketone (1 mol), and 1.0 ml of BF_3 ethereate was dissolved in benzene. The solution was refluxed and the water formed removed

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by azeotropic distillation. The benzene was then distilled off at atmospheric pressure and the remaining thick oil distilled under vacuum. A 75% yield of product [bp 100° (0.5 mm)] was realized. The integrated nmr spectrum in CCl_4 revealed the correct ratios for the ethyl (δ 0.7–1.8), methyl (δ 0.78), ring methylene (δ 3.53), and hydroxymethyl methylene (δ 3.58) absorptions.

Equimolar amounts of the above acetal and tosyl chloride were refluxed in pyridine for 24 hr. After cooling, the pyridinium tosylate was removed by filtration, excess pyridine was evaporated by atmospheric distillation and the remaining liquid was vacuum distilled to give the chloro acetal derivative in 50% yield, bp 80° (0.5 mm). The integrated nmr spectrum of the neat liquid revealed the correct ratios for the ethyl (δ 0.7–2.0), methyl (δ 0.81), ring methylene (δ 3.58), and chloromethyl methylene (δ 3.67) absorptions.

Equimolar amounts of the above chloro acetal and water, with a catalytic amount of HCl, were heated at 100° for 4 hr. Diethyl ketone was removed by atmospheric distillation. The diol was recrystallized from benzene in 80% yield. The integrated nmr spectrum in $CDCl_3$ revealed the correct ratios for the methyl (δ 0.95), chloromethyl methylene (δ 3.68), and hydroxymethyl methylene (δ 3.61) absorptions.

***meso*- and *dl*-2,4-Pentanediol.** Both *ca.* 1:1 mixtures of the diastereomeric alcohols and pure *meso*-2,4-pentanediol were prepared according to a slight modification of the procedure described by Pritchard and Vollmer.[23] The isomeric cyclic sulfites were separated with a 16-in. platinum spinning band column in conjunction with a vacuum regulator. One distillation with reflux ratios no lower than 15:1 gave 96% *meso*-sulfite along with 4% *dl*-sulfite and distillation of this mixture reduced the latter isomer to less than 1%. The thionyl chloride was freshly purified by a procedure described by Friedman and Wetter.[24]

1-*tert*-Butoxy-4,4-dimethyl-1-phospha-2,6-dioxacyclohexane (II). To a well-stirred ether suspension of 3.50 g of sodium *tert*-butoxide (36.4 mmol), prepared *in situ* from sodium amalgam and *tert*-butyl alcohol, was added dropwise 6.04 g of XVII (35.8 mmol). The ether refluxed during the addition, and external heating was applied to reflux the ether for an additional hour. The mixture was filtered and the residue was washed with ether. The ether was removed from the combined filtrates by atmospheric distillation and II was obtained in about 30% yield as a solid (mp *ca.* 30°) by distillation at less than 1 mm. The small quantity of product precluded a measurement of the boiling point. The ^{1}H nmr spectrum consists of methylene multiplets (δ 3.98–4.30 and 2.95–3.35), and a *tert*-butoxy singlet (δ 1.37), and broad (δ 1.18) and narrow (δ 0.68) methyl singlets.

Cyclic Phosphites Prepared by Transesterification. A modification of the general transesterification procedure described by Wadsworth and Emmons[25] was used to prepare the compounds below. Equimolar quantities of trimethyl phosphite and the appropriate diol were heated at about 100° until methanol began to reflux. The methanol was removed by distillation at atmospheric pressure at oil bath temperatures up to 130° and the desired product was obtained by reduced pressure distillation or sublimation. The yields were usually greater than 50%.

a. **1-Methoxy-1-phospha-2,6-dioxacyclohexane (XXIX).** Distillation under a presssure of 38 mm took place at 76–78° [lit.[26] bp 65–66° (23 mm), bp 50–51° (11 mm)]. The ^{1}H nmr spectrum taken neat consisted of a C_3C_5-methylene triplet of multiplets (δ 4.14–4.65) and multiplet (δ 3.29–3.91), a methoxyl doublet (δ 3.48, J(POCH) = 11.7), and C_4-methylene multiplets (δ 1.93–2.72 and 1.30–1.73).

b. **1-Methoxy-4,4-dimethyl-1-phospha-2,6-dioxacyclohexane (VII).** Distillation under a pressure of 36 mm took place at 87–88° [lit.[27] bp 66° (18 mm)].

c. **1-Methoxy-4-chloromethyl-4-methyl-1-phospha-2,6-dioxacyclohexane (IXa,b).** This mixture was prepared by the transesterification method of Wadsworth and Emmons[25] using 2-chloromethyl-1,3-propanediol rather than 2-chloromethyl-2-ethyl-1,3-propanediol. The compound was purified by vacuum distillation [bp 95° (2 mm)] in 50% yield. The ratio of IXa to IXb was 3.6:1.

d. **1-Methoxy-*cis*-3,5-dimethyl- and 1-Methoxy-*trans*-3,5-dimethyl-1-phospha-2,6-dioxacyclohexane (Xa and XI, Respectively).** Preparation of these compounds by transesterification has been reported,[8] but not in detail. The phosphite Xa [bp = 58–59° (11 mm)] and a *ca.* 1:1 mixture of Xa and XI (bp 58° (8 mm), bp 75–77° (18 mm)) were prepared from *meso*-2,4-pentanediol and a *ca.* 1:1 mixture of *meso*- and *dl*-2,4-pentanediol, respectively.

1-Methoxy-*trans*-3,5-dimethyl-1-phospha-2,6-dioxacyclohexane (XI) and the Isomeric 1-Methoxy-*cis*-3,5-dimethyl-1-phospha-2,6-dioxacyclohexanes (Xa and Xb). Denney and Denney have reported the preparation of a 1.3:1.0:2.9 mixture of Xa, XI, and Xb by the action of sodium methoxide on a mixture of XXa and XXI derived from a *ca.* 4:1 mixture of *meso*- and *dl*-2,4-pentanediol.[8] A tertiary base and methanol was used here in place of sodium methoxide in two adaptations of the procedure described by Aksnes, *et al.*,[7] for preparing the unstable isomer IIIb. The ratio Xb:Xa was between 2:1 and 4:1 in four preparations. These nonequilibrium mixtures can be kept for at least a month in a stoppered, nitrogen-filled flask in a Dry Ice chest without appreciable change of the isomer ratio.

a. **Procedure A.** Both a mixture of XI, Xa, and Xb and mixtures of Xa and Xb were prepared by this procedure. For example, 7.10 g of XXa (42.1 mmol) was added dropwise to an ice-cooled, well-stirred ether solution of 1.36 g of methanol (42.5 mmol) and 4.31 g of triethylamine (42.5 mmol). The triethylamine hydrochloride was filtered off and washed with ether and the ether and excess reactants were distilled at reduced pressure below room temperature. A nearly quantitative yield of a 1:2.3 mixture of Xa and Xb was obtained upon distillation [bp 60–61° (10 mm)].

b. **Procedure B.** To an ice-cooled, well-stirred ether solution of 5.22 g of XXa (31.0 mmol) was added dropwise 0.968 g of methanol (31.1 mmol) and 3.0 g of pyridine (38 mmol). The remainder of the procedure was as described in procedure A. The yield was again nearly quantitative.

1-Fluoro-4,4-dimethyl-1-phospha-2,6-dioxacyclohexane (XV). Following a modified version of the procedure of Schmutzler,[28] to 10 g of 1-chloro-1-phospha-4,4-dimethyl-2,6-dioxacyclohexane was added 23 g of SbF_3. The heterogeneous mixture was magnetically stirred under nitrogen at 50° for 4 hr. The precipitate was filtered off and the filtrate was vacuum distilled [bp 62° (43 mm)] in 80% yield. The ^{1}H nmr spectrum consists of methyl groups at 0.75 and 1.23 ppm. The methylenes appear as a triplet of triplets (δ 3.15–3.57) and a broad doublet of doublets (δ 3.97–4.20).

1-Fluoro-4-chloromethyl-4-methyl-1-phospha-2,6-dioxacyclohexane (XVIa,b). Preparation of this compound was analogous to that of XV [bp 98–99° (38 mm)]. The ratio of a to b was 3.9:1 and the yield of the a–b mixture was 80%.

1-Chloro-4,4-dimethyl-1-phospha-2,6-dioxacyclohexane (XVII). This compound was obtained following a procedure which was briefly outlined by Edmundson.[29] To a well-stirred, ice-cooled ether solution of 44 ml of phosphorus trichloride (0.50 mol) were added dropwise 49 g of 2,2-dimethyl-1,3-propanediol (0.47 mol) and 75.7 ml of pyridine (0.94 mol). The pyridine hydrochloride was removed by filtration and washed with ether. The ether was distilled from the combined filtrates at atmospheric pressure and the product was obtained by distillation [bp 70° (12 mm), lit.[29] bp 66° (13 mm)].

1-Chloro-4-chloromethyl-4-methyl-1-phospha-2,6-dioxacyclohexane (XVIIIa,b). In 100 ml of ether were dissolved 6.3 ml (0.07 mol) of PCl_3 and 11.7 ml (0.14 mol) of pyridine. The 500-ml two-neck flask containing the mixture was equipped with an addition funnel and a reflux condenser. While magnetically stirring, 10.0 g (0.07 mol) of 2-chloromethyl-2-methyl-1,3-propanediol dissolved in 100 ml of ether was added over a period of 2 hr. The pyridinium hydrochloride was then filtered off under nitrogen, the ether removed by distillation at atmospheric pressure, and the remaining liquid distilled under vacuum in 92% yield [bp 55° (5 mm)]. The ratio of a to b was 3.9:1.

1-Chloro-*cis*-3,5-dimethyl- and 1-Chloro-*trans*-3,5-dimethyl-1-phospha-2,6-dioxacyclohexanes (XXa and XXI, Respectively). These compounds have been reported but their preparation has not been fully described.[8] The procedure described for XVII was used to prepare XXa (bp 72–73° (12 mm), 35–40% yield) as well as *ca.* 1:1 mixtures of XXa and XXI [bp 77–79° (12 mm)] from *meso*-

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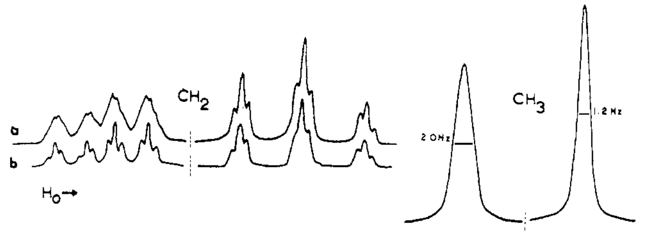

Figure 1. The ^{1}H nmr spectrum of 1-chloro-4,4-dimethyl-1-phospha-2,6-dioxacyclohexane: (a) the ring methylene proton resonance and the two 4-methyl resonances (the widths at half-height ($W_{1/2}$) shown for the expanded latter two resonances), (b) the ring methylene proton resonance when the protons giving the broader methyl resonance are decoupled.

2,4-pentanediol, and *ca.* 1:1 mixtures of *meso*- and *dl*-2,4-pentanediol, respectively. In one instance the preparation of XXa was modified in that triethylamine instead of pyridine was used as a base. The ^{1}H nmr spectrum of XXa consists of a C_3C_5-methyl doublet (δ 1.24, J = 6.2), C_4-methylene multiplet (δ 1.59–1.96), and a C_3C_5-methine multiplet (δ 4.41–5.03). The resonances for XXI are broad at room temperature and are discussed later.

1-Bromo-4,4-dimethyl-1-phospha-2,6-dioxacyclohexane (XXIV). To 7.8 ml of pyridine (0.10 mol), 4.56 ml of PBr_3 (0.05 mol), and 50 ml of ether in a two-neck 250-ml flask fitted with an addition funnel and a condenser was slowly added 5 g (0.05 mol) 2,2-dimethyl-1,3-propanediol. After addition was complete, the pyridinium hydrobromide was filtered off and the ether removed by distillation at atmospheric pressure. The remaining liquid was vacuum distilled in 30% yield [bp 72° (18 mm)]. The ^{1}H nmr spectrum of XXIV is dependent on contaminants, such as traces of water, which apparently alter the rate of Br exchange. Basically it consists of two methyl proton absorptions at 0.85 and 1.23 ppm. The methylene protons absorb at 3.42–3.77 and 4.03–4.32 ppm.

1-Bromo-4-chloromethyl-4-methyl-1-phospha-2,6-dioxacyclohexane (XXVa, b). The preparation of this compound in 30% yield was analogous to that of XXIV [bp 105° (5 mm)].

1-Phenyl-4,4-dimethyl-1-phospha-2,6-dioxacyclohexane (XXVI). This compound was prepared by a modification of the method described by Harwood[30] or Gagnaire, *et al.*[12] To a well-stirred, ice-cooled ether solution of 19.9 g of $C_6H_5PCl_2$ (0.111 mol) were added dropwise 11.6 g of 2,2-dimethyl-1,3-propanediol (0.111 mol) and 17.9 ml of pyridine (0.222 mol). After removal of the pyridine hydrochloride by filtration and after washing of the residue with ether, the solution was concentrated by atmospheric distillation of the ether and XXVI was isolated in greater than 50% yield by distillation (bp 120° (6 mm), lit.[30] bp 100° (1.5 mm), mp 82–83°). Gagnaire, *et al.*, have pointed out the deliquescent nature of XXVI and its reaction with CCl_4, $CDCl_3$, C_6D_6, and CD_3COCD_3.[12] However, a ^{1}H nmr spectrum of triply sublimed XXVI in C_6H_6 dried with $LiAlH_4$ showed only approximately 5% impurities.

1-Thiophenoxy-4,4-dimethyl-1-phospha-2,6-dioxacyclohexane (XXVII). To an ice-cooled, well-stirred ether solution of 4.95 g of XVII (29.4 mmol) were added dropwise 3.82 g of thiophenol (34.6 mmol) and 2.98 g of triethylamine (29.4 mmol) in *ca.* 20 ml of *ca.* 3:1 ether–benzene. The mixture was stirred for an additional 30 min at room temperature and then filtered. The residue was washed with ether and the combined filtrates were concentrated to give the crude product, which was purified by two recrystallizations from a *ca.* 1:1 mixture of hexane and ether (mp 70–75°). Another recrystallization and two sublimations at *ca.* 75° at less than 1 mm did not narrow the melting range, even when the sample was placed in a capillary in a nitrogen-filled dry bag and the capillary evacuated before being sealed. The solid soon becomes moist in humid surroundings. The ^{1}H nmr spectrum in $CDCl_3$ consists of a phenyl multiplet (δ 7.08–7.55), methylene multiplets (δ 3.34–3.72 and δ 4.06–4.39), and broad (δ 1.20) and narrow (δ 0.69) methyl singlets.

3,9-Dimethoxy-2,4,8,10-tetraoxa-3,9-diphosphaspiro[5.5]undecane $(CH_3O)P(OCH_2)_2C(CH_2O)_2P(OCH_3)$ **(XXVIII).** Transesterification of trimethyl phosphite with pentaerythritol was carried out as described for VII, IX, X, and XI, except that the process is significantly slower than with other alcohols, possibly because pentaerythritol is not appreciably soluble in trimethyl phosphite even at 110°. The product was sublimed twice at *ca.* 90° (<1 mm) (mp 124–127°, lit.[31] mp 124–127°).

1-Chloro-1-phospha-2,6-dioxacyclohexane (XXXI). This compound was synthesized according to the procedure of Lucas, Mitchell, and Scully.[32] The product was distilled and the fraction boiling at 36–38° (5 mm) was retained. A ^{1}H nmr spectrum of the neat liquid showed complex multiplets from 1.4 to 2.9 and 3.2 to 4.9 ppm.

Results

1-R-4,4-Dimethyl-1-phospha-2,6-dioxacyclohexanes. The ^{1}H nmr spectra (neat or in solution) of II, VII, XV, XVII, XXIV, XXVI, and XXVII have several common features which are exemplified in the spectrum of XVII shown in Figure 1a. The two methyl resonances are separated by at least 0.42 ppm and the one at lower field is broader. The methylene resonance consisting of two nonoverlapping halves appears at still lower fields. The low-field half is distinguished by its broadness relative to the high-field half, which consists of sharp unsymmetrical triplets. When the protons associated with the broader methyl resonance in II (neat), XVII (neat), and XXVI (C_6H_6) were decoupled from the methylene protons, a spectrum similar to that shown in Figure 1b resulted. The sharp unsymmetrical triplets are now evident in both halves of the methylene resonance. Decoupling of both methyl groups gives a methylene resonance essentially the same as in Figure 1b, and these spectra were analyzed[21] as AA′BB′X systems with the aid of the LAOCN3 iterative least-squares computer program.

Gagnaire, *et al.*,[11,12] have reported the analyses of the ^{1}H nmr spectra of CS_2 or CCl_4 solutions of I, VII, XIV, XV, XVII, and XXVI. Comparison of solution spectra of XIV and XXVI at 100 and 60 MHz allowed them to conclude that the two values of J(POCH) are of the same sign. The similarity of the magnitudes of these couplings for XXVI and those for I, VII, XV, and XVII led them to postulate that this coupling has the same sign in all of these compounds.

The spectra of XV (neat), XXIV (C_6H_6), and XXVII ($CDCl_3$, C_6H_6) were analyzed as AA′KK′X systems. The lack of spectra with the methyl protons decoupled increases the uncertainty of $J(POCH_K)$ and bromide exchange broadens the resonance of XXIV. Approximate values of $J(POCH_A)$ and $J(POCH_K)$ for these compounds are given in Table II.

3,9-Dimethoxy-3,9-diphospha-2,4,8,10-tetraoxaspiro-[5.5]undecane (XXVIII). The analysis[21] of the ^{1}H spectrum of this compound leads to the conclusion that for the nuclei designated in the structure below $J(POCH_C) = J(POCH_{C'}) = J(POCH_Q) = J(POCH_{Q'}) = 10.3 \pm 0.1$ Hz and that $J(POCH_G) = J(POCH_{G'}) = 2.8 \pm 0.1$ Hz. These couplings appear to correspond to $J(POCH_A)$ and $J(POCH_B)$ in II.

The 1-R-4-Methyl-4-chloromethyl-1-phospha-2,6-dioxacyclohexanes. The compounds IXa,b; XVIa,b; XVIIIa,b; and XXVa,b are pairs of geometrical isomers. No attempts were made to separate the a and b isomers of any of these pairs. As a result, overlapping

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[30] H. J. Harwood, U. S. Patent 3,270,092 (1966); *Chem. Abstr.*, 65, 15425*ef* (1966).

[31] E. T. Mukmenev and G. Kamai, *Dokl. Akad. Nauk SSSR*, 153, 605 (1963); *Chem. Abstr.*, 60, 6737*c* (1964).

[32] H. J. Lucas, F. W. Mitchell, Jr., and C. N. Scully, *J. Amer. Chem. Soc.*, 72, 5491 (1962).

Table II. Values of J(POCH) for Some 1-R-1-Phospha-2,6-dioxacyclohexanes

Compound	R	$J(\mathrm{POCH_A})^a$	$J(\mathrm{POCH_B})^a$	Solvent
XXVI	C_6H_5	10.2	3	$CS_2{}^b$
		10.0	2.85	C_6H_6
VII	OCH_3	10.8	2.8	$CCl_4{}^b$
VIII	OCH_3	10.98	2.89	$CDCl_3$
		9.40	3.90	$CS_2{}^d$
Xa	OCH_3		2.1	Neat[e]
			2.2 ± 0.2	Neat
Xb	OCH_3		3.1 ± 0.2	C_6H_6
IXa	OCH_3	10.5 ± 0.5	3.1 ± 0.1	Neat, $CDCl_3$
IXb	OCH_3	10.5 ± 0.5	3.5 ± 0.2	Neat
II	$O\mathit{t}C_4H_9$	10.7	3.0	Neat
I	OC_6H_5	10.8	2.8	$CCl_4{}^b$
XXVII	SC_6H_5	9.5 ± 0.2	4.3 ± 0.3	$CDCl_3$, C_6H_6
XV	F	10.8	2.8	$CCl_4{}^b$
		10.9 ± 0.3	3.0 ± 0.5	Neat
XVIa	F	10.5 ± 0.5	3.5 ± 0.2	Neat
XVll	Cl	10.8	6	$CCl_4{}^b$
		11.2	5.7	Neat
XIXa	Cl	11.28	5.24	$CDCl_3{}^c$
XXa	Cl		4.8	Neat[e]
XVIIIa	Cl	10.5 ± 0.5	5.7 ± 0.2	Neat, C_6H_6
XXVa	Br	10.5 ± 0.5	6.5 ± 0.5	C_6H_6
XXIV	Br	10.5 ± 0.5	6.4 ± 0.5	C_6H_6
XIV	$N(CH_3)_2$	19.6	3.8	$CCl_4{}^b$

[a] AA′ protons resonate at higher field than BB′ protons. [b] No uncertainties were given (ref 12). [c] Approximately 20% solution, 35° (ref 9). [d] Approximately 20% solution, −62° (ref 9). [e] No uncertainties were given (ref 13).

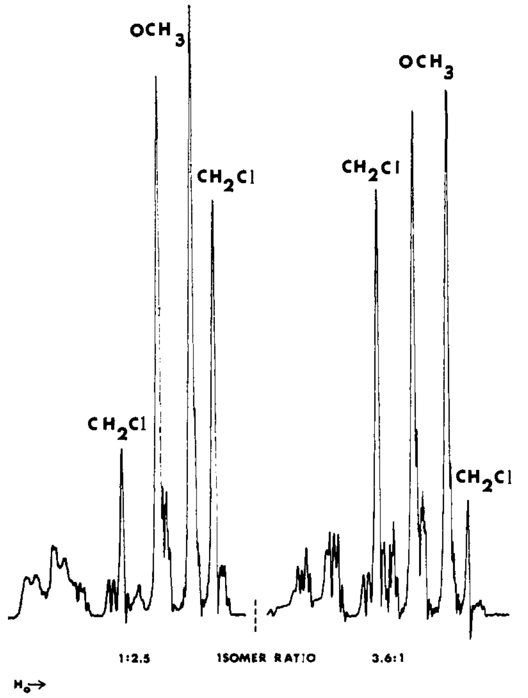
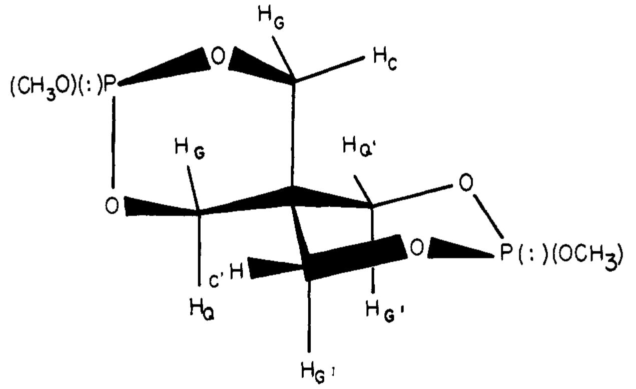


Figure 2. Partial ^{1}H nmr spectra of mixtures of *cis*- and *trans*-1-methoxy-4-methyl-4-chloromethyl-1-phospha-2,6-dioxacyclohexane (IXa,b). The left- and right-hand spectra correspond to the methoxyl, chloromethyl, and ring methylene resonances for 1:2.5 and 3.6:1 isomer ratios, respectively.

of ring methylene resonances occurs and, except for IXa,b, only the features due to the dominant isomer are evident. Values of $J(\mathrm{POCH_A})$ and $J(\mathrm{POCH_B})$ are given in Table II.



The methyl resonances of IXa,b are at 0.761 (IXa) and 1.28 ppm (IXb), the chloromethyl resonances are at 3.80 (a) and 3.27 ppm (b), and the methylene resonances, by approximate AA′KK′X analysis, are at 4.15 and 3.57 (a) and 4.25 and 3.37 ppm (b). The methylene, chloromethyl, and methoxyl resonances of a and b are shown in Figure 2. The left-hand spectrum corresponds to a 1.0:2.5 mixture and the right-hand spectrum to a 3.6:1.0 mixture of a and b. The observable parts of the high-field half of the methylene resonance of both a and b consist of sharp triplets which overlap with the sharp methoxyl doublet at 3.48 ppm ($J(\mathrm{POCH_3})$ = 11.9). The low-field half of the methylene resonance for isomer b consists of a doublet of doublets of unresolved multiplets reminiscent of those in Figure 1, but that for isomer a consists of sharp lines. Expansion of the methyl resonances ($CDCl_3$ solution) exposes a peak with $W_{1/2}$ = 1.02 Hz for isomer a and a triplet ($J(\mathrm{HCCCH_3})$ = 0.7) with $W_{1/2}$ = 1.80 Hz for isomer b.

The spectral features of the major fluoro isomer XVIa are qualitatively like those of IXa. The methyl resonances of XVI a and b are at 0.82 and 1.33 ppm and the chloromethyl resonances are at 3.79 and 3.26 ppm, respectively. The high-field half of the methylene resonance of isomer a is centered at 3.71 ppm and the low-field half at 4.17 ppm. Estimates of the corresponding centers for isomer b, assuming the coupling constants for a given in Table II, are 3.52 and 4.32 ppm.

The spectral features of the chloro isomers XVIIIa,b are broadened somewhat by an exchange phenomenon to be discussed later. The methyl resonances of isomers a and b are at 0.87 and 1.33 ppm and the chloromethyl resonances are at 3.76 and 3.29 ppm. The two halves of the methylene resonance of isomer a are centered at 3.84 and 4.35 ppm, but those of the b isomer cannot be located accurately.

The spectral features of the neat bromo isomers XXVa,b are very much broadened and the two methyl, two chloromethyl, etc. resonances cannot be distinguished unless the compound is diluted in benzene.

1-R-3,5-Dimethyl-1-phospha-2,6-dioxacyclohexanes. Spectra of Xa and mixtures of Xa,b derived from *meso*-2,4-pentanediol, were obtained with and without benzene as a solvent. In the absence of benzene, the methine (R_2,R_6) resonance for Xa is a multiplet (0.58 ppm wide) 0.35 ppm downfield from the corresponding resonance for Xb (0.58 ppm wide), which is centered at 4.15 ppm. The methoxyl proton chemical shifts at about 3.43 ppm are distinct but differ by less than 0.017 ppm with that for Xb at higher field. These protons exhibit couplings to phosphorus of 11.8 (Xa) and 10.8 Hz (Xb). The multiplet methylene resonances appear at 1.40–1.87 ppm for Xa and at roughly 1.50–2.33 ppm for Xb. The ring methyl resonances appear as a doublet ($J(HCCH_3)$ = 6.3) at 1.13 (Xa) and 1.22 ppm (Xb).

The phosphite XI derived from *dl*-2,4 pentanediol differs from Xa and Xb in having chemically nonequivalent methyl groups (R_1,R_6). The doublet resonances of these methyl protons appear at 1.43 ppm ($J(HCCH_3)$ = 6.8) and 1.20 ppm ($J(HCCH_3)$ = 6.3). Only spectra of mixtures of XI and Xa; and XI, Xa, and Xb have been obtained, but one comparison is worthy of note. The doublet methoxyl resonances of Xa, Xb, and XI appear in this order from low to high field with a range of chemical shifts of 0.020 ppm. Dilution with benzene causes all the doublets to appear at higher field, but, whereas those for Xa and XI (J = 12.0) are still separated by 0.017 ppm with the doublet of XI at higher field, the doublet for Xb now appears 0.043 ppm to lower field of the one of Xa. A magnitude of 2.5 ± 0.5 Hz for J(POCCH) for Xb was obtained from the ^{31}P spectrum which consisted of a quartet of quartets. The larger quartet splitting (10.5 ± 0.5 Hz) is due to $J(POCH_3)$ and the smaller quartets can be considered triplets of doublets owing to a J(POCH) involving the methine protons at C_3 and C_5 and J(POCCH) involving one of the methylene protons at C_4, respectively. The magnitude of the remaining J(POCCH) associated with the other C_4 methylene proton is probably less than 1 Hz, but the small signal-to-noise ratio prevented an accurate evaluation.

Temperature and Concentration Dependencies. The spectra of compounds in Table I that have been described thus far have been of samples near room temperature and often without solvent. Those compounds whose nmr spectra have been obtained at more than one temperature can be divided into two classes based on the presence or absence of spectral lines which broaden with increased temperature. Those that exhibit such broadening are XVII and XXIIIa,b; XXI; and XXVa,b, while those which do not, up to about 160°, are IXa,b; Xa; XI; XV; XVIa,b; and XXa. Several of the compounds in the former group have also been examined at various concentrations in benzene and deuteriochloroform. Compound XXIV exhibited a broad spectrum at room temperature and no temperature studies were performed.

The compounds giving broadened spectral lines contain a phosphorus–chlorine or phosphorus–bromine bond. The methyl resonances of XVII are 0.430 ppm apart at 40° (see Figure 1). At 158°, the maxima are separated by about 0.30 ppm, with very little drop in intensity between them. Gagnaire, *et al.*,[12] did not observe any apparent modification of coupling constants and chemical shifts between −40 and +155°. The discrepancy between the two observations may be due to the presence of a trace of water in the sample exhibiting the line broadening. Slight but distinct sharpening of the spectrum of XVII occurs on dilution in $CDCl_3$.

The isomers XVIIIa,b are present in a 3.9:1 ratio at 40° but the lines are slightly broader than those of XVII. Dilution of the mixture with benzene caused a sharpening of the lines and a separation of the two halves of the methylene resonances, the two chloromethyl peaks, and the two methyl peaks. An increase in temperature from 40 to 148° caused the two chloromethyl (3.76 and 3.29 ppm) and two methyl resonances (0.87 and 1.33 ppm) to coalesce to apparent single peaks at 3.59 and 0.99 ppm, respectively, in the neat mixture. These coalesced peaks are positioned 36 and 26%, respectively, of the separation of the uncoalesced peaks at 40° from the peaks of the major isomer. The lines are sharper at 148° than at intermediate temperatures but not as sharp as at 40°.

The chloro derivatives XXa and XXI were examined from −30 to 158°. At −30°, the methyl resonance of XXa consists of a sharp doublet and that of XXI consists of two sharp doublets separated by 0.30 ppm. Qualitatively, the doublet of XXa does not broaden up to 158°. However, the two doublets of XXI coalesce to one doublet ($J(H_3CCH)$ = 6.3 ± 0.2) which is still broad at 158°. The coalescence temperature for XXI is about 50 ± 10° (60 MHz) or 70 ± 10° (100 MHz). Dilution of this mixture of XXa and XXI at 40° with benzene causes the partially coalesced doublets of XXI to separate to about 0.40 ppm and sharpen. Addition of tetraphenylarsonium chloride to a dilute benzene solution has no effect on the width of the methyl doublet of XXa, but causes the doublets of XXI to broaden to more than twice their original width.

The bromine derivatives XXIV and XXVa,b have broader spectral lines at room temperature than do the corresponding chlorine compounds. Moreover, spectra of different samples of a given compound run under the same conditions differed in broadness. The resonances of a mixture of XXVa,b coalesce into four sharp peaks at 1.01 (CH_3), 3.58 (CH_2Cl), 4.01 (OCH_2), and 4.15 ppm (OCH_2) with relative areas 1.5:1.0:1.0:1.0 at 161°. The high-field halves of the methylene resonances do not coalesce as rapidly as the low-field halves so that the two peaks are of unequal height (1.13:1) at 161°. Dilution of XXIV or a mixture of XXVa,b with benzene or XXIV with $CDCl_3$ at room temperature causes the broadened and partially coalesced lines to separate and sharpen. The sum of the POCH couplings in XXVa (17 Hz) is twice the separation between the two apparent methylene peaks for the neat XXVa,b mixture at 161°.

The compounds exhibiting no broadening at elevated temperature are alkoxyl, fluoro, and chloro derivatives. The one chloro derivative, XXa, has been discussed already. In the case of the fluoro compound, XV, the chemical shift between the methylene protons, that between the methyl protons, and the splittings dependent on J(POCH) change less than 1 Hz from 40 to 161°. Although the methyl and chloromethyl proton resonances of the fluoro isomers XVIa,b do not change more than 1 Hz from 40 to 161°, the isomer ratio changes from 3.9:1 to about 2.0:1. The ring methylene resonance of XVIa, which masks that of XVIb, exhibits changes of less than 1 Hz.

The two methoxyl derivatives, Xa and XI, were examined as an approximately 1:1 mixture. The spacing between the two methyl doublet resonances of XI narrows in $CDCl_3$ from 0.27 ppm at −62° to 0.22 ppm at 40° and in the neat mixture from 0.23

ppm at 40° to 0.16 ppm at 157°, but the methyl doublet resonance of neat Xa shifts less than 0.017 ppm from 60 to 157°. Obvious changes in line spacings and intensities in the methylene and methine resonances occur throughout this temperature range, but overlap of the resonances of Xa and XI prevent attributing the changes to a specific compound.

The spectral behavior of the methoxyl isomers IXa,b upon changes in temperature can be compared to that of the fluoro isomers XVIa,b. In contrast, the isomer ratio decreases less than 5% from 3.6:1 at 40–157°, although the time of observation was at least as long as that of the fluoro isomers. The two halves of the methylene resonance of IXa approach from 0.62 to 0.57 ppm and J(POCH) changes less than 1 Hz. Also the chloromethyl and methyl resonances of both isomers change less than 0.033 ppm. The isomer ratio in deuteriochloroform was not reproducible. One sample contained a 4.7:1 ratio at −61 and at 40° 3 days later. The ratio in another sample at 40° was 3.3:1, while that of a third, kept in a Dry ice chest for about a week before being examined at 40°, was 6.9:1. When a nonequilibrium mixture of ratio 1:1.75 was kept at 70°, the ratio changed to 2.0:1 after 40 hr and to 3.0:1 after another 27 hr.

^{31}P Nmr Spectra. Table III contains data obtained from ^{31}P spectra of the compounds in Table I. The a and b isomers were always examined as a mixture. Unfortunately, the nature of the fine structure of the resonances of the minor components IXb, Xa, and XVIb could not be determined because of a small signal-to-noise ratio and/or overlap with the resonance of the major component. The broadness of the resonance of the chloro derivative XVII may be due to the quadrupole moment of chlorine.

Table III. ^{31}P Spectral Parameters of Some 1-Phospha-2,6-dioxacyclohexanes

Compound	Chemical shift, ppm	Appearance[a]	Splittings, Hz
XXIX	−131	bd q	
VII	−123, −122.7[b]	bd q	
II	−117.5 ± 0.8	bd t	10.5 ± 0.5
IXa	−123.5	1:3:6:3:1 m of t	11.5, 3.0 ± 0.5
IXb	−122.6		
Xa	−133	bd q	
Xb	−129	q of q	10.5 ± 0.5, 2.5 ± 0.5
XV[c]	−111.5, −132.9[b]	d of t of t	1180, 10.8, 3.5 ± 0.5
XVIa[d]	−112.8	d of t of t	10.3 ± 0.3, 3.6 ± 0.3
XVIb[e]	−112.2	d of t of t	
XXXI	−154, −153,[f] −153.9[f]	bd	
XVII	−146, −146.5[b] −146.7[f]	bd, $W_{1/2}$ = 30 ± 5	

[a] q = quartet, bd = broad, t = triplet, m = multiplet, d = doublet, $W_{1/2}$ = width at half height. [b] Reference 12. [c] δ ^{19}F 6.14 ppm relative to internal $CFCl_3$, J(P–F) = 1174 Hz. [d] ^{19}F 5.12 ppm, J(P–F) = 1182 Hz. [e] δ ^{19}F 6.05 ppm, J(P–F) = 1180.8 Hz. [f] V. Mark, C. H. Dungan, M. M. Crutchfield, and J. R. Van Wazer, *Top. Phosphorus Chem.*, **5**, 227 (1967).

Discussion

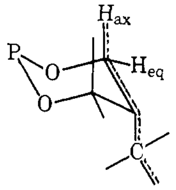
Geometrical Isomerism. There are two possible geometrical isomers for compounds III–VI, VIII–X, XII, XVI, XVIII–XX, XXII, XXIII, and XXV. The ^{1}H nmr resonances of two isomers have been observed at equilibrium for IV,[14] VI,[8] VIII,[9] XXII,[14] and XXIII,[14] and to this list we now add IX, XVI, XVIII, and XXV (dilute benzene). The ratio of isomers is about 9:1 for VIII and 3–4:1 for VI and the last four compounds. The ratios for IV (2.6:1), XII (1.5:1), and XXIII (1.5:1) are uncertain, however, because of peak overlaps.[14] Only one isomer has been found for III,[7] V,[8] XIX,[9] and XXII,[7,8] and we find the same result for X and XX.

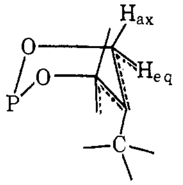
The Denneys,[8] Aksnes, *et al.*,[7] and Hargis and Bentrude[9] have concluded that an equilibrium mixture of isomeric six-membered ring phosphites (R = OAlk) results when a trialkyl phosphite is transesterified with an appropriately substituted diol. On the other hand, these workers found that a nonequilibrium mixture is formed when an alcohol and tertiary amine or, alternatively, an alkoxide ion reacts with an appropriately substituted 1-chloro-1-phospha-2,6-dioxacyclohexane. We find this also to be the case for the phosphites IXa,b and Xa,b. Ratios of IXa to IXb of 1:2.6 and Xa to Xb as great as 1:4 are formed from the chloro derivatives, whereas transesterification leads to a ratio of 3.5:1 for IXa:IXb, and essentially all Xa. Preparation of alkoxy derivatives from the chloro compounds is thought to involve a Walden inversion at phosphorus and should give an isomer ratio the inverse of that formed by transesterification, since the ratio of chloro isomers is very similar to the ratio of phosphite isomers at equilibrium. The fact that complete inversion does not always occur has been attributed to excess strength of the nucelophile (alkoxide ion), excessively high reaction temperatures, and/or the presence of nucleophiles after reaction.[7,8]

The existence of nonequilibrium isomer mixtures implies that thermal atomic inversion of phosphorus is slow at room temperature. In a mixture of Xa,b, the unstable b isomer does not isomerize appreciably in a Dry Ice chest even after a month. A 1:1.75 mixture of IXa,b at 70° does not completely return to the equilibrium value after 40 hr and this must be considered a minimum time because isomerization catalysts may have been present. It is not known whether the rate-controlling mechanism, in the absence of catalysts, involves a thermal intramolecular inversion or an intermolecular alkoxyl exchange similar to the halide exchange to be discussed later.

Ring Conformations. Each of the compounds in Table I might exist in one or more conformations such as those analogous to the chair, boat or skew-boat forms of cyclohexane. Although no solid-state or gas-phase structural determination has been reported for any 1-R-1-phospha-2,6-dioxacyclohexanes, one of the possible chair conformers has been found by solid-state X-ray diffraction methods for each of three 1-R-1-oxo-1-phospha-2,6-dioxacyclohexanes. In each compound, the phosphorus end of the chair-like ring is flattened 10–20° with respect to a cyclohexane chair. This flattening is probably due to the less-than-tetrahedral OPO angle and larger-than-tetrahedral POC angles since the P–O and C–C bond lengths are similar. The OPO angle would be expected to be even smaller when phosphorus is in the trivalent state and, therefore, the ring flattening should be even more prominent in 1-R-1-phospha-2,6-dioxacyclohexanes. Also, the possibility that the solid-state and solution structures are different cannot be ruled out.

The results of the nmr spectral analysis of the 1-R-1-phospha-4,4-dimethyl-2,6-dioxacyclohexanes can be rationalized in terms of possible ring conformations. The fact that no variation of values of ring J(POCH) was found from 40 to 161° for XIV and from −40 to 155° for I, VII, XV, and XVII strongly indicates that one conformer is very dominant.[12] As a result of the ^{1}H–^{1}H decoupling experiments described earlier, it may be concluded that just one pair of methylene protons, BB′, couples appreciably (0.7–0.8 Hz) to just one of the methyl groups of protons. There is even greater HCCCH coupling (2.5–2.9 Hz) between the A and A′ protons, but very little between the B and B′ pair. These enhanced HCCCH couplings are usually found when the bonds linking the coupled nuclei form a planar *W*.[33] Such a pathway exists between the equatorial methylene protons and between each of the axial methylene protons and an appropriately positioned axial methyl proton of either a chair or boat conformer, as shown





Thus, the equatorial methylene protons are more shielded and couple more strongly to phosphorus than the axial methylene protons. Also, the axial 4-methyl protons are less shielded than the equatorial 4-methyl protons. These long-range coupling results rule out unsymmetrical boats or twist-boats, inasmuch as they would not possess all of the appropriately positioned protons.

Also ruled out are comparable quantities of rapidly interconverting chair or boat conformers because the enhanced long-range coupling would then be averaged among all of the methylene and methyl protons according to the ratio of conformers. However, a rapid equilibrium between the chair and boat shown above, which differ only at the phosphorus end of the ring, would allow the same protons to always exist in an environment favorable for enhanced long-range coupling. The usual steric arguments against a boat conformer are not as applicable here as for substituted cyclohexanes, if the phosphorus end of the ring is flattened as in the chairs of the solid-state pentavalent derivatives. This flattening not only would reduce the bowsprit–flagpole interactions but also would allow the oxygen electron lone pairs and the methylene protons to be staggered.

The ring POCH coupling constants of the 4,4-dimethyl derivatives (Table II) may be taken as evidence against the dominant presence of a boat conformer, however. If a dihedral angular dependence of J(POCH) similar to that of J(HCCH) exists, as has been suggested,[34–38] the two values of J(POCH) for a boat, with dihedral angles of approximately 120°, should be similar, but those for a chair, with dihedral angles of approximately 180° and 60°, should be different. Such differences indeed exist and vary from 4.1 Hz for the bromo derivative XXIV to 15.8 Hz for the dimethylamino derivative XIV (Table II).

The ^{1}H nmr spectral studies of the 1-R-4-methyl-4-chloromethyl-1-phospha-2,6-dioxacyclohexanes IXa,b; XVIa; XVIIIa; and XXVa indicate a conformational similarity to the analogous 4,4-dimethyl derivatives. The ring POCH coupling constants for IXa and XVIa do not change from 40 to 160°. An exchange phenomenon to be discussed later, prevents analysis of the spectra of XVIIIa and XXVa over most of this temperature range. The J(POCH) values listed in Table II for these compounds are very similar to those for the corresponding 4,4-dimethyl derivatives. The relatively narrow 4-methyl resonance for IXa and the relative broadness of the same resonance for IXb indicate that the a isomer possesses an equatorial and the b isomer an axial 4-methyl group. The $\Delta W_{1/2}$ of 0.7 Hz in the 4-methyl resonance of IXb is the same as the splitting found by Gagnaire, *et al.*,[12] and ourselves for the 4,4-dimethyl compounds and is attributable to coupling of axial methyl protons with axial methylene protons. The presence of a broadened low-field half of the ring methylene resonance for isomer b (Figure 2) is in agreement with this conclusion. Similarly, the absence of a broadened ring methylene resonance for IXa (Figure 2) is in agreement with the absence of an axial 4-methyl group. The ring methylene resonances of XVIa, XVIIIa (C_6H_6), and XXVa (C_6H_6) are also relatively sharp. Apparently the axial 4-chloromethyl protons in the a isomers are seldom appropriately positioned for *W* coupling to the axial methylene protons. This would be the case if the chlorine were positioned as far away from the center of the ring as possible. The features of the methylene resonances of XVIb, XVIIIb, and XXVb are masked by those of the a isomers, but the large chemical shifts between both the a and b methyl and chloromethyl resonances and the similarity of these shifts to those for IXa and IXb are evidence for a conformational similarity of all the b isomers.

If the a and b isomers exist as chair conformers rather than as chair–boat equilibria, then the R group at phosphorus must be axial in all of them or equatorial because the isomers of each pair differ in configuration at C_4. The similar isomer ratios of 3–4:1 for the four pairs leads to an axial–equatorial free-energy difference for a chloromethyl and methyl group of approximately 0.7 kcal/mol at 40°. The fact that the isomers with an axial chloromethyl group are favored may be due to the fact that the C–Cl bond is longer than the C–H bond. Consequently, steric interactions of the axial chloromethyl group with other atoms in the molecule may be less than those of the axial methyl group. A very recent study of the phosphite shown below by Kainosho and Nakamura[38] tends to confirm our coupling assignments if their assumed stereochem-

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[33] S. Sternhell, *Pure Appl. Chem.*, 14, 15 (1964).

[34] J. G. Verkade and R. W. King, *Inorg. Chem.*, 1, 948 (1962).

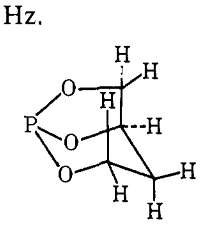
[35] E. J. Boros, K. J. Coskran, R. W. King, and J. G. Verkade, *J. Amer. Chem. Soc.*, **88**, 1140 (1966).

[36] M. Tsuboi, F. Kuriyagawa, K. Matsuo, and Y. Kyogoku, *Bull. Chem. Soc. Jap.*, **40**, 1813 (1967).

[37] L. D. Hall and R. B. Malcolm, *Chem. Ind.* (*London*), 92 (1968).

[38] M. Kainosho and A. Nakamura, *Tetrahedron*, **25**, 4071 (1969); see however D. W. White and J. G. Verkade, *J. Magn. Resonance*, **3**, 111 (1970).

istry as shown is correct. In the six-membered chair ring, $J(\mathrm{POCH_{eq}})$ was slightly more than 9 Hz, while $J(\mathrm{POCH_{ax}})$ was 2.5 Hz.

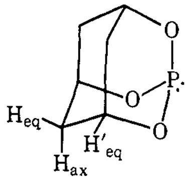


The ^{1}H and ^{31}P nmr results for the isomeric phosphites Xa,b derived from *meso*-2,4-pentanediol strongly suggest that they differ in configuration at phosphorus. The values of $J(\mathrm{HCCH})$ of 11.6 and 2.2 Hz for isomer a[13] and of approximately 11.2 and 3.1 Hz for isomer b imply equatorial 3,5-methyl groups.[39] Moreover, the 3,5-methyl proton shifts of 1.14 ppm for Xa, 1.23 for Xb, and 1.20 and 1.43 ppm for the phosphite XI derived from *dl*-2,2-pentanediol indicate a similar environment for the methyl groups of Xa,b and one of the methyl groups of XI. On steric grounds, equatorial methyl groups would be favored. The values of the ring $J(\mathrm{POCH})$ for Xa,b are similar to the values of $J(\mathrm{POCH})$ assigned to an axial methylene proton in all of the other phosphites in Table II except VIIIb.[40] Since Xa,b are geometrical isomers, the methoxyl group should be axial in one and equatorial in the other unless one isomer prefers a boat conformation. If both were boat conformers, they would still differ in configuration at phosphorus and the methoxyl disposition could still be called axial and equatorial. The δ ^{31}P values for Xa,b differ by 4 ppm, whereas those for IXa,b or XVIa,b, which are concluded to have the same configuration at phosphorus, differ by less than 1 ppm (Table III). Also, the contrast in the effect of benzene on the methoxyl chemical shift of Xb and that on the corresponding shifts of Xa and XI indicates different environments of the methoxyl group in Xa,b.

The limited information about the phosphite XI indicates that it is not conformationally pure at room temperature. The main evidence for a conformational equilibrium is the decrease in the separation of the 3,5-methyl resonances with increasing temperature. This behavior is very similar to that found for the analogous 1-oxo-*trans*-3,5-dimethyl-1-thia-2,6-dioxacyclohexane by Overberger, *et al.*[41] These investigators interpreted their data in terms of an equilibrium between two rapidly interconverting chair conformers. The benzene dilution study of Xa,b and XI cited above suggests that the major conformer of XI in benzene is stereochemically similar to that of Xa.

Stereochemistry at Phosphorus. Five groups of workers have attempted to deduce the stereochemistry at phosphorus in 1-R-1-phospha-2,6-dioxacyclohexanes. On the one hand, Gagnaire, *et al.*,[12] have concluded from nmr studies that the R group in I, VII, XIV, XV, XVII, and XXVI occupies the equatorial position in a chair conformer. Similarly, Bogat-skii, *et al.*,[14] concluded that IVa,b and XIIa,b possess an equatorial alkoxyl group from the form of the ring methylene proton resonance, but the reasoning was not given. In contrast, first White, *et al.*,[18] followed by Bodkin and Simpson[15] and more recently by Bentrude and Hargis[10] concluded that the alkoxyl group occupies the axial position of a chair conformation in at least the more stable isomer of three different pairs of geometrically isomeric phosphites.[42]

The conclusion of Gagnaire, *et al.*,[12] that the preferred stereochemistry is equatorial R, axial phosphorus lone pair is based on a steric argument and the dependence of the magnitude of $J(\mathrm{POCH})$ on the POCH dihedral angle and the disposition of the phosphorus lone pair relative to the coupled nuclei. Similar arguments have been given and the same conclusion deduced by Albrand, *et al.*,[13] in a discussion of the phosphorus stereochemistry in Xa and XXa. In the latter work[13] the POCCH couplings were the primary evidence. The steric argument seems to lose some of its attractiveness in view of the probable ring flattening at the phosphorus end of the ring. In the coupling arguments,[13] the values of the cyclic $J(\mathrm{POCCH})$ (Xa) and $J(\mathrm{POCH})$ (VII) were compared with those of the adamantane phosphite XXX.



XXX

It should be noted that the pseudoexocyclic oxygen in XXX is axial relative to the six-membered ring. The differences in the magnitudes of $J(\mathrm{POCH_{eq}})$ = 6 Hz in XXX[43] *vs.* 10.8 Hz in VII,[12] $J(\mathrm{POCCH_{eq}})$ = 0.5 Hz in XXX *vs.* 3.6 Hz in Xa, and $J(\mathrm{POCCH_{ax}})$ = 0 Hz in XXX *vs.* 0.5 Hz in Xa implied to these authors[13] that the methoxyl group in VII[12] and Xa could not be axial and must therefore be equatorial. In other words, as found earlier for the five-membered analogs,[44] there exists a great influence of the stereochemical disposition of the phosphorus lone pair on phosphorus–hydrogen coupling constants.[12,13] Because the bonding and structures of VII, Xa, and Xb are not accurately known, comparison of the coupling constants may not be justified. The fact that the $J(\mathrm{POCH_{ax}})$ values in Xa and Xb differ by only 1 Hz (provided the signs are the same) indicates that the phosphorus lone pair disposition is not very important, at least for a dihedral angle of about 60°. Furthermore, one of the values of $J(\mathrm{POCCH})$ is about 2.5 Hz for Xb, which is believed to have a stereochemistry at phosphorus different from that in Xa. Thus, neither Xa nor Xb has four-bond couplings similar to those of XXX. Unless Xb is

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[39] $J(\mathrm{H_{4ax}H_{5eq}})$ = 3.1–3.9 Hz, $J(\mathrm{H_{4ax}H_{5ax}})$ = 9.5–10.9 Hz for *cis*-4,6-dimethyl-1,3-dioxacyclohexanes: E. L. Eliel and M. C. Knoeber, Sr., *J. Amer. Chem. Soc.*, **90**, 3444 (1968).

[40] The phosphite VIIIb is felt to be a mixture of two rapidly interconverting chair conformers for which the spectral parameters are weighted time average values (see ref 9).

[41] C. G. Overberger, T. Kurtz, and S. Yaroslavsky, *J. Org. Chem.*, **30**, 4363 (1965).

[42] The preference for this stereochemistry is apparently great enough to force a 4-*tert*-butyl group to be axial approximately 75% of the time in VIIIb at room temperature (ref 9). Also, the 3-methyl group in the less stable isomer IIIb apparently does not prefer the equatorial position strongly enough to force the ethoxyl group and phosphorus lone-pair electrons exclusively into an unfavored configuration at room temperature (ref 15).

[43] J. G. Verkade, R. W. King, and C. W. Heitsch, *Inorg. Chem.*, **3**, 884 (1964).

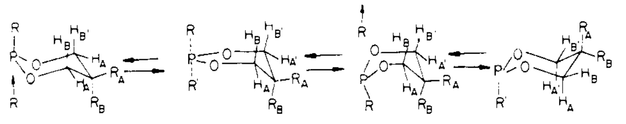
[44] D. Gagnaire, J. B. Robert, J. Verrier, and R. Wolf, *Bull. Soc. Chim. Fr.*, 3719 (1966).

other than a chair conformer, the reasoning of Albrand, *et al.*,[13] loses its applicability to these systems.

The conclusions of White, *et al.*,[18] Bentrude and Hargis,[10] and Bodkin and Simpson[15] are based on dipole moment measurements[15,18] or an X-ray structural investigation[10] on reaction products of the phosphites which form in a stereospecific manner by an assumed retention or inversion mechanism. Thus the BH_3 group reacts with the phosphorus lone pair at low temperature with retention of configuration at phosphorus,[18] while sulfur does so in the case of IIIa and IIIb.[15] Dipole moment measurements agreed with calculated values based on vectorial summation of bond moments.[45] X-Ray diffraction results[10] on one compound obtained from the reaction of methyl iodide and on another from the *tert*-butyl hydroperoxide oxidation of VIIIa,b coupled with ^{1}H nmr evidence,[9] strongly suggest that the methoxyl group of VIIIa is axially disposed in a chair conformer. Similarly, an X-ray diffraction study of the BH_3 adduct of Xa shows[46] the BH_3 group to occupy the equatorial position, as would be expected if the parent phosphite possessed an axial methoxy group. The preponderance of the evidence indicates that an axial 1-R group is so strongly favored that usually the conformational preferences of the other exocyclic substituents do not force a dominance of another conformation at phosphorus. Only in Xb and possibly IIIb[15] does the equatorial R, axial lone pair stereochemistry predominate. The results for compounds such as II and XV and the spiro compound XXVIII, which are not capable of geometrical isomerism, indicate that they are conformationally pure; moreover, a phosphorus stereochemistry in these derivatives different from that in VIIIa or IXa, for example, would be very surprising. The halogen analogs to the above isomers can tentatively be concluded to have a halogen in the axial position if two reasonable assumptions are made concerning the reaction of XXa with methanol to give mostly Xb. First, the dominant conformer of XXa (wherein the ring methyl groups are equatorial, as shown from nmr studies[13]) is at least as reactive in this reaction as the axial dimethyl conformer with which the diequatorial conformer equilibrates. Second, the reaction with methanol takes place by an S_N2 mechanism. This line of reasoning leads to an axial disposition of the 1-chloro group in XXa.

The adoption of a stereochemistry contrary to that expected on steric grounds is not unknown in heterocyclic chemistry. The axial oxygen, equatorial sulfur electron lone-pair stereochemistry has been concluded to be generally preferred in 1-oxo-1-thia-2,6-dioxacyclohexanes.[47] Also, an axial alkoxyl, equatorial hydrogen stereochemistry is preferred in 2-alkoxy-1,3-dioxacyclohexanes[48a] and the proton nmr spectrum of phosphorinane at −90° has been interpreted in terms of an axial pH proton.[48b]

Temperature and Concentration Dependencies. A process that will account for the temperature and concentration dependencies of the ^{1}H nmr spectra where they are observed for the 1-R-1-phospha-2,6-dioxacyclohexanes (R = OCH_3, F, Cl, Br) is an intermolecular exchange of the exocyclic R group at phosphorus involving an inversion of the bonds to phosphorus. A mechanism for this process is shown below. The R group and phosphorus lone pair are assumed in this discussion to prefer the axial and equatorial positions, respectively, of a chair conformer. Also, the mechanism is assumed to be the same for all the molecules investigated. In the initial structure H_A, H_A' and R_B are trans to R while H_B, H_B', and R_A are cis to R. In the final chair conformer, the cis, trans relationships of these atoms are reversed. Also, H_A, H_A', and R_A are initially in equatorial positions but move to axial positions as a result of the exchange process; H_B, H_B' and R_B similarly change from axial to equatorial positions.



The process is believed to be an intermolecular exchange rather than a thermal intramolecular inversion at phosphorus for two reasons. First, dilution with chloroform of compounds that exhibit partially coalesced resonances causes the resonances to separate and sharpen. Goldwhite and Fontal[49] found that the process causing the two methyl resonances of the five-membered cyclic compound 1-chloro-3,3,4,4-tetramethyl-1-phospha-2,5-dioxacyclopentane to coalesce could be slowed by diluting the compound with benzene, toluene, chloroform, and dioxane. These authors determined coalescence temperatures for a neat sample (−23°) and two toluene solutions and determined peak positions as a function of concentration in benzene. While the results for the aromatic solvents are meaningless if these solvents cause $\Delta\delta CH_3$ in the absence of exchange to be altered with concentration, the changes observed with chloroform and dioxane suggest that the rate-controlling process is intermolecular. The slight but distinct sharpening of the spectra of XVII and XXIV upon dilution in $CDCl_3$ at room temperature is also in accord with this hypothesis. Second, tetraphenylarsonium chloride causes the 3,5-dimethyl resonances of XXI to broaden. This is reasonable if the rate-controlling step of the process involves attack of chloride on the cyclic molecule.

The proposed mechanism can readily account for the temperature dependence of the spectra of the two pairs of isomers XVIIIa,b and XXVa,b. In each isomer, R_A and R_B are different, *i.e.*, CH_2Cl and CH_3. For both pairs, an increase of the temperature causes resonances characteristic of two isomers to coalesce. The mechanism shown above allows the phosphorus lone pair and R group to remain in their favored stereochemistry and also allows the carbon end of each molecule to flip rapidly. Thus for the isomeric pairs, this process is an isomerization. The ratio of axial to equatorial R_A is determined by the relative prefer-

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(45) Difficulties with this method and the validity of conclusions drawn using it are treated elsewhere: D. W. White and J. G. Verkade, to be published.

(46) J. Rodgers, D. W. White, and J. G. Verkade, *J. Chem. Soc. A*, in press.

(47) J. G. Tillett, *Quart. Rep. Sulfur Chem.*, **2**, 227 (1967).

(48) (a) E. L. Eliel and C. A. Giza, *J. Org. Chem.*, **33**, 3754 (1968); (b) J. B. Lambert, W. L. Oliver, L. Wallace, and G. F. Jackson, *Tetrahedron Lett.*, 2027 (1969).

(49) H. Goldwhite and B. Fontal, *Tetrahedron*, **22**, 3275 (1966).

ences of R_A and R_B for the axial and equatorial positions. This ratio is about 1.8–2.8:1 at 148° for R_A = CH_2Cl in XVIIIa,b as determined by the positions of the coalesced chloromethyl and methyl resonances relative to the resonances in the absence of exchange. This ratio is similar to the ratio of fluoro isomers XVa,b at 161° and indicates that the stereochemistry at phosphorus is the same in both chloro and fluoro isomers. Since H_A, H_A', H_B, and H_B' do not change their cis, trans roles relative to R_A and R_B' the chemical shifts of H_A and H_A' are not expected to become equal to those of H_B and H_B' at any temperature. The methylene resonance of a mixture of XXVa,b changes from a complex resonance at 40° to two observable lines of different width at 161°. Unfortunately, all that can be concluded is that $[\nu_{AB} + {}^1/_2(J_{AX} - J_{BX})]^2/(2J_{AB})$ is becoming small.[50] Rapid flipping of the carbon end of the molecule should cause $(J_{AX} - J_{BX})$ to be less than the 4 ± 1 Hz observed for XXVa at 40° (C_6H_6). Since the methylene protons are changing their axial, equatorial roles, ν_{AB} should also be less than when one pair is always axially and the other equatorially positioned. Thus, when coalescence is complete, the coupling constants and chemical shifts of all protons should be averages weighted according to the ratio of time spent by each nucleus in different environments.

The 1-chloro derivative XXa exhibits no spectral broadening from −30 to 158° and tetraphenylarsonium chloride does not cause the 3,5-dimethyl resonance to broaden. The proposed exchange mechanism can account for this behavior in the following way. Although the stereochemistry at phosphorus is the same in the initial and final structures, the 3,5-methyl groups change from equatorial to axial positions. The latter positions should be sterically very unfavorable, and even if flipping of the carbon end of the ring is rapid, the weighted average chemical shift of the methyl groups would be practically identical with the shift in nonexchanging XXa and no broadening would be observed. In other words, the two sites of the methyl groups have very different probabilities of being occupied.

If the proposed mechanism is correct, the 1-chloro derivative XXI derived from *dl*-2,4-pentanediol should exhibit one 3,5-methyl resonance at high enough temperatures. The two doublets do coalesce, but the peaks of the resulting doublet at 139° still have $W_{1/2}$ = 3.2 ± 0.2 compared to $W_{1/2}$ = 0.8 ± 0.1 for the XXa in the same sample.

The rate of exchange for the isomeric pairs IXa,b; XVIa,b; XVIIIa,b; and XXVa,b depends on the exo cyclic R in the order $CH_3O < F < Cl < Br$. The order $CH_8O < F$ is based on the fact that the ratio of the fluoro isomers changed appreciably from 40 to 161°; whereas the ratio of methoxyl isomers did not during approximately the same length of time.[51] The extent of spectral broadening at a given temperature can be used as an indication of relative exchange rate for a series of compounds if the uncoalesced lines are equally separated in all the compounds. Thus, the 4-methyl resonances in the first three pairs being discussed are separated by 0.52, 0.51, and 0.46 ppm, respectively, at room temperature. The separation for the bromo compound is probably similar to that for the others and, if so, the order Cl < Br follows. Likewise, the separations of the 4,4-dimethyl resonances in VII, XV, and XVII are 0.49, 0.48, and 0.43 ppm, respectively, at room temperature. If the separation for the chloro and bromo isomers is approximately the same, then the exchange rate order is $(CH_3O,F) < Cl < Br$. The methoxyl and fluoro derivatives cannot be compared because no temperature dependence was observed in this investigation or by Gagnaire, *et al.*[12]

^{31}P Nmr Spectra. Geometrical isomers differ in ^{31}P chemical shift in the three a–b pairs examined. In fact, the ^{31}P shift is almost as sensitive to isomerism as the ^{19}F shift in XVIa and XVIb. The upfield shift compared to $P(OMe)_3$ (−137 ppm) for the rings could arise from a slight narrowing of the OPO bond angle in ring formation.[52] There is also a ring substituent effect on the shift whose origin is not entirely obvious. The pair of phosphites differing only in methyl substitution at the 4 position, XXIX and VII, and the analogous pair of 1-chloro derivatives (XXXI and XVII) have shifts differing by 7–8 ppm in each pair. A similar upfield shift is noted in the case of the 4-methyl-4-chloromethyl derivatives (IXa and IXb). Narrowing of the OPO bond angle in the ring is expected to cause a marked upfield shift in the ^{31}P resonance.[52] Since alkyl substitution of hydrogens on carbon is expected to cause a decrease in CCC angles,[53] the OPO angles in a six-membered ring could be expected to decrease in response and thereby cause an unfield shift in the ^{31}P chemical shift.[54]

Acknowledgments. The authors are grateful to the National Science Foundation for support of this research in the form of a grant to J. G. V. and funds to the university toward the purchase of the nmr instrumentation. Stimulating conversations with Professor Bentrude are also acknowledged.

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(50) R. J. Abraham and H. J. Bernstein, *Can. J. Chem.*, **39**, 216 (1961).

(51) A difference in the rate of intramolecular inversion of the bonds to phosphorus or the presence of an isomerization catalyst in the sample of fluoro isomers could also account for this observation. Nevertheless, the exchange rate for IXa,b appears to be quite small.

(52) V. Mark and J. R. Van Wazer, *J. Org. Chem.*, **32**, 1187 (1967).

(53) P. v. R. Schleyer, *J. Amer. Chem. Soc.*, **83**, 1368 (1961).

(54) V. Mark, private communication.