150° (lit.[22] by 145°), which was quaternized with ethyl bromide to yield **1d**, mp >300° (ethanol–ethyl acetate).

Anal. Calcd for $C_8H_{18}BrP$: C, 42.67; H, 8.07. Found: C, 42.67; H, 8.27.

Cleavage of **1d** with potassium hydroxide in 70% dimethyl sulfoxide was shown by glpc analysis to give two phosphine oxide products which were found to be identical with **21** and diethyl-*n*-butylphosphine oxide (**22**). Compound **22** was prepared by reaction of diethylphenylphosphine, bp 108° (13 mm) (lit.[27] bp 108–109° (20 mm)), with *n*-butyl bromide to give diethyl-*n*-butylphenylphosphonium bromide, an oil, which was cleaved with 2 *M* sodium hydroxide to yield diethyl-*n*-butylphosphine oxide, bp 160° (1 mm) (lit.[31] bp 85.5–86° (0.1 mm)).

1,1,2,2,3,4,4-Heptamethylphosphetanium Bromide (2). This compound was prepared with minor modification by literature methods,[32] mp >300°.

Anal. Calcd for $C_{10}H_{22}BrP$: C, 47.45; H, 8.75. Found: C, 47.28; H, 9.05.

Cleavage of **2** with potassium hydroxide in 70% dimethyl sulfoxide yielded phosphine oxides which were identical by glpc analysis with 1,2,2,3,4,4-hexamethylphosphetane 1-oxide, mp 120–130° (mixture of isomers) (lit.[1f] mp 170–171° for the cis isomer), and dimethyl(1,1,2,3-tetramethylbutyl)phosphine oxide,[1f] bp *ca.* 110° (0.1 mm) (kugelrohr).

Tetramethylphosphonium Bromide (3). To a rapidly stirred Grignard reagent prepared from 1.42 mol of methyl iodide and 2.00 g-atoms of magnesium turnings in 500 ml of ether and cooled to −78° was added 0.25 mol of phosphorus trichloride. After standing overnight the solution was distilled without prior hydrolysis and the distillate collected to 95°.[33] Treatment with methyl bromide yielded 8.4 g of **3**, mp >300°.

Anal. Calcd for $C_4H_{12}BrP$: C, 28.09; H, 7.07. Found: C, 28.17; H, 7.33.

The only cleavage product of **3** detected, other than methanol and methane, when **3** was treated with alkaline 70% dimethyl sulfoxide was trimethylphosphine oxide (**23**), identical with the product of 2 *M* sodium hydroxide decomposition of trimethylphenylphosphonium iodide, mp 234–235° (lit.[6] mp 236°), which melted at 139–141° (lit.[6] mp 140–141°).

Diethyldimethylphosphonium Bromide (4). The same general procedure was employed as for the preparation of **3** except for the use of ethyl iodide and methyldichlorophosphine and isolation of methyldiethylphosphine (**24**), bp 110°, by distillation. Quaternization of **24** with methyl bromide yielded 64% of **4**, mp >300°.

Anal. Calcd for $C_6H_{16}BrP$: C, 36.20; H, 8.10; Br, 40.14. Found: C, 36.50; H, 8.09; Br, 40.24.

Phosphine oxide products obtained by treatment of **4** with potassium hydroxide in 70% dimethyl sulfoxide were found to have the same retention times as methyldiethylphosphine oxide (**25**) and dimethylethylphosphine oxide (**26**). Compound **25**, bp 124–128° (16 mm) (lit.[24] by 230°), was prepared by oxidation of **24** with 70% *tert*-butyl hydroperoxide.[8] Dimethylphenylphosphine, when quaternized with ethyl bromide, yielded dimethylethylphenylphosphonium bromide (**27**), mp 200–201°.

Anal. Calcd for $C_{10}H_{16}BrP$: C, 48.60; H, 6.52. Found: C, 48.65; H, 6.66.

Cleavage of **27** with 2 *M* sodium hydroxide yielded **26**, bp 112° (14 mm), mp 76–77° (lit.[6] mp 73–75°).

Methyltriethylphosphonium Bromide (5). Methyldiethylphosphine (**24**) upon quaternization with ethyl bromide yielded **5**, mp >300°.

Anal. Calcd for $C_7H_{18}BrP$: C, 39.47; H, 8.46. Found: C, 39.28; H, 8.35.

Phosphine oxides resulting from treatment of **5** with potassium hydroxide in 70% dimethyl sulfoxide were demonstrated by glpc to be identical with methyldiethylphosphine oxide (**25**) and triethylphosphine oxide (**28**). Compound **28** was prepared by quaternizing diethylphenylphosphine, bp 108° (13 mm) (lit.[27] bp 108–109° (20 mm)), with ethyl bromide to give triethylphenylphosphonium bromide, mp 184–186° (lit.[24] mp 187–189°). Cleavage of the bromide salt with 2 *M* sodium hydroxide gave triethylphosphine oxide, bp 230° (lit.[34] bp 243°).

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Chemical Implications of Phosphorus Configuration in Isomeric 2-Substituted 2-Oxo-1,3,2-dioxaphosphorinanes

J. A. Mosbo[1] and J. G. Verkade*

Contribution from the Department of Chemistry, Iowa State University, Ames, Iowa 50010.

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Abstract: From the known configuration of the methoxy cyclic ester given in ref 11 and 12, the stereochemistry at phosphorus in isomers IIIa and IIIb was deduced from the stereospecific course of the Michaelis–Arbuzov-like reaction of the methoxy ester (IIa) with HBr. The isolable isomers equilibrate at higher temperatures and $\Delta H°$ for the conversion of IIIa to IIIb is 4.4 ± 1.5 kcal/mol. Comparison of the physical, chemical, and spectroscopic properties of VIIa and VIIb with those of IIIa and IIIb led us to conclude that a previous stereochemical assignment (ref 22) is incorrect. Under mild conditions, water destroys IIIb and VIIb, leaving the a isomers intact. Similarly, acetone at room temperature attacks only the b isomers to produce cyclic phosphonates which may well possess the stereochemistry shown in IX and X. Pmr chemical shift results of VIIa and VIIb in the presence of $Eu(fod)_3$ are also consistent with the stereochemical assignments.

The preferred stereochemical disposition of phosphorus substituents in 2-R-2-oxo-1,3,2-dioxaphosphorinanes (Ia, Ib) is still not known with certainty.[2] In the six solid-state structures reported in the literature, configuration Ia was observed when R = OPh,[3] OH,[4,5] Br,[6] Ph,[7] or Me[8] although configuration

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(1) National Science Foundation Trainee.

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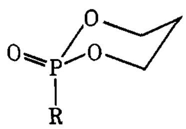
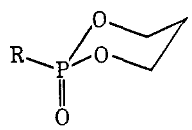


Ia



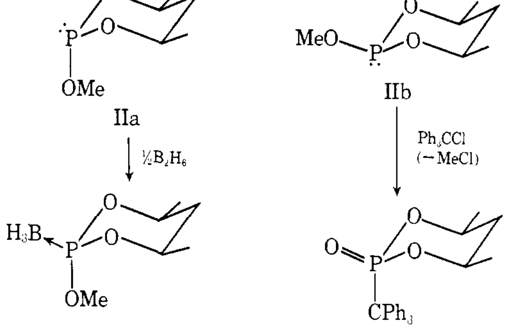
Ib

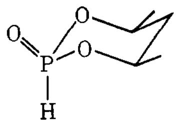
R = alkyl, aryl, alkoxy, aryloxy, alkylamino or halo and ring substituents may be present

Ib apparently does occur when R = NR_2.[9] In solution, however, nmr and ir studies point to the presence of conformational equilibria between Ia and Ib in several instances but it is not possible to assign the phosphorus stereochemistries of the conformers unambiguously.[2]

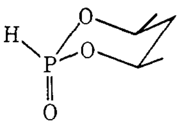
Even though cyclic phosphorus systems are conformationally mobile in solution, they produce configuration Ia in the solid state in most cases. It is unsafe, therefore, to draw conclusions concerning the relative stability of configuration Ia *vs.* b based on solid-state diffraction data since crystal packing forces may be dominant.

Recently we approached the problem of assigning the phosphorus configurations in isomeric 2-alkoxy-1,3,2-dioxaphosphorinanes by locking the cyclic ring with two equatorial methyl groups on C-4 and C-6, thereby sterically precluding appreciable concentrations of the other conformer in solution. Thus the liquid isomeric phosphites IIa and IIb can be synthesized[10] and their configurational assignments were accomplished *via* X-ray diffraction studies[11,12] on crystalline derivatives made with reagents whose stereochemical reaction pathways are known with reasonable certainty. Thus IIa is expected to behave as a symmetrical cleavage agent for B_2H_6[11] and Ph_3CCl should follow the classical Michaelis–Arbuzov pathway,[12] both reactions transpiring with retention of configuration at phosphorus. In this paper we report our assignment of the configurations for the cyclic phosphorus acid esters as shown in IIIa and IIIb based on the reaction of IIa with HBr. On the basis of equilibrium studies, a comparison of the relative thermodynamic stability of these structures is made and spectroscopic evidence is presented for their surprisingly contrasting reactivities toward water and acetone. The use of a lanthanide shift reagent produced nmr data which corroborates the structural assignments.





IIIa



IIIb

Experimental Section

***meso*-2,4-Pentanediol.** The synthesis was performed as reported previously.[13]

2-Chloro-1,3,2-dioxaphosphorinane. These starting materials for the preparation of IIIa,b, VIIa,b, and VIII were prepared as described previously for 2-chloro-4,6-α,α-dimethyl-1,3,2-dioxaphosphorinane (IV)[13] from PCl_3 and the appropriate diol.

2β-Hydro-2α-oxo-4α,6α-dimethyl-1,3,2-dioxaphosphorinane (IIIa) and 2α-Hydro-2β-oxo-4α,6α-dimethyl-1,3,2-dioxaphosphorinane (IIIb). To a solution of 21.9 g (0.13 mol) of IV dissolved in 20 ml of dioxane was added dropwise with stirring 2.5 ml (about 0.13 mol) of water in 20 ml of dioxane. After completion of addition, the dioxane was removed under vacuum. The liquid product formed in about 90% yield of which *ca.* 70% was isomer IIIa and 30% isomer IIIb (see Discussion). A synthesis of IIIa,b in which a small excess of the molar amount of pyridine was mixed with the water–dioxane solution resulted in essentially the same yield of diester and the same distribution of isomers (molecular weight by osmometry = 151; calcd 150).

To obtain pure isomer IIIb the above mixture was vacuum distilled (74° at 0.55 Torr) using a platinum spinning-band column with a pot temperature in excess of 140°. A slow reflux was maintained at the column head and a reflux ratio of one employed. The product which readily supercools was sublimed twice at *ca.* 0.1 Torr and 40° before further use. The white crystalline, deliquescent product (mp 38–39°) obtained in quantitative yield with respect to the diester mixture (owing to complete conversion of IIIa to IIIb) gave a high resolution mass spectrum parent peak of *m/e* 150.043957 (theoretical *m/e* 150.044581) as expected. The molecular weight was determined by osmometry to be 153 amu.

Upon heating IIIb to 145° for 12 hr a mixture of *ca.* 75% IIIa and 25% IIIb was obtained which gave a molecular weight of 151 amu from osmometric measurement. Repeated fractional crystallization from hot heptane led to isolation of pure IIIa (mp 50–52°). A low resolution mass spectrum exhibited a parent peak of 150 *m/e*.

2β-Hydro-2α-oxo-4α-methyl-1,3,2-dioxaphosphorinane (VIIa) and 2α-hydro-2β-oxo-4α-methyl-1,3,2-dioxaphosphorinane (VIIb). The method of preparation of these two compounds was the same as for IIIa,b above. The reaction yielded 80–85% VIIa and 20–15% VIIb *in a solid mixture (total yield ca.* 90%) which upon repeated recrystallization from hot heptane yielded pure VIIa (mp 52–54°). Isomer VIIb was prepared from the isomer mixture as described above for IIIb but with a boiling point of 78° at 0.45 Torr. Although VIIb remained a liquid, supercooling cannot be ruled out. The parent peaks of both isomers were identified from their mass spectra. The synthesis for VIIa,b has been described previously,[14,15] but the ratio of the isomers was not fully determined (see Discussion).

2-Hydro-2-oxo-5,5-dimethyl-1,3,2-dioxaphosphorinane (VIII). The synthesis was accomplished as described above for IIIa,b and it has also been described elsewhere.[14,15]

2β-Methoxy-4α,6α-dimethyl-1,3,2-dioxaphosphorinane (IIa). This compound was synthesized as described previously.[13]

2α-[2′-(2′-Hydroxypropyl)]-2β-oxo-4α,6α-dimethyl-1,3,2-dioxaphosphorinane (IX). To a few grams of IIIb was added a two- to threefold molar excess of acetone, and 2 to 3 drops of concentrated $HClO_4$. After stirring the solution for 36 hr, the acetone was removed under vacuum and the white crystalline precipitate was filtered and washed three times with small quantities of acetone. The yield of the product (mp 125–128°) was essentially quantitative. A high resolution mass spectrum of the parent peak gave a value for *m/e* of 208.084103, calculated as 208.086445 for the compound as formulated, and it exhibited a major fragment due to loss of acetone.

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Table I. Spectroscopic Properties of 2-R-2-oxo-1,3,2-dioxaphosphorinanes

Compound	δ_{PH}[a]	$^1J_{PH}$	δ_{CH_3}[a]	$^4J_{POCCH_3}$	$^3J_{HCCH_3}$	δ_{CH}[a]	δ_{CH_2}[a]	δ_{OH}[a]	$\delta_{^{31}P}$[b]	ν (P=O)[c]	ν (HP)[c]
IIIa	6.90d	664	1.41dd	1.7	6.2	4.6m[d]	1.8m[e]		−3.1	1283	2406
IIIb	6.95d	719	1.39dd	1.8	6.2	4.6m[d]	1.8m[e]		+1.2	1254	2470
VIIa	6.89d[f]	670[f]	1.42dd[f]	1.9[f]	6.2[f]	4.5m[d,g]	1.8m[h,j] 4.5m[g,i]			1287	2414
VIIb	7.00d[f]	712[f]	1.45dd[f]	1.3[f]	6.3[f]	4.5m[d,g]	1.8m[h,j] 4.5m[g,i]			1265	2477
VIII	6.90d[k]	675[k]	0.95s[k] 1.35s[k]				3.9m			1296[l] 1287[l]	2410[l] 2450[l]
IX			1.35dd[m] 1.48d[n]	1.5	6.3	4.7m	1.8m	3.48s	−24.2	1247	
X			1.22dd[m] 1.48d[n]	1.6	6.3	4.5m[g]	1.8m[h] 4.5m[g,i]	3.33s		1249	
XI			1.07s[o] 1.10s[o] 1.53d[n]				4.2m	2.98s	−22.3	1288 1258	

[a] $CDCl_3$ solution relative to TMS internal standard, s = singlet, d = doublet, m = multiplet. [b] Relative to 85% H_3PO_4 external (negative sign denotes downfield with respect to the standard). [c] $CHCl_3$ solution (cm^{-1}). [d] In the presence of Eu(fod)$_3$ shift reagent, $^3J_{H_{ax}CCH_{ax}}$ is 11 Hz. [e] In the presence of Eu(fod)$_3$ shift reagent, H_{ax} is indicated by the large spacing of 11 Hz (owing to coupling to the axial protons on C-4 and C-6) in the pair of triplets separated by a 14 Hz geminal coupling. H_{eq} is a 14 Hz doublet of unresolved multiplets. [f] Compares favorably with literature value (ref 22). [g] δ values of CH_2 protons at C-6 and CH at C-4 could not be distinguished. [h] CH_2 at C-5. [i] CH_2 at C-6. [j] Same as *e* above except that a further doubling of H_{eq} was found to be due to coupling to H_{ax} of C-5 (5 Hz). [k] Compares favorably with literature values (K. D. Bartle, R. S. Edmundson, and D. W. Jones, *Tetrahedron*, **21,** 2379 (1965)). [l] Reference 15 (see text). [m] C-4 and/or C-6 CH_3 protons. [n] $C(CH_3)_2OH$ protons. $^3J_{PCCH}$ = 15.6, 15.7, and 15.5 in IX, X, and XI, respectively. [o] C-5 CH_3 protons.

The acetone could be removed from IX to re-form IIIb by heating to 110° followed by applying vacuum until IX was observed to sublime up to the walls of the flask. Air was then admitted and the sublimate scraped down. After twice repeating this sequence, the residue was heated to 130° and vacuum distilled to obtain pure IIIb.

2α-[2′-(2′-Hydroxypropyl)]-2β-oxo-4α-methyl-1,3,2-dioxaphosphorinane (X). This synthesis differed from that of IX only in that the product was an oil for several weeks before eventually crystallizing (mp 109–110°). The parent ion was observed in its mass spectrum and there was again a major fragment from loss of acetone.

2-[2′-(2′-Hydroxypropyl)]-2-oxo-5,5-dimethyl-1,3,2-dioxaphosphorinane (XI). This compound was prepared identically to that of IX (mp 181–183°). Its mass spectrum exhibited a parent peak of *m/e* 208 and a major fragment of 150 amu due to loss of acetone.

Determination of Thermodynamic and Kinetic Data for IIIa,b. Heating pure IIIb at various temperatures resulted in formation of equilibrium mixtures of IIIa and IIIb. A total of five points at 10° increments from 120 to 160° gave isomer ratio *extrema* for IIIa/IIIb of 4.39 (81.4% IIIa) and 2.30 (69.7% IIIa), respectively. The time required for obtaining equilibrium ranged from no more than 72 hr for the former to 12 hr for the latter. A least-squares analysis yielded a slope of 9.65×10^2 and an intercept of −1.82 for a plot of log K *vs.* $1/T$. From the slope a value of -4.4 ± 1.5 kcal/mol was obtained for $\Delta H°$ of the reaction IIIb → IIIa using the relationship $\log K = (-\Delta H°/2.303R)(1/T) + I$, where K is the ratio of IIIa to IIIb and I is the intercept. A value for $\Delta S°$ was calculated as −8.3 cal/(deg mol). The reaction was found to be acid catalyzed and a sixth point was obtained at 40° under catalytic conditions. Unfortunately, the reaction had a half-life of approximately 36 hr and after only 4 half-lives there was severe decomposition. To obtain K_{eq}, the values of the known K's were plotted *vs.* time and the curved line was extrapolated to the asymptotic approach of K_{eq}. The value so obtained was used in a least-squares analysis which included the data taken at higher temperatures and the enthalpy recalculated to give $\Delta H° = -3.7 \pm 1.5$ kcal/mol and $\Delta S° = -6.5$ cal/(deg mol). The value for $\Delta G°$ calculated at 40° *via* the relationship $\Delta G° = -RT(2.303) \log K_{eq}$ is −1.6 kcal/mol.

The product distribution in converting IIIb to IIIa was observed at 150° after four different periods of time (total time 9.17 hr). A least-squares analysis of a plot of $-\log [(C - C_\infty)/(C_0 - C_\infty)]$ *vs. t* gave a slope of 0.1577 from which a value for the first-order rate constant k_{obsd} of 0.363 hr^{-1} (or 6.05×10^3 min^{-1}) was calculated ($t_{1/2}$ = 1.91 hr).

Michaelis–Arbuzov-Like Reaction of IIa with HBr. The triester IIa was dissolved in 3 ml of acetonitrile-d_3 to give a *ca.* 30% solution in a three-neck indented 25-ml flask equipped with reflux condenser and magnetic stirrer. After flushing the system and solution with nitrogen, anhydrous HBr diluted with nitrogen to about 50% was bubbled through the solution while maintaining the reaction at 65°. After 2 hr the reaction was complete as evidenced by the pmr spectrum which revealed *ca.* a 1:1 mole ratio of IIIa to IIIb. Methyl bromide was also observed in the spectrum.

Pmr Spectral Analysis of IIIa and IIIb. The coupling constants for IIIa and IIIb (Table I) were readily detectable in solutions containing the shift reagent tris(1,1,1,2,2,3,3-heptafluoro-4,6-octanedione)europium(III) (Eu(fod)$_3$). Carbon tetrachloride solutions which were 0.4 *M* in a IIIa,b mixture (75% IIIa and 25% IIIb) and 0.2 *M* in IIIb were employed. In both cases, and as found by Yee and Bentrude,[16] a 0.5 mole ratio of Eu(fod)$_3$/diester was optimum. The data derived for VIIa and VIIb in the presence of Eu(fod)$_3$ were obtained from 0.2 *M* solutions of each phosphonate in $CDCl_3$ employing the same mole ratio of shift reagent to phosphonate as above.

Instrumentation. Pmr spectra were obtained on a Varian Associates A-60 nmr spectrometer or a Varian Associates HA-100 instrument. ^{31}P chemical shifts were determined relative to H_3PO_4 external standard using a Varian Associates HR-60 instrument operating at 24 MHz employing a supercooled liquid sample in the case of IIIb and neat liquid isomer mixture (75% IIIa and 25% IIIb) for IIIa. For the ^{31}P chemical shifts of VIII, IX, and XI, however, the same instrument operating at 60 MHz was used employing standard indor techniques. The chemical shifts were determined relative to benzene lock signal from which they were calculated relative to H_3PO_4. Ir data were obtained on a Beckman IR-12 spectrometer. High resolution mass spectra were determined on an AEI MS-902 spectrometer while routine spectra were provided by an Atlas CH-4 mass spectrometer.

Results and Discussion

Hydrolysis of 2-chloro-1,3,2-dioxaphosphorinane (IV) in acidic (HCl is formed in the reaction) or basic media (excess pyridine) produced 70% IIIa and 30% IIIb which suggests dominance of SN2 mechanisms similar to those shown below if the stereochemical assignment of IIIa is correct (*vide infra*). Evidence for the likelihood of the configuration shown for IV is presented elsewhere.[13]

Although IIIa can be purified by repeated crystallization of the reaction mixture, IIIb is obtained pure by vacuum distillation of a mixture of the two isomers. The physical and spectroscopic parameters of the iso-

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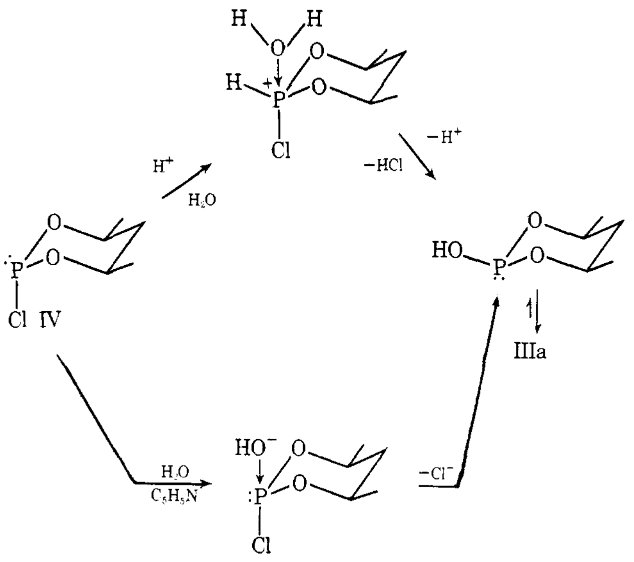
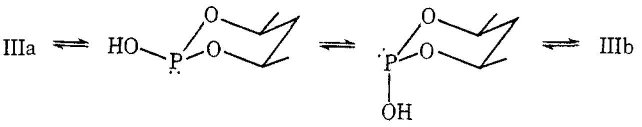
(16) K. C. Yee and W. G. Bentrude, *Tetrahedron Lett.*, 2775 (1971).



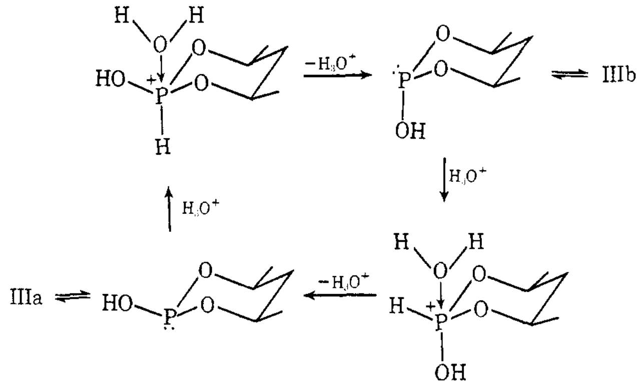
mers are tabulated in Table I and proof of their monomeric nature is found in their molecular weights measured in solution.

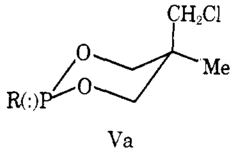
The equilibrium between the two isomers indicated by the distillation experiment was followed in the range 120–160° by means of nmr integration of the downfield half of the P–H protons and the enthalpy for conversion of IIIa to IIIb was calculated to be 4.4 ± 1.5 kcal/mol. Equilibrium at room temperature is reached undetectably slowly and even at 74° where IIIb distilled from the mixture, equilibrium establishment was sufficiently slow to allow it to be obtained pure. In fact, 72 hr are required for equilibrium to occur at 120°. The free-energy difference at 40° is $\Delta G° = -1.6 \pm 1$ kcal/mol favoring IIIa over IIIb in the acid catalyzed equilibrium.

It seems quite reasonable to assume that tautomers of IIIa and IIIb are probably important in the equilibrium process[17] and some evidence for tautomerism is presented later. The conversion of IIIb to IIIa at 150° was found by us to be first order and this was also found to be the case by Nifant'ev and Borisenko[18] for transforming VIIb to VIIa. These workers further stated that the activation energy for the conversion of VIIb to VIIa was 23.0 ± 0.8 kcal/mol.[18] Such an activation energy value is quite low for a phosphorus inversion process (~50 kcal/mol[19]) even if an anionic species is involved (~30 kcal/mol[19]) as suggested by the Russian authors.[18] Postulating other possible mechanisms at this time would be too speculative and further investigations designed to answer this question are under way. The catalysis of isomerization by aqueous acid can be understood in terms of an Sn2 attack by water (Scheme I). It should be pointed out that evidence for a similar bimolecular pathway for the facile interconversion of isomers Va and Vb has been put forth where R = halogen since isomerization is accelerated in the presence of halide ion.[13] Since the keto form might be expected to predominate, the mechanism in Scheme II for the acid-catalyzed interconversion is a viable alternative.[20]

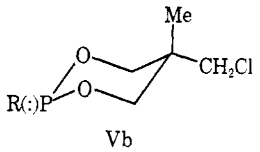


Scheme I



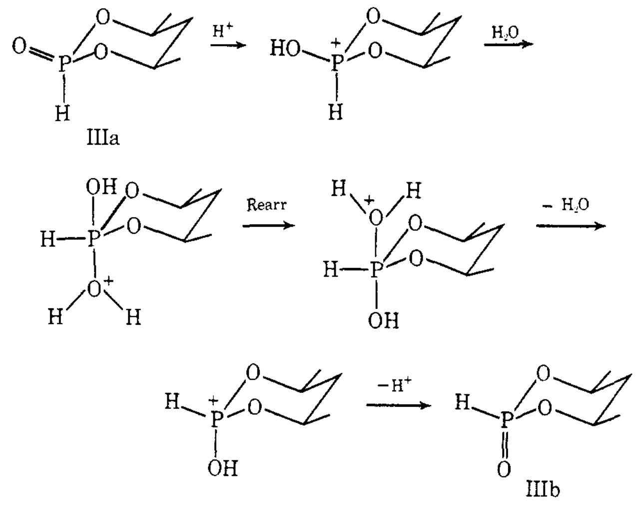


Va

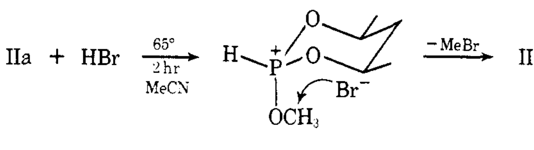


Vb

Scheme II



The stereochemistry at phosphorus in IIIa and IIIb is strongly implied by the Michaelis–Arbuzov-like reaction of IIa with gaseous HBr. Although IIIb would be expected to constitute the major product, a *ca.* 50–50 mixture of IIIb and IIIa was formed. This result suggests that at 65° isomerization of IIa to IIb (in which case the latter could react with HBr to form IIIa) and/or isomerization of IIIb to IIIa was occurring. Although the second process is undetectably slow at 65° using pure IIIb, it is catalyzed using aqueous



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(17) A single ring cleavage would not account for isomerization although its involvement in the IIIa–IIIb equilibrium cannot be ruled out. It seems unduly complicated to invoke the necessity of two simultaneous ring cleavages to cause isomerization.

(18) E. E. Nifant'ev and A. A. Borisenko, *Tetrahedron Lett.*, 309 (1972).

(19) A. Rauk, J. D. Andose, W. G. Frick, R. Tang, and K. Mislow, *J. Amer. Chem. Soc.*, **93**, 6507 (1971).

(20) We thank one of the referees and Dr. D. W. White for calling this alternate mechanism to our attention.

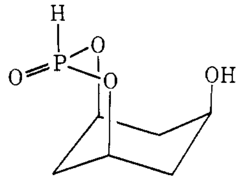
Table II. Pmr Chemical Shifts (δ) of VIIa and VIIb in Presence of Eu(fod)$_3$[a]

			C-5		C-6	
Compound	$C\mathit{H}_3CHCH_2CH_2$	C-4 $CH_3C\mathit{H}CH_2CH_2$	CH_3CH-$C(\mathit{H}_{ax})HCH_2$	CH_3CH-$C(\mathit{H}_{eq})HCH_2$	CH_3CH-$CH_2C(\mathit{H}_{ax})H$	CH_3CH-$CH_2C(\mathit{H}_{eq})H$
VIIa						
With Eu(fod)$_3$	2.6	6.1	4.0	3.2	6.1	6.1
$\Delta\delta^b$	1.2	1.6	2.2	1.4	1.6	1.6
VIIb						
With Eu(fod)$_3$	2.7	9.1	4.4	3.8	8.6	6.2
$\delta\Delta^b$	1.3	4.6	2.6	2.0	4.1	1.7

[a] Chemical shifts with respect to TMS measured in solutions 0.2 *M* in phosphonate and 0.1 *M* in Eu(fod)$_3$. [b] Chemical shift difference with and without Eu(fod)$_3$.

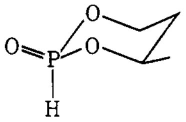
$HClO_4$ and a *ca.* 50–50 mixture of IIIa and IIIb is formed in the same length of time the HBr reaction was allowed to take place. Furthermore, when a mixture of IIa and IIIb was treated with HBr by the same procedure, a 1:1 ratio of IIIa to IIIb was obtained. Thus isomerization of the starting compound does not seem to be important, for no IIb was detected at any point during this reaction. Excess HBr could well be responsible for partial conversion of IIIb to IIIa if trace amounts of water were present.

Of importance to the configurational assignment of IIIb in the HBr reaction is the fact that equilibrium was not attained during the reaction. Even at 120°, equilibrium occurs with only about 20% IIIb present and so more than a twofold excess of IIIb was formed in the HBr reaction than could be accommodated at equilibrium at 65°. Extrapolation of the equilibrium data obtained in the 120–160° range indicates an equilibrium point of about 10% IIIb and 90% IIIa. Acid-catalyzed equilibrium approached at 40° after 5 days (see the Experimental Section) using pure IIIb or IIIa corroborates the extrapolated result. While these observations support the stereochemical assignments of IIIa and IIIb, the question of whether either or both isomers are boat or chair conformers still remains, especially in view of our solid-state structure determination of VI.[21]

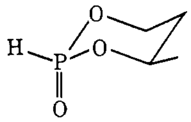


VI

A few years ago, it was reported that the isomeric VIIa and VIIb were formed upon hydrolysis of the parent 2-chloro compound in the presence of base.[22] Our configurational assignments for these isomers are opposite to those arrived at in the earlier report,[22] however. The original assignment was based on the tenuously small deshielding (0.02 ppm) of the predominantly equatorial ring methyl group when cis to P=O (VIIa) than when trans (VIIb), as might be expected if P=O groups deshielded analogously[23] to S=O groups. Repetition of this work and further studies in our laboratories, however, force us to conclude that application of the P=O deshielding criterion yields incorrect assignments in this case. The grounds for this contention follow. (1) Isomers VIIa and VIIb possess melting points, boiling points, $^1J_{PH}$ values, P=O stretching frequencies, and P—H stretching frequencies (Table I) which compare closely with those of isomers IIIa and IIIb, respectively, whose configurations were deduced from data discussed earlier in this paper. (2) Like IIIb, VIIb can be distilled in pure form from a mixture of VIIb and VIIa, and at 145° the a/b isomer equilibrium ratio is about 3:1 in both pairs of compounds. (3) The chemical properties (*vide infra*) of IIIa and VIIa are very similar as are those of IIIb and VIIb but configurations a and b do exhibit contrasting chemical behavior. (4) The proton chemical shifts in the presence of the lanthanide shift reagent Eu(fod)$_3$ are consistent with this assignment.



VIIa



VIIb

The chemical shifts of VIIa and VIIb in the presence of Eu(fod)$_3$ are listed in Table II. The chemical shift difference of protons in the presence and absence of shift reagent ($\Delta\delta$) is expressed as[24]

$$\Delta\delta_1 = k(3\cos^2\theta - 1)/R^3$$

where θ is the angle between the symmetry axis of the complex and the vector from the lanthanide ion to the proton, *R* is the distance from the lanthanide to the proton, and *k* is a collection of constants. Yee and Bentrude[16] observed in a similar system that the ring oxygens did not contribute to complexing with the shift reagent, but that the phosphoryl oxygen was involved. A model of VIIa in the chair conformer indicates that if the lanthanide coordinates through the phosphoryl oxygen, the two axial protons of the 4 and 6 positions and the equatorial proton of the 6 position are all in rather similar environments with respect to distance and angle to the lanthanide ion. The chemical shifts of these protons are expected to be very similar, and this is found experimentally. A model of the chair conformer of VIIb, however, indicates that the two axial protons are much closer to the lanthanide than is the equatorial proton which suggests that a larger shift difference for axial protons *vs.* the equatorial protons should be expected. These differences were found experimentally to be substantial (see Table II).

Our stereochemical assignment for VIIa and b, while

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(21) D. M. Nimrod, D. R. Fitzwater, and J. G. Verkade, *Inorg. Chim. Acta*, **2**, 149 (1968).

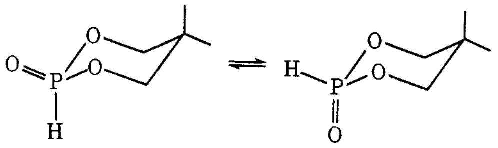
(22) M. Mikolajczyk, *J. Chem. Soc. D*, 1221 (1969).

(23) F. Ramirez, A. V. Patwardhan, N. B. Desai, and S. R. Heller, *J. Amer. Chem. Soc.*, **87**, 549 (1965).

(24) B. L. Shapiro, J. R. Hlubucek, and G. R. Sullivan, *ibid.*, **93**, 3281 (1971).

in disagreement with that of Misolajczyk,[22] does confirm the identical conclusion reached in a recent Russian report[25] on the basis of the measured dipole moments of these isomers.

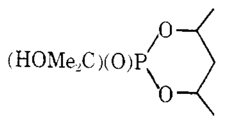
Since IIIa and IIIb form an equilibrium mixture at 40°, it is reasonable to suppose that VIII is similar in nature. The intermediacy of $^1J_{PH}$ for VIII between



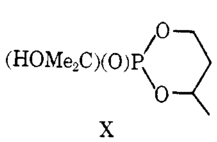
VIIIa VIIIb

the values measured for each pair of a and b isomers supports this idea to some extent. On the faster ir time scale, it might be expected that VIII would exhibit two P=O and two P—H stretching frequencies since the a and b isomers of III and VII possess rather characteristic values for these modes (Table I). Although Zwierzak has reported[15] a pair of P—H bands as well as two P=O bands for VIII (Table I), in our hands the ir spectrum does not appear quite so definitive. The band we see at 2444 cm^{-1} seems rather broad and weak compared to that at 2409 cm^{-1} and the 1296-cm^{-1} absorption has two shoulders on the low-frequency side. Thus we are uncertain as to whether the 2444-cm^{-1} band and one of the shoulders on the 1296-cm^{-1} absorption represent a second conformer and isotope substitution experiments are planned to clarify this point.

The behaviors of IIIa, IIIb, VIIa, VIIb, and VIIIa,b in the presence of water and acetone are rather remarkable. When an equimolar mixture of IIIa and IIIb or VIIa and VIIb is allowed to react (in the absence or presence of acid) with enough water to hydrolyze half of the diester completely to phosphorous acid and diol, the b isomers are completely destroyed after 24 hr at room temperature while the a isomers remain intact as shown from the ^{1}H nmr spectra. Compound VIIIa,b also hydrolyzes. Furthermore, IIIb, VIIb, and VIIIa,b all react quantitatively with acetone in the presence of a catalytic amount of aqueous acid over a period of 36 hr to form IX, X, and XI,

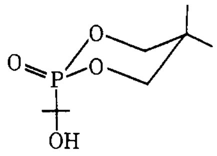


IX

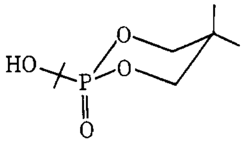


X

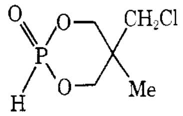
respectively, while no reaction is observed using IIIa or VIIa. Although we have already disclosed a preliminary report[26] of the reaction of acetone with XII and XIII to form similar products, the present work reveals the stereospecific dependence of acetone attack on the configuration at phosphorus. While the configuration at phosphorus in the acetone reaction products IX and X is uncertain, it is apparently the same in these two compounds as judged from the similarity of the δ ^{31}P chemical shifts and P=O stretching frequencies. The observation of two P=O frequencies in XI indicates the presence of the two conformers XIa and XIb.



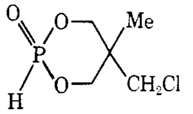
XIa



XIb

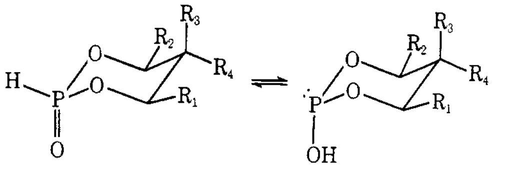


XII



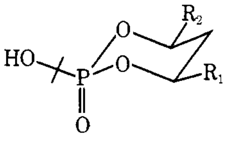
XIII

The hydrolyses and the acetone reactions of IIIb, VIIb, and VIIIa,b may reflect a greater ease of tautomer formation on the part of isomers of the "b" configuration.



IIIb, $R_1 = R_2 = Me$; $R_3 = R_4 = H$
VIIb, $R_1 = Me$; $R_2 = R_3 = R_4 = H$
VIIIb, $R_1 = R_2 = H$; $R_3 = R_4 = Me$

Thus like the OR groups,[12,13] an OH group may well be thermodynamically more stable in the axial than in the equatorial position demanded by the a isomers. Moreover, equatorial attack of the "b" tautomer by nucleophiles such as H+ in the hydrolysis (probably followed by water attack on P and cleavage of a ring P—O bond) and carbonyl carbon in the acetone reaction (followed by proton attack of the carbonyl oxygen) is perhaps somewhat more sterically favored than axial attack on the "a" tautomers. The available evidence seems to suggest that the configuration of IX and X is that shown below, but further studies are needed before a less ambiguous structural assignment is possible.



IX, $R_1 = R_2 = Me$
X, $R_1 = Me$; $R_2 = H$

Acknowledgments. The authors are grateful to the National Science Foundation for funds to Iowa State University which were used toward the purchase of the nmr instrumentation and a grant to J. G. V. They also thank Mr. R. Bowen for furnishing compound XI.

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[25] E. E. Nifant'ev, A. A. Borisenko, I. S. Nasonovskii, and E. I. Matrosov, *Dokl. Akad. Nauk SSSR*, **196**, 28 (1971).

[26] R. D. Bertrand, T. J. Kistenmacher, R. L. Kolpa, G. K. McEwen, and J. G. Verkade, Abstracts, 162nd National Meeting of the American Chemical Society, Washington, D. C., 1971, No. ORGN-071.