X-Ray Analysis of *cis*-1-Iodomethyl-3-methyl-1-phenylphospholanium Iodide and Assignment of Configuration to Stereochemically Related Phospholane Derivatives

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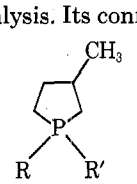
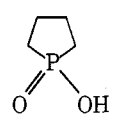
The crystal and molecular structure of the isomer of 1-iodomethyl-3-methyl-1-phenylphospholanium iodide of mp 192–193 °C (**1c**) has been determined by x-ray analysis and the methyl group found to be trans to the phenyl substituent. The phospholanium ring appears to be in the envelope form with the methyl group at the point of the flap. The crystals are monoclinic of space group $P2_1/c$ with a = 7.217 (3) Å, b = 14.261 (6) Å, and c = 14.778 (6) Å, β = 106.54 (3)°. The structure was solved from the three-dimensional Patterson function by location of the iodine positions and refined by using full-matrix least squares to an R factor of 4.5% for the observed data. Bond distances around phosphorus range from 1.78 (1) to 1.82 (1) Å while the endocyclic angle at phosphorus is 96.0 (4)°. The exocyclic angles at phosphorus average 112°. By the use of stereospecific reactions, the trans and cis configurations of isomers of the following constitution are now known: 3-methyl-1-phenylphospholane, 3-methyl-1-phenylphospholane 1-oxide, 1,3-dimethyl-1-phenylphospholanium bromide, 1-benzyl-3-methyl-1-phenylphospholanium bromide, 1-iodomethyl-3-methyl-1-phenylphospholanium iodide, 1-methoxy-3-methyl-1-phenylphospholanium hexafluorophosphate, 1,3-dimethylphospholane, 1,3-dimethylphospholane 1-oxide, and 1-benzyl-1,3-dimethylphospholanium bromide. The x-ray structure determination also reveals that catalytic addition of hydrogen to 3-methyl-1-phenyl-2-phospholene 1-oxide occurs stereospecifically to the oxide side of the phospholene ring.

Several reasons prompted this structural analysis of a derivative of 3-methyl-1-phenylphospholane (**1a**). We have chosen the isomer of 1-iodomethyl-3-methyl-1-phenylphospholanium iodide (**1c**) of mp 192–193 °C for this study because of its stability and the suitability of the crystals for x-ray analysis. Its configuration has been found to be cis.[1]



1a, R = Ph; R′ = lone pair
b, R = Me; R′ = lone pair
c, R = Ph; R′ = CH_2I



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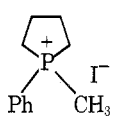

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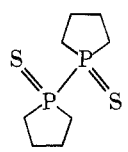

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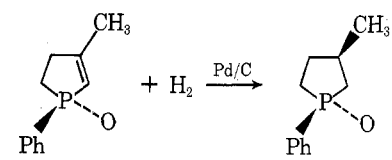
Although structure determinations for three compounds possessing simple phospholane rings (**2**,[2] **3**,[3] **4**[4]) are reported in the literature, none of these substances possess substituents on ring carbons, and thus the effect of substitution on ring structure has remained unknown.

One of us (K.L.M.) has participated in rather extensive investigations into the stereochemistry of nucleophilic substitution reactions at phosphorus in phospholane ring systems employing geometrically isomeric derivatives of **1a** and **1b**.[5] Although conclusions could be drawn concerning the stereochemistry of most reactions studied because of the completion of stereochemical cycles, the actual geometric configurations of the isomers used were unknown. Because of the similarity of ^{1}H NMR (60 MHz) and ^{31}P NMR (100 MHz) spectra of the trans and cis isomers of these phospholane derivatives, stereochemical assignments could not be made with confidence by NMR. During the course of these studies nine sets of geometrical isomers, structurally related to **1**, were prepared in analytical and isomeric purity and characterized. These are shown in Chart I together with their configurational assignments and certain physical properties. Their geometric configurations were determined by relating these compounds through reactions of known stereochemistry (Chart I) to the structure of *cis*-1-iodomethyl-3-methyl-1-phenylphospholanium iodide (**5**) whose crystal structure analysis is reported in this paper. Knowledge of the configurations of these compounds will also be useful in future stereochemical studies.

The x-ray structure determination of **5** has enabled us to assign stereochemistry to two reactions of previously undemonstrated stereochemistry. First, it has been noted that the reduction of 3-methyl-1-phenyl-2-phospholene 1-oxide[6] (**6**) with hydrogen in the presence of palladium on carbon catalyst yields only one of two possible diastereomers as a racemic mixture.[5d] This work has established the fact that addition of hydrogen occurs *exclusively from the oxygen side of the heterocycle* to yield the trans isomer (shown for one enantiomer in eq 1). It should be noted that



6 **7** (1)

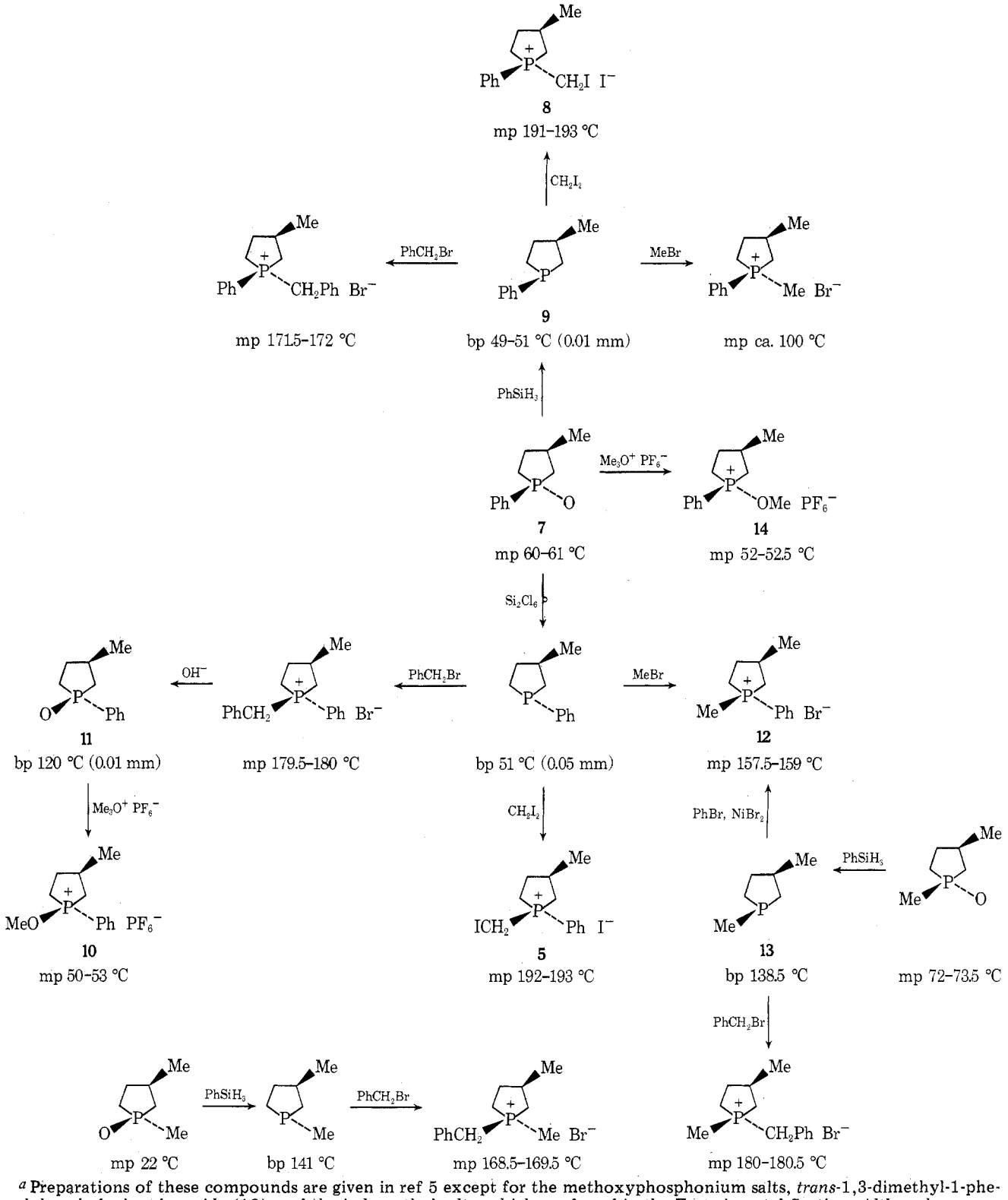
catalytic hydrogenation of 1,3-dimethyl-3-phospholene 1-oxide yields a mixture of the trans and cis isomers of the corresponding phospholane 1-oxide.[5d] Secondly, although it has been shown that acyclic tertiary phosphines may be arylated with bromobenzene in the presence of $NiBr_2$ with retention of configuration at phosphorus,[7a] the stereochemistry of this reaction with cyclic tertiary phosphines has not been tested. Chart I indicates that this arylation has now been demonstrated to occur with predominant if not complete retention of configuration at phosphorus.

Experimental Section

Preparation of *cis*-1-Iodomethyl-3-methyl-1-phenylphospholanium Iodide (5). To 13.6 g (0.070 mol) of *trans*-3-methyl-1-

phenylphospholane 1-oxide (7) in 300 ml of dry benzene under nitrogen was added slowly 24.5 g (0.0911 mol) of hexachlorodisilane. The reaction mixture was quenched by dropwise addition of 60 ml of 30% sodium hydroxide at 0 °C and the benzene layer separated

Chart I. Stereochemical Relationships of Phospholanes Using Reactions of Known Stereochemistry[a,b]



[a] Preparations of these compounds are given in ref 5 except for the methoxyphosphonium salts, *trans*-1,3-dimethyl-1-phenylphospholanium bromide (12), and the iodomethyl salts, which are found in the Experimental Section. Although one enantiomer is shown for each reaction, the reactions and physical properties are for *racemic mixtures* of pure geometrical isomers. [b] Stereochemistry of reactions shown in this chart: quaternization of phosphines with alkyl halides occurs with retention of configuration at phosphorus [L. D. Quin and T. P. Barket, *J. Am. Chem. Soc.*, 92, 4303 (1970); L. Horner, *Pure Appl. Chem.*, 9, 225 (1964)]; phenylsilane reduction of phosphine oxides also occurs with retention of configuration at phosphorus [K. L. Marsi, *J. Org. Chem.*, 39, 265 (1974)]; methylation of phosphine oxides takes place with retention of configuration since no bonds are cleaved at phosphorus; hexachlorodisilane reduction of phospholane oxides is accompanied by predominant inversion of configuration at phosphorus;[5c] hydroxide cleavage of *trans*- and *cis*-1-benzyl-3-methyl-1-phenylphospholanium bromide occurs with retention of configuration at phosphorus[5d] as does the hydroxide cleavage of *trans*- and *cis*-1-benzyl-1,3-dimethylphospholanium bromide.[5a,b]

and dried. Methylene iodide (30.0 g, 0.133 mol) was added with stirring to the benzene layer, the mixture refluxed gently for 1 h, and 17.6 g of crude **5** obtained after filtration. Seven recrystallizations from water gave a material of mp 192–193 °C dec.

Anal. Calcd for $C_{12}H_{17}I_2P$: C, 32.31; H, 3.84. Found: C, 32.04; H, 3.94.

Preparation of *trans*-1-Iodomethyl-3-methyl-1-phenylphospholanium Iodide (8). To 5.0 g (0.0258 mol) of **7** under nitrogen was added 2.8 g of phenylsilane via pipet. The mixture was warmed to about 60 °C. After effervescence ceased (about 0.5 h) the reaction mixture was distilled to give *cis*-3-methyl-1-phenylphospholane (**9**), bp 130–136 °C (5 mm). The distillate was quaternized by adding 6.85 g (0.0257 mol) of methylene iodide in 15 ml of benzene with stirring. The mixture was stored overnight and yielded 5.8 g (0.0130 mol) of **8** upon filtration. One recrystallization from ethanol–ethyl acetate gave **8** of mp 191–193 °C dec. A mixture melting point with **5** gave 177–178 °C.

Anal. Calcd for $C_{12}H_{17}I_2P$; C, 32.31; H, 3.84. Found: C, 32.39; H. 3.91.

Preparation of the Trans and Cis Isomers of 1-Methoxy-3-methyl-1-phenylphospholanium Hexafluorophosphate. For the preparation of the trans isomer (**14**) 2.98 g (0.0153 mol) of the phosphine oxide **7** was dissolved in 25 ml of dry methylene chloride. This solution was added to a suspension of 3.51 g (0.0170 mol) of trimethyloxonium hexafluorophosphate in 50 ml of dry methylene chloride and the resulting mixture stirred at room temperature overnight. Traces of insoluble residue were removed by centrifugation and the supernatant solution evaporated to dryness in vacuo. The glassy residue crystallized upon standing and the resulting crystals were extracted with 150 ml of ether in 10-ml portions. The crystals were then dissolved in methylene chloride and ether added until an oil separated. The oil was washed twice with ether, and upon drying in vacuo it crystallized to yield 1.60 g (0.00452 mol) of **14**, mp 50–52.5 °C.

Anal. Calcd for $C_{12}H_{18}OP_2F_6$: C, 40.69; H, 5.12. Found: C, 40.95; H, 5.40.

The cis isomer (**10**) was similarly prepared from **11**,[5d] mp 50–53 °C; a mixture melting point with **14** gave 29–44 °C.

Anal. Calcd for $C_{12}H_{18}OP_2F_6$: C, 40.69; H, 5.12. Found: C, 40.80; H, 5.39.

Preparation of *trans*-1,3-Dimethyl-1-phenylphospholanium Bromide (12). This compound was prepared from *cis*-1,3-dimethylphospholane (**13**)[5a,b] by the method of Horner,[7a] mp 157.5–159 °C (lit.[5d] 158.5–159 °C).

X-Ray Crystallographic Data. A colorless, transparent parallelepiped of dimensions 0.486 × 0.076 × 0.064 mm^3 was used for the x-ray analysis. Since the material appeared hygroscopic, a crystal was mounted on a glass fiber and sealed in a Lindemann glass capillary tube for collection of the x-ray data. Preliminary Weissenberg and precession photographs showed the following conditions for reflection: *hkl*, no conditions; 0*k*0, $k = 2n$; *h*0*l*, $l = 2n$, uniquely determining space group at $P2_1/c$. A pseudo-A-centering condition was also exhibited which helped in interpretation of the Patterson map.

Precise unit cell parameters were obtained by a least-squares refinement of 18 independent 2θ values obtained from a manual G.E. XRD-5 diffractometer equipped with a scintillation counter as a detector and using Mo Kα radiation. (Crystal data are given in Table I.)

Table I. Crystal Data

Mol wt 446.051	$F(000) = 840$
Monoclinic, space group $P2_1/c$	
$a = 7.217$ (3) Å	
$b = 14.261$ (6) Å	$\beta = 106.54°$ (3)
$c = 14.778$ (6) Å	
Volume of the unit cell = 1458 Å^3	$D_{calcd} = 2.03$ g/cm^3
Molecules/unit cell = 4	$D_{exp} = 2.12$ g/cm^3

Linear absorption coefficient, μ(Mo K$_\alpha$) = 44.473 cm^{-1}
Crystal dimensions: 0.486 × 0.076 × 0.064 mm
Crystal was bound by faces {100}, {0$\bar{1}$1}, and {011}, respectively.

Data were collected out to a 2θ of 45° using 60-s scans at a scan rate of 2° min^{-1}, counting backgrounds for 10 s on either side of the peak. Three standard reflections were measured every 2 h. A scale factor calculated from these was used to scale each block of data to zero time. The average value of the scale factor over the complete data collection was 1.006 with a standard deviation of 0.026, indicating no significant deterioration of the crystal or variation of conditions. The crystal did change to a yellowish-brown color during the course of the data collection. A total of 1946 reflections was measured with 1434 considered observed based on the criteria $I > 3\sigma(I)$. Unobserved data were given zero weight and not included in the refinement.

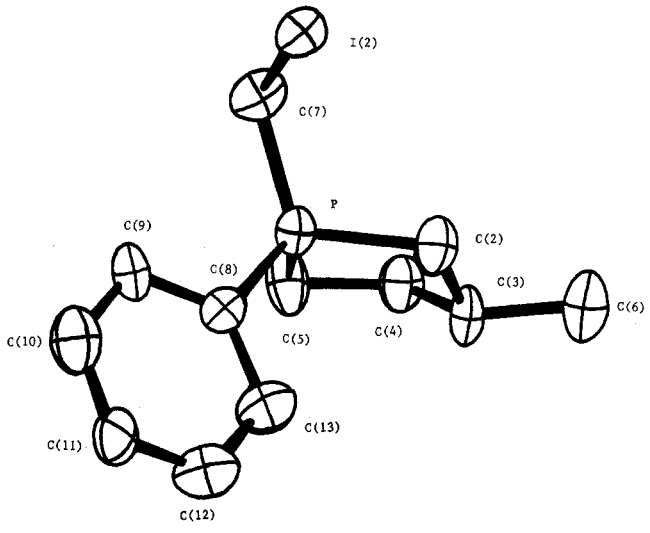


Figure 1. ORTEP drawing of the molecule. Thermal ellipsoids have been scaled to include 50% probability.

Backgrounds were corrected for counting times and Lorentz and polarization factors were applied in the normal manner.[8] Initially the data were not corrected for absorption, but a final correction using Tompa's method[9] gave maximum and minimum transmission coefficients of 0.77 and 0.72, respectively. Weights were calculated according to the method proposed by Stout and Jensen,[10] $\sigma(F) = \{(k/4LpI)[\sigma^2(I) + (0.05I)^2]\}^{1/2}$. Scattering factors for the iodide ion were taken from Cromer and Mann.[11] Scattering factors for all other nonhydrogen atoms were from the International Tables[12] with hydrogen scattering factors taken from the calculations of Stewart, Davidson, and Simpson.[13] Anomalous scattering corrections were assumed to be the same for both the iodine atom and iodide ion and were from the International Tables for Crystallography.[12] No correction was made for extinction but 39 reflections were finally removed from the data because of obvious error in crystal setting, irregularly shaped backgrounds, short-term variations in instrumental stability, and other errors related to the data collection.

Structure Analysis and Refinement. The structure was solved from the three-dimensional Patterson function by location of the iodine positions. The Fourier synthesis phased on the iodine atom showed the locations of all the other atoms except hydrogen. Refinement of these atomic positions and the anisotropic thermal parameters gave a standard R factor of 0.066. A difference Fourier map failed to indicate well-defined hydrogen atom positions. Examination of the data indicated some obvious errors in data collection indicated above. After removal of the 39 reflections with these obvious experimental errors all hydrogen atoms were evident in the difference Fourier. Four additional cycles of full matrix refinement of positional parameters of all atoms, anisotropic thermal parameters of heavy atoms, and isotropic temperature factors of the hydrogen atoms produced an R factor of 0.045 for the observed data only; the R factor for both the observed and unobserved data was 0.085. The weighted $R(\Sigma w\Delta F^2/\Sigma wF_o^2)^{1/2}$ was 0.059 and S, the standard deviation of an observation of unit weight $[\Sigma w\Delta F^2/(m - n)]^{1/2}$ (m is the number of observations and n is the number of parameters), was 1.87. Final shifts in heavy atom parameters were less than 10% of their standard deviations and the corresponding shifts in the hydrogen parameters were less than 25% of their standard deviations. A final difference map was essentially flat except for areas around the iodine atom and ion, where peak heights varied from +1.30 to −0.51 eA^{-3}. A $\delta(R)$ normal probability plot[14] was calculated and was essentially linear; the equation of the least-squares straight line had a slope of 1.7 and an intercept of −0.04. The slope of this line indicates that the $\sigma(F)$ are underestimated by a factor of about 1.7.

Table II lists final positional and thermal parameters, Figure 1 is an ORTEP drawing of the molecule, and Table III gives the bond distances and angles.

Table II. Positional and Thermal Parameters with Their Standard Deviations in Parentheses

Atom	x/a	y/b	z/c	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
I(1)	0.90818 (10)[a]	0.88611 (5)	0.22996 (5)	0.02025 (20)	0.00576 (5)	0.00565 (5)	0.00011 (7)	0.00348 (7)	0.00087 (3)
I(2)	0.30387 (9)	0.61494 (5)	0.24359 (4)	0.01933 (18)	0.00569 (5)	0.00376 (4)	0.00044 (7)	0.00286 (6)	0.00012 (3)
P	0.3556 (3)	0.7580 (2)	0.0815 (2)	0.0127 (5)	0.0034 (1)	0.0042 (1)	0.0004 (2)	0.0022 (2)	0.0000 (1)
C(2)	0.1005 (12)	0.7451 (7)	0.0187 (6)	0.0165 (23)	0.0045 (6)	0.0047 (6)	0.0011 (9)	0.0036 (9)	0.0006 (4)
C(3)	0.0556 (13)	0.8258 (8)	−0.0483 (7)	0.137 (22)	0.0057 (7)	0.0065 (6)	0.0020 (10)	0.0033 (10)	0.0011 (5)
C(4)	0.1750 (15)	0.9089 (7)	−0.0017 (7)	0.0193 (24)	0.0042 (6)	0.0064 (7)	0.0018 (10)	0.0049 (11)	0.0009 (5)
C(5)	0.3791 (13)	0.8767 (6)	0.0427 (7)	0.0155 (23)	0.0034 (5)	0.0057 (6)	0.0000 (8)	0.0029 (9)	−0.0004 (4)
C(6)	−0.1623 (16)	0.8452 (9)	−0.0486 (5)	0.0195 (28)	0.0072 (7)	0.0075 (8)	−0.0005 (12)	−0.0019 (12)	−0.0003 (7)
C(7)	0.3939 (14)	0.7515 (7)	0.2060 (7)	0.0193 (25)	0.0046 (6)	0.0048 (6)	−0.0005 (9)	0.0027 (9)	−0.0016 (5)
C(8)	0.5047 (12)	0.6768 (6)	0.0426 (5)	0.0126 (20)	0.0041 (5)	0.0030 (5)	−0.0014 (8)	0.0025 (8)	0.0003 (4)
C(9)	0.4522 (16)	0.6515 (7)	−0.0516 (7)	0.0275 (29)	0.0038 (6)	0.0048 (6)	0.0010 (11)	0.0040 (11)	0.0004 (5)
C(10)	0.5658 (17)	0.5905 (7)	−0.0825 (6)	0.0348 (35)	0.0056 (7)	0.0027 (5)	0.0022 (12)	0.0063 (11)	−0.0005 (5)
C(11)	0.7267 (14)	0.5531 (7)	−0.0230 (8)	0.0187 (26)	0.0033 (6)	0.0072 (8)	−0.0025 (9)	0.0042 (12)	−0.0017 (5)
C(12)	0.7787 (14)	0.5771 (7)	0.0651 (8)	0.0148 (23)	0.0048 (6)	0.0068 (7)	−0.0001 (10)	−0.0004 (10)	−0.0002 (6)
C(13)	0.6677 (13)	0.6387 (6)	0.1052 (7)	0.0147 (23)	0.0047 (6)	0.0050 (6)	−0.0006 (9)	0.0023 (9)	−0.0001 (5)
H2(1)	0.057 (16)	0.670 (9)	−0.013 (7)	8. (3)[b]					
H2(2)	0.017 (13)	0.736 (6)	0.55 (6)	5. (2)					
H3(3)	0.097 (11)	0.843 (6)	−0.091 (5)	3. (2)					
H4(4)	0.119 (11)	0.929 (6)	0.037 (6)	4. (2)					
H4(5)	0.171 (14)	0.970 (7)	−0.051 (7)	6. (3)					
H5(6)	0.440 (13)	0.875 (6)	−0.002 (6)	4. (2)					
H5(7)	0.449 (8)	0.907 (4)	0.094 (4)	0. (1)					
H6(8)	−0.234 (14)	0.791 (7)	−0.112 (7)	6. (3)					
H6(9)	−0.233 (18)	0.868 (7)	−0.032 (8)	7. (3)					
H6(10)	−0.213 (15)	0.893 (7)	−0.129 (7)	8. (3)					
H7(11)	0.510 (15)	0.758 (6)	0.234 (6)	5. (2)					
H7(12)	0.310 (8)	0.805 (4)	0.222 (4)	0. (1)					
H9(13)	0.351 (11)	0.678 (6)	−0.093 (5)	4. (2)					
H10(14)	0.536 (8)	0.576 (4)	−0.144 (4)	0. (1)					
H11(15)	0.774 (12)	0.502 (6)	−0.045 (6)	5. (2)					
H12(16)	0.874 (10)	0.550 (5)	0.114 (5)	3. (2)					
H13(17)	0.714 (9)	0.662 (4)	0.178 (4)	1. (1)					

[a] The form of the anisotropic temperature factor expression is exp $(\Sigma_{i=1}^{3} \Sigma_{j=1}^{3} h_i h_j \beta_{ij})$. [b] Isotropic temperature factors are given for hydrogen atoms.

Table III. Bond Distances and Angles with Their Standard Deviations in Parentheses

A. Bond Distances

P(1)–C(2)	1.82 (1)	C(2)–H(21)	1.2 (1)
C(2)–C(3)	1.49 (1)	C(2)–H(22)	0.9 (1)
C(3)–C(4)	1.51 (1)	C(3)–H(31)	0.8 (1)
C(4)–C(5)	1.50 (1)	C(4)–H(41)	0.8 (1)
P(1)–C(5)	1.81 (1)	C(4)–H(42)	1.1 (1)
P(1)–C(7)	1.78 (1)	C(5)–H(51)	0.9
C(3)–C(6)	1.54 (1)	C(5)–H(52)	0.90
P(1)–C(8)	1.78 (1)	C(6)–H(61)	1.0
P(1)–C(7)	1.78 (1)	C(6)–H(62)	1.3
C(7)–I(2)	2.17 (1)	C(6)–H(63)	0.9 (1)
C(8)–C(9)	1.38 (1)	C(7)–H(72)	1.04
C(9)–C(10)	1.36 (2)	C(7)–H(71)	0.8
C(10)–C(11)	1.35 (2)	C(9)–H(91)	0.9
C(11)–C(12)	1.35 (2)	C(10)–H(101)	0.9
C(12)–C(13)	1.39 (1)	C(11)–H(111)	0.9
C(13)–C(8)	1.38 (1)	C(12)–H(121)	0.9
		C(13)–H(131)	1.08

B. Bond Angles

C(2)–P–C(5)	96.0 (4)	C(3)–C(6)–H(8)	112 (6)
C(2)–P–C(8)	112.7 (4)	C(3)–C(6)–H(9)	111 (5)
C(2)–P–C(7)	111.0 (4)	H(10)–C(6)–H(9)	102 (8)
C(5)–P–C(7)	112.0 (5)	H(10)–C(6)–H(8)	104 (9)
C(5)–P–C(8)	112.7 (4)	H(9)–C(6)–H(8)	104 (8)
P–C(5)–C(4)	104.8 (7)	C(3)–C(2)–H(2)	116 (6)
C(5)–O(4)–C(3)	108.7 (8)	C(3)–C(2)–H(1)	117 (6)
C(4)–C(3)–O(2)	108.3 (8)	H(2)–C(2)–H(1)	87 (8)

B. Bond Angles

C(3)–O(2)–P	104.9 (7)	P–C(2)–H(1)	114 (6)
C(4)–C(3)–C(6)	114.3 (9)	C(8)–C(9)–H(13)	121 (5)
P–C(8)–C(9)	118.5 (7)	H(13)–C(9)–C(13)	120 (5)
P–C(8)–C(13)	121.0 (7)	C(9)–C(10)–H(14)	120 (4)
C(8)–C(9)–C(10)	119.1 (9)	H(14)–C(10)–C(11)	119 (4)
C(9)–C(10)–C(11)	122 (1)	C(10)–C(11)–H(15)	115 (6)
C(10)–C(11)–C(12)	120 (1)	H(15)–C(11)–C(12)	123 (6)
C(11)–C(12)–C(13)	121 (1)	C(11)–C(12)–H(16)	124 (5)
C(12)–C(13)–C(8)	117.6 (9)	H(16)–C(12)–C(13)	114 (5)
P–C(5)–H(7)	105 (4)	C(12)–C(13)–H(17)	122 (3)
H(7)–C(5)–H(6)	112 (7)	C(8)–C(13)–H(17)	121 (3)
C(4)–C(5)–H(6)	108 (6)		
C(5)–C(4)–H(5)	111 (5)		
H(5)–C(4)–H(4)	105 (8)		
C(3)–C(4)–H(4)	105 (6)		
C(4)–C(3)–H(3)	80 (5)		
H(3)–C(3)–C(6)	104 (6)		
C(3)–C(6)–H(10)	122 (7)		

Discussion

The methyl group is trans to the phenyl group and is in an equatorial position, thus establishing the stereochemical configuration. The phospholanium ring system appears to be in the envelope form with the methyl group equatorial at the point of flap [C(3)] (Figure 1). A comparison of the phospholanium ring system with the half-chair form and the envelope form of cyclopentane is given in Figure 3.[17] The longer P–C bonds, compared to normal C–C bonds, cause considerable variations in the bond angles when compared to cyclopentane.

The equations for the various planes are given in Table

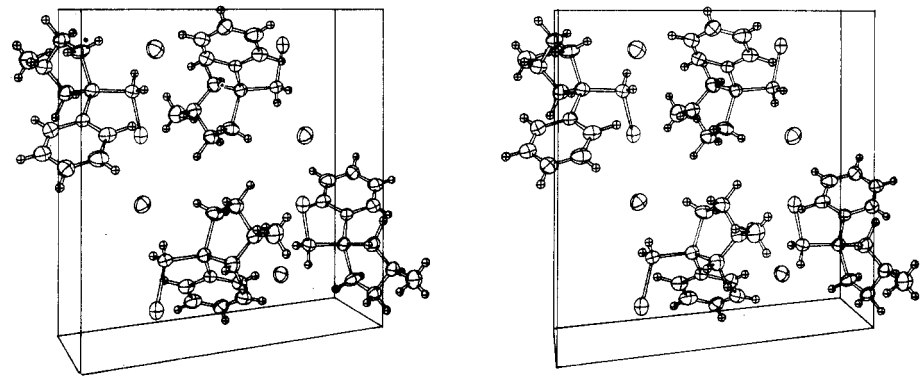
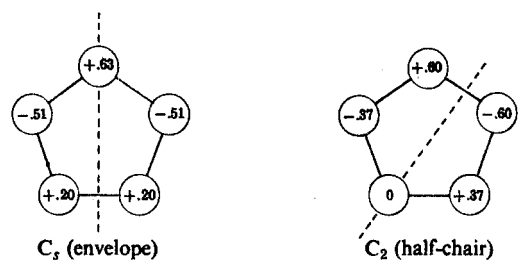


Figure 2. ORTEP drawing illustrating the packing of the molecules in the unit cell. Thermal ellipsoids have been scaled to include 50% probability; hydrogen atoms have been assigned an isotropic temperature factor of 1.0 for the sake of clarity.



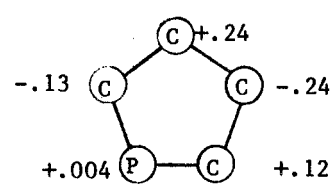


Figure 3. Comparison of the envelope and half-chair forms of cyclopentane[17] and the phospholanium ring system. Figures indicate displacement of atoms in angstroms, above (positive) or below (negative) the plane of the paper.

Table IV

Atoms in Plane	*l*	*m*	*n*	$p^{a,b}$	$S(\Delta^2)^c$
C(8), C(9), C(10) C(11), C(12), C(13)	0.618	0.763	−0.189	9.38	0.0002
P, C(2), C(4), C(5)	−0.438	0.272	0.857	2.89	0.019
C(2), C(3), C(4)	−0.880	0.282	0.382	2.53	
C(8), P, C(2)	0.310	0.659	−0.686	7.02	
P, C(2), C(3) C(4), C(5)	−0.559	0.290	0.776	2.80	0.151

[a] Least-squares plane; $lX + mY + nZ - p = 0.0$. [b] Coordinate system for plane is X along a, Y in a–b plane, z along c. [c] $S(\Delta^2)$ is the sum of the squares of the deviations of atoms from the planes.

IV. The angle formed between the plane of the phenyl group and the C(8)–P–C(2) plane is 34°. The plane of the phenyl group makes an angle of 77° with the C(5)–C(4)–P–C(2) plane. The plane of C(2)–C(3)–C(4) forms an angle of 38° with P–C(5)–C(4)–C(2).

Comparison of this structure to the structure of methylphenylphospholanium iodide[3] shows that all angles and distances are within three standard deviations of one another. The sum of the angles in the phospholanium ring of methylphenylphospholanium iodide is 516° while the sum of the internal angles in the phospholanium ring in this structure is 523°.

A packing diagram is shown in Figure 2. An iodide–iodine distance of 3.672 (1) Å is observed in this structure, which is significantly less than the sum of the van der Waals radii of 4.3 Å.[15] An intermolecular distance of 3.76 Å between two iodine atoms has been observed in hexaiodobenzene.[16] The polarizable nature of the iodine atom probably accounts for the unusually close approaches observed in these structures. There appear to be no other intermolecular interactions that are significantly less than the sum of the van der Waals radii.

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Registry No.—**5,** 57664-91-2; **7,** 57664-92-3; **8,** 57664-93-4; **9,** 57664-94-5; **10,** 55043-89-5; **12,** 57664-95-6; **14,** 55043-91-9.

References and Notes

(1) The cis and trans designations are in accordance with the *Chemical Abstracts* system by which, for example, the cis isomer has the senior groups (as defined by the sequence rule) on the same side of reference plane of the ring; cf. *Chem. Abstr.*, **76,** 851 (1972), and also *J. Chem. Inform. Computer Sci.*, **15,** 67 (1975).
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(8) Computer programs used were by F. R. Ahmed and co-workers (NRC-2, Data Reduction: NRC-8, Fourier for Distorted and Undistorted Nets; and NRC-12, Scan of Interatomic Distances and Angles, National Research Council, Ottawa, Ontario, Canada), Busing and Levy (ORFLS), and Carrol K. Johnson (ORTEP). These programs were locally modified for use with the XDS Sigma 7 computer. Other programs were written locally by G. D. Smith, E. L. Enwall, and C. N. Caughlan.
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Synthesis of Monoesters of Aryl- (or alkyl-) phosphonic Acids of Selected Arenols. A Study of the Effect of Dimethylformamide on the Preparation of 2-Naphthylphenylphosphonic Acid via Proton and Phosphorus-31 Nuclear Magnetic Resonance Analysis[1]

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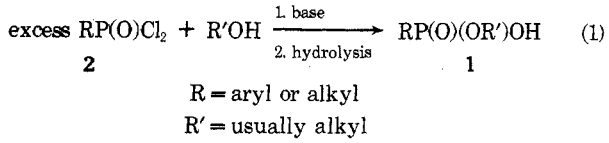
The general synthesis of aryl- (or alkyl-) phosphonate monoesters of selected arenols has been accomplished in good yield by reaction of the substituted phosphonic dichloride with the arenol in pyridine solvent. Careful hydrolysis of the reaction mixture gave the phosphonate monoester which was isolated as the ammonium salt from acetone–ether (1:2). A comprehensive study of the preparation of 2-naphthyl phenylphosphonate revealed that the yield was enhanced by premixing of the phosphonic dichloride with dimethylformamide in pyridine prior to the addition of the arenol in pyridine. The influence of dimethylformamide on the reaction path has been studied by ^1H NMR and ^{31}P NMR analysis.

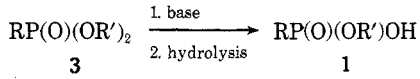
It has recently been shown that monoesters of phosphonic acids **1** are good substrates for certain phosphodiesterase enzymes which are widely distributed in nature.[3] Phosphonate monoesters have several advantages over conventional substrates, usually complex nucleotide phosphodiesters, or the simple diester, bis(4-nitrophenyl)phosphate, for assaying these enzymes.[4] For example, phosphonate monoesters readily and conveniently distinguish[4] between 5′-nucleotide phosphodiesterases and other phosphodiesterases.[5] In light of the elevated levels of 5′-nucleotide phosphodiesterase activity in fast-growing rat hepatomas[6] and the suggested diagnostic value of 5′-nucleotide phosphodiesterase isoenzyme patterns in the sera of human hepatic cancer patients,[7,8] considerable interest in phosphonate monoesters as enzyme substrates for diagnostic and analytical purposes can be expected. We have thus investigated the preparation of these compounds.

The preparation of phosphonate monoesters **1** has normally been accomplished via (a) reaction of an excess of an appropriate phosphonic dichloride **2** with an aliphatic alcohol (thus minimizing diester formation)[9] and subsequent hydrolysis to the phosphonate monoester or (b) by the synthesis of the aliphatic phosphonate diester **3** by known methods[10] followed by a controlled basic hydrolysis to the monoacid ester **1** (2).[11] These procedures, although affording good yields, have been primarily limited to the preparation of monoacid esters derived from aliphatic alcohols and not arenols.



(1)

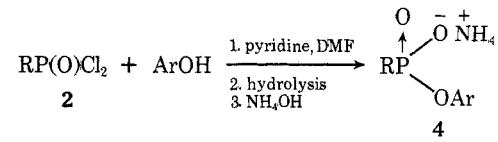
R = aryl or alkyl
R′ = usually alkyl



(2)

R = aryl, alkyl
R′ = alkyl

The scarcity of good methods for phosphonate monoesters of arenols is likely the result of the known low reactivity of the oxygen atom of the arenol with respect to a weak electrophilic center such as the phosphorus atom of a phosphonic dichloride. However, we have synthesized several phosphonate monoesters in good yield (isolated as the ammonium salts **4**), via the reaction in pyridine solvent of a selected phosphonic dichloride with a suitable arenol. The results of 11 such syntheses are listed in Table I. An observation that dimethylformamide (DMF) greatly influenced the reaction prompted us to make a careful study of the process with one case. As can be noted from Table II, the influence of dimethylformamide on the yield of the overall reaction (eq 3) (R = C_6H_5; Ar = 2-$HOC_{10}H_7$) is dramatic. Without DMF, the variation in the yield of monoester is considerable and, as expected, is very dependent upon the concentration of both the phosphonic dichloride and the arenol. Owing to the expense and difficulty in obtaining



(3)

R = C_6H_5, C_6H_{11}, C_3H_7, CH_3, $ClCH_2$
Ar = 2-$HOC_{10}H_7$, 4-$O_2NC_6H_4$

most of the initial phosphonic dichlorides, maintenance of their concentrations at a minimum level during the synthesis is economically desirable. For example, the yield of isolated monoester **4** (R = C_6H_5; Ar = 2-$C_{10}H_7$) decreases with decreasing concentration of phenylphosphonic dichloride and increasing concentration of 2-naphthol. This result is