Cyclic Organophosphorus Compounds. Part 21.[1] Crystallographic and Spectroscopic Assignments of Configuration at Phosphorus in 2-Chloro-4-isopropyl-5,5-dimethyl-1,3,2λ⁵-dioxaphosphorinan-2-ones and in 2-Methoxy-4-isopropyl-5,5-dimethyl-1,3,2-dioxaphosphorinanes

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The crystal and molecular structures of *cis*- and *trans*-2-chloro-4-isopropyl-5,5-dimethyl-1,3,2λ⁵-dioxaphosphorinan-2-ones have been determined by single-crystal X-ray analyses. In the solid state, these structures possess equatorial and axial phosphorus–chlorine bonds, respectively, with $(S)_p$ and $(R)_p$ configurations. The temperature-independent formation of the *cis*-phosphorochloridate by chlorination of the thermodynamically more stable 2-methoxy-4-isopropyl-5,5-dimethyl-1,3,2-dioxaphosphorinane suggests that the latter has the *trans* geometry with the $(R)_p$ configuration. The geometries thus assigned to the diastereoisomeric methyl phosphites are consistent with the ³¹P n.m.r. data for the corresponding 2-selenides.

The stereochemical changes which occur during reactions at a chiral, tetraco-ordinate phosphorus atom have been widely studied using *inter alia* appropriately substituted cyclic esters of phosphoric and related phosphorus acids. Among these compounds, derivatives of the 4-methyl-1,3,2-dioxaphosphorinane system have proved to be particularly popular substrates, and the epimeric methyl phosphites based on this ring system have been employed in the study of reactions involving valence expansion at phosphorus.[2]

Although in such studies the stereochemistries of individual compounds may be determined by dipole-moment or i.r. measurements, more often n.m.r. spectroscopy is utilized.[2,3] ¹H N.m.r. spectroscopy normally provides information about the conformations of groups at carbon centres, but not about those of groups on phosphorus, although J_{PH} data have been examined briefly as indicators of stereochemistry at phosphorus in some cyclic esters of tervalent phosphorus. More recently, assignments of conformation (and hence of configuration) at phosphorus in diastereoisomeric 4-methyl-1,3,2λ⁵-dioxaphosphorinanes have been made on the basis of ³¹P chemical shifts and $J(^{31}P^{1}H)$ or $^{1}J(^{31}P^{77}Se)$ data; ¹³C chemical shifts and $J(^{31}P^{13}C)$ couplings have also been measured.[2] However, the value of such data in configurational assignments has been questioned.[4]

Aside from the complexities of analysis of the ¹H n.m.r. spectra, the use of the 4-methyl-1,3,2λ⁵-dioxaphosphorinane system also presents practical difficulties. Some derivatives stereomutate relatively rapidly in a process which appears to be solvent-dependent; for some of the more important compounds, *e.g.* the cyclic phosphorochloridates and phosphorochlorothioates, the physical properties render them unsuitable for structural analysis by other techniques such as X-ray diffraction.

Successive replacement of ring-hydrogen atoms in 1,3,2-dioxaphospholanes and 1,3,2-dioxaphosphorinanes by methyl groups increases the stability of single bonds at phosphorus in displacement reactions.[5] At least for the dioxaphospholanes, this may be attributed to increased resistance to pseudorotation in reaction intermediates containing pentaco-ordinate phosphorus.[6] The role of pentaco-ordinate intermediates in the displacement reactions of 1,3,2-dioxaphosphorinanes is by no means so clear, but, in the event that they are involved, it would seem reasonable to suppose that the presence of even bulkier groups on the larger ring would also restrict pseudorotation and thus result in higher configurational stability.
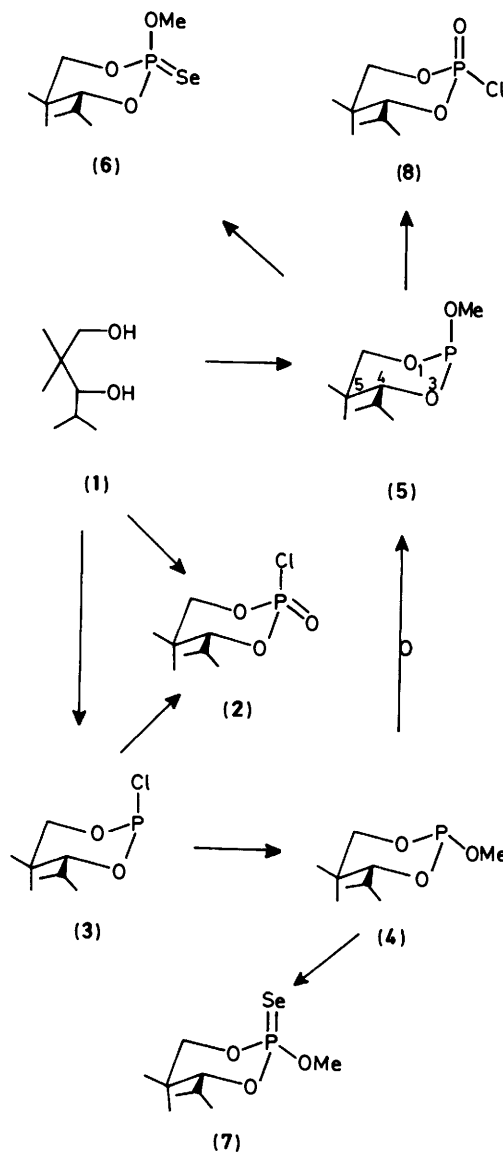
Scheme 1.

Derivatives of the 4-isopropyl-5,5-dimethyl-1,3,2-dioxaphosphorinane system were chosen to initiate a study of the effects of ring substitution on the reactivity of 1,3,2-dioxaphosphorinanes, partly because of the ready availability of the precursor diol; a few compounds in the series have already been reported.[7]

Experimental

General Procedure.—Solutions and solvents were dried by conventional means. Light petroleum refers to the fraction of b.p. 60—80 °C unless otherwise stated. Triethylamine was dried over CaO and fractionally distilled. Tervalent phosphorus compounds were distilled in an atmosphere of nitrogen. T.l.c. and column chromatography were performed with Merck Kieselgel; a solution of iodine in ethanol was used as indicator for t.l.c. I.r. spectra were determined on a Perkin-Elmer model 681 spectrophotometer for KBr discs (solids) or NaCl plates (liquids). Mass spectra were determined on an AEI MS9 instrument operating at 70 eV with the ion-source temperature 150 °C. 100 MHz ^{1}H N.m.r. spectra were determined for deuteriochloroform solutions (unless otherwise stated) with SiMe$_4$ as internal standard on a JEOL JNM-MH-100 spectrometer. ^{31}P N.m.r. spectra were recorded for chloroform solutions, with phosphoric acid as external standard (chemical shifts to lower field are positive), through the S.E.R.C. low-field multinuclear n.m.r. spectroscopy service unit at the City of London Polytechnic.

trans-2-*Chloro-4-isopropyl-5,5-dimethyl-1,3,2-dioxaphosphorinane* (3).—A solution of 2,2,4-trimethylpentane-1,3-diol (1) (39.5 g, 0.27 mol) and triethylamine (57.4 g, 0.54 mol) in benzene (350 ml) was added dropwise to a stirred and cooled solution of freshly distilled phosphorus trichloride (37.3 g, 0.27 mol) in benzene in a nitrogen atmosphere during 2 h. The mixture was stirred for 4 h at ambient temperature and filtered. Ether (500 ml) was added to the filtrate and the combined solution was chilled overnight; then it was refiltered, the filtrate evaporated, and the residue distilled to give the *cyclic phosphorochloridite* (3) (39—43 g, 69—76%), b.p. 71—74 °C at 1 mmHg; n_D^{23} 1.4772 (Found: C, 45.5; H, 7.7. C$_8$H$_{16}$ClO$_2$P requires C, 45.6; H, 7.65%); n.m.r., ^{1}H δ 2.0 (C*H*Me$_2$), 1.23 (3 H) and 0.88 (3 H) (CMe$_2$), 4.3 (2 H, 4- and 6-H$_{ax}$), and 3.45 p.p.m. (1 H, 6-H$_{eq}$): the 4-isopropyl methyl groups (6 H) were indicated at 92, 96, 98, and 104 Hz; ^{31}P, δ 151.1 p.p.m.; $v_{max.}$ 1 043s, 1 028s, 990s, 945s, 777s, and 632s cm^{-1}.

trans-2-*Chloro-4-isopropyl-5,5-dimethyl-1,3,2λ^5-dioxaphosphorinan-2-one* (2).—(a) A solution of freshly distilled phosphorus trichloride oxide (52 g) in benzene (100 ml) was added dropwise to a stirred solution of 2,2,4-trimethylpentane-1,3-diol (1) (49.5 g) and triethylamine (68.7 g) in benzene. After the addition was complete, the mixture was kept overnight at ambient temperature. The mixture was filtered, the filtrate evaporated, and the solid residue crystallized from benzene. The cyclic phosphorochloridate (2) (48—51 g, 62—66%) had m.p. 120—121.5 °C (lit.,[7] 119.5—120 °C); ^{31}P n.m.r., δ −1.1 p.p.m.; $v_{max.}$ 1 300s (P=O), 1 043s, 1 018s, and 988s (POC) cm^{-1}.

(b) A solution of *trans*-2-chloro-4-isopropyl-5,5-dimethyl-1,3,2-dioxaphosphorinane (3) (3.5 g) in dichloromethane (75 ml) was treated with dry gaseous dinitrogen tetraoxide until the colour of the solution persisted; excess of oxidant was removed in a stream of nitrogen. Evaporation of the solution gave the cyclic phosphorochloridate (2) (3.5 g, 93%), identical (m.p., mixed m.p., and i.r. spectrum) with that prepared from phosphorus trichloride oxide.

4-*Isopropyl-2-methoxy-5,5-dimethyl*-1,3,2-dioxaphosphorinane (4) *and* (5).—(a) The cis-*phosphite* (4). A solution of *trans*-2-chloro-4-isopropyl-5,5-dimethyl-1,3,2-dioxaphosphorinane (3) (10.5 g) in diethyl ether (25 ml) was added dropwise to a stirred solution of methanol (1.6 g, dried over molecular sieve) and triethylamine (5.05 g) in ether (25 ml) at ambient temperature; the mixture was then stirred during 0.5 h. After filtration, the filtrate was distilled to give the cis-*phosphite* (4) (6.2—7.5 g, 60—73%), b.p. 68.5 °C at 3 mmHg; n_D^{18} 1.4583 (Found: C, 52.6; H, 9.3. C$_9$H$_{19}$O$_3$P requires C, 52.4; H, 9.3%); n.m.r.: ^{1}H, δ 3.52 [OCH$_3$, ^{3}J(POC*H*$_3$) 9.6 Hz] and 1.84 (1 H, C*H*Me$_2$) p.p.m.; signals for CMe$_2$ overlapped with those for CH*M*e$_2$, and those for 4- and 6-H overlapped with those for the OMe group; ^{31}P, δ 134.0 p.p.m.; $v_{max.}$ 1 468m, 1 390m, 1 367m, 1 215w, 1 173w, 1 112m, 1 048s, 1 015s, br, 978s, 948s, 917m, 890m, 818s, 760s, and 730s cm^{-1}.

During storage at 0—5 °C for 8 weeks, the cis-phosphite (4) underwent complete stereomutation to the more stable *trans*-form (5). (b) The trans-*phosphite* (5). A mixture of trimethyl phosphite (30 ml) and 2,2,4-trimethylpentane-1,3-diol (1) (36.5 g, dried azeotropically with benzene) containing triethylamine (6 drops) was set aside at ambient temperature for 60 h, warmed to dissolve the remaining solid, and then slowly fractionally distilled to give the *trans*-phosphite (5) (34.5 g, 71%), b.p. 65—67 °C at 0.5 mmHg; n_D^{18} 1.4552; n.m.r.: ^{1}H, δ 3.34 [OMe, ^{3}J(POC*H*) 11.1 Hz], 1.8 (1 H, C*H*Me$_2$), 1.12 (3 H), and 0.75 (3 H) (CMe$_2$), 3.0 (1 H, 6-H$_{eq}$), and 3.9 (2 H, 4- and 6-H$_{ax}$) p.p.m. The isopropyl methyl groups were indicated at 96, 94, 90, and 88 Hz (6 H); ^{31}P, δ 127.4 p.p.m.; $v_{max.}$ 1 468m, 1 390m, 1 367m, 1 290s, 1 212w, 1 175w, 1 110m, 1 096m, 1 045s, 1 015s, 982s, 940s, 912m, 892m, 843m, 818m, 760m, 745m, 723s, and 627s cm^{-1}.

4-*Isopropyl-2-methoxy-5,5-dimethyl*-1,3,2λ^5-dioxaphosphorinane 2-selenide (6) *and* (7).—(a) Selenium (0.4 g) was added in portions to the cis-phosphite (4) (1.05 g). When the exothermic reaction had subsided, the mixture was diluted with benzene, the solution filtered, and the solvent removed under reduced pressure to leave cis-*selenide* (7) (1.3 g) as an oil (Found: C, 36.6; H, 6.5. C$_9$H$_{19}$O$_3$PSe requires C, 37.9; H, 6.7%); ^{31}P n.m.r., δ 72.1 p.p.m., ^{1}J(^{31}P^{77}Se) 958 Hz; $v_{max.}$ 1 030s, br and 1 010s, br (POC) cm^{-1}.

(b) The above reaction was repeated using the *trans*-phosphite (5). The oily product crystallized, and was recrystallized from light petroleum to give the trans-*selenide* (6) (1.15 g), m.p. 72—73 °C (Found: C, 38.1; H, 6.75%); n.m.r.: ^{1}H, δ 3.77 [3 H, OMe, ^{1}J(POC*H*) 15 Hz], 2.0 (C*H*Me$_2$), 1.24 (3 H), and 0.88 (3 H) (CMe$_2$), and 1.08 (3 H) and 1.00 (3 H) (CH*M*e$_2$); ^{31}P, δ 67.6 p.p.m., ^{1}J(^{31}P^{77}Se) 991 Hz; $v_{max.}$ 1 050s, 1 032s, and 1 010s (POC) cm^{-1}.

Chlorination of 4-*Isopropyl-2-methoxy-5,5-dimethyl*-1,3,2-dioxaphosphorinane.—(a) The trans-*phosphite* (5). A solution of the *trans*-phosphite (5) (2.1 g) in dichloromethane (20 ml) was added dropwise to a solution of a slight excess of chlorine (0.5 g) in dichloromethane (30 ml) stirred magnetically at −75 °C. When the addition was complete, the solution was stirred at 0 °C for 1 h and then concentrated to an oil (2.2 g); this showed ^{31}P signals at δ 2.4 and −1.1 p.p.m. in the ratio 96:4, together with other signals at 8.1, 5.05, −4.4, and −5.1 p.p.m. When the reaction was performed at room temperature, the product showed signals at 2.4 and −1.1 p.p.m. in the ratio 98:2 with other main signals at 6.4, 3.8, 3.4, 0.6, and −5.5 p.p.m. In several reactions, the product solidified, and was recrystallized from carbon tetrachloride—light petroleum, to give cis-2-*chloro-4-isopropyl-5,5-dimethyl*-1,3,2λ^5-dioxaphosphorinan-2-one (8), m.p. 55—56 °C (Found: C, 42.4; H, 7.35. C$_8$H$_{16}$ClO$_3$P requires C, 42.4; H, 7.1%), free from the epimeric phosphorochloridate;

Table 1. Final fractional unit-cell co-ordinates for atoms of *trans*-(2); e.s.d.s in parentheses

Atom	x	y	z
P(1)	0.748 6(1)	0.199 3(1)	0.313 4(1)
Cl(1)	0.920 8(1)	0.142 1(1)	0.417 5(1)
O(1)	0.737 9(1)	0.295 6(1)	0.428 1(2)
O(2)	0.655 1(2)	0.116 9(1)	0.300 7(2)
O(3)	0.752 8(1)	0.246 3(1)	0.143 3(1)
C(1)	0.809 5(2)	0.393 3(2)	0.420 4(3)
C(2)	0.783 2(2)	0.436 0(1)	0.241 9(2)
C(3)	0.823 4(2)	0.348 9(1)	0.138 0(2)
C(4)	0.648 3(2)	0.468 7(2)	0.176 4(3)
C(5)	0.867 7(3)	0.534 0(2)	0.252 1(4)
C(6)	0.813 5(2)	0.368 9(2)	−0.047 0(2)
C(7)	0.899 6(3)	0.291 4(3)	−0.102 1(3)
C(8)	0.683 0(2)	0.360 6(3)	−0.167 1(3)
H(11)	0.901 9(21)	0.376 2(18)	0.466 2(27)
H(12)	0.783 4(20)	0.444 4(19)	0.492 0(29)
H(31)	0.910 2(17)	0.330 8(14)	0.192 7(22)
H(41)	0.590 3(24)	0.407 2(22)	0.161 9(32)
H(42)	0.629 0(24)	0.514 6(22)	0.256 1(33)
H(43)	0.633 2(22)	0.507 3(19)	0.069 1(32)
H(51)	0.854 2(25)	0.583 3(24)	0.332 1(34)
H(52)	0.849 6(23)	0.571 5(22)	0.147 6(34)
H(53)	0.960 3(28)	0.512 1(23)	0.280 9(34)
H(61)	0.841 1(20)	0.440 4(18)	−0.052 7(27)
H(71)	0.983 6(29)	0.298 8(24)	0.973 6(37)
H(72)	0.870 2(29)	0.218 8(26)	0.913 7(39)
H(73)	0.897 1(23)	0.301 1(21)	−0.218 7(33)
H(81)	0.631 1(31)	0.417 8(29)	−0.145 4(42)
H(82)	0.643 5(36)	0.291 0(34)	−0.158 5(49)
H(83)	0.682 5(26)	0.372 0(21)	−0.278 0(37)

Table 2. Final fractional unit-cell co-ordinates for atoms of *cis*-(8); e.s.d.s in parentheses

Atom	x	y	z
P(1)	0.789 8(1)	0.426 3(1)	0.013 2(1)
Cl(1)	0.629 5(1)	0.320 9(2)	0.020 3(1)
O(1)	0.812 5(3)	0.481 9(3)	0.129 6(2)
O(2)	0.875 5(3)	0.313 1(4)	−0.027 7(3)
O(3)	0.764 0(3)	0.582 5(3)	−0.052 1(2)
C(1)	0.861 3(4)	0.641 5(5)	0.155 7(3)
C(2)	0.801 3(3)	0.779 1(4)	0.092 0(3)
C(3)	0.822 7(3)	0.741 4(4)	−0.025 0(2)
C(4)	0.670 4(4)	0.794 9(6)	0.121 2(3)
C(5)	0.872 8(4)	0.934 2(5)	0.122 9(3)
C(6)	0.780 2(4)	0.816 0(4)	−0.111 2(3)
C(7)	0.646 2(5)	0.865 2(7)	−0.134 3(4)
C(8)	0.846 3(5)	0.825 4(6)	−0.212 3(3)
H(11)	0.949 3	0.641 4	0.141 2
H(12)	0.849 5	0.662 6	0.232 8
H(31)	0.912 6	0.742 7	−0.027 7
H(41)	0.631 9	0.885 4	0.079 1
H(42)	0.665 5	0.820 1	0.198 5
H(43)	0.627 5	0.689 7	0.105 4
H(51)	0.859 8	0.960 5	0.199 1
H(52)	0.960 5	0.914 9	0.112 0
H(53)	0.844 6	1.027 9	0.077 7
H(61)	0.799 0	0.972 9	−0.083 0
H(71)	0.818 7	0.903 5	−0.268 9
H(72)	0.934 9	0.838 6	−0.198 9
H(73)	0.828 8	0.710 6	−0.235 6
H(81)	0.628 1	0.947 0	−0.191 5
H(82)	0.603 5	0.897 2	−0.068 7
H(83)	0.618 3	0.754 4	−0.157 9

n.m.r.: ^{1}H, δ 1.16 (3 H) and 1.08 (3 H) (CMe_2), 1.12 (6 H, CHMe_2), and 2.08 (1 H, C$H$$Me_2$); ^{31}P, δ 2.40 p.p.m.; ν_{max}. 1 098m, 1 042s, 1 033s, 990s, 966s, and 635s cm^{-1}.

(b) *The* cis-*phosphite* (4). Similar reactions were performed with the cis-phosphite (4). At −75 °C, the ^{31}P n.m.r. signals at 2.4 and −1.1 p.p.m. were in the ratio 14 : 86, with other main signals at 5.1, 2.0, −4.5, and −5.1 p.p.m. At room temperature, the signals at 2.4 and −1.1 p.p.m. were in the ratio 93 : 7, with other signals at 6.4, 3.7, 3.4, and 0.6—5.2 p.p.m.

Crystal Structure Determination of the trans-*Cyclic Phosphorochloridate* (2).—*Crystal data.* trans-$C_8H_{16}ClO_3P$, M = 226.5. Monoclinic, a = 11.208(3), b = 12.423(3), c = 8.319(3) Å, β = 106.51(1)°, U = 1 110.2 Å^3 (by least-squares refinement of diffractometer angles for 25 reflections with 23 $\leqslant$ 2θ $\leqslant$ 25°, λ = 0.7107 Å), space group $P2_1/a$ (non-standard; alt. $P2_1/c$, No. 14), D_m = 1.35 g cm^{-3} (flotation in carbon tetrachloride–hexane), D_x (for Z = 4) = 1.42 g cm^{-3}. Mottled square-sectioned needles recrystallized from benzene; data-collection crystal 0.3 × 0.4 × 0.4 mm sliced from large needle, μ(Mo-K_α) = 4.72 cm^{-1}, $F(000)$ = 480.

Data collection and processing.—Enraf–Nonius CAD-4F diffractometer (Rothamstead), $\omega/2\theta$ variable-scan mode, maximum time per reflection 100 s, graphite-monochromatized Mo-K_α radiation. 2 829 Intensity measurements (including standards 342 and 012 measured every 2 h, which showed 5% intensity diminution during collection) encompassed 2.8 $\leqslant$ 2θ $\leqslant$ 50° of $\pm h, + k, + l$ quadrant of limiting sphere and included some overlap. Removal of 126 systematic absences from scaled, Lorentz–polarization-corrected data yielded 1 950 unique reflections (merging R = 0.017). Centric intensity statistics consistent with $P2_1/a$ space group.

Structure analysis and refinement. The structure was solved by direct methods (MULTAN 78) which gave 11 out of 13 non-hydrogen atoms, with the chlorine and a methyl carbon atom missing. The 13-atom structure was completed from a Fourier calculation and gave an initial R index of 0.55. After isotropic full-matrix least-squares refinement had reduced R from 0.26 to 0.14, anisotropic refinement (in two blocks) of the 13-atom structure lowered R to 0.07 over 1 725 F_o with $|F_o| > 5\sigma|F_o|$. General and slant-plane Fourier difference syntheses containing expected hydrogen positions located all except H(31) and H(82) which were geometrically placed. Anisotropic refinement with three blocks including all atoms decreased R to 0.032 over 1 725 reflections. For the final blocked-matrix least-squares refinement (block 1: co-ordinates for all 29 atoms; block 2: overall scale factor and thermal parameters, isotropic for hydrogen atoms, anisotropic for other atoms), the 180 weakest reflections ($1 \leqslant |F_o| \leqslant 4$) were suppressed, shift factors of 0.5 were applied to all refined parameters (to 'dampen' oscillations), and weights were based on a truncated Chebyshev series having three terms (18.6, 23.2, 5.9). This gave a final R index of 0.027 (R_w = 0.035) for 182 least-squares parameters and 1 543 data. Table 1 lists the final atomic positional parameters. Tables of thermal parameters are available in Supplementary Publication No. SUP 56093 (17 pp.).*

Crystal Structure Determination of the cis-*Cyclic Phosphorochloridate* (8).—*Crystal data.* cis-$C_8H_{16}ClO_3P$, M = 226.5. Monoclinic, a = 11.105(1), b = 8.169(1), c = 12.624(1) Å, β = 91.56(1)°, U = 1 144.8 Å^3 (by least-squares refinement on diffractometer angles), λ = 1.5418 Å, space group $P2_1/n$ (alt. $P2_1/c$, No. 14), D_m = 1.31 g cm^{-3}, D_x (for Z = 4) = 1.31$_5$ g cm^{-3}; μ(Cu-K_α) = 40.8 cm^{-1}, $F(000)$ = 480.

Data collection and processing. Enraf–Nonius CAD-4F diffractometer (Nottingham University), $\omega/2\theta$ mode, nickel-filtered, Cu-K_α radiation. 1 996 Reflection measurements ($2\theta \leqslant 66°$) yielded 1 448 unique reflections with $I \geqslant 3\sigma(I)$.

Structure solution and refinement. A combination of direct (SHELX) and Patterson methods led to the location of the chlorine and phosphorus atoms. Difference syntheses enabled first the carbon and oxygen atoms to be located and subsequently the hydrogen atoms, although the latter were included in calculated positions for the final stages of the least-squares refinement (isotropic, $U = 0.05$ Å², for hydrogens, anisotropic for other atoms) to $R = 0.050$. Table 2 lists the final atomic positional parameters. Tables of thermal parameters and observed and calculated structure factors are available as Supplementary Publication No. SUP 56093/17 pp.

Results and Discussion

Preparation and N.m.r. Spectroscopy.—The reaction between phosphorus trichloride oxide and 2,2,4-trimethylpentane-1,3-diol (**1**) in the presence of triethylamine yields the cyclic phosphorochloridate (**2**), for which the ^{31}P chemical shift is -1.1 p.p.m.* The isopropyl group is evidently disposed equatorially as judged from [1]H n.m.r. data recorded elsewhere,[7] but the configuration at phosphorus has not been determined. *A priori* arguments,[3] backed by X-ray analyses of other cyclic phosphorohalidates,[8] would suggest that, at least for the solid state, an axial conformation for the phosphorus–chlorine bond is most likely. A single-crystal X-ray analysis of compound (**2**) (discussed more fully later) shows that the phosphorus–chlorine bond is indeed orientated axially and in the *trans*† disposition to the isopropyl group (Figure 1). Of course, these conformations do not necessarily obtain in solution, but steric interactions between *gem*-dimethyl and isopropyl groups would be expected to reduce the extent of conformation changes. The phosphorochloridate (**2**) is also formed on stereoretentive oxidation, using dinitrogen tetraoxide,[9] of the tervalent chloride (**3**) obtained from (**1**) and phosphorus trichloride. The configuration at phosphorus in (**3**) can thus be defined as $(R)_p$.

The treatment of the stereoisomerically pure *trans*-compound (**3**) with methanol in the presence of triethylamine gave a mixture of stereoisomeric methyl phosphites, the major component of which ($>90\%$) had a ^{31}P resonance at 134.0 p.p.m., and to which the *cis*-geometry (**4**) and $(S)_p$ configuration were assigned, based initially on the premise that the replacement of chlorine in (**3**) by methanol takes place mostly with inversion of configuration at phosphorus.[10] The minor component (**5**), with *trans*-geometry and $(R)_p$ configuration, was almost certainly formed as a result of replacement of chlorine with ultimate retention of configuration at phosphorus rather than by rapid stereomutation of the $(S)_p$ phosphite, although this process does occur during several weeks at 0—5 °C.

When a mixture of the diol (**1**) and trimethyl phosphite was heated, 4-isopropyl-2-methoxy-5,5-dimethyl-1,3,2-dioxaphosphorinane was obtained as its thermodynamically more stable stereoisomer (**5**), with a ^{31}P chemical shift of 127.4 p.p.m., always $>98\%$ stereoisomeric purity. It was identical (^{31}P and ^{1}H chemical shifts) with the minor component derived from (**3**).

Surprisingly, transesterification between a diol and a trialkyl phosphite is a process which appears not to have been widely adopted for the preparation of the thermodynamically more stable diastereoisomeric alkyl cyclic phosphites, although aryl cyclic phosphites have been prepared in this way.[11] More

frequently, the acid-induced stereomutation of the kinetically preferred phosphites has been the preparative procedure adopted.[12]

The phosphites (**4**) and (**5**) can be distinguished by means of (a) their ^{31}P chemical shifts, (b) their $^3J(POCH_3)$ values (9.6 Hz for the *cis*-phosphite, with equatorial methoxy, and 11.1 Hz for the *trans*-phosphite), and (c) the n.m.r. properties of their derived selenides.

Addition of selenium to the *trans*-phosphite (**5**) gave a crystalline 2-selenide (**6**) with a ^{31}P chemical shift of 67.6 p.p.m. and $^1J(^{31}P^{77}Se)$ 991 Hz. Crystals of this compound exhibited very broad X-ray reflections, indicative of extreme molecular disorder, thus preventing the X-ray crystallographic determination of its molecular structure and hence, definitively, that of the phosphite (**5**) from which it is derived with stereoretention. The *cis*-phosphite (**4**) gave an oily 2-selenide (**7**) with a ^{31}P chemical shift of 72.1 p.p.m., and $^1J(^{31}P^{77}Se)$ 958 Hz. It is to be noted that the more positive (present convention) ^{31}P chemical shift is associated with the numerically smaller coupling constant; such behaviour has been observed for other 1,3,2-dioxaphosphorinane 2-selenides[13] and, in the case of the 2-t-butylamino-4-methyl-1,3,2λ^5-dioxaphosphorinane 2-selenides, X-ray crystallographic examination has shown that the more positive (present convention) ^{31}P chemical shift is associated with an axial selenophosphoryl bond,[14] as it would appear to be here.

Chlorination of the *trans*-methyl phosphite (**5**) under mild conditions yielded a cyclic phosphorochloridate (**8**), m.p. 55 °C, with a ^{31}P chemical shift of 2.66 p.p.m., which can be isolated in high purity. At either room temperature or -75 °C, the reaction product is a mixture containing one principal component; the ratio of (**8**) to (**2**) was 97:3 at room temperature and 96:4 at -75 °C, so that the product composition appears to be independent of temperature. An X-ray structure analysis of the lower-melting phosphorochloridate showed that the isopropyl group and the P–Cl bond are both equatorial, and the compound thus has the *cis*-geometry with the $(S)_p$ configuration. Stereomutation of (**8**) to the more stable *trans*-phosphorochloridate (**2**) takes many months at 0 °C, but occurs more rapidly in dimethylformamide solution.

When the *cis*-methyl phosphite (**4**) was chlorinated under the same conditions as for the *trans*-phosphite (**5**), the product mixtures were more complex but, more importantly, the reaction appeared to be temperature-dependent. Thus, at -75 °C, the main product was the $(R)_p$ phosphorochloridate (**2**) (the ratio of phosphorochloridates was 86:14 but, at room temperature, the ratio was 7:93).

Thus, care must be exercised in the presentation of arguments for chirality based upon the supposed stereospecificity of the chlorination reaction formulated in general terms in Scheme 2. Nevertheless, our results would appear to be consistent with, particularly, the presence of an equatorial methoxy group in the *cis*-methyl phosphite (**4**), and with the formation of an intermediate dichlorophosphorane from phosphite(s) and chlorine (possibly *via* biphilic attack) with resistance to pseudorotational interconversion by the isopropyl group, prior to breakdown to phosphonium salts[15] followed by phosphorochloridate formation. Very recently, the formation of a trichlorophosphorane during the chlorination of 2-chloro-1,3,2-dioxaphospholane at -100 °C has been observed,[16] and similar

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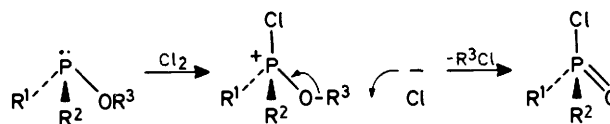
*[31]P Chemical shifts are positive unless otherwise stated.
†The terms *cis* and *trans* refer to the spatial dispositions of the C-4 substituent and the single-bonded substituent at phosphorus.
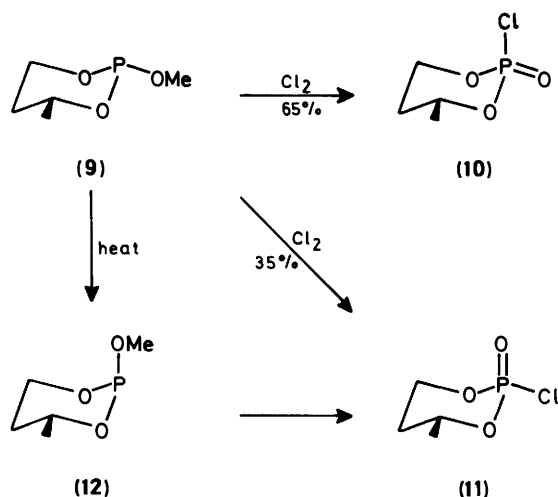
Scheme 2.

Scheme 3.

Table 3. Selected m/z values and relative intensities for mass spectra of the epimeric *trans*- and *cis*-compound (2) and (8)

m/z	117	95	68	67	57	56	55	41	40
trans-(2)	23.3	20.2	11.6	8.7	4.0	31.5	100	1.5	14.6
cis-(8)	24.3	14.5	5.3	9.9	4.6	29.1	100	1.4	14.9

m/z	$M - 55$	$M - 43$	$M - 42$	$M - 41$	$M - 40$	$M - 35$
trans-(2)	16.8	1.9	3.4	1.0	1.1	0.8
cis-(8)	14.6	2.7	1.3	0.9	0.5	0.2

Figure 1. View of the molecular structure of *trans*-(2) from the POCl end of the molecule

intermediates have been recognised in reactions between cyclic phosphites and sulphenyl chlorides at low temperatures;[17] a similar mechanism has been proposed for the reaction between 2-methoxy-4-methyl-1,3,2-dioxaphosphorinane and alkyl hypochlorites.[18] On the other hand, tetraco-ordinated ionic intermediates have been isolated, *e.g.* following halogenation of 1-phosphabicyclo[2.2.2]octanes.[19]

Some comparison can be made between the 4-isopropyl-5,5-dimethyl- and 4-methyl-1,3,2-dioxaphosphorinane systems with regard to the formation of their respective cyclic phosphoro-chloridate derivatives. Thus, chlorination of the *cis*-phosphite (9) at -50 °C yields a mixture of *trans*- and *cis*-2-chloro-4-methyl-1,3,2-dioxaphosphorinan-2-one (10) and (11), respectively, in the ratio 65:35;[20] at -60 °C, the *trans*-phosphite (12) is reported to give the *cis*-phosphorochloridate, presumably as the major, if not the only, product.[21] Even allowing for the slight but measurable effect which 5,5-*gem*-dimethyl groups have on reactivity at phosphorus in 1,3,2-dioxaphosphor-inanes,[5] it would appear that, at least for the *cis*-methyl phosphites, the presence of isopropyl rather than methyl at C-4 results in a greater overall stereoselectivity of reaction with chlorine. Secondly, in the reaction between phosphorus trichloride oxide and the respective diol,[10,22] the formation of (2) in >95% stereoisomeric yield is to be contrasted with the formation of (10) and (11) in the ratio 75—80:25—20, indicative of a probable steric effect in the ring-closure stage of the reaction sequence.

The mass spectra of the diastereoisomeric phosphorochlor-idates (2) and (8) are very similar (Table 3); each has the base peak at m/z 100, and neither exhibits the $M - 15$, $M - 28$, $M - 30$, $M - 67$, or $M - 85$ fragments characteristic of 5,5-dimethyl-1,3,2-dioxaphosphorinan-2-ones lacking substituents at position 4.[23,24] The fragment at m/z 117, represented by ion (a), corresponds to loss of $C_8H_{13}\cdot$. One of the few differences
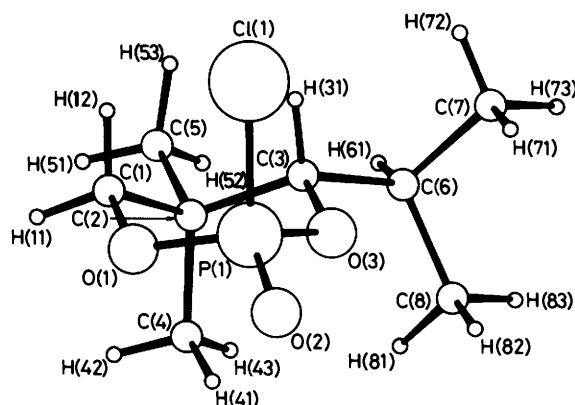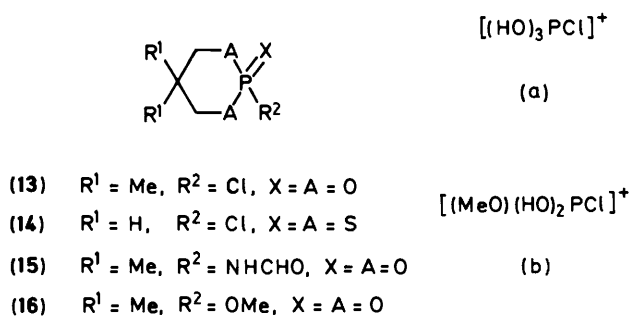
between the spectra is shown by ion (b), m/z 95, which corresponds to loss of $C_7H_{11}\cdot$. Of the low-mass hydrocarbon fragments, only that at m/z 68 shows a pronounced difference. Loss of the isopropyl group as propene following transfer of $H\cdot$ leads to the $M - 42$ ion. Whether the $H\cdot$ is captured by a ring oxygen or by a phosphoryl oxygen is not known, but the small difference in intensities could be the result of a difference between the electron densities of axial and equatorial phosphoryl oxygens (known to exhibit different basicities[3]) or of a relay of this difference to the ring oxygens. For 2-chloro-5,5-dimethyl-1,3,2λ^5-dioxaphosphorinan-2-one, fragments at m/z 117, 100, 68, 56, and 41 are all important.[23]

Crystal and Molecular Structures of trans- *and* cis-2-*Chloro*-4-*isopropyl*-5,5-*dimethyl*-1,3,2λ^5-*dioxaphosphorinan*-2-*one* (2) *and* (8).—Although the structures are not isomorphous, and they have different monoclinic *b*-axes, the unit-cell lengths are almost identical. Molecular shapes, both in chair conformation, are shown in Figures 1 and 2, while molecular dimensions are listed in Tables 4—7. The crystal structure of the *trans*-compound (2) is one of the most precisely determined of any 1,3,2-dioxaphosphorinane compound; even the apparent (*i.e* to electron density maxima) C–H distances cluster very closely round 0.97 Å (Table 6). Agreement between lengths of corresponding bonds in *trans*- and *cis*-structures (Table 4) is very close except for the two exocyclic bonds at the phosphorus, where the slight lengthening of the precisely determined axial P–Cl bond in (2) to 2.007(1) Å (possibly a consequence of differences in orbital overlap between axial and equatorial bonds) is formally significant and consistent with the less precisely determined[8] axial P–Cl bond length of 2.004(7) Å in 2-chloro-5,5-dimethyl-1,3,2λ^5-dioxaphosphorinan-2-one (13); the axial P–Cl bond at 2.053(4) Å is longer[25] in the rather less flattened 2-chloro-1,3,2λ^5-dithiaphosphorinane-2-thione (14).
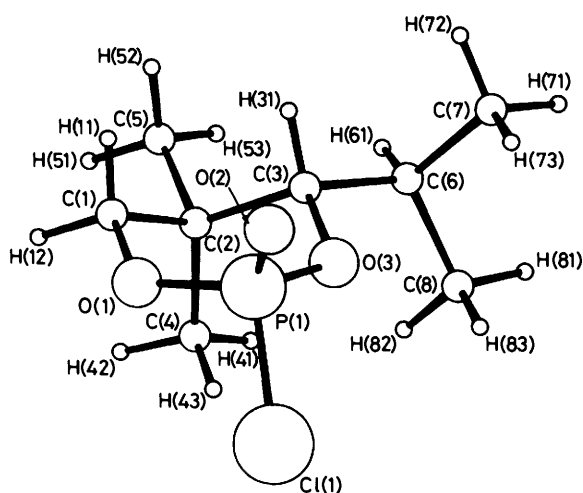
Figure 2. View of the molecular structure of cis-(8) from a similar viewpoint to that of Figure 1.

Table 4. Bond lengths (Å) between non-hydrogen atoms of the trans- and cis- (2) and (8) with e.s.d.s in parentheses

	trans-(2)	cis-(8)
P–Cl	2.007(1)	1.982(1)
P=O(2)	1.448(2)	1.433(2)
P–O(1)	1.556(2)	1.551(3)
P–O(3)	1.553(1)	1.541(2)
C(1)–O(1)	1.465(3)	1.446(5)
C(3)–O(3)	1.487(2)	1.488(4)
C(2)–C(1)	1.525(3)	1.525(5)
C(2)–C(3)	1.530(2)	1.533(5)
C(2)–C(4)	1.530(3)	1.540(5)
C(2)–C(5)	1.529(3)	1.515(6)
C(3)–C(6)	1.531(2)	1.527(5)
C(6)–C(7)	1.523(3)	1.509(6)
C(6)–C(8)	1.523(3)	1.518(6)

Phosphoryl bonds (unless hydrogen-bonded) in 1,3,2-dioxaphosphorinanes are generally around 1.44—1.46 Å [1.461(6) Å in compound (15)[26] and 1.444(4) Å in (16)[22]], although in (13) P=O appears to be only 1.39(1) Å, a measurement possibly affected by very anisotropic thermal motion; P=O is slightly shorter in the cis-compound (8) than in (2).

There are small differences among the bond angles (Table 5) around the phosphorus: O–P–Cl angles are about 2° larger and O–P–O angles smaller in the trans- than in the cis-compound. Angles at phosphorus in (13) [Cl–P=O, 112°; O(1)–P–O(3), 105°] and mean angles [O–P=O, 115.7°; O(1,3)–P–Cl, 104.6°] are in good agreement with the corresponding angles in (2). Carbon–carbon bond lengths in the trans-structure are all remarkably close to (or just under) 1.53 Å [methyl C–C bonds determined in (13) with a gem-5,5-dimethyl group are disparate at 1.49(1) and 1.59(1) Å owing to large-amplitude thermal vibrations but are 1.53—1.54 Å in (16)].

The close correspondence between torsion angles (Table 7), except where the stereochemistry demands otherwise, emphasises the similarity in ring conformations in the two phosphorochloridates (2) and (8). Although not, of course, required by crystallographic symmetry, the plane through C(1,2,3) is perpendicular to the dimethyl plane C(2,4,5) in the trans-compound as is, at the phosphorus end of the molecule, the plane through O(1)–P–O(3) to that through O(2)–P–Cl.

Table 5. Bond angles (not involving hydrogen) for the trans- and cis-isomer (2) and (8) (°) with e.s.d.s in parentheses

	trans-(2)	cis-(8)
O(1)–P(1)–O(2)	114.1(1)	115.9(2)
O(1)–P(1)–O(3)	106.6(1)	106.7(1)
O(1)–P(1)–Cl	103.9(1)	102.0(2)
O(2)–P(1)–Cl	111.6(1)	110.0(1)
O(2)–P(1)–O(3)	114.8(1)	117.2(2)
O(3)–P(1)–Cl	105.0(1)	103.3(1)
P(1)–O(1)–C(1)	118.1(1)	122.0(2)
P(1)–O(3)–C(3)	120.7(1)	121.6(2)
O(1)–C(1)–C(2)	112.0(2)	112.9(3)
O(3)–C(3)–C(2)	109.4(1)	108.6(3)
C(1)–C(2)–C(3)	107.3(2)	106.4(3)
C(1)–C(2)–C(4)	109.6(2)	110.0(3)
C(1)–C(2)–C(5)	106.1(2)	104.9(3)
C(4)–C(2)–C(5)	110.5(2)	111.1(3)
C(4)–C(2)–C(3)	114.4(2)	115.3(3)
C(3)–C(2)–C(5)	108.5(2)	108.5(3)
C(2)–C(3)–C(6)	120.3(2)	120.3(3)
O(3)–C(3)–C(6)	106.2(1)	105.6(2)
C(3)–C(6)–C(7)	109.2(2)	109.2(3)
C(3)–C(6)–C(8)	115.5(2)	115.9(3)
C(7)–C(6)–C(8)	109.5(2)	109.8(4)

Table 6. Bond lengths (Å) to hydrogen in trans-(2); e.s.d.s in parentheses

C(1)–H(1)	1.02(2)	C(6)–H(61)	0.95(2)
H(12)	0.97(2)	C(7)–H(71)	0.98(3)
C(3)–H(31)	0.98(2)	H(72)	0.98(3)
C(4)–H(41)	0.98(3)	H(73)	0.97(3)
H(42)	0.94(3)	C(8)–H(81)	0.97(4)
H(43)	0.99(3)	H(82)	0.98(4)
C(5)–H(51)	0.95(3)	H(83)	0.93(3)
H(52)	0.96(3)		
H(53)	1.03(3)		

Table 7. Torsion angles (°) for rings in the trans- and cis-isomer (2) and (8)

	trans-(2)	cis-(8)
O(1)–P(1)–O(3)–C(3)	39.2	33.2
P(1)–O(3)–C(3)–C(2)	−52.1	−53.1
O(3)–C(3)–C(2)–C(1)	59.3	61.8
C(3)–C(2)–C(1)–O(1)	−61.9	−59.9
C(2)–C(1)–O(1)–P(1)	54.5	45.6
C(1)–O(1)–P(1)–O(3)	−39.4	−28.6
O(2)–P(1)–O(1)–C(1)	−167.3	103.9
O(2)–P(1)–O(3)–C(3)	166.5	−98.7
Cl–P(1)–O(1)–C(1)	71.1	−136.6
Cl–P(1)–O(3)–C(3)	−70.6	140.2
O(1)–C(1)–C(2)–C(5)	−177.6	−174.8
O(3)–C(3)–C(2)–C(5)	173.2	174.3
O(1)–C(1)–C(2)–C(4)	63.0	65.6
O(3)–C(3)–C(2)–C(4)	−63.0	−60.5
C(6)–C(3)–C(2)–C(1)	−177.4	−175.8
C(6)–C(3)–C(2)–C(4)	60.4	61.9
C(6)–C(3)–C(2)–C(5)	−63.5	−63.3
C(6)–C(3)–O(3)–P(1)	176.6	177.0
C(7)–C(6)–C(3)–C(2)	159.5	162.4
C(7)–C(6)–C(3)–O(3)	−75.7	−74.3
C(8)–C(6)–C(3)–C(2)	−76.4	−73.8
C(8)–C(6)–C(3)–O(3)	48.5	49.3

However, the dimethyl plane C(2,4,5) is inclined at about 6° to the O(2)–P–Cl plane. Other characteristic inclinations between least-squares best planes through ring atoms in the trans-

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structure, 125° (compared with 130° in cyclohexane) between C(1,2,3) and C(1)–O(1)–C(3)–O(3), and 143° between C(1)–O(1)–C(3)–O(3) and O(1)–P–O(3), are very close to the average inclinations found in slightly flattened 'chair' conformations typical of 1,3,2-dioxaphosphorinanes.

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