Some diphenylphosphorus(v) group monosaccharide compounds derived from methyl 2,3-*O*-isopropylidene-α-D-mannofuranoside

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Methyl 6-*O*-diphenylphosphinoyl-2,3-*O*-isopropylidene-α-D-mannofuranoside 2 is obtained by aerial oxidation of the product of the reaction of methyl 2,3-*O*-isopropylidene-α-D-mannofuranoside 1 and Ph_2PCl in the presence of a base. Methyl 2,3-*O*-isopropylidene-5,6-bis-*O*-methylsulfonyl-α-D-mannofuranoside 4; R = Me reacts with Ph_2PLi to give, after aerial oxidation, methyl 6-deoxy-6-*C*-diphenylphosphinoyl-2,3-*O*-isopropylidene-5-*O*-methylsulfonyl-α-D-mannofuranoside 5 and methyl 6-deoxy-6-*C*-diphenylphosphinoyl-2,3-*O*-isopropylidene-β-L-gulofuranoside 6. Also prepared are the 5-*O*-toluene-*p*-sulfonyl analogue of compound 2 and 2,3 : 5,6-bis-*O*-isopropylidene-1-*O*-diphenylphosphinoyl-α-D-mannofuranoside 8. Crystal structures of compounds 4; (R = Me) and 2 are determined: the furanose ring in both compounds is in a °*E* conformation. Intermolecular H-bonding, involving the P=O and OH groups, links the molecules of compound 2 into chains.

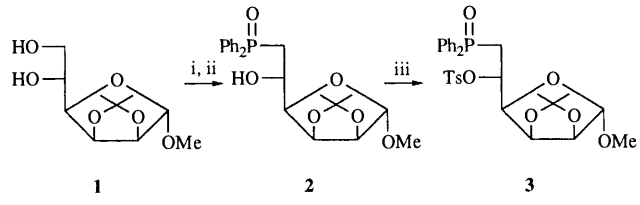
Introduction

Monosaccharide derivatives containing phosphorus-group substituents constitute a diverse and important array of compounds. The significance of pentose phosphates, *e.g.*, as structural units of nucleotides or in metabolic biochemical systems,[1] and the utility of *C*- and *O*-phosphino-carbohydrate derivatives as chiral ligands in transition-metal-catalysed asymmetric synthesis[2] provide major impetus for their study. In addition to the phosphate and phosphino groups, other important phosphorus(III)- and phosphorus(V)-containing substituents found in carbohydrate derivatives include the phosphite,[3] phosphinoyl[4,5] and phosphonoyl groups.[5] Furthermore, phosphorus-containing sugar derivatives are known in which the phosphorus atoms are part of the furanose or pyranose rings.[6]

As part of a study of carbohydrate derivatives with arsenic- and phosphorus-containing substituents,[7-10] *O*- and *C*-diphenylphosphinoyl monosaccharide species have been synthesized from methyl 2,3-*O*-isopropylidene-α-D-mannofuranoside and its 5,6-bis-*O*-methylsulfonyl derivative.

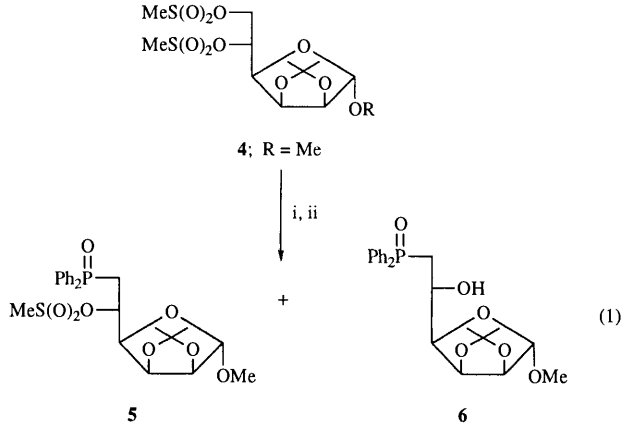
Results and discussion

Reactions of Ph_2PCl and Ph_2PLi with appropiate derivatives of methyl 2,3-*O*-isopropylidene-α-D-mannofuranoside **1** have been shown to produce 6-(*P*–*O*)- and 6-(*P*–*C*)-linked phosphorus group-monosaccharide derivatives, respectively. The very ready aerial oxidation of the initial phosphorus(III) products made it more convenient to characterize them as their phosphorus(V) analogues, Scheme 1 and eqn. (1). Phosphorus NMR spectra of small-scale reactions, carried out under strictly oxygen-free conditions, clearly indicated the presence of phosphorus(III) products. The reaction of Ph_2PCl with substrate **1** occurs selectively at the primary hydroxy group, to give, after aerial oxidation, methyl 6-*O*-diphenylphosphinoyl-2,3-isopropylidene-α-D-mannofuranose **2**. The reduced reactivity of the secondary hydroxy group at C-5 in substrate **1** is clearly evident from its lack of reaction with excess of Ph_2PCl. Although no reaction occurred between compound **2** and Ph_2PCl, compound **2** did react with toluene-*p*-sulfonyl chloride, to give compound **3**. Attempts to obtain other



1 **2** **3**

Scheme 1 *Reagents:* i, Ph_2PCl; ii, air; iii, TsCl



5 **6** (1)

Reagents: i, Ph_2PCl; ii, air

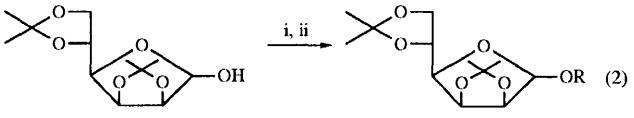
phosphorus group derivatives, from compound **3**, were thwarted by the inertness of the 5-*p*-tosyloxy group in compound **3**, *e.g.* as shown by the lack of reaction of compound **3** with Ph_2PLi. Work-up of the reaction mixture of compound **3** with Ph_2PLi led to the complete recovery of the sugar starting material.

From the reaction of Ph_2PLi with compound **4**; (R = Me), two products, **5** and **6**, were isolated after oxidation, eqn. (1): both products **5** and **6** contained 6-*C*-diphenylphosphinoyl substituents. Compound **5** is formed from dimesyl ester **4**; R = Me by direct nucleophilic substitution at C-6 and has an unchanged stereochemistry at C-5. The 6-mesyloxy group in compound **4**; R = $PhCH_2$ has previously been shown to be the more easily substituted sulfonate group in reaction with potassium acetate in the presence of a crown ether.[11] The mesyloxy group in compound **5** does not react with additional Ph_2PLi. The formation of compound **6** is considered to involve

the intermediacy of the epoxide, methyl 5,6-anhydro-2,3-*O*-isopropylidene-β-L-gulofuranoside **9**,[12] and proceeds with overall inversion of configuration at C-5, Scheme 2. Presumably, compound **6** results from attack of Ph_2P- at sulfur of the 6-$MeS(O)_2$ group. The epoxide **9** has been isolated from the reactions of methyl 2,3-*O*-isopropylidene-5-*O*-methylsulfonyl-α-D-mannofuranoside with such bases[13] as NaOMe, NaH or KOBu^t. The intermediacy of epoxides has also been invoked in reactions of compound **4**; R = Me or CH_2Ph with acetate[13,14] and benzoate,[15] from which products with inverted configurations at C-5, *i.e.* L-gulofuranoside derivatives, have been isolated. Examples include the reaction between compound **4**; R = Me and excess of sodium benzoate in dimethylformamide (DMF), which produced methyl 5,6-di-*O*-benzoyl- and methyl 6-*O*-benzoyl-2,3-isopropylidene-β-L-gulofuranoside,[15] and that between compound **4**; R = Me and sodium acetate in boiling DMF from which benzyl 5,6-di-*O*-acetyl-2,3-isopropylidene-β-L-gulofuranoside was isolated.[14]

In contrast to the reaction of Ph_2PLi with compound **4**; R = Me, no mannofuranosyl-arsenic product was obtained from lithium diphenylarsinide, Ph_2AsLi, and compound **4**; R = Me; the only arsenic-containing product isolated on work-up of the reaction mixture was diphenylarsinic acid, $Ph_2As(O)OH$.

Compound **8**; R = $P(O)Ph_2$, which was obtained from compound **7** as shown in eqn. (2), has been previously

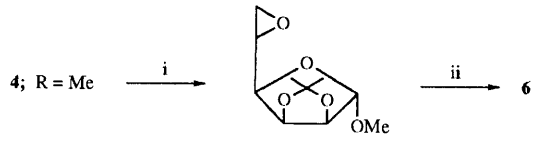


(2)

7 **8**; R = $Ph_2P(O)$

Reagents: i, Ph_2PCl; ii, air

prepared[16] from $Ph_2POC(Me)=CC(O)Me$ and (compound **8**; R = BEt_2), followed by reaction with H_2O_2.



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Scheme 2 *Reagents:* i, Ph_2PLi; ii, water

Spectra

The ^1H–^1H coupling constants in the ^1H NMR spectra of compounds **2**, **3** and **4**; R = Me, **5**, **6** and **8**; R = $P(O)Ph_2$ indicate similar furanose ring conformations, with $J(H^1$–$H^2) < 0.5$, $J(H^2$–$H^3) = 5.8$–6.0 and $J(H^3$–$H^4) = 2.8$–3.7 Hz. Similar coupling constants have been reported for compound **8**; R = CH_2SnR_3.[17] Differences are, however, seen in the proton–proton coupling constants involving the acyclic hydrogens. The assignments of the carbon signals in the solution ^{13}C NMR spectra were aided by ^1H–^{13}C correlations. The two phenyl groups in each of compounds **2**, **3**, **5** and **8** are diastereotopic as shown by the two sets of signals for the ring carbons in the ^{13}C NMR spectra.

Solid-state ^{13}C and ^{31}P NMR spectra were also obtained for compound **2**; the largest differences in the δ_C-values (1.8 ppm) of aliphatic carbons between the solution and solid-state spectra are for C-6 and one of the methyl carbon atoms in the isopropylidene group. There is a change of ~3 ppm in the δ_P-values between the two phases.

The ν(P=O)-values for compounds **2**, **5**, **6** and **8** in the IR spectra were at 1200, 1230, 1210 and 1210 cm^{-1} respectively. The ν(OH)-values were between 3600–3300 for compound **2**, and at 3500 cm^{-1} for compound **6**. The ν(P=O)- and ν(OH)-values for compounds **2**, **3**, **5**, **6** and **8** are in the same regions as reported[7,8] for methyl 4,6-*O*-benzylidene-2-deoxy-2-*C*-diphenylphosphinoyl-α-D-altropyranoside **10** and methyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-diphenylphosphinoyl-α-D-altropyranoside **11**, respectively. Intermolecular H-bonding, involving the P=O and the OH groups, in compound **2** was clearly indicated by X-ray crystallography; see below.

Crystal structures

Crystal structures were determined for compounds **2** and **4**; R = Me.

Crystal structure of compound 2. The atomic arrangement of compound **2** and the numbering system used in the crystallographic study are shown in Fig. 1. The atomic coordinates are listed in a Supplementary Publication† and selected bond lengths and angles are given in Table 1. The pentavalent phosphorus atom has a distorted tetrahedral geometry with the valency angles at P ranging from 101.7(2) [C(17)–P–O(2)] to 115.8(3)° [O(4)–P–O(2)]. The P–C bond lengths in compound **2** are 1.788(3) and 1.797(3) Å: these are somewhat shorter than the reported values[7,8] in compounds **10** [1.808(5)–1.829(6) Å] and **11** [1.819(8)–1.851(8) Å]. The P=O bond length [1.470(5) Å] is similar to the values found for other phosphinoyl-carbohydrates, *e.g.* 1.488(5) Å in **10**, 1.490(5) Å in **11** and 1.480(5) Å in 1,2,3,5-tetra-*O*-acetyl-4-deoxy-4-*C*-[(*S*)-ethylphosphinoyl]-α-D-ribofuranose.[18] The solid-state conformations of the isopropylidene and the furanose rings are envelopes: the latter can be designated the °*E* form. Torsional angles, [H–C–C–H], involving hydrogens on the furanose-ring carbon atoms, are shown in Table 2: these solid-state values can be compared in Table 2 with the estimates of the solution values calculated from ^1H NMR coupling-constant data, using a version of the Karplus equation.

Molecules of compound **2** are linked into chains *via* intermolecular H-bonds involving P=O(4) and H(O3); the bond lengths and angles of the O–H · · · O moiety are O(3)–H(O3) = 0.80(7) Å; O(4) · · · H($O3^i$) = 1.97(8) Å; O(4) · · · O(3^i) = 2.740(7) Å and O(4) · · · H($O3^i$)–O(3^i) = 161(8)° [symmetry operation $i = x, y - 1, z$]. See Fig. 2.

The exocyclic angles the phosphorus atom makes with one of the phenyl rings [involving C(17)–C(22)] are significantly different: C(18)–C(17)–P = 123.8(1) and C(22)–C(17)–P = 116.1(1)°.

The exocyclic angles to the other phenyl ring are the same [120.0 ± 3°].

Molecular structure of compound 4; R = Me. The atomic arrangements of compound **4**; R = Me and the crystallographic numbering system are shown in Fig. 3. Atomic coordinates are listed in a Supplementary Publication,† bond lengths and valency angles are shown in Table 3. The conformation of the furanose ring in compound **4**; R = Me is essentially the same as that in compound **2**, *i.e.* the °*E* conformation. A mean-plane calculation on the furanose ring indicates that the oxygen atom [O(1)] is 0.535(9) Å out of the best plane of the four C atoms (r.m.s. deviation of the C atoms = 0.003 Å). A similar calculation for the isopropylidene ring shows C(7) to be −0.440(8) Å out of the best plane of the other four ring atoms (r.m.s. deviation = 0.003 Å). Cremer–Pople ring-puckering parameters were calculated, using the Pucker program,[19] to be $Q = 0.362$, $q2 = 0.362$, $\psi = 0.7$ for the furanose ring; and $Q = 0.285$, $q2 = 0.285$, $\psi = 34.8$ for the isopropylidene ring. The furanose and isopropylidene rings were calculated to adopt 96 and 93% envelope conformations, respectively.

The calculated H–C–C–H torsional angles for hydrogens on furanose-ring carbons in compound **4**; R = Me are listed in

† *Supplementary Publication:* Tables of atomic coordinates and structure factors and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See *Instructions for Authors*, January issue.

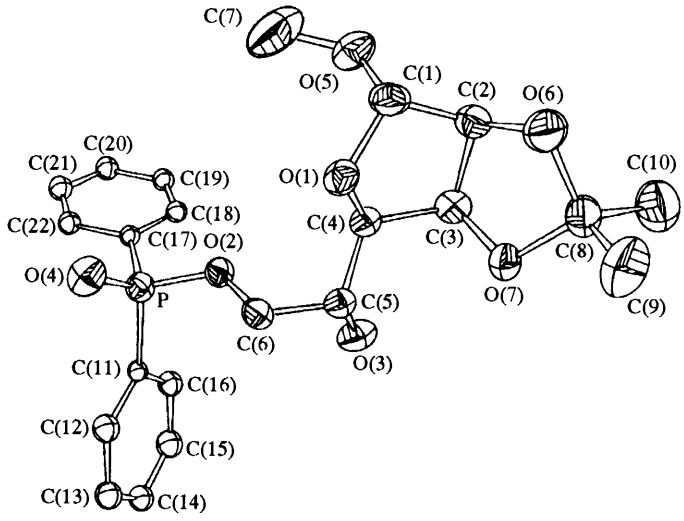


Fig. 1 Atom arrangement and numbering system for compound **2**. H-Atoms have been omitted for clarity and thermal ellipsoids are drawn at the 40% probability level.

Table 1 Selected bond lengths (Å) and angles (°) for compound **2**

O(2)–P	1.584(4)	O(4)–P	1.470(5)
C(11)–P	1.797(3)	C(17)–P	1.788(3)
C(1)–O(1)	1.421(7)	C(4)–O(1)	1.430(7)
C(6)–O(2)	1.457(6)	C(5)–O(3)	1.411(8)
C(1)–O(5)	1.388(7)	C(7)–O(5)	1.410(10)
C(2)–O(6)	1.413(7)	C(8)–O(6)	1.423(7)
C(3)–O(7)	1.434(7)	C(8)–O(7)	1.424(7)
C(2)–C(1)	1.491(10)	C(3)–C(2)	1.531(8)
C(4)–C(3)	1.513(8)	C(5)–C(4)	1.516(7)
C(6)–C(5)	1.500(8)	C(9)–C(8)	1.507(10)
C(10)–C(8)	1.505(10)		
O(4)–P–O(2)	115.8(3)	C(11)–P–O(2)	105.3(2)
C(11)–P–O(4)	111.0(3)	C(17)–P–O(2)	101.7(2)
C(17)–P–O(4)	113.8(3)	C(17)–P–C(11)	108.5(2)
C(4)–O(1)–C(1)	105.4(5)	C(6)–O(2)–P	118.4(4)
C(7)–O(5)–C(1)	113.9(7)	C(8)–O(6)–C(2)	107.6(5)
C(8)–O(7)–C(3)	107.4(4)	O(5)–C(1)–O(1)	112.5(5)
C(2)–C(1)–O(1)	105.8(5)	C(2)–C(1)–O(5)	107.8(6)
C(1)–C(2)–O(6)	110.8(5)	C(3)–C(2)–O(6)	106.0(4)
C(3)–C(2)–C(1)	104.4(5)	C(2)–C(3)–O(7)	103.4(4)
C(4)–C(3)–O(7)	110.7(5)	C(4)–C(3)–C(2)	103.9(5)
C(3)–C(4)–O(1)	104.2(4)	C(5)–C(4)–O(1)	109.4(5)
C(5)–C(4)–C(3)	115.7(5)	C(4)–C(5)–O(3)	110.8(5)
C(6)–C(5)–O(3)	112.5(4)	C(6)–C(5)–C(4)	112.9(5)
C(5)–C(6)–O(2)	109.0(5)	O(7)–C(8)–O(6)	104.9(5)
C(9)–C(8)–O(6)	108.9(6)	C(9)–C(8)–O(7)	107.7(6)
C(10)–C(8)–O(6)	111.6(6)	C(10)–C(8)–O(7)	110.6(6)
C(10)–C(8)–C(9)	112.7(6)	C(12)–C(11)–P	119.7(2)
C(16)–C(11)–P	120.3(2)	C(18)–C(17)–P	123.8(1)
C(22)–C(17)–P	116.1(1)		

Hydrogen bond distances and angles

O(3)···H	0.80(7)	O(4)···H	1.97(8)
O(4)···O(3^{i})	2.740(7)	O(4)···H–O(3^{i})	1.61(8)

Symmetry operation i $x, y - 1, z$.

Table 2. As can be seen, these are similar to the values found in compound **2**.

There are, as expected, staggered arrangements of substituents on the C(5)–C(6) acyclic fragments in both compounds **2** and **4**; R = Me; however, the C(6)-substituent is directed between the substituents on C(5) in both cases; see Fig. 4.

Experimental

NMR spectra were obtained on a Bruker 250 MHz instrument; J-values are given in Hz. IR spectra were recorded on a Philips Analytical PU9800 Fourier-transform spectrometer. The following EPSRC services were used: solid-state NMR spectroscopy, based at the University of Durham; mass spectrometry, based at the University of Wales, Swansea; and X-ray data collection, based at the University of Wales, Cardiff.

Methyl 2,3-*O*-isopropylidene-α-D-mannofuranoside[14] **1**, methyl 2,3-*O*-isopropylidene-5,6-bis-*O*-methylsulfonyl-α-D-mannofuranoside[14,15] **4**; R = Me, and 2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranose[20] **7** were obtained by published procedures. The ^{1}H and ^{13}C NMR spectra of compound **4**; R = Me are given here as only partial NMR data have been reported previously.

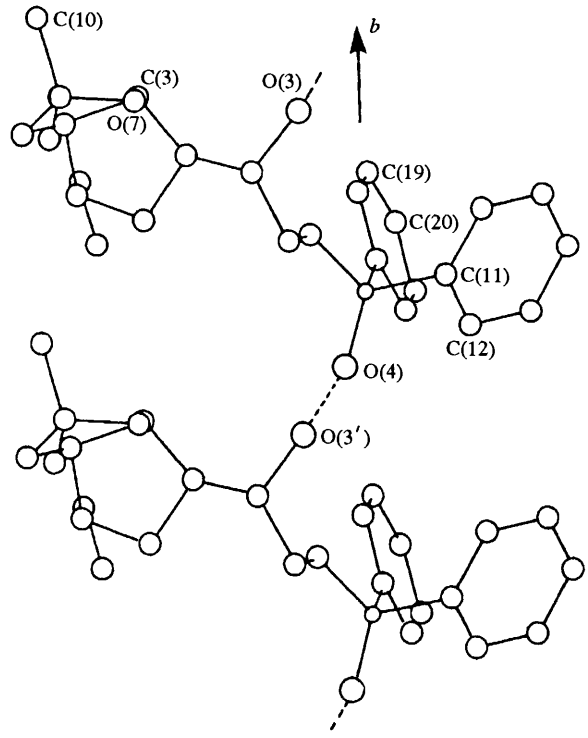


Fig. 2 H-Bonding in compound **2**. Two molecules are shown associated with a unit cell viewed down c. Dashed lines indicate the H-bonding interactions between O(4) and O(3^{i}) (symmetry operation: $x, y - 1, z$).

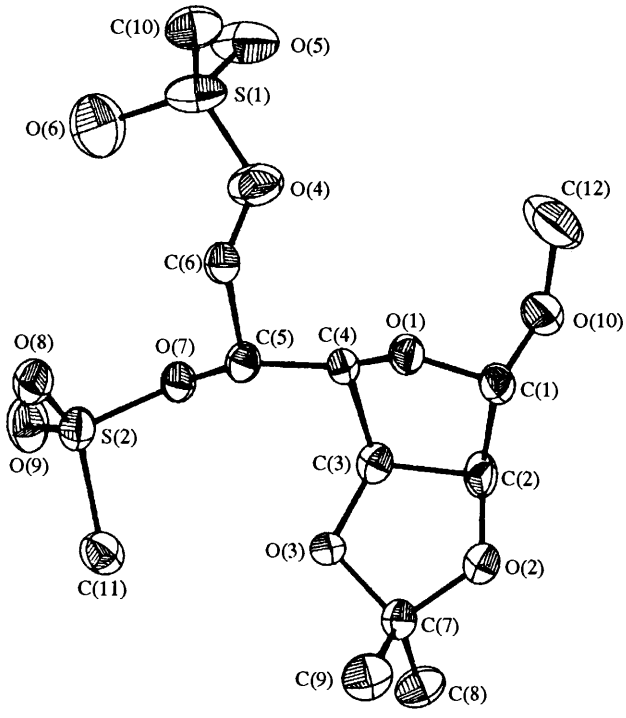
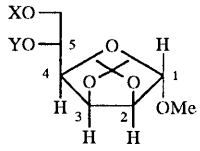


Fig. 3 Atom arrangement and numbering system for compound **4**; R = Me

Table 2 Calculated torsion (dihedral) angles in solutions and in the solid state for compounds **2** and **4**; R = Me



Torsion (dihedral) angle (°)	Compound **4** [X = Y = $MeS(O)_2$] Solid state	Solution[a]	[$J(^1H^N–^1H^{N+1})$] (Hz)	Compound **2** [X = $Ph_2P(O)$, Y = H] Solid state	Solution[a]	[$J(^1H^N–^1H^{N+1})$] (Hz)
$H^N–C^N–C^{N+1}–H^{N+1}$						
$H^1–C^1–C^2–H^2$	−95.6	90	0	−93.9	90	0
$H^2–C^2–C^3–H^3$	−0.1	32	5.8	+3.1	31	5.9
$H^3–C^3–C^4–H^4$	−27.4	47	3.6	−28.5	48	3.5
$H^4–C^4–C^5–H^5$	+175.7	150	7.8	+170.3	162	8.3

[a] Dihedral angles, calculated from the $J(^1H–^1H)$ coupling constant data, using the Karplus equation, $J = X\cos^2\theta - 0.28$ ($X = 8.5$, $\theta < 90°$; $X = 9.5$, $\theta > 90°$).

Table 3 Bond angles (°) and lengths (Å) for compound **4**; R = Me

S(1)–O(5)	1.394(5)	O(3)–C(7)	1.429(7)
S(1)–O(6)	1.478(6)	O(4)–C(6)	1.451(7)
S(1)–O(4)	1.526(5)	O(7)–C(5)	1.470(7)
S(1)–C(10)	1.737(7)	O(10)–C(1)	1.394(8)
S(2)–O(9)	1.420(5)	O(10)–C(12)	1.432(9)
S(2)–O(8)	1.426(5)	C(1)–C(2)	1.529(8)
S(2)–O(7)	1.581(4)	C(2)–C(3)	1.536(8)
S(2)–C(11)	1.759(6)	C(3)–C(4)	1.537(8)
O(1)–C(1)	1.388(7)	C(4)–C(5)	1.516(7)
O(1)–C(4)	1.417(7)	C(5)–C(6)	1.505(8)
O(2)–C(7)	1.415(7)	C(7)–C(9)	1.470(10)
O(2)–C(2)	1.420(7)	C(7)–C(8)	1.516(9)
O(3)–C(3)	1.421(6)		
O(5)–S(1)–O(6)	115.8(4)	O(10)–C(1)–C(2)	107.0(6)
O(5)–S(1)–O(4)	106.4(3)	O(2)–C(2)–C(1)	110.6(5)
O(6)–S(1)–O(4)	107.4(3)	O(2)–C(2)–C(3)	105.3(5)
O(5)–S(1)–C(10)	113.4(4)	C(1)–C(2)–C(3)	103.3(5)
O(6)–S(1)–C(10)	107.8(4)	O(3)–C(3)–C(2)	104.0(5)
O(4)–S(1)–C(10)	105.4(4)	O(3)–C(3)–C(4)	111.2(5)
O(9)–S(2)–O(8)	119.8(3)	C(2)–C(3)–C(4)	103.4(5)
O(9)–S(2)–O(7)	104.0(3)	O(1)–C(4)–C(5)	106.5(5)
O(8)–S(2)–O(7)	109.0(2)	O(1)–C(4)–C(3)	105.0(5)
O(9)–S(2)–C(11)	110.2(3)	C(5)–C(4)–C(3)	117.6(5)
O(8)–S(2)–C(11)	108.4(3)	O(7)–C(5)–C(6)	111.4(5)
O(7)–S(2)–C(11)	104.3(3)	O(7)–C(5)–C(4)	105.2(4)
C(1)–O(1)–C(4)	106.2(5)	C(6)–C(5)–C(4)	111.2(5)
C(7)–O(2)–C(2)	107.6(5)	O(4)–C(6)–C(5)	109.3(5)
C(3)–O(3)–C(7)	108.2(4)	O(2)–C(7)–O(3)	105.0(9)
C(6)–O(4)–S(1)	122.2(4)	O(2)–C(7)–C(9)	110.2(6)
C(5)–O(7)–S(2)	119.1(3)	O(3)–C(7)–C(9)	109.5(5)
C(1)–O(10)–C(12)	109.8(7)	O(2)–C(7)–C(8)	109.8(5)
O(1)–C(1)–O(10)	113.5(6)	O(3)–C(7)–C(8)	110.5(6)
O(1)–C(1)–C(2)	106.0(5)	C(9)–C(7)–C(8)	111.7(5)

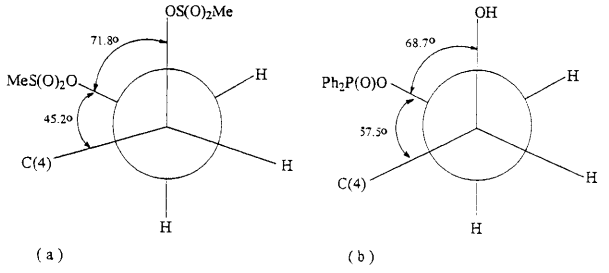


Fig. 4 Arrangement of substituents at the C(5)–C(6) acyclic moieties in solid compounds **2** and **4**; R = Me

Compound 4; R = Me

$\delta_H(CDCl_3$; 250 MHz) 5.05 [1 H, ddd, $J(H^5–H^{6'})$ 2.2, $J(H^5–H^6)$ 4.4, $J(H^4–H^5)$ 7.8, 5-H], 4.93 (1 H, s, 1-H), 4.78 [1 H, dd, $J(H^2–H^3)$ 5.8, $J(H^3–H^4)$ 3.6, 3-H], 4.73 [1 H, dd, $J(H^5–H^{6'})$ 2.2, $J(H^6–H^{6'})$ 11.8, 6′-H], 4.62 [1 H, d, $J(H^2–H^3)$ 5.8, 2-H], 4.54 [1 H, dd, $J(H^5–H^6)$ 4.4, $J(H^6–H^{6'})$ 11.8, 6-H], 4.23 [1 H, dd, $J(H^3–H^4)$ 3.6, $J(H^4–H^5)$ 7.8, 4-H], 3.34 (3 H, s, OMe), 3.15 and 3.11 (6 H, 2 s, 2 × $MeSO_3$) and 1.50 and 1.33 (6 H, 2 s, Me_2C); $\delta_C(CDCl_3$; 62.9 MHz) 113.2 (Me_2C), 107.2 (C-1), 84.8 (C-3), 78.8 (C-2), 76.5 (C-4), 76.3 (C-5), 68.8 (C-6), 55.0 (OMe), 38.6 and 37.6 (2 × $MeSO_3$) and 26.0 and 24.7 (Me_2C).

Methyl 6-*O*-diphenylphosphinoyl-2,3-*O*-isopropylidene-α-D-mannofuranoside 2

To a stirred solution of compound **1** (2.34 g, 10 mmol) in dry Et_3N (100 cm^3) was added a solution of Ph_2PCl (2.43 g, 11 mmol) in dry tetrahydrofuran (THF) (100 cm^3). The reaction mixture was stirred at room temp. overnight and filtered, and the filtrate was evaporated. The residual oil was separated on a chromatotron, with $CHCl_3$ as eluent, to give *compound* **2**, which was recrystallized from EtOAc–hexane (2.30 g, 53%), mp 172–174 °C (Found: C, 61.0; H, 6.3; P, 7.0. $C_{22}H_{27}O_7P$ requires C, 60.8; H, 6.3; P, 7.1%); $\delta_H(CDCl_3$; 250 MHz) 7.86–7.71 (4 H, m, *o*-H), 7.59–7.44 (6 H, m, *m*- + *p*-H), 4.87 (1 H, s, 1-H), 4.87 [1 H, dd, $J(H^2–H^3)$ 5.9, $J(H^3–H^4)$ 3.5, 3-H], 4.54 [1 H, d, $J(H^2–H^3)$ 5.9, 2-H], 4.34 [1 H, ddd, $J(H^6–H^{6'})$ 11.7, $J(H^5–H^6)$ 10.2, $J(H^6–^{31}P)$ 1.7, 6-H], 4.27 [1 H, dd, $J(H^6–H^{6'})$ 11.7, $J(H^5–H^{6'})$ 5.3, 6′-H], 4.20 [1 H, m, $J(H^5–H^6)$ 10.2, $J(H^5–H^{6'})$ 5.3, $J(H^5–^{31}P)$ 1.9, 5-H], 3.95 [1 H, dd, $J(H^4–H^5)$ 8.3, $J(H^3–H^4)$ 3.5, 4-H], 3.25 (3 H, s, OMe) and 1.45 and 1.32 (6 H, 2 s, Me_2C); $\delta_C(CDCl_3$; 62.9 MHz) 132.5 [$J(^{13}C–^{31}P)$ 2.5, C-*p*], 132.4 [$J(^{13}C–^{31}P)$ 2.5, C-*p*], 131.8 [$J(^{13}C–^{31}P)$ 10.2, C-*p*], 131.6 [$J(^{13}C–^{31}P)$ 10.1, C-*o*], 130.5 [$J(^{13}C–^{31}P)$ 138, C-*i*], 130.3 [$J(^{13}C–^{31}P)$ 138, C-*i*], 128.6 [$J(^{13}C–^{31}P)$ 13.5, C-*m*], 128.6 [$J(^{13}C–^{31}P)$ 13.4, C-*m*], 112.5 (Me_2C), 107.2 (C-1), 84.7 (C-2), 79.8 (C-3), 78.5 (C-4), 68.5 [$J(^{13}C–^{31}P)$ 3, C-5], 69.0 [$J(^{13}C–^{31}P)$ 6, C-6], 54.4 (OMe) and 26.0 and 24.6 (Me_2C); $\delta_P(CDCl_3$; 101.3 MHz) 36.5; δ_C(solid state; 75.43 MHz) 135.5, 133.0 and 128.0 (protonated aryl C), 131.8 and 130.0 (non-protonated aryl C), 111.7 (Me_2C), 106.8 (C-1), 84.4 (C-4), 78.9 (C-3), 78.3 (C-4), 68.5 (C-5), 67.2 (C-6), 54.0 (OMe) and 27.8 and 25.5 (Me_2C); δ_P(solid state; 121.4 MHz) 33.4; ν_{max}(KBr)/cm^{-1} 3600–3300 (OH) and 1200 (P=O); *m*/*z* (%) 435 (18%), 261 (100), 233 (20), 219 (80) and 201 (72).

Methyl 6-*O*-diphenylphosphinoyl-2,3-*O*-isopropylidene-5-*O*-(*p*-tolylsulfonyl)-α-D-mannofuranoside 3

A solution of compound **2** (4.34 g, 10 mmol) and toluene-*p*-sulfonyl chloride (2.30 g, 12 mmol) in anhydrous pyridine (70 cm^3) was stirred at room temp. for 48 h, and poured into ice–water. The syrup which separated was collected and dissolved in $CHCl_3$ (100 cm^3). The $CHCl_3$ solution was successively washed with cold 5% aq. HCl, saturated aq. $NaHCO_3$ and water, dried over $CaCl_2$, and rotary evaporated. The syrupy

residue was crystallized from EtOH to give fine needles of *compound* **3** (3.75 g, 66%), mp 94–95 °C (Found: C, 59.3; H, 5.7. $C_{29}H_{33}O_9PS$ requires C, 59.2; H, 5.7%); δ_H($CDCl_3$; 250 MHz) 7.88–7.75 (6 H, m, *o*-H + 2 H from tosyl), 7.56–7.22 (6 H, m, *m*- + *p*-H), 7.20 [2 H, d, *J*(H–H) 8, tosyl], 5.00 [1 H, ddd, $J(H^4–H^5)$ 7.1, $J(H^5–H^6)$ 5.0, $J(H^5–H^{6'})$ 2.1, 5-H], 4.75 (1 H, s, 1-H), 4.42 [1 H, d, $J(H^2–H^3)$ 5.9, 2-H], 4.49 [1 H, ddd, $J(H^5–H^{6'})$ 2.1, $J(H^6–H^{6'})$ 11.6, $J(H^{6'}–^{31}P)$ 4.9, 6-H′], 4.31 [1 H, dt, $J(H^5–H^6)$ 5.0, $J(H^6–H^{6'})$ 11.6, $J(H^6–^{31}P)$ 5.0, 6-H], 4.30 [1 H, dd, $J(H^2–H^3)$ 5.9, $J(H^3–H^4)$ 2.8, 3-H], 4.17 [1 H, dd, $J(H^3–H^4)$ 2.8, $J(H^4–H^5)$ 7.1, 4-H], 3.18 (3 H, s, OMe), 2.37 (3 H, s, Me), 2.03 (br s, OH) and 1.21 and 1.09 (6 H, 2 s, Me_2C); δ_C($CDCl_3$; 62.3 MHz) 144.5 and 133.8 (tosyl), 132.2 [$J(^{13}C–^{31}P)$ 2.8, C-*p*], 132.1 [$J(^{13}C–^{31}P)$ 2.8, C-*p*], 131.9 [$J(^{13}C–^{31}P)$ 10.3, C-*o*], 131.5 [$J(^{13}C–^{31}P)$ 10.3, C-*o*], 131.3 [$J(^{13}C–^{31}P)$ 139, C-*i*], 130.6 [$J(^{13}C–^{31}P)$ 139, C-*i*], 129.4 and 128.6 [$J(^{13}C–^{31}P)$ 13.3, C-*m*], 128.4 [$J(^{13}C–^{31}P)$ 13.3, C-*m*], 128.3 (tosyl), 112.6 (Me_2C), 106.9 (C-1), 84.5 (C-2), 78.7 (C-3), 77.5 [$J(^{13}C–^{31}P)$ 9.0, C-5], 77.1 (C-4), 63.3 [$J(^{13}C–^{31}P)$ 4.0, C-6], 54.7 (Me), 25.7 and 24.3 (Me_2C) and 21.6 (Me); δ_P($CDCl_3$; 101.3 MHz) 32.9; ν_{max}(KBr)/cm^{-1}, 1220 (P=O).

Methyl 6-deoxy-6-*C*-diphenylphosphinoyl-2,3-*O*-isopropylidene-5-*O*-methylsulfonyl-α-D-mannofuranoside 5 and methyl 6-deoxy-6-*C*-diphenylphosphinoyl-2,3-*O*-isopropylidene-β-L-gulofuranoside 6

Lithium pieces (0.28 g, 40 mmol) were added, under nitrogen, to a solution of PPh_3 (5.24 g, 20 mmol) in anhydrous THF (50 cm^3). The mixture was agitated in an ultrasonic bath for 4 h at room temp., and Bu^{t}Cl (20 mmol) was added to destroy the PhLi co-product. To this stirred solution of $LiPPh_2$ was added under nitrogen, a solution of compound **4**; R = Me (3.90 g, 10 mmol) in anhydrous THF (50 cm^3). The reaction mixture was left overnight, water (100 cm^3) was added, and the THF was removed under reduced pressure. The residue was extracted with benzene (3 × 100 cm^3); the combined extracts were dried over $MgSO_4$ and rotary evaporated to give a syrup. This was separated, using a chromatotron, into two fractions. The more mobile material was *compound* **5**, which was crystallized from EtOAc–hexane as needles (1.5 g, 31%), mp 73–75 °C (Found: C, 55.7; H, 5.6. $C_{23}H_{29}O_8PS$ requires C, 55.6; H, 5.9%); δ_H($CDCl_3$; 250 MHz) 7.86–7.71 (4 H, m, *o*-H), 7.54–7.28 (6 H, m, *m*- + *p*-H), 5.46 (1 H, m, 5-H), 4.91 (1 H, s, 1-H), 4.84 [1 H, dd, $J(H^3–H^4)$ 3.7, $J(H^2–H^3)$ 5.8, 3-H], 4.54 [1 H, d, $J(H^2–H^3)$ 5.9, 2-H], 4.49 [1 H, dd, *J*(H–H) 3.5, *J*(H–H) 3.7, 4-H], 3.35 (3 H, s, OMe), 3.03 (2 H, m, 6-H_2), 2.94 (3 H, s, $MeSO_3$) and 1.34 and 1.28 (Me_2C); δ_C($CDCl_3$; 62.9 MHz) 133.3 [$J(^{13}C–^{31}P)$ 101.3, C-*i*], 131.9 [$J(^{13}C–^{31}P)$ 2.7, C-*p*], 131.8 [$J(^{13}C–^{31}P)$ 2.7, C-*p*], 130.7 [$J(^{13}C–^{31}P)$ 9.4, C-*o*], 130.6 [$J(^{13}C–^{31}P)$ 9.5, C-*o*], 128.7 [$J(^{13}C–^{31}P)$ 12.0, C-*m*], 128.6 [$J(^{13}C–^{31}P)$ 11.9, C-*m*], 112.7 (Me_2C), 106.6 (C-1), 84.5 (C-2), 80.5 [$J(^{13}C–^{31}P)$ 7.2, C-4], 79.2 (C-3), 75.4 [$J(^{13}C–^{31}P)$ 4.7, C-5], 54.8 (OMe), 38.4 ($MeSO_3$), 31.0 [$J(^{13}C–^{31}P)$ 71.6, C-6] and 24.2 and 25.5 (Me_2C); δ_P($CDCl_3$; 101.3 MHz) 29.1; ν_{max}(KBr)/cm^{-1} 1230 (P=O).

The less mobile compound was the gulo-*product* **6**, which was crystallized from EtOAc–hexane (1.3 g, 32%), mp 118–120 °C (Found: C, 63.3; H, 6.7. $C_{22}H_{27}O_6P$ requires C, 63.2; H, 6.5%); δ_H($CDCl_3$; 250 MHz) 7.86–7.71 (4 H, m, *o*-H), 7.59–7.44 (6 H, m, *m*- + *p*-H), 4.85 (1 H, s, 1-H), 4.85 [1 H, dd, $J(H^2–H^3)$ 6.0, $J(H^3–H^4)$ 3.6, 3-H], 4.55 [1 H, d, $J(H^2–H^3)$ 6.0, 2-H], 4.45 [1 H, dddd, $J(H^4–H^5)$ 7.9, $J(H^5–H^6)$ 2.1, $J(H^5–H^{6'})$ 10.4, $J(H^5–^{31}P)$ 10.1, 5-H], 4.00 (v br, OH), 3.88 [1 H, dd, $J(H^3–H^4)$ 3.6, $J(H^4–H^5)$ 7.9, 4-H], 3.28 (3 H, s, OMe), 2.85 [1 H, ddd, $J(H^5–H^6)$ 2.1, $J(H^6–H^{6'})$ 15.1, $J(H^6–^{31}P)$ 8.1, 6-H], 2.55 [1 H, ddd, $J(H^5–H^{6'})$ 10.4, $J(H^6–H^{6'})$ 15.1, $J(H^{6'}–^{31}P)$ 21.2, 6′-H] and 1.32 and 1.30 (6 H, 2 s, Me_2C); δ_C($CDCl_3$; 62.9 MHz) 133.1 [$J(^{13}C–^{31}P)$ 100, C-*i*], 131.6 [$J(^{13}C–^{31}P)$ 100, C-*i*], 132.0 [$J(^{13}C–^{31}P)$ 1, C-*p*], 131.9 [$J(^{13}C–^{31}P)$ 1, C-*p*], 130.9 [$J(^{13}C–^{31}P)$ 9.5, C-*o*], 130.3 [$J(^{13}C–^{31}P)$ 9.8, C-*o*], 128.6 [$J(^{13}C–^{31}P)$ 12, C-*m*], 112.4 (Me_2C), 106.9 (C-1), 84.7 (C-2), 82.3 [$J(^{13}C–^{31}P)$ 12, C-4], 79.3 (C-3), 65.4 [$J(^{13}C–^{31}P)$ 4.7, C-5], 54.5 (OMe), 33.5 [$J(^{13}C–^{31}P)$ 71.8, C-6] and 24.6 and 25.7 (Me_2C); δ_P($CDCl_3$; 101.3 MHz) 35.8; ν_{max}(KBr)/cm^{-1} 3500 (OH) and 1210 (P=O).

1-*O*-Diphenylphosphinoyl-2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranoside 8; R = $Ph_2P(O)$

A solution of Ph_2PCl (4.49 g, 20 mmol) in anhydrous THF (50 cm^3) was added to a solution of 2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranose **7** (5.20 g, 20 mmol) in anhydrous Et_2NH (100 cm^3). The reaction mixture was stirred for 48 h, filtered, and the filtrate was rotary evaporated to give a syrupy residue. The residue was crystallized from EtOAc–hexane (7.45 g, 81%), mp 168–169 °C (lit.,[16] 162–164 °C) (Found: C, 62.6; H, 6.3. $C_{24}H_{29}O_7P$ requires C, 62.6; H, 6.3%); δ_H($CDCl_3$; 250 MHz) 7.86–7.72 (4 H, m, *o*-H), 7.58–7.28 (6 H, m, *m*- + *p*-H), 5.94 [1 H, d, $J(H–^{31}P)$ 6.3, 1-H], 4.94 [1 H, d, $J(H^2–H^3)$ 5.8, 2-H], 4.90 [1 H, dd, $J(H^3–H^4)$ 3.3, $J(H^2–H^3)$ 5.8, 3-H], 4.32 [1 H, ddd, $J(H^4–H^5)$ 8.2, $J(H^5–H^{6'})$ 6.3, $J(H^5–H^6)$ 4.33, 5-H], 4.01 [1 H, dd, $J(H^3–H^4)$ 3.3, $J(H^4–H^5)$ 8.2, 4-H], 3.91 [1 H, dd, $J(H^5–H^{6'})$ 6.3, $J(H^6–H^{6'})$ 8.8, 6′-H], 3.45 [1 H, dd, $J(H^5–H^6)$ 4.3, $J(H^6–H^{6'})$ 8.8, 6-H] and 1.43, 1.40, 1.35 and 1.34 (12 H, 4 s, Me_2C); δ_C($CDCl_3$; 62.9) 132.3 [$J(^{13}C–^{31}P)$ 3.3, C-*p*], 132.2 [$J(^{13}C–^{31}P)$ 3.3, C-*p*], 131.6 [$J(^{13}C–^{31}P)$ 10.4, C-*o*], 131.3 [$J(^{13}C–^{31}P)$ 138, C-*i*], 131.2 [$J(^{13}C–^{31}P)$ 134, C-*i*], 131.1 [$J(^{13}C–^{31}P)$ 10.4, C-*o*], 128.4 [$J(^{13}C–^{31}P)$ 13.3, C-*m*], 113.0 (Me_2C), 109.2 (Me_2C), 102.6 [$J(^{13}C–^{31}P)$ 5.7, C-1], 86.3 [$J(^{13}C–^{31}P)$ 7.9, C-2], 82.0 (C-4), 79.1 (C-3), 72.3 (C-5), 66.5 (C-6) and 26.8, 25.8, 25.1 and 24.6 (2 × Me_2C); δ_P($CDCl_3$; 101.3 MHz) 30.6; ν_{max}(KBr)/cm^{-1} 1210 (P=O).

X-Ray analysis of compound 4; R = Me

Data were collected on a Delft instruments' FAST diffractometer with monochromated Mo-Kα radiation. Corrections were made for Lorentz and polarization effects only. The data were collected as triclinic; however, the unit-cell dimensions were entered into Lepage[21] and a monoclinic centred cell was suggested. Errors on the cell dimensions were assumed to be the same as those found for the triclinic data. Crystal data and refinement details are listed in Table 4. All non-hydrogens were located using SHELXS86[22] and refined using SHELXL-93.[23] The hydrogen atoms were allowed to ride on their attached carbon atoms with ideal bond lengths and common isotropic temperature factors according to type. Full-matrix least-squares calculations with anisotropic temperature factors for the S, O and C atoms were calculated. The absolute configuration is based on the known stereochemistry of the carbohydrate moiety and the low absolute structure parameter (Table 4). The diagram of the atomic arrangement was obtained using ZORTEP.[24]

X-Ray analysis of compound 2

Data were collected on a Nicolet P3 diffractometer with monochromated Mo-Kα radiation. Data collection used $\bar{\omega}$ scan rates of 1.0 (I_p < 150) to 29.3 (I_p > 2500)° min^{-1}, where I_p was the prescan intensity. Scan width was 0.6 $\bar{\omega}$ with background counts taken at ±1.0 $\bar{\omega}$. Data reduction was made using the RDNIC program.[25] Refinement was by full-matrix least-squares. Crystal data and refinement details are given in Table 4. The phenyl groups [C(11)–C(16) and C(17)–C(22)], and the attached H-atoms were refined as rigid bodies with C–C and C–H set to 1.395 and 0.95 Å, respectively, and with C vibrating isotropically. All other non-H-atoms were refined anisotropically. The hydroxy group H was found in a difference map and refined isotropically. All other H-atoms were placed in calculated positions with C–H = 0.95 Å and refined with separate group U_{iso}-values for primary and secondary methyl and phenyl H. The methyl groups were also treated as rigid

Table 4 Crystal data and structure refinement

	Compound **4**; R = Me	Compound **2**
Empirical formula	$C_{12}H_{22}O_{10}S_2$	$C_{22}H_{27}O_7P$
Formula weight	390.42	434.43
Temperature (K)	293(2)	298
Radiation type	Mo-Kα	Mo-Kα
Wavelength (Å)	0.710 69	0.710 69
Crystal system	Monoclinic	Monoclinic
Space group	*C*2	$P2_1$
Unit-cell dimensions		
a (Å)	19.923(6)	13.418(14)
b (Å)	5.434(7)	5.976(6)
c (Å)	17.985(3)	13.971(16)
α (°)	90	90
β (°)	112.25(10)	102.81(9)
γ (°)	90	90
Volume (Å)^3	1802(2)	1092(2)
Z	4	2
Density (calc.) (Mg m^{-3})	1.439	1.321
Absorption coefficient (mm^{-1})	0.342	0.16
F(000)	824	
Crystal size (mm)	0.18 × 0.15 × 0.20	0.8 × 0.3 × 0.06
Range	2.08 to 24.85	0 to 25
Index ranges	$-22 \leqslant h \leqslant 21$	$-15 \leqslant h \leqslant 15$
	$0 \leqslant k \leqslant 6$	$0 \leqslant k \leqslant 7$
	$0 \leqslant l \leqslant 19$	$0 \leqslant l \leqslant 16$
Independent reflections	1552	2005
Observed reflections	1114	1633
	$[I > 2\sigma(I)]$	$[F > 4\sigma(I)]$
Refinement method	Full-matrix l.s. on F^2	Full-matrix l.s. on F^2
Number of parameters	224	202
Goodness of fit on F^2(s)	0.914	
Final *R* indices $[I > 2\sigma(I)]$	$R1 = 0.0467$, $wR2 = 0.1036$	$R = 0.059$, $wR = 0.059$
R indices (all data)	$R1 = 0.0634$, $wR2 = 0.1077$	
Final weighting scheme	$w = 1/[\sigma^2(F_o^2) + (0.0546P)^2]$	$w = 1/[\sigma^2(F) + 0.000\,572F^2]$
Residual diffraction max. (e Å^{-3})	0.467	0.47
Residual diffraction min. (e Å^{-3})	−0.214	−0.37

bodies. All computations were performed on the SUN SPARCserver (UNIX operating system) of the University of Aberdeen. Structure solution and refinement was achieved using SHELXS86[22] and SHELX76.[26] Molecular graphics programs used were ORTEX[27a] and PLOTAID.[27b]

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