The Synthesis of Sugars with Highly Halogenated Side-chains

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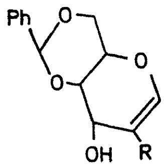
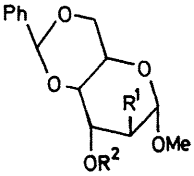
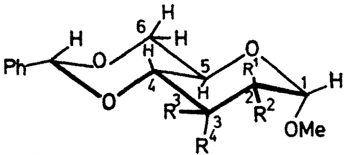
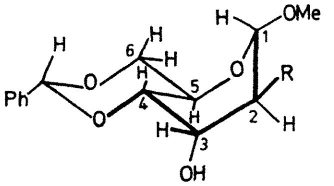
Summary A synthesis of sugars with a pentachlorophenyl side-chain which leads to a 4,6-*O*-benzylidene-*altro*-pyranoside with a boat conformation, and a new route to furanose-1-enes are outlined.

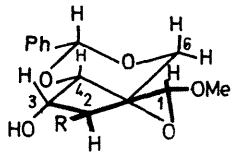
FEAST, OVEREND, and WILLIAMS[1] isolated 4,6-*O*-benzylidene-2-phenyl-D-allal (Ia) as the major product from the reaction of phenyl-lithium with methyl-2,3-anhydro-4,6-*O*-benzylidene-α-D-allopyranoside (II). We have examined the reaction of (II) with pentachlorophenyl-lithium (III) and find, in contrast, that the major product [m.p. 181—182° $[\alpha]_D - 34°$ ($CHCl_3$, *c* 0·4)] gave correct elemental analysis and i.r. spectrum for methyl-4,6-*O*-benzylidene-2-dexoy-2-pentachlorophenyl-α-D-altroside (IVa). However the ^{1}H n.m.r. spectrum was not consistent with either the D-*altro* [diaxial ring opening, (V)] or the D-*gluco* [diequatorial ring opening, (VI)] configuration in the normal (chair) forms. In both (V) and (VI) $J_{1\text{-H},\,2\text{-H}} = ca.$ 3 Hz. whereas the observed value is 7 Hz. Coxon[2] has studied the conformation of several 4,6-*O*-benzylidene altrosides by n.m.r. and found that they all adopt the chair conformation (V). However, the bulky pentachlorophenyl group in an axial position will considerably reduce the stability of this conformer. The most likely alternative conformations are the boat forms (VII) and (VIII) and the skew boat form (IX). All three conformers have a 1-H–2-H dihedral angle of 180° and should give rise to a large $J_{1\text{-H},\,2\text{-H}}$ value. The only other resolved signal is a low-field quartet at τ 4·9. This is assigned to 2-H as this proton is deshielded by the pentachlorophenyl group. The value of 9 Hz. for $J_{2\text{-H},\,3\text{-H}}$ excludes conformer (VIII). The 2-H–3-H dihedral angle is 180° and 153° for conformers (VII) and (IX), respectively. The n.m.r. evidence therefore favours conformer (VII) but does not entirely exclude conformer (IX).

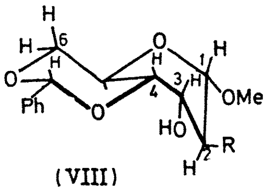

(I)a; R = C_6H_5
b; R = C_6Cl_5

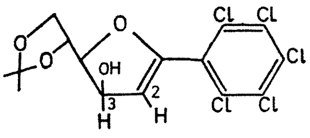

(IV) a; R^1 = C_6Cl_5, R^2 = H
b; R^1 = C_6Cl_5, R^2 = MeCO


(V) R^1 = C_6Cl_5, R^2 = OH, R^3 = C_6Cl_5, R^4 = H
(VI) R^1 = C_6Cl_5, R^2 = R^3 = H, R^4 = OH


(VII)


(IX)


(VIII)


(XI)

On acetylation (IVa) gave a crystalline product [m.p. 136—138°, [α]D −24.9° ($CHCl_3$, *c* 0·46)] which was identified as (IVb) by elemental analysis and i.r. and n.m.r. spectra.

A second carbohydrate product [m.p. 154—156°, [α]D 65·4 ($CDCl_3$, *c*. 0·8)] was identified as 4,6-*O*-benzylidene-2-pentachlorophenyl-D-allal (Ib) by elemental analysis and spectra: i.r. 3550 (OH) and 1640 (C=C–O) cm.$^{-1}$; n.m.r. ($CDCl_3$) τ 2·5 (br s, ArH), 3·55 (s, 1-H), 4·25 (s, PhC*H*), *ca.* 5·7 (m, 3-H, 4-H, 5-H, 6-H, 6′-H), and 7·6 (br s, OH, exchanges with D_2O).

From the reaction of methyl-2,3-anhydro-4,6-*O*-benzylidene-α-D-mannoside (X) with pentachlorophenyl-lithium, only methyl-4,6-*O*-benzylidene-α-D-altroside (28%) and starting material were isolated. In this case attack at the 3-position, as required for diaxial ring opening of (X), is more hindered sterically and attack even with small nucleophiles such as OMe$^-$ requires forcing conditions.[3]

The reaction of pentachlorophenyl-lithium with 2,3 : 5,-6-di-*O*-isopropylidene-α-D-mannosyl chloride was examined. The major product, which was unstable, had an i.r. spectrum 3500 (OH), 1660 (C=C–O), and 720 (C–Cl) cm.$^{-1}$ and an n.m.r. spectrum τ ($CDCl_3$) 4·6 (d, 2-H) 4·9 (m, simplifies into q on shaking with D_2O, 3-H), *ca.* 5·5 (m, 2H) *ca.* 5·9 (m, 2H), 7·9 (br d, exchanges with D_2O, OH), 8·55 (s, CH_3), and 8·65 (s, CH_3), which is consistent with the structure being 5,6-*O*-isopropylidene-1-pentachlorophenyl-1,2-dideoxy-D-arabofuranose-1-ene (XI).

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[1] A. A. J. Feast, W. G. Overend, and N. R. Williams, *J. Chem. Soc.*, 1965, 7378.
[2] B. Coxon, *Tetrahedron*, 1965, **21**, 3481.
[3] G. J. Robertson and C. F. Griffith, *J. Chem. Soc.*, 1935, 1193.