

Note

1,2-*O*-Trichloroethylidene- α -D-galactofuranose*

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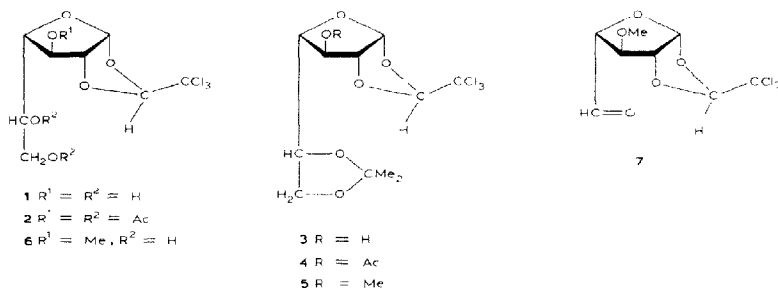
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Previously known cyclic acetal derivatives of D-galactose usually contain the sugar ring in the pyranoid form^{1,2}. The reaction of D-galactose with acetone affords mainly 1,2:3,4-di-*O*-isopropylidene- α -D-galactopyranose, and only a small proportion of 1,2:5,6-di-*O*-isopropylidene- α -D-galactofuranose² is formed. The lower preference for the furanoid derivative may be due to the non-bonded interactions between the *endo*-methyl group of the 1,2-*O*-isopropylidene ring and the 5,6-*O*-isopropylidene ring. From D-glucose, the corresponding glucofuranose derivative is obtained in good yield; similar interactions are not possible as the 5,6-*O*-isopropylidene ring is *exo* with respect to the fused-ring system.

After the reaction of D-galactose and chloral catalysed with sulphuric acid, only one of the two possible isomers of 1,2-*O*-trichloroethylidene- α -D-galactofuranose (**1**) was isolated. The n.m.r. spectra provide evidence that, in **1** and its derivatives, the trichloromethyl groups occupy the *exo* position (*S*-isomer). For cyclic acetals, the n.m.r. signals for acetal protons that are *endo* appear³ at lower fields than those for the corresponding *exo* protons. As expected, the acetal-proton singlets of known 1,2-*O*-trichloroethylidene- α -D-glucofuranose derivatives were observed⁴ in the range δ 5.27-5.34 for the *R*-isomers, whereas the values for the *S*-isomers were in the range δ 5.58-5.63. The acetal-proton singlets for derivatives of **1** appeared at even lower fields (δ 5.65-5.78), suggesting that the protons occupy the *endo* position (*S*-isomer). The other diastereoisomer is not formed, probably because of the interactions between the trichloromethyl group and the *endo* substituent on C-4. Molecular models indicate that, for galactochloralose derivatives in ²*T*₃ or *E*₀ conformations, interactions between the 1,2-acetal ring and the *endo* substituent on C-4 should be small as these groups diverge from each other. In such a situation, however, H-3 and H-4, and even H-2 and H-3, would be almost *trans*, and hence relatively large *J*_{2,3} and *J*_{3,4} values are to be expected. In the n.m.r. spectra of all of the chloralose derivatives, the H-1 and H-2 signals appear as low-field doublets^{4,5}. The *J*_{1,2} and *J*_{2,3} values are invariably ~4 and ~0 Hz, respectively,

*Trichloroethylidene Acetals. Part I.

and the values of $J_{3,4}$ are in the range of 0–4 Hz. (cf. 0–2 Hz for the galactochloralose derivatives⁶). Conformational analysis of 1,2:5,6-di-*O*-isopropylidene- α -D-galactofuranose⁷ indicated that the dihedral angle for H-1/H-2 should be small ($\sim 10^\circ$), with those for H-2/H-3 and H-3/H-4 being 118 and 132°, respectively. The observed coupling constants were 3.8, 1.0, and 4.0 Hz, respectively, consistent with a conformation $^7(E_0 \rightleftharpoons ^1T_0 \rightleftharpoons E_1)$ in which the 5,6-ring is slightly away from the 1,2-ring but not at the most extreme distance. For the galactochloralose derivatives, the $J_{3,4}$ values are smaller, which suggest a furanose ring more distorted towards the 3T_2 conformation in spite of the undesirable interactions mentioned above.



The structure of compound **1** was shown by chemical means. A triacetate **2** and an isopropylidene derivative **3** of **1** were prepared, and **3** was also characterised as its monoacetate **4** and monomethyl ether **5**. Hydrolysis of **5** to remove the isopropylidene ring gave **6**, which was converted into 3-*O*-methyl-1,2-*O*-trichloroethylidene- α -L-*arabino*-pentodialdo-1,4-furanose (**7**) by glycol fission. The crude pentodialdose **7** was directly converted into its crystalline 2,4-dinitrophenylhydrazone, the n.m.r. spectrum of which was consistent with the suggested structure. Further evidence is provided by the similarities with the n.m.r. data for 3-*O*-methyl-1,2-*O*-trichloroethylidene-D-*xylo*-pentodialdose 2,4-dinitrophenylhydrazone⁵.

EXPERIMENTAL

T.l.c. was performed on Kieselgel (Merck, 7731) with toluene–methanol (9:1). N.m.r. spectra were recorded for solutions in $CDCl_3$ at 100 MHz (Varian HA-100) with Me_4Si as internal standard. Melting points are uncorrected. Optical rotations were determined with a Perkin–Elmer 141 polarimeter.

1,2-O-Trichloroethylidene- α -D-galactofuranose (**1**). — D-Galactose (90 g) was added to chloral (150 mL) in portions with mechanical stirring. Sulphuric acid

(4 mL; sp. gr. 1.84) was added, the mixture was boiled under reflux for 2 h, and chloroform (100 mL) was added to the mixture while it was still warm. After cooling, the mixture was diluted to 500 mL with chloroform and kept at room temperature overnight. The precipitate was collected, washed with chloroform, and air-dried. The light-brown product (80 g, 52%), which appeared to be a single compound by t.l.c. and n.m.r. spectroscopy, was recrystallised from boiling water and then from hot methanol, to give **1**, m.p. 205–207°, $[\alpha]_D^{19} -38^\circ$ (c 2, methanol) (Found: C, 31.06; H, 4.05; Cl, 34.25. $C_8H_{11}Cl_3O_6$ calc.: C, 31.04; H, 3.58; Cl, 34.36%).

Acetylation (pyridine-acetic anhydride) of **1** gave the 3,5,6-triacetate **2** (95%), m.p. 128–130° (from ethanol), $[\alpha]_D^{19} +0.5^\circ$ (c 3.1, chloroform) (Found: C, 38.69; H, 4.05; Cl, 24.30. $C_{14}H_{17}Cl_3O_9$ calc.: C, 38.60; H, 3.93; Cl, 24.41%). N.m.r. data: δ 6.23 (d, 1 H, $J_{1,2}$ 3.8 Hz, H-1), 4.97 (d, 1 H, $J_{2,3}$ 0 Hz, H-2), 5.17 (s, 1 H, $J_{3,4}$ ~0 Hz, H-3), 4.24 (d, 1 H, $J_{4,5}$ 6.7 Hz, H-4), 5.34 (m, 1 H, $J_{5,6}$ 4.0 Hz, $J_{5,6'}$ 6.7 Hz, H-5), 4.40 (q, 1 H, $J_{6,6'}$ 11.4 Hz, H-6), 4.18 (q, 1 H, H-6'), 2.05, 2.10, 2.13 (9 H, 3 Ac), and 5.78 (s, 1 H, CCl_3CH).

5,6-O-Isopropylidene-1,2-O-trichloroethylidene- α -D-galactofuranose (**3**). — Conventional methods, using 2,2-dimethoxypropane and toluene-*p*-sulphonic acid or acetone and hydrochloric acid, both converted **1** into **3** (80%); the solvent for **1** was *N,N*-dimethylformamide. After recrystallisation from methanol, **3** had m.p. 214–216° (dec.), $[\alpha]_D^{19} +18^\circ$ (c 4.8, pyridine) (Found: C, 37.74; H, 4.22; Cl, 30.70. $C_{11}H_{15}Cl_3O_6$ calc.: C, 37.79; H, 4.32; Cl, 30.42%).

Acetylation of **3** gave the 3-acetate **4** (95%), m.p. 139–140° (from ethanol), $[\alpha]_D^{19} -10.5^\circ$ (c 2.5, chloroform) (Found: C, 39.89; H, 4.30; Cl, 27.00. $C_{13}H_{17}Cl_3O_7$ calc.: C, 39.87; H, 4.37; Cl, 27.16%). N.m.r. data: δ 6.30 (d, 1 H, $J_{1,2}$ 4.0 Hz, H-1), 5.02 (d, 1 H, $J_{2,3}$ ~0.5 Hz, H-2), 5.10 (s, 1 H, $J_{3,4}$ ~0 Hz, H-3), 3.80–4.50 (m, 4 H, H-4,5,6,6'), 2.10 (3 H, Ac), 1.40, 1.46 (6 H, 2 Me), and 5.71 (s, 1 H, CCl_3CH).

5,6-O-Isopropylidene-3-O-methyl-1,2-O-trichloroethylidene- α -D-galactofuranose (**5**). — A solution of compound **3** (5 g) in *N,N*-dimethylformamide (50 mL) was treated with silver oxide (10 g) and methyl iodide (15 mL) for 24 h. The usual work-up procedure⁵ gave **5** as a syrup (4.8 g, 92%), which, after crystallisation, had m.p. 65–67° (from ethanol-water), $[\alpha]_D^{19} -34^\circ$ (c 2.4, chloroform), (Found: C, 39.32; H, 4.70; Cl, 29.02; OMe, 8.40. $C_{12}H_{17}Cl_3O_6$ calc.: C, 39.63; H, 4.71; Cl, 29.25; OMe, 8.53%). N.m.r. data: δ 6.23 (d, 1 H, $J_{1,2}$ 4.0 Hz, H-1), 4.98 (d, 1 H, $J_{2,3}$ 0 Hz, H-2), 3.68 (d, 1 H, $J_{3,4}$ 2.0 Hz, H-3), 3.93–4.06 (m, 4 H, H-4,5,6,6'), 3.35 (s, 3 H, OMe), 1.28, 1.30 (6 H, 2 Me), and 5.73 (s, 1 H, CCl_3CH).

3-O-Methyl-1,2-O-trichloroethylidene- α -D-galactofuranose (**6**). — Compound **5** (4 g) was hydrolysed with *M* hydrochloric acid (10 mL) in ethanol (15 mL) by boiling under reflux for 1 h. Chloroform extraction gave a syrup which crystallised to give **6** (1.8 g, 51%), m.p. 72–73° (from methanol-water), $[\alpha]_D^{19} -58^\circ$ (c 5.1, methanol) (Found: C, 33.36; H, 4.02; Cl, 32.54; OMe, 9.40. $C_9H_{13}Cl_3O_6$ calc.: C, 33.40; H, 4.05; Cl, 32.87; OMe, 9.59%).

3-O-Methyl-1,2-O-trichloroethylidene- α -L-arabino-pentodialdo-1,4-furanose

2,4-dinitrophenylhydrazon. A solution of **6** (0.8 g) in a mixture of methanol (20 mL) and water (30 mL) was treated with sodium metaperiodate (0.5 g) overnight. Extraction of the solution with chloroform and removal of the solvent gave a syrup (0.7 g) which was conventionally converted into the title compound (80%), m.p. 178–179° (from chloroform), $[\alpha]_D^{19} = -18.5^\circ$ (c 1.9, chloroform) (Found: C, 35.37; H, 2.85; Cl, 22.75; N, 11.89; OMe, 6.51. $C_{14}H_{13}Cl_3N_4O_8$ calc.: C, 35.65; H, 2.77; Cl, 22.55; N, 11.87; OMe, 6.58%). N.m.r. data: δ 6.38 (d, 1 H, $J_{1,2} = 4.0$ Hz, H-1), 5.12 (d, 1 H, $J_{2,3} = 0$ Hz, H-2), 4.32 (s, 1 H, $J_{3,4} = 0$ Hz, H-3), 5.00 (d, 1 H, $J_{4,5} = 4.8$ Hz, H-4), 7.58 (d, 1 H, H-5), 3.55 (s, 3 H, OMe), 5.50 (s, 1 H, CCl_3CH), 7.96 (d, 1 H, $J_{ortho} = 8.7$ Hz, Ph), 8.36 (q, 1 H, $J_{meta} = 2.0$ Hz, Ph), 9.12 (d, 1 H, Ph), and 11.12 (s, 1 H, NH).

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