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Note

Transformation of uronic acids catalysed by boron trifluoride etherate. Synthesis of 4-*O*-acetyl-1,2-*O*-isopropylidene-3-*O*-toluene-*p*-sulphonyl-α-D-xylopyranurono-5,1-lactone

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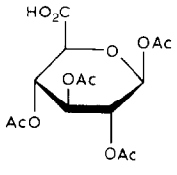
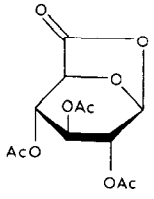
The transformation of uronic acids with participation of the carboxyl group and Lewis acids may be illustrated by the conversion[1] of 1,2,3,4-tetra-*O*-acetyl-β-D-glucopyranuronic acid (**1**) into 2,3,4-tri-*O*-acetyl-β-D-glucopyranurono-6,1-lactone (**2**) by $SnCl_4$ in boiling benzene.



1



2

Acetolysis of alkyl pento- and hexo-furanosides yields the pyranose acetates which, as a rule, possess greater thermodynamic stability. Thus, acetolysis of glycosides of pentofuranuronic acids would be expected to yield pentopyranurono-5,1-lactones.

When 1,2-*O*-isopropylidene-3-*O*-toluene-*p*-sulphonyl-α-D-xylofuranuronic acid[2] (**3**) was acetolysed ($AcOH/Ac_2O/H_2SO_4$), a complex mixture of products was obtained which was not amenable to column chromatography on silica gel. However, 10% of 4-*O*-acetyl-1,2-*O*-isopropylidene-3-*O*-toluene-*p*-sulphonyl-α-D-xylopyranurono-5,1-lactone (**4**) was obtained on treatment of **3** with acetic anhydride and a catalytic amount of $BF_3 \cdot Et_2O$ at room temperature for 12 h. A reaction time of 10–15 min was optimal for the conversion **3**→**4**, and the yield was then in the range 50–60%. When the reaction was performed in ethyl acetate using a small excess of acetic anhydride, the yield of **4** was almost quantitative.

The conversion **3**→**4** appears to involve an acyclic intermediate formed as a result of the attachment of BF_3 or Ac^+ to the ring oxygen atom of **3**.

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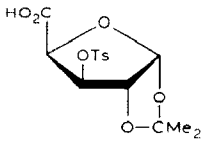

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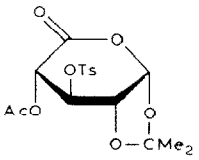
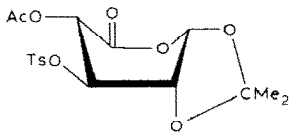


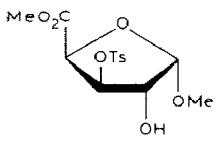
4

The structure of **4** was established by the ^{1}H-n.m.r. data (see Experimental). In addition to signals for Ts, CMe_2, and Ac groups, the coupling values $J_{1,2}$ 2.5, $J_{2,3}$ 2.5, and $J_{3,4}$ 10.0 Hz accord with a pyranose structure in the $B^{1,4}$ conformation (**5**) in which H-3,4 are *trans*-diaxial and H-1,2 are axial and equatorial.



5 ($B^{1,4}$)

The i.r. absorption at 1773 cm^{-1} for **4** accords with the data of Cheung *et al.*[3] and also indicates a boat conformation. When $BF_3 \cdot Et_2O$ was added to a solution of **4** in chloroform, rapid polymerisation occurred, yielding a product that was insoluble in most organic solvents. Treatment of **4** with methanolic hydrogen chloride afforded methyl (methyl 3-*O*-toluene-*p*-sulphonyl-α-D-xylofuranosid)uronate[2] (**6**) and, with triethylamine in benzene, 4-*O*-acetyl-3-deoxy-1,2-*O*-isopropylidene-α-D-*glycero*-pent-3-enopyranurono-5,1-lactone (**7**) was formed.



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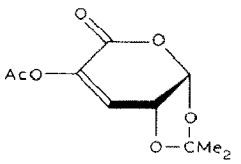
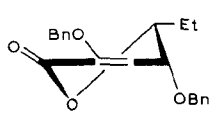


7

The ^{1}H-n.m.r. signals for the three protons of the six-membered ring of **7** appeared as 2 d and a dd with $J_{1,2}$ 4.0 and $J_{2,3}$ 6.0 Hz. The latter value is typical for the quasi-equatorial orientation of the allylic proton[4]. Hence, **7** exists in solution in the half-chair conformation $^1H_0$ (**9**) or sofa S^1 (**10**) conformation with C-1 out of the plane of the ring.

The ^{1}H-n.m.r. and c.d. data of the lactone **7** agree well with the spectral characteristics of the unsaturated lactone **8** to which the half-chair conformation $^1H_0$ was assigned[5]. The i.r. band at 1773 cm^{-1} for **7** indicates the sofa conformation S^1 to a greater degree.



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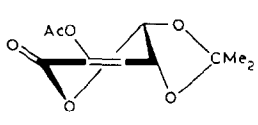
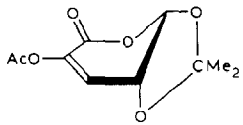


$^9(^1H_0)$



$10(S^1)$

In the c.d. spectrum of **7**, a negative Cotton effect of the optically active band at 210 nm was observed with a molecular ellipticity value, $[\theta]$, of $-18{,}600$.

EXPERIMENTAL

^{1}H-N.m.r. spectra (internal Me_4Si) were recorded with a JNM PS-100 spectrometer (Jeol). U.v. spectra were recorded with a Zeiss Specord UV-Vis spectrophotometer, c.d. spectra and optical rotations with a JASCO-20 spectropolarimeter, and i.r. spectra with a Zeiss UR-20 spectrometer. Reactions were monitored, and the purity of compounds was assessed, by t.l.c. on Silufol 254, using chloroform–methanol (95:5, 4:1). Melting points were measured on a Boetius hot-stage unit.

4-O-*Acetyl-1,2*-O-*isopropylidene-3*-O-*toluene*-p-*sulphonyl*-α-D-*xylopyranurono-5,1-lactone* (**4**). — Acetic anhydride (1 mL) and boron trifluoride etherate (0.2 mL) were added to a solution of 1,2-*O*-isopropylidene-3-*O*-toluene-*p*-sulphonyl-α-D-xylofuranuronic acid (**3**, 1.0 g) in ethyl acetate (25 mL). After 3 days, the solution was poured into ice–water and extracted with chloroform (3 × 25 mL). The combined extracts were washed with saturated aqueous $NaHCO_3$ and water, dried (Na_2SO_4), and concentrated to dryness to yield **4** (1.1 g, 98%), m.p. 143–145° (from methanol), $[\alpha]_D^{20}$ +22° (*c* 1, *N,N*-dimethylformamide); λ_{max}^{MeOH} 227 nm (ε 12.6 × 10^{-3}). C.d. (MeOH) 222 nm ($[\theta]$ 7.3 × 10^{-3}). ^{1}H-N.m.r. data ($CDCl_3$): δ 7.8 (d, 2 H, Ts), 7.32 (d, 2 H, Ts), 5.94 (d, 1 H, $J_{1,2}$ 2.5 Hz, H-1), 5.36 (d, 1 H, $J_{3,4}$ 10.0 Hz, H-4), 4.88 (dd, 1 H, $J_{2,3}$ 2.5 Hz, H-3), 4.44 (dd, 1 H, H-2), 2.44 (s, 3 H, Me), 2.00 (s, 3 H, OAc), 1.50 and 1.32 (2 s, 6 H, CMe_2).

Anal. Calc. for $C_{17}H_{20}O_9S$: C, 51.00; H, 5.00; S, 8.00. Found: C, 50.86; H, 4.98; S, 7.90.

Methyl (methyl 3-O-*toluene*-p-*sulphonyl*-α-D-*xylofuranosid)uronate* (**6**). — To a stirred, ice-cold solution of **4** (1.0 g) in methanol (25 mL) was added acetyl chloride (1.2 mL) dropwise. The mixture was stirred for 48 h at room temperature and then concentrated to dryness. Methanol was evaporated thrice from the residue which was then recrystallised from methanol to give **6** (0.6 g, 70%), m.p. 146–148°; lit.[2] m.p. 146–148°. ^{1}H-N.m.r. data ($CDCl_3$): δ 7.76 (d, 2 H, Ts), 7.44 (d, 2 H, Ts), 5.16 (d, 1 H, $J_{1,2}$ 4.5 Hz, H-1), 4.94 (d, 1 H, H-2), 4.90 (s, 2 H, H-3,4), 3.54 (s, 3 H, CO_2Me), 3.30 (s, 3 H, OMe), 2.40 (s, 3 H, Ts).

4-O-*Acetyl-3-deoxy-1,2*-O-*isopropylidene*-α-D-glycero-*pent-3-enopyranurono-5,1-lactone* (**7**). — A solution of **4** (0.4 g) in benzene (15 mL) was stirred with triethylamine (1 mL) at room temperature for 5 h and then concentrated to dryness.

A solution of the residue in chloroform was washed with water, dried (Na_2SO_4), and concentrated to give **7** (0.2 g, 88%), m.p. 152–156°, $[\alpha]_D^{20}$ −43° (*c* 0.9, chloroform); λ_{max}^{MeOH} 205 nm (ε 9 × 10^{-3}), 221 nm (sh ε 5.7 × 10^{-3}). C.d. (MeOH) 215 nm ([θ] −18.6 × 10^{-3}). ^{1}H-N.m.r. data ($CDCl_3$): δ 6.38 (d, 1 H, $J_{2,3}$ 6.0 Hz, H-3), 5.92 (d, 1 H, $J_{1,2}$ 4.0 Hz, H-1), 4.62 (dd, 1 H, H-2), 2.16 (s, 3 H, OAc), 1.44 and 1.35 (2 s, 6 H, CMe_2).

Anal. Calc. for $C_{10}H_{12}O_6$: C, 52.63; H, 5.26. Found: C, 52.56; H, 5.19.

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