A Synthesis of L-Psicose

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L-Psicose has been obtained by hydrolysis of the product of the stereoselective reduction of methyl 1,3-*O*-benzylidene-5-*O*-*p*-tolylsulphonyl-α-L-*erythro*-hexo-2,4-diulopyranoside.

In the course of our work on the synthesis of amino-deoxy-ketohexoses it was necessary to prepare a number of derivatives of L-psicose for comparison with the corresponding amino-compounds. D-Psicose has been prepared by two groups of workers by a route involving stereoselective reduction of 1,2 : 4,5-*O*-isopropylidene-β-D-*erythro*-hexo-2,3-diulopyranose [1,2] or of the corresponding 1,2 : 4,5-di-*O*-cyclohexylidene derivative.[1] We have found that L-psicose can be prepared in reasonable yield by a similar route from L-sorbose.

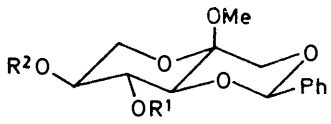
Treatment of methyl 1,3-*O*-benzylidene-α-L-sorbopyranoside [3] (1) with toluene-*p*-sulphonyl chloride (1 mol)

[1] K. James, A. R. Tatchell, and P. K. Ray, *J. Chem. Soc.* (*C*), 1967, 2681.

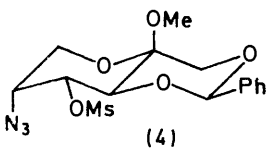
[2] E. J. McDonald, *Carbohydrate Res.*, 1967, **5**, 106.

[3] D. Murphy, *J. Chem. Soc.* (*C*), 1967, 1732.

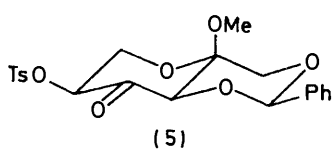
in pyridine at low temperature gave a single crystalline mono-*p*-tolylsulphonyl ester (2), characterised as the acetate and methanesulphonate (3) derivatives. Although it appears (from a study of molecular models) that the approach by a reagent to the 5-hydroxy-group



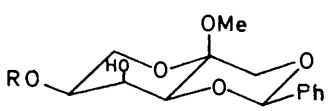
(1) $R^1 = R^2 = H$
(2) $R^1 = H, R^2 = Ts$
(3) $R^1 = Ms, R^2 = Ts$



(4)



(5)



(6) R = Ts
(7) R = H

(Ts = *p*-$MeC_6H_4 \cdot SO_2$; Ms = $MeSO_2$)

is easier than that to the 4-hydroxy-group, the sulphonate (2) may have been the 4- or the 5-sulphonate. That it was in fact methyl 1,3-*O*-benzylidene-5-*O*-*p*-tolylsulphonyl-α-L-sorbopyranoside was proved by reaction of the methanesulphonate (3) with sodium azide to give the known[3] methyl 5-azido-1,3-*O*-benzylidene-5-deoxy-4-*O*-methylsulphonyl-β-D-fructopyranoside (4). Thus, in compound (3), the 5-*O*-*p*-tolylsulphonyl group was displaced, showing that the 5-hydroxy-group in the sorbopyranoside (1) was selectively sulphonated.

Oxidation of the 5-*O*-*p*-tolylsulphonylsorbopyranoside (2) with dimethyl sulphoxide–phosphorus pentoxide[4] gave methyl 1,3-*O*-benzylidene-5-*p*-tolylsulphonyl-α-L-*erythro*-hexo-2,4-diulopyranoside (5) in 70% yield. The oxidation was also attempted using the Pfitzner–Moffatt reagent,[5] but great difficulty was experienced in the purification of the product.

Reduction of the ketone (5) with sodium borohydride gave a crystalline hydroxy-compound different from the sorbopyranoside (2). The product was therefore assumed to be methyl 1,3-*O*-benzylidene-5-*O*-*p*-tolylsulphonyl-α-L-psicopyranoside (6). None of the expected small quantity of the sorbopyranoside (2) could be isolated from the mixture. Reductive desulphonation of the psicopyranoside (6) with lithium aluminium hydride gave methyl 1,3-*O*-benzylidene-α-L-psicopyranoside (7), characterised as the bis-*p*-nitrobenzoate ester.

Hydrolysis of the psicopyranoside (7) with 50% aqueous acetic acid gave the syrupy reducing sugar, L-psicose, which was characterised by conversion into L-*ribo*-hexose phenylosazone[6] and into 1,2 : 3,4-di-*O*-isopropylidene-L-psicofuranose.[6]

[4] K. Onodera, S. Hirano, and N. Kashimura, *J. Amer. Chem. Soc.*, 1965, **87**, 4651.

[5] K. E. Pfitzner and J. G. Moffatt, *J. Amer. Chem. Soc.*, 1963, **85**, 3027; 1965, **87**, 5661.

EXPERIMENTAL

Solutions were concentrated under reduced pressure. Optical rotations were measured at 20—22° for solutions in chloroform unless otherwise stated. Where possible, compounds were identified by mixed m.p. and by i.r. spectroscopy; new compounds had i.r. spectra consistent with their assigned structures.

Methyl 1,3-O-*Benzylidene*-5-O-p-*tolylsulphonyl*-α-L-*sorbopyranoside* (2).—A solution of methyl 1,3-*O*-benzylidene-α-L-sorbopyranoside (1) (20 g) in pyridine (200 ml) was cooled to *ca.* −20°, and then treated with toluene-*p*-sulphonyl chloride (13·5 g), dissolved in a little pyridine. The solution was kept for 16 h at 0°, and then poured with stirring into ice–water (2 l) to give the *product* (65%), m.p. 135—136° (from propan-2-ol), $[\alpha]_D$ −45·4 (*c* 1·0) (Found: C, 57·6; H, 5·9; S, 7·2. $C_{21}H_{24}O_8S$ requires C, 57·8; H, 5·6; S, 7·3%).

Chloroform extraction of the aqueous mother liquors gave unchanged starting material (1) (20%), m.p. 183—184°.

Methyl 4-O-*Acetyl*-1,3-O-*benzylidene*-5-O-p-*tolylsulphonyl*-α-L-*sorbopyranoside*.—Treatment of the toluene-*p*-sulphonate (2) with acetic anhydride–pyridine in the usual way gave the 4-O-*acetyl compound*, m.p. 150—151° (from propan-2-ol), $[\alpha]_D$ −33·7° (*c* 0·8) (Found: C, 57·8; H, 5·2. $C_{23}H_{26}O_9S$ requires C, 57·7; H, 5·4%).

Methyl 1,3-O-*Benzylidene*-4-O-*methylsulphonyl*-5-O-p-*tolylsulphonyl*-α-L-*sorbopyranoside* (3).—Treatment of the toluene-*p*-sulphonate (2) with methanesulphonyl chloride–pyridine gave the 4-O-*methylsulphonyl compound* (3), m.p. 148—149° (from propan-2-ol), $[\alpha]_D$ −48·8° (*c* 1·1) (Found: C, 51·2; H, 5·2. $C_{22}H_{26}O_{10}S_2$ requires C, 51·2; H, 5·1%).

Treatment of the methylsulphonyl compound (3) with sodium azide in boiling *NN*-dimethylformamide gave methyl 5-azido-1,3-*O*-benzylidene-5-deoxy-4-*O*-methylsulphonyl-β-D-fructopyranoside[3] (4), m.p. 174—175° (decomp.), identical with an authentic sample obtained from methyl 1,3-*O*-benzylidene-4,5-bis-*O*-methylsulphonyl-α-L-sorbopyranoside.[3]

Methyl 1,3-O-*benzylidene*-5-O-p-*tolylsulphonyl*-α-L-erythro-*hexo*-2,4-*diulopyranoside* (5).—A mixture of the sorbopyranoside (2) (5 g), dimethyl sulphoxide (3·5 g), phosphorus pentoxide (6 g), and *NN*-dimethylformamide (200 ml) was stirred for 2 h at 65—70°. The solution was poured into ice–water (500 ml) and the mixture kept overnight at 0° to give the *product* (5) (70%), m.p. 155° (decomp.) (from ethanol), $[\alpha]_D$ −61·2° (*c* 1·0) (Found: C, 58·0; H, 5·2. $C_{21}H_{22}O_8S$ requires C, 58·1; H, 5·1%). Attempted oxidation with the Pfitzner–Moffatt reagent[5] gave a product, m.p. 145—155°, in which impurities could still be detected (t.l.c.) after five recrystallisations from ethanol.

Methyl 1,3-O-*Benzylidene*-5-O-p-*tolylsulphonyl*-α-L-*psicopyranoside* (6).—The ketone (5) (10 g) was dissolved in *NN*-dimethylformamide (50 ml), and then boiling methanol (1000 ml) was added to the solution. The solution was stirred at 20° for 1 h during which time sodium borohydride (10 g) was added in small portions. When the addition was complete the solution was boiled for 15 min. Evaporation gave a syrup which was extracted with chloroform–water. Evaporation of the chloroform layer gave a white solid which after two recrystallisations gave the *product*

[6] M. Steiger and T. Reichstein, *Helv. Chim. Acta*, 1935, **18**, 790.

(6) (80%), m.p. 168—169° (decomp.), $[\alpha]_D$ −47·3° (*c* 1·0) (Found: C, 57·8; H, 5·5. $C_{21}H_{24}O_8S$ requires C, 57·8; H, 5·6%).

Methyl 1,3-O-*Benzylidene*-α-L-*psicopyranoside* (7).—The 5-*O*-methylsulphonylpsicopyranoside (6) (10 g) was added cautiously to a suspension of lithium aluminium hydride (5 g) in ether–benzene (1 : 1; 500 ml). The mixture was boiled under reflux for 120 h. The excess of lithium aluminium hydride was destroyed by the addition of a little water, and the solids were removed by filtration. The solid residue was boiled for 1 h with chloroform–ethanol (1 : 1; 500 ml), and the mixture was filtered through Keiselguhr. Evaporation of the combined filtrates gave a syrup which crystallised to give the *psicopyranoside* (7) (62%), m.p. 209—210° (from propan-2-ol), $[\alpha]_D$ −25·2° (*c* 1·0) (Found: C, 59·5; H, 6·4. $C_{14}H_{18}O_6$ requires C, 59·6; H, 6·4%). Hydrolysis of methyl 1,3-*O*-benzylidene-α-L-psicopyranoside (1 g) in boiling 50% aqueous acetic acid gave, after evaporation of the solvent, a clear syrup (0·6 g), $[\alpha]_D$ +3° (*c* 1·0 in H_2O). The syrup reduced Fehling's solution and gave a silver mirror when heated with ammoniacal silver nitrate. Treatment of the syrup with phenylhydrazine–acetic acid in the usual way gave L-*ribo*-hexose phenylosazone, m.p. 169—171°, $[\alpha]_D^{20}$ +77·9° (*c* 1·0 in pyridine) {lit.,[6] m.p. 174°, $[\alpha]_D^{20}$ +78·6° (*c* 2·164 in pyridine)}.

1,2 : 3,4-*Di*-O-*isopropylidene*-L-*psicofuranose*.—The syrupy L-psicose (0·6 g) in acetone (20 ml) was treated with conc. sulphuric acid (2 drops) and the solution was shaken for 24 h at room temperature. Chloroform (100 ml) was added, and the solution washed with water and with a solution of sodium hydrogen carbonate. The chloroform extract was dried (Na_2SO_4) and evaporated to give the product (32%), m.p. 55—56° (from pentane), $[\alpha]_D^{20}$ +98·7° (*c* 1·0 in acetone) {lit.,[6] m.p. 56·5—57°, $[\alpha]_D^{20}$ +99° (*c* 2·5 in acetone)}.

Methyl 1,3-O-*Benzylidene*-4,5-*bis*-O-p-*nitrobenzoyl*-α-L-*psicopyranoside*.—The psicopyranoside (7) was heated with *p*-nitrobenzoyl chloride–pyridine to give the *bis*-p-*nitrobenzoyl compound* (69%), m.p. 178—180° (decomp.) (from ethanol), $[\alpha]_D$ −17·1° (*c* 1·0) (Found: C, 57·8; H, 4·3; N, 4·9. $C_{28}H_{24}N_2O_{12}$ requires C, 57·9; H, 4·2; N, 4·8%).

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