Potential Hexokinase Inhibitors. Synthesis and Properties of 2,3-Anhydro-D-allose, 2,3-Anhydro-D-ribose, and 2-*O*-Methylsulphonyl-D-mannose

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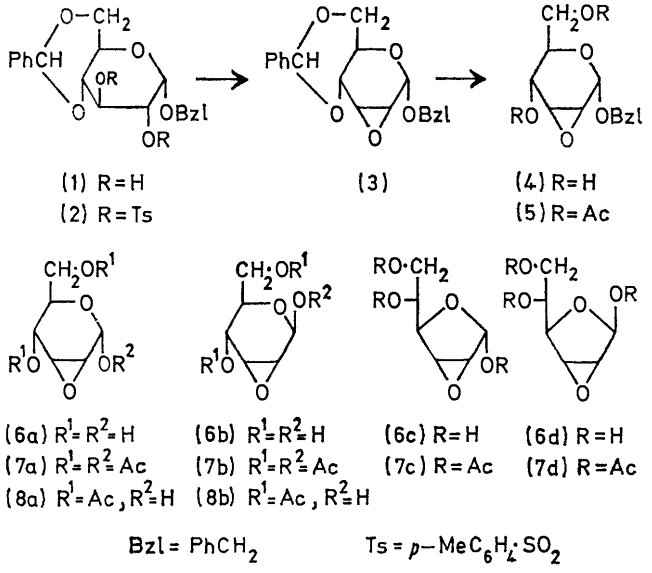
Hydrogenolysis of benzyl 2,3-anhydro-α-D-allopyranoside (4) in tetrahydrofuran over palladium–charcoal afforded crystalline 2,3-anhydro-α-D-allopyranose (6a). When dissolved in water this sugar underwent rapid mutarotation to give an equilibrium mixture containing mainly the α-pyranose (6a) (41%) and the β-furanose (6d) (42%), together with the β-pyranose (6b) and the α-furanose (6c) (5 and 12%, not individually assigned). 2,3-Anhydro-D-ribose, as an equilibrium mixture (13), has been prepared by hydrogenolysis of benzyl 2,3-anhydro-α-D-ribopyranoside (12).

2-*O*-Methylsulphonyl-α-D-mannopyranose (18) has been prepared and shown to give 1,6-anhydro-β-D-glucopyranose (20) with base.

In earlier work [1] we described the synthesis of free sugars containing the oxiran ring as potential inhibitors of hexokinases.[2,3] Hexokinases are known to have wide specificity and it was hoped that alkylation of the enzyme at its active site by the oxiran would lead to irreversible inhibition.[1] We have now examined the preparation of 2,3-anhydro-D-allose (6), as shown in Scheme 1.



Scheme 1

The disulphonate (2) was prepared from the diol (1), essentially by Inch and Lewis's method.[4] We found it necessary to warm the tolylsulphonylation reaction mixture to ensure complete introduction of the second sulphonyl group. The anhydro-alloside (3), obtained from the disulphonate (2) by treatment with methanolic sodium methoxide,[4] was converted into the crystalline 4,6-diol (4) by acidic hydrolysis. Hydrogenolysis of the benzyloxy-group in the glycoside (4) proceeded smoothly in tetrahydrofuran, which was chosen as solvent to minimise mutarotation of the product.[1,5] Crystalline 2,3-anhydro-α-D-allopyranose (6a) was isolated in 47% yield [from (4)]. The α-pyranose structure was confirmed by its ^{1}H n.m.r. spectrum, measured in [$^2H_6$]dimethyl sulphoxide, in which mutarotation is slow.[1] The signal due to H-1 appeared as a double doublet, $J_{1,2}$ 3.0 Hz, in agreement with earlier work [6,7] on derivatives of 2,3-anhydro-α-D-allopyranose ($J_{1,2}$ *ca.* 2.5 Hz) and with the values found for the glycosides (3) and (4) in the present paper.

When the crystalline 2,3-anhydroallose was acetylated in pyridine a pure syrup was obtained whose n.m.r. spectrum was consistent with the α-pyranose structure (7a), the H-1 signal being a doublet ($J_{1,2}$ 2.5 Hz). Furthermore, when the diacetate (5) was debenzylated by hydrogenolysis and the resulting mixture of sugars (8a and b) was acetylated the n.m.r. spectrum of the syrupy product was clearly that of a mixture of triacetates (7a and b) in the ratio 4 : 1. The signal due to H-1 in the β-anomer (7b) appeared as a broad ' singlet ' ($J_{1,2}$ 0.8 Hz) at higher field, as expected.[8]

The crystalline sugar (6a) was dissolved in water and allowed to undergo mutarotation. After evaporation of solvent the components of the mixture were converted into their trimethylsilyl (Tms) ethers, which were subjected to g.l.c.[9] The four peaks that appeared, corresponding presumably to the Tms ethers of the four anhydro-sugars (6a—d), were designated A—D, in order of elution from the column. The retention times, relative to the Tms ether of α-D-glucose, were 0.91, 0.93, 1.39, and 2.16 respectively, and the relative intensities 5 : 12 : 42 : 41. A gas chromatogram of the Tms ether of the crystalline sugar (6a) showed a single component corresponding to component D. The α-pyranose (6a) is therefore one of the major components of the equilibrium mixture. In order to assign structures to the remainder a study was

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made of the mixture of triacetates (7a—d) obtained by acetylation.

When the mixture of anhydro-sugars (6a—d) was treated with acetic anhydride and pyridine a crystalline triacetate was isolated in 36% yield. It differed from the syrupy triacetate (7a) of the α-pyranose and from the triacetate (7b) of the β-pyranose, and was therefore a furanose triacetate (7c or d). This was confirmed by first-order analysis of its n.m.r. spectrum, which was well resolved. The signal for H-5 was at low field (τ 4.91), owing to deshielding by the acetyl group, and showed coupling to H-4, -6, and -6'. The signal due to H-1 was a low-field singlet (τ 3.72), but this could not be used, in the furanose series, to assign the anomeric configuration of the 1-acetoxy-group. On the basis of its specific rotation, $[\alpha]_D$ −62° ($CHCl_3$), it is probably the β-anomer (7d) [the specific rotations [10] of the α- and β-anomers of methyl 2,3-anhydro-D-ribofuranoside are +13.1 and −109° (in $CHCl_3$), respectively].

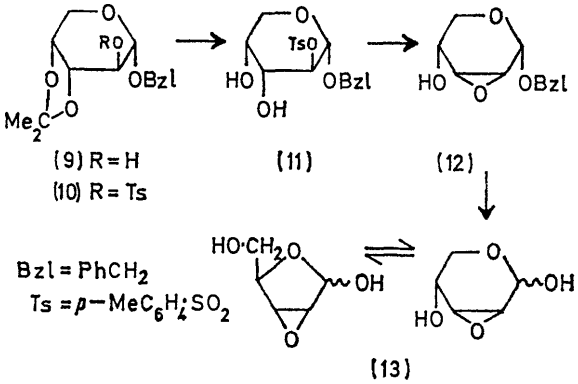
The mutarotation of crystalline 2,3-anhydro-α-D-allopyranose (6a) in aqueous solution was studied polarimetrically. At room temperature equilibrium was reached after approximately 90 min. The plot of log $(r_t - r_\infty)$ against time [1] was a straight line, extrapolation of which to zero time gave a specific rotation of +62° for the pure α-pyranose (6a).

The mutarotation in deuterium oxide was studied by ^1H n.m.r. spectroscopy. In the low-field region of the spectrum a doublet due to H-1 in the α-pyranose (6a) (τ 4.60, $J_{1,2}$ 3.0 Hz) gradually subsided with time and a singlet due to H-1 in the β-furanose (6d) (τ 4.55) became of comparable intensity. In addition, two broad singlets of low intensity [τ 4.44, H-1 of α-furanose (6c) and 4.84, H-1 of β-pyranose (6b)] appeared.

We conclude that at equilibrium an aqueous solution of 2,3-anhydro-D-allose contains 41% of the α-pyranose form (6a), 42% of a furanose form, probably β-(6d), and 12 and 5% of the two other forms (6b and c), not fully identified. The presence of a furanose form as a major component of the equilibrium mixture is not surprising in view of the earlier work on 2,3-anhydro-D-mannose.[1] A comparison of the behaviour of oxirans with that of five-membered cyclic acetals and carbonates was made in the earlier paper.[1]

Because of the stereochemical relationship between allose and ribose we also undertook the synthesis of 2,3-anhydro-D-ribose. Previously this sugar had been obtained on a small scale, together with 2,3-anhydro-D-lyxose, by oxidation of 3,4-anhydro-D-altritol with periodate.[11] We have prepared it by the more orthodox route outlined in Scheme 2. Benzyl α-D-arabinoside [12] was converted into the acetal (9) and the sulphonate (10) by conventional means. The isopropylidene group was removed with hot 90% acetic acid, affording the diol (11), which gave the oxiran (12) on treatment with sodium methoxide. Hydrogenolysis gave 2,3-anhydro-D-ribose (13) as a syrup which did not crystallise. We also examined the hydrogenolysis of the known benzyl 2,3-anhydro-β-D-ribopyranoside,[13] but hydrogenolysis was very slow and was accompanied by another reaction, presumably reductive opening of the oxiran ring.

We considered 1,2-anhydro-α-D-glucopyranose (19) or 1,2-anhydro-β-D-mannopyranose as possible inhibitors of hexokinase. The glucose anhydride is known only as its



SCHEME 2

triacetate (Brigl's anhydride) and as a non-isolable intermediate in the alkaline hydrolysis of Brigl's anhydride and of aryl β-D-glucopyranosides.[14,15] The mannose anhydride is the probable major intermediate in the oxidation of 1,5-anhydro-2-deoxy-D-*arabino*-hex-1-enitol ('D-glucal') by perbenzoic acid which leads eventually to D-mannose.[16] We suspected that the anhydride (19) and its *manno*-isomer would be unstable even under neutral aqueous conditions, and confirmed this when attempts to prepare them by careful epoxidation [17] of D-glucal were unsuccessful. It was therefore decided to approach the problem in a different way.

It is believed that the hexitol 1,6-disulphonates owe their tumour-inhibiting properties to epoxide formation *in situ*.[18] We envisaged that 2-*O*-methylsulphonyl-D-mannose (18) might be sufficiently stable to penetrate cells, and yet be a potential precursor of 1,2-anhydro-D-glucopyranose (19). D-Mannose is a substrate for mammalian hexokinases [2] and we hoped that the methylsulphonyl group might be sufficiently small to permit binding. An axially oriented *O*-methylsulphonyl group is favourably situated for epoxide formation and it is known that 2-sulphonates of certain free sugars readily

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[16] M. Bergmann and H. Schotte, *Ber.*, 1921, **54**, 440.
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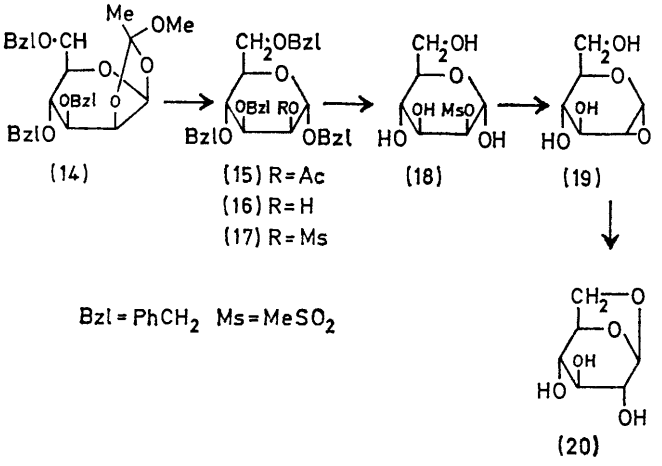
undergo 1,2-anhydride formation.[19-21] The conversion of the sulphonate (18) into the epoxide (19) might occur while the former was attached to the enzyme, leading possibly to glycosylation at the active site.

The sulphonate (18) was prepared as shown in Scheme 3. The orthoester (14) [22] was converted into the syrupy



SCHEME 3

benzyl α-D-mannoside (15) in 61% yield by the procedure of Kochetkov *et al.*[23] Alkaline methanolysis removed the ester group affording the mannoside (16), which gave the sulphonate (17) on treatment with methanesulphonyl chloride in pyridine. Finally, hydrogenolysis over palladium–charcoal yielded the crystalline free sugar (18). As expected,[14,15] when the sulphonate was treated with alkali the 1,6-anhydride (20) resulted, presumably through 1,2-anhydro-α-D-glucopyranose (19) as an intermediate.

2,3-Anhydro-D-allose (6), 2,3-anhydro-D-ribose (13), and 2-*O*-methylsulphonyl-D-mannose were tested as inhibitors of yeast hexokinase by Dr. E. M. Bessell and Professor A. B. Foster (Chester Beatty Research Institute). Each potential inhibitor, having reached mutarotational equilibrium, was incubated with crystalline yeast hexokinase for 24 h at pH 7.5. After dialysis to remove the excess of inhibitor the solution was tested for hexokinase activity. None of the compounds was active. In separate experiments it was shown that 2,3-anhydro-D-allose was a substrate for yeast hexokinase at high enzyme concentration (K_m value 0.13M). It is interesting to note that D-allose has been reported as a substrate, also with a high K_m value.[24]

EXPERIMENTAL

Evaporations were carried out under reduced pressure, with a rotary evaporator. Other general methods are described in ref. 1.

Benzyl 4,6-O-*Benzylidene*-α-D-*glucopyranoside* (1).—This compound was prepared from D-glucose essentially by Inch and Lewis's method,[4] except that in the initial formation of the benzyl glucoside the mixture of D-glucose, benzyl alcohol, and toluene-*p*-sulphonic acid was shaken overnight prior to heating. The 4,6-*O*-benzylidene compound (1) had m.p. 151—152°, $[\alpha]_D$ +95° (*c* 3.0 in $CHCl_3$) (lit.,[4] m.p. 152°). Dr. Inch has informed us that the specific rotation given in ref. 4 is incorrect.

Benzyl 2,3-*Anhydro*-4,6-O-*benzylidene*-α-D-*allopyranoside* (3).—To a solution of the diol (1) (4.0 g) in anhydrous pyridine (25 ml) toluene-*p*-sulphonyl chloride (8.0 g, 3.75 mol. equiv.) was added, and the mixture was stirred at 60 °C for 12 h. T.l.c. (9 : 1 benzene–ether) showed that none of the monosulphonate remained. A small amount of water was added and after 15 min the mixture was poured into ice–water. The crude disulphonate was filtered off, washed with water, and purified by reprecipitation with water from a methanolic solution. The n.m.r. spectrum of the resulting amorphous solid was consistent with the structure (2). It was dissolved in methanol (250 ml) containing sodium methoxide [from sodium (3 g, *ca.* 12 mol. equiv.)] and heated under reflux until t.l.c. (9 : 1 benzene–ether) showed that no disulphonate remained. After cooling the solid was filtered off and recrystallised from ethanol to give the anhydroalloside (3) (2.1 g, 55%), m.p. 182—183°, $[\alpha]_D$ +124° (*c* 3.0 in $CHCl_3$) (lit.,[4] m.p. 185°). Dr. Inch has informed us that the rotation given in ref. 4 is incorrect.

Benzyl 2,3-*Anhydro*-α-D-*allopyranoside* (4).—A suspension of the benzylidene compound (3) (2.0 g) in 0.005M-sulphuric acid (100 ml) and methanol (100 ml) was heated under reflux until the solid had dissolved (3 h). T.l.c. (9 : 1 benzene–ether) showed that no starting material remained. After neutralisation ($BaCO_3$) and filtration the solution was evaporated to dryness and the resulting crystals recrystallised from ether–light petroleum to give the *epoxide* (4) (0.88 g, 59%), m.p. 106—108°, $[\alpha]_D$ +123° (*c* 1.0 in EtOH) (Found: C, 61.6; H, 6.1. $C_{13}H_{16}O_5$ requires C, 61.9; H, 6.35%); τ (100 MHz; [$^2H_5$]pyridine) 2.40—3.00 (5 H, unresolved, Ph), 3.77br (1 H, s, OH), 4.72 (1 H, dd, *J* 1.8 and 1.1 Hz, H-1), 4.82—5.46 (3 H, q and broad s, benzylic and OH), 5.5—6.0 (4 H, unresolved), and 6.36 (2 H, unresolved, H-2 and -3).

A solution of the epoxide (4) (0.1 g) in anhydrous pyridine (2 ml) and acetic anhydride (2 ml) was kept at room temperature for 16 h. Isolation with chloroform gave the *diacetate* (5) as a syrup which was homogeneous by t.l.c. (9 : 1 benzene–ether); τ (60 MHz; $CDCl_3$) 2.58 (5 H, s, Ph), 4.8—5.0 (2 H, unresolved, H-1 and -4), 5.6—6.0 (3 H, unresolved), 6.35—6.55 (2 H, unresolved, H-2 and -3), and 7.88 and 7.94 (6 H, 2s, 2MeCO).

2,3-*Anhydro*-D-*allose* (6a—d).—5% Palladium–charcoal (0.5 g) was added to a solution of the benzyl glycoside (4) in tetrahydrofuran (30 ml) and the mixture was shaken at room temperature with a slight overpressure of hydrogen. After 2 h uptake was complete and the catalyst was removed. T.l.c. (6 : 3 : 1 light petroleum–ethyl acetate–ethanol) showed the absence of starting material. The solution was evaporated to give a syrup that crystallised spontaneously. Acetone–light petroleum was added to the solid which was

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then filtered off (0.15 g, 47%). The filtrate was evaporated to give syrupy 2,3-anhydro-D-allose (6a—d) (0.14 g). Recrystallisation of the solid from acetone–light petroleum gave 2,3-*anhydro*-α-D-*allopyranose* (6a), m.p. 88—90°, $[\alpha]_D$ +27° (equil.; *c* 1.0 in H_2O) (Found: C, 44.4; H, 6.2. $C_6H_{10}O_5$ requires C, 44.45; H, 6.15%); τ [100 MHz; $(CD_3)_2SO$] 3.77 (1 H, d, $J_{1.OH}$ 6.3 Hz, HO-1), 4.86 (1 H, dd, $J_{1.2}$ 3.0 Hz, H-1), 4.92 (1 H, d, $J_{4.OH}$ 5.8 Hz, HO-4), 5.66 (1 H, t, $J_{6.OH} = J_{6'.OH}$ = 6.0 Hz), and 6.1—6.9 (6 H, unresolved).

Paper chromatography (3 : 1 : 1 butan-1-ol-pyridine–water) of the crystals or of the syrup showed a single component, R_{Glc} 2.43, detected by aniline phthalate [25] (reducing sugar) or by sodium iodide–Methyl Red [26] (vicinal epoxide).

The mutarotation of the crystalline anhydride (6a) (20 mg) in water (1 ml) was studied by the method in ref. 1, The equilibrated mixture was converted into a mixture of Tms ethers and examined by g.l.c.[1] The results of both of these experiments are given in the Discussion section.

1,4,6-*Tri*-O-*acetyl*-2,3-*anhydro*-α-D-*allopyranose* (7a).—The crystalline anhydro-allose (6a) (50 mg) was acetylated with acetic anhydride and pyridine in the normal way to give the title compound as a homogeneous syrup [t.l.c. (9 : 1 benzene–ether)]; τ (100 MHz; $CDCl_3$) 3.77 (1 H, d, $J_{1.2}$ 2.5 Hz, H-1), 4.87 (1 H, dd, $J_{4.5}$ 9.5, $J_{3.4}$ 1.3 Hz, H-4), 5.6—6.0 (3 H, unresolved), 6.26—6.43 (2 H, unresolved, H-2 and -3), and 7.85, 7.88, and 7.94 (9 H, 3s, 3MeCO).

1,4,6-*Tri*-O-*acetyl*-2,3-*anhydro*-αβ-D-*allopyranose* (7a *and* b).—5% Palladium–charcoal (0.2 g) was added to a solution of the diacetate (5) [prepared from (4) (0.1 g)] in methanol (15 ml) and the mixture was shaken at room temperature with a slight overpressure of hydrogen. After 30 min uptake was complete and the catalyst was removed. T.l.c. (9 : 1 benzene–ether) showed a single component of R_F value lower than that of the starting material. The anomeric mixture (8a and b) was obtained as a syrup [90 mg, 92% from (4)]; τ (60 MHz; D_2O) 4.5—5.0 (2 H, unresolved), 5.7—5.9 (3 H, unresolved), 6.32 (2 H, unresolved, H-2 and -3), and 7.91 and 7.98 (6 H, 2s, 2MeCO).

The above anomeric mixture (90 mg) was treated with acetic anhydride (1 ml) and pyridine (1 ml) at room temperature for 16 h. The resulting syrup, consisting of the triacetates (7a and b), was homogeneous by t.l.c.; τ (100 MHz; $CDCl_3$) 3.77 and 3.92 (1 H, 2 doublets, $J_{1,2}$ 2.5 and 0.8 Hz in the ratio 4 : 1, H-1), 4.7—5.0 (1 H, unresolved, H-4), 5.6—6.7 (5 H, unresolved), and 7.85, 7.87, and 7.94 (9 H, 3s, 3MeCO).

1,5,6-*Tri*-O-*acetyl*-2,3-*anhydro*-β-D-*allofuranose* (7d).—Syrupy 2,3-anhydro-D-allose (6a—d) (0.14 g) was acetylated in the normal manner to give a syrup that crystallised spontaneously. After trituration with ethyl acetate–light petroleum the crystals were filtered off (90 mg, 36%). Recrystallisation from ethyl acetate–light petroleum afforded the *triacetate* (7d), m.p. 120—121°, $[\alpha]_D$ −62° (*c* 0.45 in $CHCl_3$) (Found: C, 49.6; H, 5.4. $C_{12}H_{16}O_8$ requires C, 50.0; H, 5.6%); τ (100 MHz; $CDCl_3$) 3.74 (1 H, s, H-1), 4.91 (1 H, ddd, $J_{4,5}$ 8.3, $J_{5,6'}$ 5.5, $J_{5.6}$ 3.0 Hz, H-5), 5.50 (1 H, dd, $J_{6,6'}$ 12.3 Hz, H-6), 5.72 (1 H, d, H-4), 5.97 (1 H, dd, H-6'), 6.1—6.25 (2 H, q, H-2 and H-3), and 7.88, 7.90, and 7.94 (9 H, 3s, 3MeCO).

Benzyl 3,4-O-*Isopropylidene*-2-O-p-*tolylsulphonyl*-α-D-*arabinoside* (10).—Benzyl α-D-arabinopyranoside [12] (6.0 g) in 2,2-dimethoxypropane (20 ml) and acetone (20 ml) containing toluene-*p*-sulphonic acid (0.2 g) was stirred for 1 h at room temperature. The clear solution was neutralised with barium carbonate, the solids were removed by filtration, and the filtrate was evaporated leaving the crude isopropylidene compound (9) as a syrup. Pyridine (30 ml) was added to the syrup, followed by toluene-*p*-sulphonyl chloride (6.0 g, 1.26 mol. equiv.), and the mixture was kept at 50 °C for 3 h. Ice–water (5 ml) was added to the cooled mixture, with stirring, and after a few minutes the solution was poured on to ice. The resulting solid was filtered off and recrystallised from aqueous ethanol to give the pure *sulphonate* (10) (9.0 g, 83%), m.p. 80—82°, $[\alpha]_D$ −12° (*c* 1.0 in $CHCl_3$) (Found: C, 60.8; H, 6.0; S, 7.2. $C_{22}H_{26}O_7S$ requires C, 60.8, H, 6.0; S, 7.4%).

Benzyl 2-O-p-*Tolylsulphonyl*-α-D-*arabinopyranoside* (11).—The acetal (10) (5 g) in aqueous acetic acid (90% v/v; 20 ml) was heated at 100 °C for 45 min. Evaporation left a solid which was recrystallised from aqueous methanol to give the pure *sulphonate* (11) (4.0 g, 90%), m.p. 110—112°, $[\alpha]_D$ +22° (*c* 1.0 in $CHCl_3$) (Found: C, 57.8; H, 5.6. $C_{19}H_{22}O_7S$ requires C, 57.9; H, 5.6%); τ (60 MHz; $CDCl_3$) 2.0—2.9 (9 H, m, Ar), 5.1—6.9 (10 H, unresolved, benzylic and sugar ring protons), and 7.65 (3 H, s, Me).

Benzyl 2,3-*Anhydro*-α-D-*ribopyranoside* (12).—The sulphonate (11) (2.0 g) was dissolved in methanol (25 ml) containing sodium methoxide [from sodium (0.3 g, *ca.* 2.5 mol. equiv.)] and heated to 50 °C for 30 min. The cooled solution was carefully neutralised with Amberlite IR 120 (H^+ form) ion-exchange resin, filtered, and evaporated, and the solid residue was extracted with ethyl acetate (3 × 15 ml). Evaporation of the combined extracts gave a syrup which crystallised from light petroleum to give the *anhydroriboside* (12) (1.0 g, 89%), m.p. 94—96°, $[\alpha]_D$ +202° (*c* 1.0 in EtOAc) (Found: C, 64.7; H, 6.25. $C_{12}H_{14}O_4$ requires C, 64.9; H, 6.3%); τ [100 MHz; $(CD_3)_2SO$] 2.65 (5 H, s, Ph), 4.8 (1 H, d, *J* 6 Hz, HO-4), 5.0 (1 H, d, *J* 3 Hz, H-1), 5.4 (2 H, q, benzylic), 6.1 (1 H, m, H-4), and 6.5—6.8 (4 H, m).

2,3-*Anhydro*-D-*ribose* (13).—The anhydro-riboside (12) (1.0 g) in ethyl acetate was stirred with 5% palladium–charcoal (0.1 g) in hydrogen for 24 h. The catalyst was removed, and the filtrate evaporated to a syrup. T.l.c. indicated that 2,3-anhydro-ribose was the major product (orange spot with the sodium iodide–Methyl Red reagent [26]). Chromatography on silica gel afforded the pure *anhydrosugar* (0.4 g, 67%) as a syrup, $[\alpha]_D$ −5° (equil.) (*c* 1.18 in H_2O) (Found: C, 45.6; H, 6.4. $C_5H_8O_4$ requires C, 45.45; H, 6.1%). The n.m.r. spectrum [100 MHz; $(CD_3)_2SO$] was complex and indicated the presence of several ring forms.

Benzyl 2-O-*Acetyl*-3,4,6-*tri*-O-*benzyl*-α-D-*mannopyranoside* (15).—A solution containing 3,4,6-tri-*O*-benzyl-β-D-mannopyranose 1,2-(methyl orthoacetate) (14) [22] (3.5 g), nitromethane (35 ml), and benzyl alcohol (4 ml) was distilled slowly and fresh nitromethane was added at such a rate as to maintain a constant volume. After 5 ml of distillate had been collected, mercury(II) bromide (100 mg) was added and the distillation continued for 1 h. The mixture was cooled and evaporated under reduced pressure to leave a syrup which was purified by chromatography on silica gel with light petroleum–ethyl acetate (9 : 1) as eluant. The pure *acetate* (15) (2.46 g, 61%) was a syrup, $[\alpha]_D$ +38.2° (*c* 1.0 in $CHCl_3$) (Found: C, 73.3; H, 6.8. $C_{36}H_{38}O_7$ requires C, 74.2; H, 6.5%); τ (60 MHz; $CDCl_3$) 2.6—2.8 (20 H, m, Ph), 4.5—6.2 (15 H, unresolved), and 7.87 (3 H, s, MeCO).

Benzyl 3,4,6-*Tri*-O-*benzyl*-α-D-*mannopyranoside* (16).—

[25] S. M. Partridge, *Nature*, 1949, **164**, 443.
[26] J. G. Buchanan and J. C. P. Schwarz, *J. Chem. Soc.*, 1962, 4770.

The acetate (15) (2.0 g) was deacetylated with methanolic sodium methoxide. The syrupy glycoside (1.84 g, 99%), had $[\alpha]_D$ +35° (*c* 1.0 in $CHCl_3$) (Found: C, 75.8; H, 6.8. $C_{34}H_{36}O_6$ requires C, 75.6; H, 6.7%).

Benzyl 3,4,6-*Tri*-O-*benzyl*-2-O-*methylsulphonyl*-α-D-*mannopyranoside* (17).—The glycoside (16) (1.0 g) in pyridine (10 ml) was treated with methanesulphonyl chloride (1 ml) at room temperature for 2 h. The excess of acid chloride was destroyed with a little water and the product isolated with chloroform. Chromatography on silica gel gave the pure *sulphonate* (17) as a syrup (0.92 g, 80%), $[\alpha]_D$ +32° (*c* 1.0 in $CHCl_3$) (Found: S, 5.7. $C_{35}H_{38}O_8S$ requires S, 5.2%).

2-O-*Methylsulphonyl*-D-*mannose* (18).—The sulphonate (17) (1.0 g) in ethanol (25 ml) was shaken with hydrogen over 5% palladium–charcoal (0.5 g) at atmospheric pressure for 4 days. The catalyst was filtered off and the solution evaporated to leave a solid. Recrystallisation from ethyl acetate gave the pure *sulphonate* (18) (0.2 g, 48%), m.p. 128—130°, $[\alpha]_D$ 0.0° (*c* 1.0 in H_2O) (Found: C, 32.8; H, 5.6; S, 12.35. $C_7H_{14}O_8S$ requires C, 32.6; H, 5.4; S, 12.4%); τ (60 MHz; D_2O) 4.6 (d, $J_{1,2}$ H-1 of α-anomer), 4.87 (s, H-1 of β-anomer) (α : β ratio *ca.* 3 : 1), 5.1 (1 H, unresolved), 5.8—6.6 (5 H, unresolved), and 6.7 (3 H, s, CH_3SO_2).

Reaction of 2-O-*Methylsulphonyl*-D-*mannose* (18) *with Alkali*.—The sulphonate (18) (50 mg) was dissolved in methanolic 10% sodium methoxide (5 ml). After 30 min the solution was carefully neutralised with Amberlite IR 120 (H^+ form) resin and evaporated to dryness. The residue was extracted with ethyl acetate and from the extract was obtained 1,6-anhydro-β-D-glucopyranose (20), m.p. 177—178°, $[\alpha]_D$ −65° (*c* 1.0 in H_2O), indistinguishable from an authentic sample.

We thank the Cancer Research Campaign for supporting this work, Dr. E. M. Bessell and Professor A. B. Foster for the enzymic tests and for discussions, and the S.R.C. for the 100 MHz n.m.r. spectra (measured at the P.C.M.U., Harwell).

[6/107 *Received*, 16*th January*, 1976]