The Epimerisation of Sugars.

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[Reprint Order No. 6354.]

De-esterification of the 2-*O*-toluene-*p*-sulphonyl or 2-*O*-methanesulphonyl derivatives of arabinose, xylose, and fucose converts them into ribose, lyxose, and talomethylose respectively. Similarly 3-*O*-methanesulphonyl-D-fructose is converted into D-psicose.

1 : 2-Anhydro-D-ribose was required for a research project. We attempted to prepare this compound from 2-*O*-methanesulphonyl-D-arabinose by alkaline hydrolysis but obtained, instead, D-ribose in high yield. This led us to study the alkaline hydrolyses of the 2-*O*-toluene-*p*-sulphonyl and 3-*O*-methanesulphonyl derivatives of the methylpentose and ketose sugars respectively.

2-*O*-Methanesulphonyl-D-arabinose was prepared from methyl 2-*O*-methanesulphonyl-3 : 4-*O*-*iso*propylidene-β-D-arabinoside. We report new constants for this compound (cf. Overend and Stacey, *J.*, 1949, 1235). Crystalline 2-*O*-toluene-*p*-sulphonyl-D-xylose was prepared from methyl 3 : 5-*O*-*iso*propylidene-2-*O*-toluene-*p*-sulphonyl-αβ-D-xylofuranoside (cf. Percival and Zobrist, *J.*, 1952, 4308), and 2-*O*-toluene-*p*-sulphonyl-L-fucose was isolated after hydrolysis of methyl 3 : 4-*O*-*iso*propylidene-2-*O*-toluene-*p*-sulphonyl-α-L-fucoside (Percival and Percival, *J.*, 1950, 690). All three of these glycosides were relatively stable to hydrolysis by acids, presumably owing to the 2-sulphonyloxy-substituent (cf. Richards, *Chem. and Ind.*, 1955, 228). 3-*O*-Methanesulphonyl-D-fructose was isolated as a syrup after acidic hydrolysis of 3-*O*-methanesulphonyl-1 : 2-4 : 5-di-*O*-*iso*propylidene-D-fructose.

In order to convert these carbohydrate sulphonic esters into the epimeric sugars they were dissolved in water and their solutions were titrated with 0·3N-barium hydroxide to a phenolphthalein end-point. The mixtures were then de-ionised with Amberlite resins, IR-120 and IR-4B, and concentrated to a syrup. The epimer from 2-*O*-toluene-*p*-sulphonyl-D-xylose contained lyxose, and also xylose and traces of sugars identified chromatographically as a keto-D-*threo*pentose and D-arabinose. This mixture was fractionated on a cellulose column and pure D-lyxose was isolated. L-Talomethylose was obtained in crystalline form from the mixture resulting when the toluene-*p*-sulphonyl group was eliminated from 2-*O*-toluene-*p*-sulphonyl-L-fucose. D-Ribose was obtained crystalline only after separation from a small amount of arabinose on a cellulose column.

D-Psicose resulting from the elimination of the methanesulphonyl group from 3-*O*-methanesulphonyl-D-fructose was obtained as a chromatographically pure syrup which was characterised as D-allosazone and as the crystalline di-*O*-*iso*propylidene derivative of D-psicose.

The mechanism of the formation of these epimeric sugars is not clear. They may be formed *via* a 1 : 2-anhydro-sugar or by direct inversion at $C_{(2)}$. However, alkaline hydrolysis of methyl 2-*O*-methanesulphonyl-3 : 4-*O*-*iso*propylidene-β-D-arabinoside yielded methyl 3 : 4-*O*-*iso*propylidene-β-D-arabinoside by elimination of the methanesulphonyl group without inversion (cf. *Adv. Carbohydrate Chem.*, 1953, **8**, 167) which by acid hydrolysis afforded methyl β-D-arabinoside. This indicates that the second mechanism may not be operative in the transformations described above. The epimers are not formed by conversion of the sugars into an equilibrium mixture under the influence of a basic catalyst as they are produced in high yield. Fructose and fucose possess the same configuration of secondary alcohol groups as arabinose and may be considered as derivatives of this sugar. Anhydro-ring formation involving the reducing hydroxyl group of these sugars would result in the formation of ribose derivatives. If, then, the 1 : 2-anhydro-ring were opened in accordance with the Fürst–Plattner rule two axially oriented hydroxyl groups would result. This may explain the high yields of epimers obtained in this reaction.

While this work was in progress the conversion of 4-*O*-formyl-2-*O*-methanesulphonyl-D-arabinose into D-ribose was reported by Smith (*Chem. and Ind.*, 1955, 92).

Experimental

Concentrations were carried out under reduced pressure. Sugars were detected on chromatograms with the *p*-anisidine hydrochloride spray. The following solvents were used in chromatographic separations on Whatman No. 1 paper: (*a*) ethyl acetate–acetic acid–formic acid–water (18 : 3 : 1 : 4); (*b*) butan-1-ol–pyridine–water (10 : 3 : 3); (*c*) butan-1-ol–ethanol–water (4 : 1 : 2); and (*d*) ethyl acetate–acetic acid–water (9 : 2 : 2) (all v/v). Solutions were de-ionised with Amberlite resins IR-4B and IR-120.

2-O-*Methanesulphonyl*-D-*arabinose*.—Methyl 2-*O*-methanesulphonyl-3 : 4-*O*-*iso*propylidene-β-D-arabinoside (6·5 g.) {m. p. 140—141°, $[\alpha]_D^{24}$ −185° (*c*, 1·0 in $CHCl_3$); reported by Overend and Stacey (*loc. cit.*) to have m. p. 136·5—137·5°, $[\alpha]_D^{24}$ −333° (*c*, 0·045 in $CHCl_3$)} was boiled under reflux with 2N-sulphuric acid (244 c.c.) for 24 hr. The solution was very carefully neutralised with barium carbonate and filtered immediately through a Celite pad. The filtrate was evaporated to dryness under diminished pressure and the residue extracted with alcohol. The extract was filtered through charcoal and evaporated to a colourless syrup (4·4 g.), $[\alpha]_D^{24}$ −85° (*c*, 4·4 in H_2O), R_{RH} 1·2 (solvent *c*), R_{RH} 1·4, and R_F 0·58 (solvent *d*), showing one component only with the *p*-anisidine or silver nitrate reagent (R_{RH} is relative to rhamnose). The material reduced Fehling's solution.

D-*Ribose*.—2-*O*-Methanesulphonyl-D-arabinose (1·09 g.) in water (25 c.c.) was titrated slowly with saturated barium hydroxide solution to a phenolphthalein end-point. The solution was de-ionised and evaporated to dryness. The residual syrup, which was contaminated with a small amount of arabinose (detected chromatographically), was purified on a small cellulose column by elution with butan-1-ol half saturated with water. The eluate was evaporated to dryness, and the residue dissolved in water and filtered through charcoal. The filtrate was evaporated to dryness, and the residue on trituration with alcohol and seeding with authentic ribose crystallised, giving D-ribose (0·18 g.), $[\alpha]_D^{24}$ −22·8° (*c*, 1·8 in H_2O), m. p. 93—94°, mixed m. p. 90—91°.

D-*Ribose Toluene*-p-*sulphonhydrazone*.—D-Ribose (0·072 g.) in methanol (10 c.c.) was boiled under reflux with a solution of toluene-*p*-sulphonhydrazide (0·7 g.) in methanol (10 c.c.) for ½ hr. The solution was stored in the refrigerator for 24 hr. The crystalline residue was collected, washed with cold methanol and dried (0·122 g.; m. p. and mixed m. p. 174°).

2-O-*Methanesulphonyl*-3 : 4-O-iso*propylidene*-D-*arabinose*.—2-*O*-Methanesulphonyl-D-arabinose (1·0 g.) in acetone (50 c.c.) was shaken with anhydrous copper sulphate (5 g.) for 10 days. The course of the reaction was followed chromatographically, the product having R_{RH} 2·1 and R_F 0·86 (solvent *d*). The mixture was filtered, the filtrate concentrated to dryness, and the residue dissolved in ether. The ethereal solution was extracted with a little water, dried ($MgSO_4$), concentrated to a small volume, and placed in the refrigerator. The crystalline residue

was collected {0·250 g.; $[\alpha]_D^{24}$ −118° (*c*, 2·06 in acetone); m. p. 127—128°}. After recrystallisation from ether–acetone, it had m. p. 130—131°, not changed by further recrystallisation (Found: C, 40·1; H, 6·0; S, 11·7. Calc. for $C_9H_{16}O_7S$: C, 40·3; H, 6·0; S, 11·9%).

Methyl 3 : 4-O-iso*Propylidene*-β-D-*arabinoside*.—Methyl 2-*O*-methanesulphonyl-3 : 4-*O*-*iso*propylidene-β-D-arabinoside (5 g.) was heated in alcohol (200 c.c.) containing sodium hydroxide (0·75 g.) for 16 hr. The solution was filtered and the filtrate concentrated to dryness. The residue was extracted with light petroleum (b. p. 40—60°), and the extract filtered and concentrated to a syrup (1·9 g.), b. p. 100° (bath-temp.)/0·5 mm., n_D^{26} 1·4622, $[\alpha]_D^{20}$ −197° (*c*, 1·848 in $CHCl_3$) (Found: OMe, 14·0. Calc. for $C_9H_{16}O_5$: OMe, 15·2%).

Methyl β-D-*Arabinoside*.—Methyl 3 : 4-*O*-*iso*propylidene-β-D-arabinoside was dissolved in ether, acidified, and set aside for 16 hr.; crystals separated, having m. p. 167—168°, $[\alpha]_D^{22}$ −235° (*c*, 1·65 in MeOH) (Found: C, 44·1; H, 7·3; OMe, 18·9. Calc. for $C_6H_{12}O_5$: C, 43·9; H, 7·3; OMe, 18·9%).

2-O-*Toluene*-p-*sulphonyl*-D-*xylose*.—Methyl 3 : 5-*O*-*iso*propylidene-2-*O*-toluene-*p*-sulphonyl-αβ-D-xylofuranoside (11·3 g.) (Percival and Zobrist, *loc. cit.*) was dissolved in ethanol–water (1 : 1; 50 c.c.) containing concentrated hydrochloric acid (5 c.c.). The solution was heated on the boiling-water bath and the hydrolysis followed chromatographically (solvent *b*). After 5 hr. the solution contained a trace of xylose and two other components which moved at rates 1·6 and 2·06 relative to rhamnose. The faster-moving component was the major product. The solution was neutralised with barium carbonate, then filtered and the filtrate extracted exhaustively with chloroform. Concentration of the extract gave a crystalline residue (7·2 g.), easily soluble in methanol, ethanol, dioxan, and ethyl acetate, sparingly soluble in chloroform and ether. The product, 2-*O*-toluene-*p*-sulphonyl-D-xylose, recrystallised from ethyl acetate–chloroform, had m. p. 148°, $[\alpha]_D$ 14° (*c*, 0·5 in H_2O), and moved at twice the rate of rhamnose in solvent (*b*) (Found: C, 47·5; H, 5·3; S, 10·0. Calc. for $C_{12}H_{16}O_7S$: C, 47·3; H, 5·3; S, 10·5%).

Conversion of 2-O-*Toluene*-p-*sulphonyl*-D-*xylose into* D-*Lyxose*.—The toluene-*p*-sulphonyl derivative (0·91 g.) was dissolved in water, and 0·1N-sodium hydroxide (30 c.c.) added slowly at 40°. At this stage the solution was alkaline to phenolphthalein. After 15 min. the solution was acidified with acetic acid and de-ionised. The neutral effluent, $[\alpha]_D$ −6° (*c*, 2·7 in H_2O), was concentrated and examined chromatographically. The major component present was lyxose; a minor component was xylose; and unchanged starting material and small quantities of arabinose and keto*threo*pentose were also detected. The concentrate was fractionated on a column of cellulose with butan-1-ol half saturated with water as eluant. Concentration of the appropriate fractions of effluent from the column gave D-lyxose (0·4 g.) which slowly crystallised. Trituration with ethanol gave pure D-lyxose, m. p. and mixed m. p. 115°, $[\alpha]_D$ −14° (equil.).

Preparation of L-*Talomethylose* (with Mr. J. L. THOMPSON).—Methyl 3 : 4-*O*-*iso*propylidene-2-*O*-toluene-*p*-sulphonyl-α-L-fucoside (1 g.) was heated in 4N-hydrochloric acid (20 c.c.) on the water-bath for 3 hr. Paper chromatography (solvent *b*) then indicated complete hydrolysis, the mixture containing one component which moved, relative to rhamnose, at a rate of 2·1 (solvent *c*). The solution was neutralised with barium carbonate and filtered. The filtrate was titrated with 0·3N-barium hydroxide (10 c.c.) until a permanent pink colour was produced (phenolphthalein), then acidified with acetic acid, de-ionised, and concentrated. The syrupy residue (0·32 g.) contained talomethylose, which moved at 1·7 times the speed of rhamnose (solvent *b*) and traces of fucose (R_{RH} 0·7). On trituration with acetone the syrup crystallised. The crystals (0·22 g.) were collected and had m. p. and mixed m. p. 118—120° (Found: C, 44·1; H, 6·8. Calc. for $C_6H_{12}O_5$: C, 43·9; H, 7·3%). The syrup remaining gave with methylphenylhydrazine solution a methylphenylhydrazone (0·092 g.), m. p. 181°.

Conversion of D-*Fructose into* D-*Psicose*.—3-*O*-Methanesulphonyl-1 : 2-*O*-*iso*propylidene-D-fructose, m. p. 142° (1·62 g.) (3 : 4-di-*O*-acetyl derivative, m. p. 81°), was heated in 0·2N-sulphuric acid (11 c.c.) on the water bath for 30 min. Chromatography then indicated complete hydrolysis. The cooled solution was neutralised with barium carbonate and filtered and the filtrate titrated with 0·3N-sodium hydroxide (20 c.c.) until the solution remained alkaline for 10 min. The mixture was then acidified (acetic acid), de-ionised, and concentrated. The resulting syrup, examined chromatographically, was found to contain a ketose which moved at the same rate as psicose. A sample gave an osazone, m. p. 165° alone or mixed with D-allosazone. The residual syrup was shaken overnight with acetone (100 c.c.) and concentrated sulphuric acid (1 c.c.). The acid catalyst was then removed with anhydrous potassium carbonate, and the solution filtered. The filtrate was concentrated, dissolved in water, and extracted with light petroleum (b. p. 40—60°). The aqueous solution was extracted with

chloroform, and the extract dried and concentrated to a syrup which rapidly crystallised (0·61 g.), having m. p. and mixed m. p. 58° after recrystallisation from light petroleum (b. p. 40—60°) (Found : C, 55·6; H, 7·3. $C_{12}H_{20}O_6$ requires C, 55·3; H, 7·7%).

We thank the Institute of Seaweed Research, Inveresk, Midlothian for a gift of L-fucose, the National Research Council of Canada for a grant which helped to defray part of the cost of this investigation, and Dr. R. B. Kelly for fruitful discussion.

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