267. *Deoxy-sugars. Part III. Methanesulphonyl Derivatives of* D-*Arabinose.*

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Attempts have been made to effect the exchange reaction between various 2-methanesulphonyl derivatives of D-arabinose and sodium iodide. In no case, however, was this achieved. Numerous new methanesulphonyl derivatives of the pentose are described.

The importance of the deoxypentose of thymus nucleic acid, 2-deoxy-D-ribose, has prompted us to explore many possible methods of its preparation. One such possibility is through the reduction of a 2-halogeno arabinoside. This has been accomplished in the case of 2-bromo β-methylarabinoside, obtained by the ring scission of 2 : 3-anhydro-β-methyl-D-riboside (see preceding paper). Now it is known that, in certain cases, methanesulphonyl residues attached to a secondary carbon atom of a sugar molecule may be replaced by an iodine atom by the simple expedient of heating the methanesulphonate with sodium iodide in acetone or other ketones of higher boiling point; for instance, 4-methanesulphonyl 1 : 2 : 3 : 6-tetra-acetyl glucose upon treatment with sodium iodide in acetone solution afforded 4-iodo 1 : 2 : 3 : 6-tetra-acetyl glucose in good yield (Helferich and Gnüchtel, *Ber.*, 1938, **71**, 712). If such a reaction were possible with a 2-methanesulphonyl derivative of D-arabinose to yield a corresponding 2-iodo derivative, this, on reduction, would lead to the formation of 2-deoxy-D-ribose. For this reason we have studied the methanesulphonyl derivatives of D-arabinose, and many new derivatives of this type are now described. In no case, however, was it possible to effect the replacement of the 2-methanesulphonyl group by iodine.

Treatment of β-methyl-D-arabopyranoside (I) with excess of methanesulphonyl chloride in pyridine affords crystalline 2 : 3 : 4-*trimethanesulphonyl* β-*methyl*-D-*arabinoside*. Similarly, α-methyl-D-arabopyranoside gave a crystalline *trimethanesulphonyl* derivative in quantitative yield.

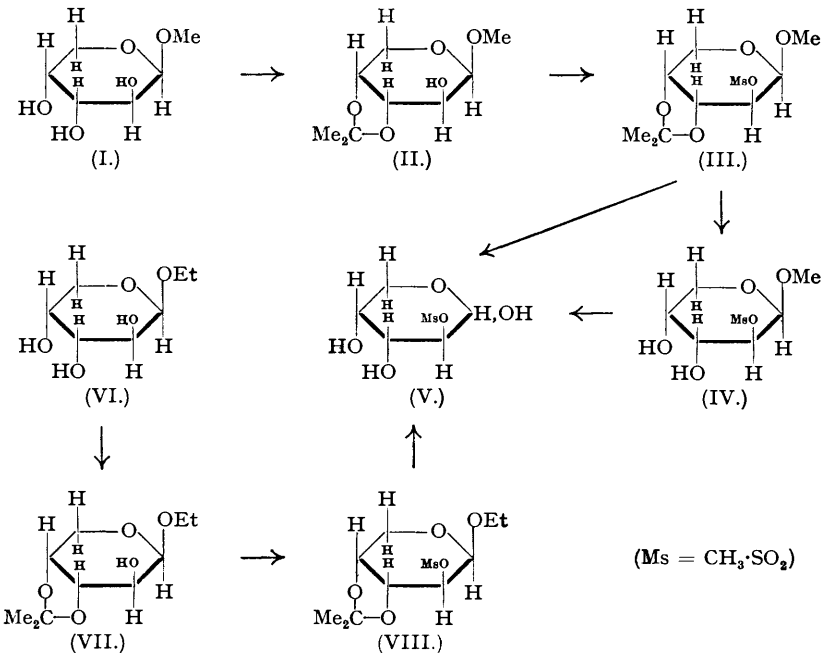
When β-methyl-D-arabinoside (I) was treated with acetone in the presence of 0·5% sulphuric acid or phosphoric oxide, syrupy 3 : 4-*iso*propylidene β-methyl-D-arabopyranoside (II) was obtained. This compound was described by Jones, Kent, and Stacey (*J.*, 1947, 1341), who also obtained the crystalline 2-toluene-*p*-sulphonyl and 2-methanesulphonyl (III) derivatives. An additional crystalline derivative, the 2-*acetyl* derivative is now described.

All attempts to convert the 2-methanesulphonyl derivative (III) into 2-iodo 3 : 4-*iso*propylidene β-methyl-D-arabopyranoside were unsuccessful. Jones, Kent, and Stacey (*loc. cit.*) have already reported that this compound (III) was unchanged after being heated with dry acetone and dry sodium iodide in a sealed tube at 112° for 48 hours. We have now recovered the material unchanged after heating it more drastically.

Removal of the *iso*propylidene residue from 2-methanesulphonyl 3 : 4-*iso*propylidene β-methyl-D-arabopyranoside (III) was effected by heating it with methyl alcohol containing 2·0% of 5N-hydrochloric acid, and crystalline 2-*methanesulphonyl* β-*methyl*-D-*arabopyranoside* (IV) was obtained. Treatment of this with hot N-sulphuric acid resulted in elimination of the glycoside group and afforded crystalline 2-*methanesulphonyl* D-*arabinose* (V). The same compound was obtained directly from (III) by hydrolysis with N-sulphuric acid. When 2-methanesulphonyl β-methyl-D-arabopyranoside (IV) was kept with acetic anhydride in dry pyridine, it yielded crystalline 2-*methanesulphonyl* 3 : 4-*diacetyl* β-*methyl*-D-*arabinoside*. Neither 2-methanesulphonyl β-methyl-D-arabopyranoside (IV) nor its 3 : 4-diacetyl derivative gave a 2-iodo compound of β-methyl-D-arabopyranoside when treated with dry acetone and sodium iodide.

It was thought that an alteration of the glycoside grouping from methyl to ethyl might have

the effect of increasing the lability of the methanesulphonyl substituent on C_2 of the arabinoside, and facilitate its exchange with iodine. Consequently 3 : 4-iso*propylidene* β-*ethyl*-D-*arabopyranoside* (VII) was prepared, treated with methanesulphonyl chloride, and the 2-*methanesulphonyl* derivative (VIII) obtained. This was isolated only as a liquid, but on hydrolysis with 1·75N-sulphuric acid, it gave 2-methanesulphonyl D-arabinose (V), identical with that prepared from 2-methanesulphonyl β-methyl-D-arabopyranoside (IV). Treatment of (VIII) with dry acetone and sodium iodide in a sealed tube gave no 2-iodo 3 : 4-*iso*propylidene β-ethyl-D-arabopyranoside, and the starting material was recovered unchanged.



It was envisaged that a change of configuration of the glycoside group in arabinose from β to α might enhance the lability of the methanesulphonyl substituent on C_2. Consequently 2-*methanesulphonyl* 3 : 4-iso*propylidene* α-*methyl*-D-*arabopyranoside* was prepared. Nevertheless, when this was heated with dry acetone and sodium iodide, no replacement of the methanesulphonyl substituent by iodine occurred.

Removal of the *iso*propylidene residue from 2-methanesulphonyl 3 : 4-*iso*propylidene α-methyl-D-arabopyranoside was effected by heating it with methyl alcohol containing 2% of 5N-hydrochloric acid, and crystalline 2-*methanesulphonyl* α-*methyl*-D-*arabopyranoside* was obtained.

Experimental.

2 : 3 : 4-*Trimethanesulphonyl* β-*Methyl*-D-*arabinoside*.—β-Methyl-D-arabinoside (0·168 g.) was dissolved in dry pyridine (5 c.c.), and the solution cooled to 0°. Methanesulphonyl chloride (3·3 mols., 0·377 g.) was slowly added, and the mixture kept at room temperature for 48 hours. After being poured into water, the material was extracted with chloroform, and the extract washed with 0·05N-sulphuric acid, then with dilute aqueous sodium hydrogen carbonate solution, and finally with water. After being dried ($MgSO_4$), the extract was evaporated to dryness, and the syrup which remained was crystallised by trituration with ethyl alcohol. Recrystallisation from absolute ethyl alcohol gave a quantitative yield of the *trimethanesulphonyl* derivative as colourless needles, m. p. 123°, $[\alpha]_D^{13.5°}$ −333·3° (*c*, 0·102 in chloroform) (Found : C, 27·2; H, 4·5; OMe, 8·0. $C_9H_{18}O_{11}S_3$ requires C, 27·1; H, 4·5; OMe, 7·8%).

2 : 3 : 4-*Trimethanesulphonyl* α-*Methyl*-D-*arabinoside*.—This was prepared by the method described above for the β-compound, and recrystallised from chloroform–pyridine in colourless needles, m. p. 186—187°, $[\alpha]_D^{18°}$ −86·95° (*c*, 0·184 in chloroform); the yield was quantitative (Found : C, 27·2; H, 4·5; OMe, 7·5%).

3 : 4-iso*Propylidene* β-*Methyl*-D-*arabinoside*.—(*a*) β-Methyl-D-arabinoside (12·34 g.) was shaken with acetone (1 l.) containing 0·5% sulphuric acid and worked up in the usual way. The product was a colourless liquid, b. p. 115° (bath temp.)/0·01 mm., $n_D^{17°}$ 1·4617, $[\alpha]_D^{18.5°}$ −197·6° (*c*, 0·344 in chloroform) {Honeyman, *J.*, 1946, 990, gives b. p. 82°/0·1 mm., $[\alpha]_D^{20°}$ +199·1° (*c*, 3·3 in chloroform) for 3 : 4-*iso*-

propylidene β-methyl-L-arabinoside} (yield 14·09 g., 92%) (Found OMe, 15·2. Calc. for $C_9H_{16}O_5$: OMe, 15·2%).

(*b*) β-Methyl-D-arabinoside (24·72 g.) was suspended in dry acetone (500 c.c.), and phosphoric oxide (16·6 g.) added; the product, obtained as usual, was a colourless oil, b. p. 115—120° (bath temp.)/0·01 mm., $[\alpha]_D^{20°}$ −198·4° (*c*, 0·54 in chloroform).

2-*Acetyl* 3 : 4-iso*Propylidene* β-*Methyl*-D-*arabinoside*.—Freshly distilled acetic anhydride (0·26 g., 50% excess) was added to a solution of 3 : 4-*iso*propylidene β-methyl-D-arabcpyranoside (0·366 g.) in dry pyridine (10 ml.). The solution was kept at room temperature for 3 hours and then poured into water. It was then neutralised with sodium hydrogen carbonate and extracted with chloroform. The extract was dried ($MgSO_4$), and the solvent removed by evaporation. The syrupy *acetyl* derivative, crystallised on trituration with acetone–water and recrystallised from hot water, had m. p. 76·5—77·5°, $[\alpha]_D^{16°}$ −125° (*c*, 0·416 in water) (Honeyman, *loc. cit.*, quotes $[\alpha]_D^{16°}$ +123·6° in water for the L-isomer) (Found: C, 53·0; H, 7·1; OMe, 12·4. $C_{11}H_{18}O_6$ requires C, 53·6; H, 7·3; OMe, 12·6%).

Attempts to prepare 2-*Iodo* 3 : 4-isc*Propylidene* β-*Methyl*-D-*arabinoside*.—(*a*) 2-Methanesulphonyl 3 : 4-*iso*propylidene β-methyl-D-arabinoside (0·133 g.) {m. p. 136·5—137·5°, $[\alpha]_D^{24°}$ −333° in chloroform (*c*, 0·045)}, obtained according to Jones, Kent, and Stacey (*loc. cit.*), was dissolved in dry acetone (25 ml.) containing dry sodium iodide (1·1 mols., 0·079 g.), and the solution was heated in a sealed tube at 125° for 5 hours. No sodium methanesulphonate separated. After cooling, the solution was evaporated to dryness and the solid residue was leached with water. The solid then remaining was collected (0·10 g.) and had m. p., alone or in admixture with the starting material, 137°.

(*b*) The above experiment was repeated, except that the time of heating was extended to 12 hours and the temperature increased to 200°, but the starting material was recovered unchanged.

2-*Methanesulphonyl* β-*Methyl*-D-*arabopyranoside*.—2-Methanesulphonyl 3 : 4-*iso*propylidene β-methyl-D-arabopyranoside (1·87 g.) was dissolved in methyl alcohol (111 c.c.) containing 5N-hydrochloric acid (2·27 c.c.), and the solution boiled for 6 hours. After being neutralised with silver carbonate, the solution was filtered, and the filtrate evaporated to dryness. The syrupy residue was extracted with chloroform. After being dried ($MgSO_4$), the extract was evaporated to a syrup, which crystallised when triturated with ethyl alcohol and water. The solid *methanesulphonyl* derivative, recrystallised from ethyl alcohol–water, formed colourless cubes (0·86 g., 54%), m. p. 69—70°, $[\alpha]_D^{17·5°}$ −161·3° (*c*, 0·310 in chloroform) (Found: C, 32·35; H, 6·3; OMe, 13·0. $C_7H_{14}O_7S,H_2O$ requires C, 32·3; H, 6·2; OMe, 11·9%).

2-*Methanesulphonyl* 3 : 4-*Diacetyl* β-*Methyl*-D-*arabinoside*.—2-Methanesulphonyl β-methyl-D-arabinoside (0·18 g.) was dissolved in dry pyridine (5 c.c.) and freshly distilled acetic anhydride (0·432 g., 50% excess) was added to the solution. The mixture was kept at room temperature for 12 hours and then poured into water. After being neutralised with sodium hydrogen carbonate, the solution was extracted with chloroform. The extract was dried ($CaCl_2$) and then evaporated to dryness. A pale yellow syrup remained which crystallised when triturated with ethyl alcohol. Recrystallisation from ethyl alcohol–water (charcoal) gave the *diacetyl* derivative in colourless cubes, m. p. 103—104°, $[\alpha]_D^{21·5°}$ −312·5° (*c*, 0·048 in chloroform); yield 0·06 g. (Found: C, 40·5; H, 5·6. $C_{11}H_{18}O_9S$ requires C, 40·4; H, 5·6%).

Attempt to prepare 2-*Iodo* β-*Methyl*-D-*arabinoside*.—2-Methanesulphonyl β-methyl-D-arabinoside (0·10 g.) was dissolved in dry acetone (10 ml.) and dry sodium iodide (1·1 mols., 0·068 g.) was added. The mixture was heated at 110° for 5 hours in a sealed tube. After cooling and filtration, the solution was evaporated to dryness, and the residue was extracted with chloroform. Evaporation of the solution gave a syrup which completely crystallised. Recrystallisation from ethyl alcohol gave colourless needles, m. p. alone or in admixture with 6-methanesulphonyl β-methyl-D-arabinoside, 69°; yield of recovered material, 0·085 g.

Attempt to prepare 2-*Iodo* 3 : 4-*Diacetyl* β-*Methyl*-D-*arabinoside*.—2-Methanesulphonyl 3 : 4-diacetyl β-methyl-D-arabinoside (0·50 g.) was dissolved in dry acetone (15 ml.), dry sodium iodide (1·1 mols., 0·23 g.) added, and the mixture heated at 110° for 5 hours in a sealed tube. After cooling, the solution was filtered and then evaporated to dryness. The residue was extracted with chloroform and evaporation of the solution gave a syrup which crystallised on standing. Recrystallised from alcohol–water, it had m. p. 103° alone or in admixture with the starting material; yield 0·42 g.

2-*Methanesulphonyl* D-*Arabinose*.—(*a*) 2-Methanesulphonyl 3 : 4-*iso*propylidene β-methyl-D-arabinoside (1·2 g.) was heated under reflux with N-sulphuric acid (40 c.c.) for 4 hours. The solution was neutralised with barium carbonate, and then filtered through a carbon pad. The filtrate was evaporated to dryness under diminished pressure, and the residue extracted with alcohol. The extract was filtered and evaporated to a colourless syrup which crystallised on trituration with ethyl alcohol. After recrystallisation from ethyl alcohol–water, colourless plates of 2-*methanesulphonyl* D-*arabinose* were obtained; m. p. 65—66°, $[\alpha]_D^{17°}$ −187·6° changing to −203·7° after 12 minutes (*c*, 0·373 in 5 parts chloroform and 1 part ethyl alcohol). The solid (yield 0·3 g.) reduced Fehling's solution in the cold (Found: C, 32·1; H, 6·2; S, 11·4. $C_6H_{12}O_7S,0·5C_2H_6O,0·5H_2O$ requires C, 32·3; H, 6·1; S, 12·2%).

(*b*) 2-Methanesulphonyl β-methyl-D-arabopyranoside (1·0 g.) was heated under reflux with N-sulphuric acid (40 c.c.) for 4 hours. The solution was neutralised with barium carbonate, and then filtered through a carbon pad. 2-Methanesulphonyl D-arabinose (0·4 g., 42·5%) was isolated as described above; m. p. 65—66°.

β-*Ethyl*-D-*arabopyranoside*.—Dry D-arabinose (13·0 g.) was heated under reflux for 7 hours with absolute ethyl alcohol (300 c.c.) containing 1% of hydrogen chloride. After cooling, the solution was neutralised with silver carbonate and filtered. The filtrate was evaporated to dryness, and after trituration with ethyl alcohol, the residue crystallised. Recrystallisation from ethyl alcohol yielded the *arabopyranoside* as shining white plates (3·0 g., 19·5%), m. p. 134·5—135·5°, $[\alpha]_D^{23°}$ −251·9° (*c*, 1·3 in water) (Found: OEt, 25·4. $C_7H_{14}O_5$ requires OEt, 25·2%). Helferich and Appel (*Z. physiol. Chem.*, 1932, **205**, 20) give m. p. 136—137°, $[\alpha]_D$ +233·5°, for β-ethyl-L-arabinoside.

3 : 4-iso*Propylidene* β-*Ethyl*-D-*arabinoside*.—β-Ethyl-D-arabopyranoside (1·76 g.) was shaken with acetone (350 c.c.) containing 0·5% of sulphuric acid until complete solution was effected. The solution was neutralised with potassium carbonate and then filtered. The filtrate was evaporated to dryness in

the presence of potassium carbonate, and the residue extracted with ether. Evaporation of the solvent yielded a mixture of syrup and solid. The solid was separated and recrystallised from acetone, forming colourless plates of 3 : 4-iso*propylidene* β-*ethyl*-D-*arabinoside*, m. p. 89—91°, $[\alpha]_D^{23.5°}$ −188·1° (*c*, 0·404 in chloroform) (Found : C, 54·5; H, 8·3; OEt, 20·2. $C_{10}H_{18}O_5$ requires C, 55·0; H, 8·3; OEt, 20·6%). The syrupy portion distilled as a colourless oil, b. p. 110—120°/0·005 mm. (0·225 g.), which crystallised on cooling. It recrystallised from acetone in long needles, which were extremely hygroscopic; m. p. *ca.* 40°, $[\alpha]_D^{21.5°}$ −128° (*c*, 0·25 in chloroform) (Found : C, 55·7; H, 8·2; OEt, 10·5%). This substance has not yet been identified.

2-*Methanesulphonyl* 3 : 4-iso*Propylidene* β-*Ethyl*-D-*arabinoside*.—3 : 4-*iso*Propylidene β-ethyl-D-arabinoside (0·064 g.) was dissolved in dry pyridine (5 c.c.), and methanesulphonyl chloride (50% excess) was added to the cooled solution. After being kept at room temperature for one day, the mixture was poured into water and extracted with chloroform. The extract was dried ($MgSO_4$) and evaporated to a syrup, which could not be induced to crystallize; $[\alpha]_D^{22°}$ −172·6° (*c*, 0·464 in chloroform) (Found : OEt, 15·0. $C_{11}H_{20}O_7S$ requires OEt, 15·2%).

Attempt to prepare 2-*Iodo* 3 : 4-iso*Propylidene* β-*Ethyl*-D-*arabinoside*.—The foregoing syrupy 2-*methanesulphonyl* 3 : 4-iso*propylidene* β-*ethyl*-D-*arabinoside* (0·133 g.) and dry sodium iodide (1·1 mols.) were dissolved in dry acetone (25 ml.) and the solution was heated at 125° for 12 hours. After being cooled, the solution was evaporated to dryness, and the residue leached with water and then extracted with chloroform. The extract was dried ($MgSO_4$) and then evaporated. A syrup remained which had $[\alpha]_D^{24°}$ −174·3° (*c*, 0·450 in chloroform). It contained sulphur, but no halogen, and was unchanged material.

3 : 4-iso*Propylidene* α-*Methyl*-D-*arabinoside*.—α-Methyl-D-arabinoside (13·40 g.) was dissolved in acetone (700 c.c.) to which concentrated sulphuric acid (3·5 ml.) was added, and the mixture shaken overnight and then filtered. The filtrate was neutralised with anhydrous potassium carbonate and filtered. This filtrate was evaporated to dryness in the presence of potassium carbonate and the residue was extracted with ether. On removal of the ether, an oil remained, which distilled in two distinct fractions, A and B. Fraction A was a colourless oil, b. p. 125° (bath temp.)/0·01 mm. (5·35 g.), $[\alpha]_D^{22°}$ −27·8° (*c*, 1·798 in water), $n_D^{19.5°}$ 1·4543, and was 3 : 4-*iso*propylidene α-methyl-D-arabinoside (Found : OMe, 14·7. Calc. for $C_9H_{16}O_5$: OMe, 15·2%). Fraction B was a colourless syrup, b. p. 145—150° (bath temp.)/0·01 mm., which crystallised; recrystallised from light petroleum (b. p. 60—80°), it formed clusters of large colourless plates (1·0 g.), m. p. 60—62°, $[\alpha]_D^{21.5°}$ −55·5° (*c*, 0·576 in water) (Found : C, 51·2; H, 7·9%). This substance has not yet been identified.

2-*Methanesulphonyl* 3 : 4-iso*Propylidene* α-*Methyl*-D-*arabinoside*.—3 : 4-*iso*Propylidene α-methyl-D-arabinoside (1·835 g.) was dissolved in dry pyridine (15 c.c.), and the solution cooled to 0°. Methanesulphonyl chloride (50% excess, 1·1 g.), also dissolved in dry pyridine (10 ml.), was added at 0°, and the mixture kept at room temperature for 48 hours. After being poured into water, the aqueous solution was extracted with chloroform, and the extract washed with dilute sulphuric acid, with sodium hydrogen carbonate solution, and finally with water. It was dried ($MgSO_4$), and the solvent removed by evaporation. The syrupy product crystallised when triturated with water and recrystallised from absolute ethyl alcohol in clusters of colourless needles (0·6 g., 24%); m. p. 135° (sinters, 118—120°), $[\alpha]_D^{17.5°}$ −81·5° (*c*, 0·466 in chloroform) (Found : C, 42·6; H, 6·4; OMe, 11·3. $C_{10}H_{18}O_7S$ requires C, 42·5; H, 6·4; OMe, 10·9%).

Attempt to prepare 2-*Iodo* 3 : 4-iso*Propylidene* α-*Methyl*-D-*arabinoside*.—The foregoing 2-*methanesulphonyl* 3 : 4-iso*propylidene* α-*methyl*-D-*arabopyranoside* (0·40 g.) and dry sodium iodide (1·1 mols., 0·23 g.) were dissolved in dry acetone (10 ml.) and the solution was heated at 110° for 5 hours in a sealed tube. After filtration the solution was evaporated to dryness, and then leached with water. The residue was dissolved in chloroform, and the extract was dried ($MgSO_4$). The solvent was removed by evaporation, and the residue was shown to be unchanged material (m. p. 133—134° alone or in admixture with original material).

2-*Methanesulphonyl* α-*Methyl*-D-*arabopyranoside*.—2-Methanesulphonyl 3 : 4-*iso*propylidene α-methyl-D-arabopyranoside (0·44 g.) was dissolved in methyl alcohol (26·1 c.c.) containing 5N-hydrochloric acid (0·53 c.c.). The solution was heated under reflux for 6 hours, neutralised with silver carbonate, filtered, and then evaporated to dryness. The syrupy residue, when triturated with ethyl alcohol–water, crystallised. Recrystallisation from ethyl alcohol–water gave small nodules of 2-*methanesulphonyl* α-*methyl*-D-*arabopyranoside*, m. p. 176—178°, $[\alpha]_D^{19.5°}$ −150° (*c*, 0·10 in methyl alcohol) (Found : C, 34·2; H, 6·0; OMe, 13·6. $C_7H_{14}O_7S$ requires C, 34·7; H, 5·8; OMe, 12·81%).

Hydrolysis of 2-*Methanesulphonyl* 3 : 4-iso*Propylidene* β-*Ethyl*-D-*arabinoside*.—This methanesulphonyl derivative (0·50 g.) was heated under reflux for 5 hours with 1·75N-sulphuric acid (40 c.c.). The solution was neutralised with barium carbonate, filtered, and the filtrate evaporated to dryness under diminished pressure. The residue was extracted with alcohol, and the extract evaporated. The syrupy product crystallised on nucleation with 2-methanesulphonyl D-arabinose; recrystallised from ethyl alcohol–water, it had m. p. 65—66°; yield 0·15 g.

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