1028. *Synthesis of Mycinose (6-Deoxy-2,3-di-O-methyl-D-allose).**

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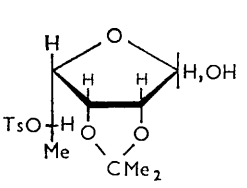
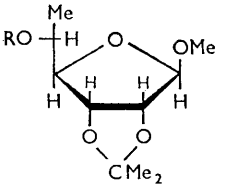
Mycinose, a sugar component of the antibiotic chalcomycin, has been synthesised and its identity with 6-deoxy-2,3-di-*O*-methyl-D-allose confirmed.

Methanolysis of the antibiotic chalcomycin [1] affords the methyl glycosides of two new sugars, chalcose and mycinose. The structure of chalcose has been established as 4,6-dideoxy-3-*O*-methyl-D-*xylo*-hexopyranose by degradative experiments,[2] synthesis,[3] and conversion [4] of desosamine (3,4,6-trideoxy-3-dimethylamino-D-*xylo*-hexopyranose) into chalcose. Mycinose has been identified [5] as 6-deoxy-2,3-di-*O*-methyl-D-allose (IV) on the basis of degradative experiments and n.m.r. studies on its methyl glycoside. We now report a stereospecific synthesis which confirms this structural assignment.

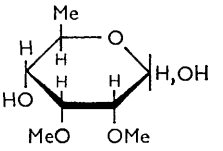
The conversion of 2,3-*O*-isopropylidene-5-*O*-tosyl-L-rhamnofuranose (I) into methyl 6-deoxy-2,3-*O*-isopropylidene-β-D-allofuranoside (II) with sodium methoxide was first reported by Levene and Compton [6] who established that inversion of configurations occurred at both C-4 and C-5 of the rhamnose derivative. This reaction provides an elegant synthesis for 6-deoxy-D-allose derivatives and has been used [7] in the synthesis of nucleosides containing this sugar; a mechanism for the reaction has also been suggested.[7]



(I)



(II: R = H)
(III: R = $PhCH_2$)



(IV)

In our synthesis, benzylation of the 5-hydroxyl group of the allofuranoside (II) was effected with benzyl chloride after formation of the alcoholate with sodium hydride, a procedure which has been used [8] in these laboratories in the alkylation of a number of carbohydrate derivatives. The derived benzyl ether (III) was deisopropylidenated in boiling methanolic hydrogen chloride and the resultant glycosides on methylation gave methyl 5-*O*-benzyl-6-deoxy-2,3-di-*O*-methyl-αβ-D-allofuranoside. After removal of the benzyl group with hydrogen over palladium–charcoal,[9] the glycoside mixture was hydrolysed with acid to give 6-deoxy-2,3-di-*O*-methyl-D-allopyranose (IV) which was identical with mycinose (see Experimental section); the direction of its mutarotation [10] indicated a β-configuration.

Experimental

Thin-layer chromatography was performed on silica gel (Merck) using either benzene–methanol (9 : 1, v/v) or ethyl acetate as the mobile phase. The dried chromatogram was sprayed with an acidified 3% (w/v) solution of vanillin in ethanol [11] and heated at 115° for 5—10 min. Solvents were generally removed under reduced pressure below 40°.

* Preliminary communication, *Proc. Chem. Soc.*, 1964, 83.

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[2] Woo, Dion, and Bartz, *J. Amer. Chem. Soc.*, 1961, **83**, 3352; Woo, Dion, and Johnson, *ibid.*, 1962, **84**, 1066.
[3] Kochetkov and Usov, *Tetrahedron Letters*, 1963, 519.
[4] Foster, Stacey, Webber, and Westwood, *Proc. Chem. Soc.*, 1963, 279.
[5] Dion, Woo, and Bartz, *J. Amer. Chem. Soc.*, 1962, **84**, 880.
[6] Levene and Compton, *J. Biol. Chem.*, 1936, **116**, 169.
[7] Reist, Goodman, Spencer, and Baker, *J. Amer. Chem. Soc.*, 1958, **80**, 3962.
[8] Jones and Willard, personal communication.
[9] Mozingo, *Org. Synth.*, 1946, **26**, 77.
[10] Hudson, *Adv. Carbohydrate Chem.*, 1948, **3**, 15.
[11] E. Merck AG, Darmstadt, "Chromatography," 2nd edn., p. 30.

Methyl 6-Deoxy-2,3-O-isopropylidene-β-D-allofuranoside (II).—This compound, b. p. 68—70°/0·2 mm., $[\alpha]_D$ −74° (*c* 2 in methanol), was prepared from L-rhamnose in three steps by a method previously described [7] {lit.,[7] b. p. 74—76°/0·7 mm., $[\alpha]_D$ −73·8° (*c* 2·3 in methanol)}.

Methyl 5-O-Benzyl-6-deoxy-2,3-O-isopropylidene-β-D-allofuranoside (III).—Sodium hydride powder (3 g.) was added gradually to a solution of methyl 6-deoxy-2,3-*O*-isopropylidene-β-D-allofuranoside (5 g.) in redistilled benzyl chloride (9 ml.); the mixture was kept at room temperature overnight and heated at 60° for 1·5 hr. On cooling, methanol (15 ml.) was added slowly, and the solution was heated under reflux for 30 min., cooled, dispersed in water (200 ml.), neutralised with 2N-hydrochloric acid, extracted with chloroform (3 × 100 ml.), and the combined chloroform extracts were washed with water (3 × 100 ml.) and dried ($MgSO_4$). Evaporation of the solvent left an oil which was fractionally distilled under reduced pressure to give the *product* (6·5 g.), b. p. 127—128°/0·2 mm., $[\alpha]_D^{30}$ −70° (*c* 2 in chloroform) (Found: C, 66·5; H, 7·9. $C_{17}H_{24}O_5$ requires C, 66·2; H, 7·8%). The infrared spectrum was in accord with the proposed structure.

Methyl 5-O-Benzyl-6-deoxy-αβ-D-allofuranoside.—A solution of the foregoing compound (6·4 g.) in methanol (50 ml.) containing concentrated hydrochloric acid (1 ml.) was heated under reflux for 2 hr. After removal of the solvent the residue was extracted with chloroform (200 ml.) and the extract washed with sodium hydrogen carbonate solution and water, dried ($MgSO_4$), and filtered; evaporation under reduced pressure gave the *products* as a pale yellow oil (4·6 g.), $[\alpha]_D^{24}$ −32° (*c* 2 in chloroform). The infrared spectrum of the glycoside mixture exhibited strong bands at *ca.* 3600 cm.$^{-1}$ (OH), and absorption at 1380 cm.$^{-1}$ (isopropylidene group) was negligible.

Methyl 5-O-Benzyl-6-deoxy-2,3-di-O-methyl-αβ-D-allofuranoside.—Sodium hydride powder (1·5 g.) was added in small portions with cooling (0°) to a solution of the foregoing glycosides (4·6 g.) in methyl iodide (12 ml.). The solution was left at room temperature overnight, unreacted sodium hydride destroyed by careful addition of methanol (5 ml.), the solution poured into chloroform (250 ml.), and the organic layer washed with water, decolourised with activated charcoal, and dried ($MgSO_4$). The filtered solution was evaporated to dryness and the residual pale yellow oil distilled, to give the *product mixture* (3·1 g.), b. p. 126°/0·1 mm., $[\alpha]_D^{35}$ −8° (*c* 2 in chloroform), which exhibited no hydroxyl stretching absorption in its infrared spectrum.

6-Deoxy-2,3-di-O-methyl-β-D-allose (IV).—A solution of the foregoing glycosides (3·0 g.) in ethanol (100 ml.) containing palladium–charcoal [9] (3 g.) was shaken under slight pressure of hydrogen at room temperature for 36 hr. The solvent was removed from the filtered solution under reduced pressure and the debenzylated material (1·9 g.) hydrolysed with N-sulphuric acid (50 ml.) at 95—100° for 3 hr. After neutralisation ($BaCO_3$), water was removed under reduced pressure and the residue dissolved in chloroform and dried ($MgSO_4$). The syrupy residue, obtained on evaporation of the solvent, crystallised from chloroform–light petroleum (b. p. 100—120°) to give the *product* (0·7 g.) as fine needles, m. p. 100—102°, $[\alpha]_D^{33}$ −41° (3 min.) ⟶ −29° (final) (*c* 1·5 in water) {lit.,[5] m. p. 102—106°, $[\alpha]_D^{25}$ −46° ⟶ −42° (2 min.) ⟶ −29° (final) (*c* 1·56 in water)} (Found: C, 50·3; H, 8·5. $C_8H_{16}O_5$ requires C, 50·0; H, 8·4%). The chromatographic properties, infrared spectrum (KBr disc), and *X*-ray powder photograph of the synthetic compound were indistinguishable from those of natural mycinose.

Methyl 6-Deoxy-2,3-di-O-methyl-β-D-allopyranoside.—6-Deoxy-2,3-di-*O*-methyl-D-allose (0·25 g.) in dry methanol (25 ml.) containing concentrated hydrochloric acid (3 ml.) was boiled under reflux for 6 hr. The cooled solution was neutralised with solid potassium carbonate, filtered, and the solvent removed. Thin-layer chromatography of the residue revealed four components. The residue was taken up in chloroform, and an aliquot part of the dried ($MgSO_4$) chloroform solution chromatographed on silica gel. The component eluted first from the column with ethyl acetate was recrystallised from n-hexane, to give the *product* (6 mg.), m. p. and mixed m. p. 83—84° (lit.,[5] m. p. 88—88·5°); the infrared spectra (KBr disc) and thin-layer chromatographic properties of the glycosides prepared from the natural and synthetic sugars were indistinguishable.

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