Carbohydrate Research, 36 (1974) 205–206

Note

An alternative synthesis of 3,6-di-*O*-methyl-D-galactose

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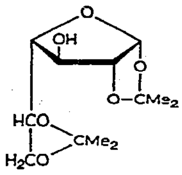
(Received February 18th, 1974; accepted for publication, March 19th, 1974)

There is interest in a convenient synthesis of 3,6-di-*O*-methyl-D-galactose in view of the presence[1] of this sugar among the products of methylation analysis of polysaccharides related to ξ-carrageenan. Although Penman and Rees[1] have recently reported a sixteen-stage synthesis of 3,6-di-*O*-methyl-D-galactose from D-galactose, the difficulties of accomplishing selective 3-*O*-substitution in the galactose series by classical methods are well known. The ease of conversion of D-glucose into 1,2:5,6-di-*O*-isopropylidene-α-D-galactofuranose (**1**) (in seven steps[2]) has overcome many of these difficulties, and the effectiveness of this approach in the synthesis of 3-*O*-substituted D-galactose derivatives is illustrated by a recent synthesis[3b] of D-digitalose (6-deoxy-3-*O*-methyl-D-galactose). An alternative and convenient synthesis of 3,6-di-*O*-methyl-D-galactose (**5**) is described below.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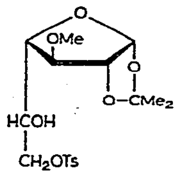
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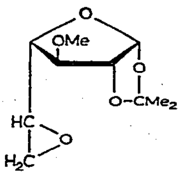
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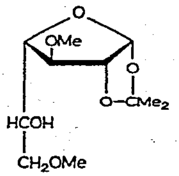
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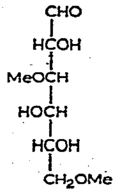
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Our synthesis[3] of D-digitalose involved the controlled treatment of 1,2-*O*-isopropylidene-3-*O*-methyl-6-*O*-toluene-*p*-sulphonyl-α-D-galactofuranose (**2**) with methanolic sodium methoxide at low temperature to furnish the 5,6-anhydro sugar **3** by intramolecular displacement of the sulphonyloxy group. However, on prolonged treatment with methanolic sodium methoxide at room temperature, the sulphonate **2** was converted into 1,2-*O*-isopropylidene-3,6-di-*O*-methyl-α-D-galactofuranose (**4**) by regiospecific opening of the intermediate oxirane **3** at C-6 with methoxide ion. Mild hydrolysis of compound **4** with acid afforded crystalline 3,6-di-*O*-methyl-D-galactose (**5**), exhibiting physical constants in close agreement with those reported[1].

EXPERIMENTAL

T.l.c. was performed on microscope slides coated with Kieselgel (Merck), and spots were detected with vanillin–sulphuric acid[4]. N.m.r. spectra were determined with a Perkin–Elmer R10 spectrometer for solutions in deuteriochloroform containing 1% of tetramethylsilane as internal standard. Optical rotations were measured with a Perkin–Elmer 141 automatic polarimeter.

1,2-O-Isopropylidene-3,6-di-O-methyl-α-D-galactofuranose (**4**). — A solution of the syrupy toluene-*p*-sulphonate **2**[3] (~1.15 g) in methanolic M sodium methoxide (100 ml) was kept at room temperature for 4 days; t.l.c. (toluene–acetone, 4:1) then showed that a single product had been formed. The excess of base was neutralized with solid carbon dioxide, the solution was concentrated, and the dimethylated sugar **4** (0.37 g), b.p. 105° (bath)/0.1 mmHg, $[\alpha]_D$ −39° (*c* 0.8, chloroform), was obtained on distillation (Found: C, 52.8; H, 8.3. $C_{11}H_{20}O_6$ calc.: C, 53.2; H, 8.1%). N.m.r. data: τ 4.05 (1H, d, $J_{1,2}$ 4 Hz, H-1), 5.38 (1H, d, H-2), 6.58 (6H, s, 2 OMe), and 8.45 and 8.66 (6H, 2s, CMe_2).

3,6-Di-O-methyl-D-galactose (**5**). — The acetal **4** (0.27 g) in 0.25M sulphuric acid (5 ml) was heated at 50° for 2 h, the acid was then neutralized with barium carbonate, and inorganic material was filtered off. The filtrate was concentrated to give a virtually quantitative yield of a syrup that slowly crystallized. Recrystallization from acetone gave **5**, m.p. 100.5–101°, $[\alpha]_D$ +93° (*equilib.*, *c* 0.6, water); lit.[1] m.p. 101–102°, $[\alpha]_D$ +93.2° (*c* 1.1, water). The infrared spectrum of this material was indistinguishable from that of an authentic sample (kindly provided by Professor D. A. Rees). Since the aqueous solution exhibited downwards mutarotation, it is assumed that the α-D-aldopyranose was obtained crystalline.

ACKNOWLEDGMENTS

We thank the University of Dundee for the award of a research scholarship (to A.J.R.), and I. Da'aboul for helpful discussion.

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