

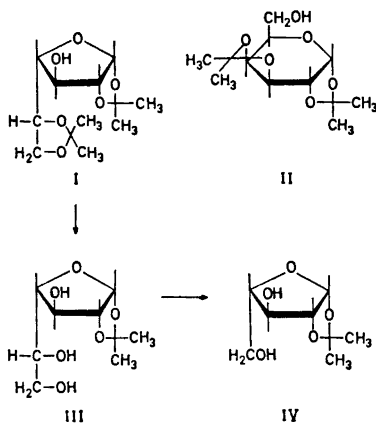
Isopropylidene Derivatives of α -D-Galactofuranose

SVEIN MORGENLIE

*Department of Chemistry, Agricultural
University, N-1432 As-NLH, Norway*

1,2:5,6-Di-*O*-isopropylidene- α -D-galactofuranose (I) has found only limited use in synthetic carbohydrate chemistry, being less accessible than the corresponding D-glucose derivative. This di-*O*-isopropylidene-galactofuranose has been synthesized by two different routes from the corresponding D-glucose derivative in three¹ and six² steps, respectively. Formation of the compound in low yield directly from D-galactose by treatment with acetone-cupric sulphate at 100°C has, however, been reported.³ Isolation of this compound from the main product, 1,2:3,4-di-*O*-isopropylidene- α -D-galactopyranose (II), was achieved by gas-liquid chromatography, and the method is not suitable on a synthetic scale. 1,2:5,6-Di-*O*-isopropylidene- α -D-galactofuranose (I) was required as precursor in the synthesis of the 1,2-*O*-isopropylidene derivative, and it was hoped that a modification of the direct acetonation method might offer a simple way to the di-*O*-isopropylidene-galactofuranose (I) also on a larger scale.

Treatment of D-galactose with cupric sulphate in refluxing acetone after prior



dissolution of the sugar in hot dimethylformamide was found to enhance the proportion of 1,2:5,6-di-*O*-isopropylidene- α -D-

galactofuranose (I) relative to the pyranose derivative (II). The total yield of di-*O*-isopropylidene derivatives was, however, reduced to 50–60%. The furanose and pyranose diacetals were formed in about equal amounts, and it was possible to isolate much of the furanose isomer by crystallization from the product mixture. The furanose diacetal (I) was obtained in this way in 20–22% yield in one step from D-galactose without chromatographic separation, and despite the low yield, the method should offer a useful alternative to the previously reported three- and six-step syntheses.^{1,2}

Partial acid hydrolysis of the 5,6-*O*-isopropylidene group of the diacetal (I) yielded 1,2-*O*-isopropylidene- α -D-galactofuranose (III). This compound could be obtained in 24% yield from D-galactose by taking advantage of the stability of 1,2:3,4-di-*O*-isopropylidene- α -D-galactopyranose (II) at conditions sufficient to remove the 5,6-*O*-isopropylidene group of the furanose isomer (I). Weak acid hydrolysis of the di-*O*-isopropylidene-galactose mixture thus gave 1,2-*O*-isopropylidene- α -D-galactofuranose (III) as the only monoisopropylidene derivative, easily separable from the unhydrolyzed 1,2:3,4-di-*O*-isopropylidene- α -D-galactopyranose (II).

The identity of the monoisopropylidene-galactose (III) was established by periodate oxidation followed by borohydride reduction to 1,2-*O*-isopropylidene- β -L-arabinofuranose (IV), and by re-acetonation of the monoisopropylidene-galactose (III) with cupric sulphate-acetone, which gave the diisopropylidene-galactofuranose (I) exclusively.

High temperature^{4,5} and dimethylformamide as a solvent^{6,7} are factors known to favor furanose formation in solutions of reducing sugars, and a furanose content higher than 50% was indicated for D-galactose under conditions similar to those employed in the synthesis of the di-*O*-isopropylidene-galactofuranose (I) by trimethylsilylation and subsequent GLC in this laboratory. This high furanose content is possibly the explanation of the relatively high yield of di-*O*-isopropylidene-galactofuranose obtained.

Experimental. Thin layer chromatography (TLC) was performed on silica gel G in benzene-ethanol 3:1 (v/v) and benzene-ethanol 4:1; the spots were detected with diphenylamine-aniline-phosphoric acid.⁸ Paper chromatography was run on Whatman No. 1 paper

in butanol-pyridine-water 5:3:2, and electrophoresis on Whatman No. 1 paper in borate buffer, pH 10; the spots were detected with aniline hydrogenphthalate. Gas-liquid chromatography (GLC) was effected with a Perkin Elmer F-11 gas chromatograph, equipped with a flame ionization detector and a stainless steel column (2 m x 3 mm) containing 3% XE-60 on Gas Chrom Q (100/120 mesh); the nitrogen flow rate was 20 ml/min. The operating temperature was 175°C.

1,2:5,6-Di-O-isopropylidene- α -D-galactofuranose (I). A solution of D-galactose (3 g) in hot dimethylformamide (30 ml) was added to rapidly stirred anhydrous cupric sulphate (15 g) in acetone (90 ml), and stirring under reflux was continued for 24 h. After addition of more cupric sulphate (5 g) and acetone (100 ml), the mixture was stirred under reflux for additional 24 h. Solid material was then filtered off, and the solution concentrated to a thin syrup. The syrup was dissolved in water (50 ml) and the water solution extracted with chloroform (5 x 10 ml). The combined chloroform extracts were dried over sodium sulphate, and the solvent was evaporated. The residue (2.3 g) contained two compounds, indistinguishable from authentic 1,2:3,4-di-O-isopropylidene- α -D-galactopyranose (II) and 1,2:5,6-di-O-isopropylidene- α -D-galactofuranose (I) by TLC and GLC, the latter having the lowest mobility by both methods. Quantitative GLC showed that the ratio of the amounts of the furanose (I) to pyranose (II) derivative was 6:5. The mixture of di-isopropylidene derivatives was extracted with light petroleum (b.p. 40–56°C) (3 x 10 ml) at 35°C to remove some of the di-isopropylidene-galactopyranose derivative (II). The residue was dissolved in light petroleum-diethyl ether, from which 1,2:5,6-di-O-isopropylidene- α -D-galactofuranose (I) crystallized, (0.95 g, 22%), m.p. after recrystallization from the same solvent mixture 97–98°C (lit.¹ 97.5–98°C), $[\alpha]_D -34^\circ$ (c 1, methanol) (lit.¹ –35.3°).

1,2-O-Isopropylidene- α -D-galactofuranose (III). A mixture of di-O-isopropylidene-galactose derivatives (I and II) prepared from D-galactose (3 g) as described above, was dissolved in 40% aqueous acetic acid (30 ml), and the solvents were evaporated in a stream of air over night. The residue was dissolved in chloroform (25 ml), and the chloroform solution was extracted with water (2 x 15 ml). The combined water extracts were re-extracted with chloroform (2 x 10 ml), and the water evaporated under reduced pressure. Crystallization of the residue from ethyl acetate gave 1,2-O-isopropylidene- α -D-galactofuranose (III) (870 mg, 24% based on galactose), m.p. 102–103°C, $[\alpha]_D -27^\circ$ (c 2, water). (Found: C 48.83; H 7.24. Calc. for C₉H₁₆O₆: C 49.08; H 7.34.)

1,2-O-Isopropylidene- β -L-arabinofuranose (IV). To 1,2-O-isopropylidene- α -D-galactofuranose (III) (40 mg) in water (2.5 ml) was added sodium periodate (60 mg) in water (3 ml). After 20 min 0.5 M barium acetate solution was added until complete precipitation, and the solution was filtered and treated with Dowex 50 W (H⁺) ion exchanger. Sodium borohydride (50 mg) in water (3 ml) was then added, the solution kept at room temperature for 2 h and then treated with Dowex 50 W (H⁺) ion exchanger once more. The solvent was evaporated, and the boric acid removed by repeated codistillation with methanol. The residue gave a single spot when subjected to TLC. Preparative TLC and crystallization from ethyl acetate gave 1,2-O-isopropylidene- β -L-arabinofuranose (IV) (9 mg), m.p. 113–115°C (lit.⁹ 117–118°C). Hydrolysis of the product at 100°C for 4 h in 30% aqueous acetic acid and subsequent removal of the solvents under reduced pressure, gave a syrup which was indistinguishable from authentic arabinose by paper chromatography and electrophoresis.

1,2:5,6-Di-O-isopropylidene- α -D-galactofuranose (I) from 1,2-O-isopropylidene- α -D-galactofuranose (III). 1,2-O-Isopropylidene- α -D-galactofuranose (III) (20 mg) in acetone (5 ml) was stirred with anhydrous cupric sulphate (0.5 g) for 2 h. TLC and GLC showed the presence of a single component, indistinguishable from authentic 1,2:5,6-di-O-isopropylidene- α -D-galactofuranose (I). Filtration of the solution and evaporation of the solvent gave a crystalline residue (22 mg, 93%) m.p. 94–97°C, mixed m.p. 95–97°C.

Acknowledgement. The author is indebted to Miss Astrid Fosdahl for valuable technical assistance.

1. Paulsen, H. and Behre, H. *Carbohydr. Res.* **2** (1966) 80.
2. Brimacombe, J. S., Gent, P. A. and Stacey, M. *J. Chem. Soc. C* **1968** 567.
3. DeJongh, D. C. and Biemann, K. *J. Am. Chem. Soc.* **86** (1964) 67.
4. Acree, T. E., Shallenberger, R. S., Lee, C. Y. and Einset, J. W. *Carbohydr. Res.* **10** (1969) 355.
5. Acree, T. E., Shallenberger, R. S. and Mattick, L. R. *Carbohydr. Res.* **6** (1968) 498.
6. Hveding, J. A., Kjølborg, O. and Reine, A. *Acta Chem. Scand.* **27** (1973) 1427.
7. Kuhn, R. and Grassner, H. *Ann.* **610** (1957) 122.
8. Schwimmer, S. and Bevenue, A. *Science* **123** (1956) 543.
9. Levene, P. A. and Compton, J. *J. Biol. Chem.* **116** (1936) 189.

Received October 11, 1973.