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Note

Derivatives of 1,2-*O*-isopropylidene-α-D-galactofuranose*

CHRIS L. BREWER, SERGE DAVID†, AND ALAIN VEYRIÈRES
Département de Chimie Organique, Bât. 420, Université de Paris-Sud, 91405 Orsay (France)
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In an extension of our work on D-galactose derivatives having positions 3 and 6 unprotected[1], we have examined the possibility of a derivative in the furanose form. The known 3-*O*-benzoyl-1,2:5,6-di-*O*-isopropylidene-α-D-galactofuranose[2] (**1**) was selected as our starting material.

Hydrolysis of the 3-benzoate **1** with 70% acetic acid selectively removed the 5,6-*O*-isopropylidene group to give 3-*O*-benzoyl-1,2-*O*-isopropylidene-α-D-galactofuranose (**2**), which underwent isomerisation to the 6-benzoate (**3**) on treatment with dilute aqueous base.

Selective benzoylations of carbohydrate derivatives with *N*-benzoylimidazole[3] have already been reported[4,5]. We found that when the monobenzoate **2** was treated with one equivalent of this reagent, 3,6-di-*O*-benzoyl-1,2-*O*-isopropylidene-α-D-galactofuranose (**4**) was obtained as the major product. That isomerisation did not occur during this reaction was demonstrated by the observation that on replacement of *N*-benzoylimidazole with imidazole, only the starting 3-benzoate (**2**) was recovered and no 6-benzoate was detected. The dibenzoate **4** was treated with dihydropyran and an acid catalyst and the benzoate groups were subsequently removed with aqueous methanol–triethylamine to give, after chromatography, 1,2-*O*-isopropylidene-5-*O*-tetrahydropyranyl-α-D-galactofuranose (**5**). Although this product is presumably a mixture of diastereo-isomers, only one spot was detected on t.l.c. in various solvents. The p.m.r. spectrum, however, showed four singlets due to the isopropylidene methyl groups. The structures of the benzoates **2**, **3**, and **4** were assigned from their p.m.r. spectra. All the compounds in which a 3-*O*-benzoyl group was present (*i.e.* **1**, **2**, **4**) had a one proton resonance, either as a broad singlet or a narrow doublet, in the region δ 5.3–5.5, attribuable to H-3. These signals were absent in the spectrum of the 6-benzoate (**3**). On the other hand, in compounds in which a 6-*O*-benzoyl group was present (*i.e.* **3** and **4**), the peaks due to H-6, H-6′ were downfield in relation to those

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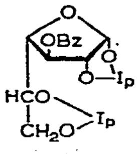
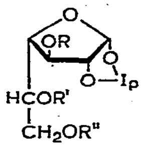
[†] To whom all correspondence should be sent concerning this note.

of **2**. 5-Benzoates were excluded on the grounds that H-5 would, in these cases, give rise to a low-field multiplet, which was not observed.



1



2 R=Bz, R'=R"=H
3 R=R'=H, R"=Bz
4 R=R"=Bz, R'=H
5 R=R"=H, R'=tetrahydropyranyl

EXPERIMENTAL

General methods. — See Part I[1].

*3-O-Benzoyl-1,2:5,6-di-O-isopropylidene-α-*D*-galactofuranose* (**1**). — This compound was prepared according to Brimacombe *et al.*[2] (yield 80%), m.p. 85–88°, $[\alpha]_D^{20}$ ±0° (*c* 5.0, chloroform); i.r. data: ν_{max}^{Nujol} 1715 cm^{-1} (CO); p.m.r. data (chloroform-*d*): δ 3,80–4,60 (H-4, H-5, H-6, H-6′), 4.76 (d, $J_{1,2}$ 6.2 Hz, H-2), 5.19 (d, J3,0 Hz, H-3), and 6.04 (d, H-1); lit.[2]: m.p. 86–87°, $[\alpha]_D^{20}$ −2° (*c* 0.5, chloroform).

*3-O-Benzoyl-1,2-O-isopropylidene-α-*D*-galactofuranose* (**2**). — The diacetal **1** (1.1 g) was treated for 4 h at 35–40° with 7:3 acetic acid–water (40 ml) whence t.l.c. (ether) showed complete reaction. The reaction mixture was diluted with ice–water and extracted with chloroform. The chloroform extracts were dried (magnesium sulfate) and evaporated to dryness. The residue (930 mg, 95%) was crystallized from methanol–water to give pure **2**, m.p. 105–107°, $[\alpha]_D^{20}$ +41.0° (*c* 1.0, chloroform); i.r. data: ν_{max}^{KBr} 1715 (CO) and 3280 cm^{-1} (broad, OH); p.m.r. data (chloroform-*d*): δ 2.95 (OH), 3.25 (OH), 3.86 (m, H-6, H-6′), 4.06 (q, $J_{4,5}$ 8.2 Hz, $J_{5,6}$ 4.5 Hz, H-5), 4.32 (q, $J_{3,4}$ 2 Hz, H-4), 4.85 (d, $J_{1,2}$ 4.5 Hz, H-2), 5.36 (d, H-3), and 6,07 (d, H-1).

Anal. Calc. for $C_{16}H_{20}O_7$: C, 59.25; H, 6.22. Found: C, 59.12; H, 6.20.

*6-O-Benzoyl-1,2-O-isopropylidene-α-*D*-galactofuranose* (**3**). — A solution of **2** (220 mg) in acetone (10 ml) was cooled in an ice–water bath and treated with 0.05M aqueous sodium hydroxide solution (10 ml). After 10 min the reaction mixture was diluted with ice–water and extracted with chloroform. The combined extracts were dried (magnesium sulfate) and evaporated to dryness. The crude residue was purified by preparative layer chromatography (Merck Silica Gel, 200×200×2 mm) (in ether) to give a syrup which cristallized (120 mg, 60%). The product was recristallized from chloroform–light petroleum (40–60°) (53 mg, 26%), m.p. 93–95°, $[\alpha]_D^{20}$ −13,8° (*c* 0.6, chloroform); i.r. data: ν_{max}^{KBr} 1715 (CO) and 3440 (OH) cm^{-1}; p.m.r. data (chloroform-*d*): δ 3.12 (broad, 2 OH), 4.06 (H-5), 4.25–4.54 (H-3, H-4, H-6, H-6′), 4.61 (d, $J_{1,2}$ 4.5 Hz, H-2), and 5.94 (d, H-1).

Anal. Calc. for $C_{16}H_{20}O_7$: C, 59.25; H, 6.22. Found: C, 59.13; H, 6.04.

*3,6-Di-O-benzoyl-1,2-O-isopropylidene-α-*D*-galactofuranose* (**4**). — To a solution of imidazole (335 mg) in dry chloroform (5 ml) at 0° was added a solution of benzoyl chloride (346 mg) in dry chloroform (2.5 ml). The imidazole hydrochloride was removed by filtration and washed with dry chloroform (2.5 ml). The combined filtrates were immediately added to a solution of **2** (795 mg) in dry chloroform (10 ml) and the mixture heated at reflux on an oil bath for 17 h. The cooled reaction mixture was diluted with a small amount of chloroform, extracted with aqueous sodium hydrogen carbonate solution and water, dried (magnesium sulfate), and evaporated to dryness to give a syrup which was purified by preparative layer chromatography (3:2 chloroform–ether). The major product was obtained as a crystalline solid wich was recrystallized from ether–light petroleum (40–60°) to give pure **4** (590 mg, 56%) m.p. 127–129°, $[\alpha]_D^{20}$ +10,2° (*c* 1, chloroform); i.r. data: ν_{max}^{KBr}: 1690 (CO), 1720 (CO), and 3495 (OH) cm^{-1}; p.m.r. data (chloroform-*d*): δ 3.04 (OH), 4.36 (H-6, H-6′), 4.48–4.63 (H-4, H-5), 4.87 (d, $J_{1,2}$ 4.5 Hz, H-2), 5.50 (H-3), and 6.07 (d, H-1).

Anal. Calc. for $C_{23}H_{24}O_8$: C, 64.48; H, 5.65. Found: C, 64.63; H, 5.59.

In large-scale preparations, **4** was crystallized directly from the crude syrup with ether–light petroleum (40–60°) and was essentially pure after one recrystallization.

1,2-O-Isopropylidene-5-O-tetrahydropyranyl-α-D-galactofuranose (**5**). — A solution of **4** (900 mg) in dry 1,4-dioxane (40 ml) containing *p*-toluenesulfonic acid (40 mg) and dihydropyran (4 ml) was stirred for 1 h at room temperature and then diluted with chloroform (100 ml). The solution was washed with saturated aqueous sodium hydrogen carbonate and water, dried (magnesium sulfate), and evaporated to dryness. The residual syrup was dissolved in methanol (40 ml) and water (10 ml), treated with triethylamine (3 ml), and kept overnight. The reaction mixture was then evaporated to dryness to give a yellow syrup which was dissolved in chloroform, dried (magnesium sulfate), and evaporated to dryness. The residue was purified by column chromatography (39:1 ether–methanol) to give a colorless syrup (671 mg, 74%), $[\alpha]_D^{20}$ 0.0° (*c* 1.25, chloroform); i.r. datum: ν_{max}^{film} 3455 cm^{-1} (broad, OH).

Anal. Calc. for $C_{14}H_{24}O_7$: C, 55.25; H, 7.95. Found: C, 55.08; H, 8.02.

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