Note

1,2,5-*O*-Ethylidyne-α-D-galactofuranose

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Helferich and co-workers[1,2], as well as Ness and Fletcher[3–5], have shown that tri-*O*-benzylidyne-hexose and -pentose derivatives can be obtained from di-*O*-(benzyloxybenzylidene)aldoses or from partially benzoylated aldosyl halides. Kochetkov *et al.*[6] have recently reported the spontaneous cyclization of 1,2-*O*-(methoxybenzylidene)-β-L-arabinofuranose to 1,2,5-*O*-benzylidyne-β-L-arabinofuranose under neutral conditions. Prior to this, Fletcher and Ness[3] had similarly observed that 1,2-*O*-(1-benzyloxybenzylidene)-α-D-ribopyranose rearranges to 1,2,4-*O*-benzylidyne-α-D-ribose in faintly acidic aqueous acetone. We now report a new *O*-alkylidyne-hexose, namely, 1,2,5-*O*-ethylidyne-α-D-galactofuranose.

3,5,6-Tri-*O*-acetyl-1,2-*O*-(1-methoxyethylidene)-α-D-galactofuranose[7] was treated with sodium methoxide in methanol. The resulting solution, containing 1,2-*O*-(1-methoxyethylidene)-α-D-galactofuranose, was passed through a column of Amberlite IRC-50(H^+) cation-exchange resin, and evaporated. The resulting syrup showed two major components by t.l.c., and was fractionated by column chromatography with silica gel. The faster-moving material (**1a**) crystallized. It was stable indefinitely when kept cold, and its rate of movement in t.l.c. was unaffected by treatment with sodium methoxide in methanol.

Compound **1a** reacted rapidly with water to yield a crystalline material (**2**) whose analysis showed it to be a mono-*O*-acetylhexose. Treatment of **2** with sodium methoxide in methanol produced a compound having the same mobility as galactose in t.l.c. When compound **1a** was treated with methanol containing a trace of *p*-toluenesulfonic acid, a low-melting, hygroscopic, crystalline substance was obtained having the elemental composition of a methyl *O*-acetylgalactoside (**3**). Treatment of **3** with sodium methoxide in methanol resulted in the formation of a compound chromatographically indistinguishable from methyl β-D-galactofuranoside. Treatment of **1a** with phenyl isocyanate in pyridine gave a crystalline dicarbanilate (**1b**). Chemical-ionization mass spectroscopy[8] of **1a** showed a strong mass peak of 205 for M+1 (see Fig. 1). The 100-MHz p.m.r. spectrum of **1a** in methyl sulfoxide-d_6 showed the following features: a doublet centered at $\delta \sim 5.90$ that persisted after the addition

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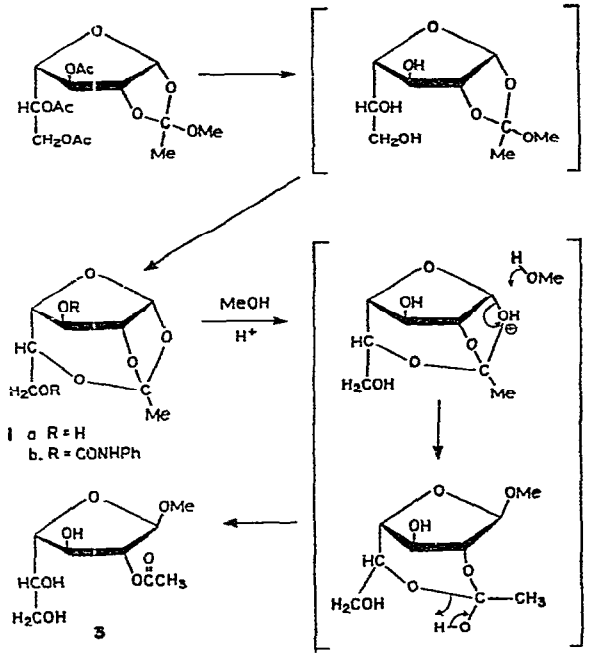

of D_2O (assigned to a β-H-1), a doublet at δ ~5.37 that disappeared upon addition of D_2O (OH-3), a triplet at δ ~4.75 that disappeared on addition of D_2O (OH-6), and a doublet at δ ~4.08 that persisted on addition of D_2O, but collapsed to a singlet (assigned to H-3). In addition, a clear signal for the C-CH_3 group was present at δ 1.48 (see Fig. 2, A and B). On g.l.c. of its per(trimethylsilyl) derivative, the methyl

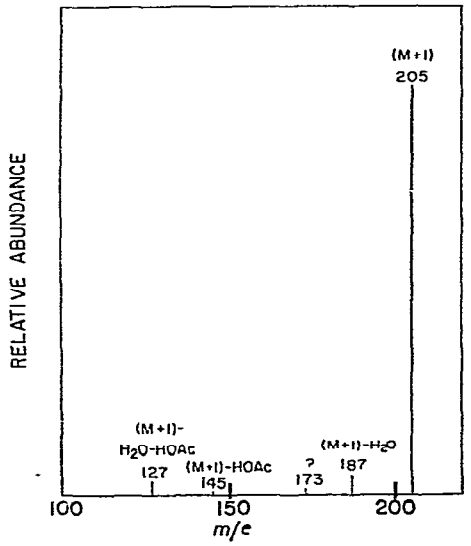

Fig. 1. Chemical-ionization mass spectrum of **1a** (CH_4, probe temp. 200°, block temp. 70°).

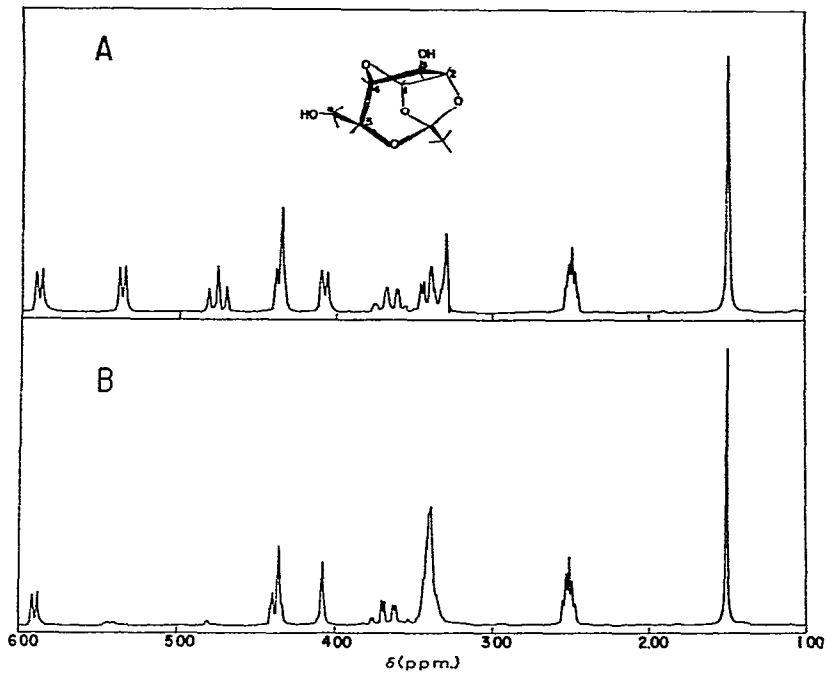

Fig 2 The 100-MHz p.m r. spectrum of **1a** (A, in methyl sulfoxide-d_6; B, in methyl sulfoxide-d_6 containing 23% of D_2O by volume).

O-acetylgalactoside **3** derived from **1a** showed a single peak that was different in its rate of movement from per(trimethylsilyl)ated methyl 6-*O*-acetyl-β-D-galactofuranoside prepared by Roy and Glaudemans[9]. Treatment of **3** with pyridine for 45 min followed by g.l.c. of its per(trimethylsilyl) derivative failed to change its rate of movement; this seemed to indicate that **3** is not methyl 5-*O*-acetyl-β-D-galactofuranoside, but, probably, the corresponding 2-acetate, as the former would be expected to rearrange rapidly to the 6-*O*-acetyl glycoside. Periodate oxidation of **3** confirmed this supposition; compound **3** consumed ~1 mole of periodate and produced ~1 mole of formaldehyde per mole of **3**. When **3** was oxidized with periodate, the resulting product reduced with sodium borohydride, and the reduction product hydrolyzed in aqueous sulfuric acid, arabinose was obtained, as shown by t.l.c. The acid-catalyzed opening of the alkylidyne system in **1a** would, at least initially, lead to either methyl 2- or 5-*O*-acetyl-β-D-galactofuranoside. It is, sterically, most unlikely that either of these two possible products would then rearrange to the corresponding 3-acetate. From the above data, it may therefore be concluded that **3** is methyl 2-*O*-acetyl-β-D-galactofuranoside. At this time, we are unable to propose a definite structure for monoacetate **2**.

EXPERIMENTAL

1,2,5-O-Ethylidyne-α-D-galactofuranose (**1a**). — β-D-Galactofuranose pentaacetate (11 g, 31.8 mmoles) was converted into the crystalline chloride[10], and this

was converted into syrupy 3,5,6-tri-*O*-acetyl-1,2-*O*-(1-methoxyethylidene)-α-D-galactofuranose as previously described[7]. This compound was dissolved in methanol (50 ml), sodium methoxide (50 mg) was added, and the solution was kept overnight at room temperature. The solution was passed through a column of Amberlite IRC-50 (H^+) cation-exchange resin (prewashed with methanol) and the eluate was concentrated. Examination by t.l.c. (5:1 ether–methanol) showed five components, the two fastest-moving of which greatly preponderated. The mixture was fractionated on a column of silica gel, with the same solvent mixture as eluant, and the fastest-moving material was collected. It was recrystallized from ethyl acetate–cyclohexane to yield pure **1a** (1.58 g; 24% based on the pentaacetate), m.p. 116–118°, $[\alpha]_D^{20}$ +34.8° (*c* 1, methanol)

Anal. Calc. for $C_8H_{12}O_6$: C, 47.06; H, 5.93. Found: C, 46.98; H, 5.73.

The 100-MHz p.m.r. spectrum of **1a** in methyl sulfoxide-d_6 is shown in Fig. 2 A. Exchangeable hydrogen atoms were then replaced by deuterium through the addition of D_2O (see Fig. 2 B), the final concentration of D_2O in the solution being 23% by volume. In view of the fact that **1a** reacts rapidly with water (see later) to yield a monoacetate of D-galactose, it was necessary to check the spectral solution afterwards for possible decomposition of **1a** following addition of D_2O. No hydrolysis product of **1a** was detected by t.l.c. on silica gel using 5:1 ether–methanol, which readily separates **2** (see later) from **1a**.

1,2,5-O-Ethylidyne-3,6-di-O-(N-phenylcarbamoyl)-α-D-galactofuranose (**1b**). Compound **1** (100 mg) was dissolved in pyridine (3 ml). Phenyl isocyanate (10 drops) was added, and the mixture was kept for six days at room temperature. The solution was evaporated to dryness, and (in order to remove pyridine) ethanol, toluene, and ethanol were successively added, and evaporated off *in vacuo*. The solid residue was recrystallized from methanol to yield **1b**, 173 mg (80%), m.p. 195–197°, $[\alpha]_D^{20}$ +46.1° (*c* 1, acetone); ν_{max}^{Nujol} 3380 (NH stretching), 1720 (Amide I), and 1600 cm^{-1} (Amide II).

Anal. Calc. for $C_{22}H_{22}N_2O_8$: C, 59.73; H, 5.01; N, 6.33. Found: C, 59.94; H, 5.14; N, 6.13.

O-Acetyl-D-galactose (**2**). — Compound **1a** (300 mg) was dissolved in water (2.5 ml). After 20 min, it had largely been converted into a new product having approximately one third the rate of movement of the starting material, in t.l.c. on silica gel with 5:1 ether–methanol. After 24 h, the solution was evaporated, and the residue was recrystallized from cold ethanol–ethyl acetate to yield a compound (241 mg, 74%) having m.p. 129–135°.

Anal. Calc. for $C_8H_{14}O_7$: C, 43.45; H, 6.38. Found: C, 43.64; H, 6.58.

Treatment of this material with sodium methoxide in methanol yielded a product having the same R_F as galactose in t.l.c. on silica gel with 5:1 ether–methanol.

Methyl 2-O-acetyl-β-D-galactofuranoside (**3**). — A solution of **1a** (200 mg) in methanol (8 ml) was treated with *p*-toluenesulfonic acid (3 mg) and kept at room temperature. Virtually no starting material could be detected after 45 min (t.l.c. on silica gel with 5:1 ether–methanol). The mixture was concentrated, immediately

added to the top of a column of silica gel, and eluted with the same solvent. Appropriate fractions were pooled, and evaporated. The resulting syrup crystallized after being kept at −17° for several days. On being recrystallized from ether, it yielded **3** (90 mg, 39%) as extremely hygroscopic, flat needles, m.p. 50–54°, $[\alpha]_D^{20}$ −95° (*c* 0.78, water).

Anal. Calc. for $C_9H_{16}O_7$: C, 45.76; H, 6.83. Found: C, 45.63; H, 6.90.

The per(trimethylsilyl) derivative showed a single peak in g.l.c. (15% SE 30 on Gaschrom Q at 218°), its rate of movement being unlike that of the per(trimethylsilyl) derivative of methyl 6-*O*-acetyl-β-D-galactofuranoside[9]. When **3** was equilibrated in pyridine for 45 min and then converted into the per(trimethylsilyl) derivative, the rate of movement remained unchanged.

Periodate oxidation of **3**. — Compound **3** (11 mg) was oxidized with sodium metaperiodate at pH 6.2 (acetate buffer) in the dark at room temperature. Uptake of periodate was determined by the Fleury–Lange method[11]. Found: 1.04 moles of periodate consumed per mole of **3** after 5 min. No further consumption was noticed up to 30 min; then there was a slight upward drift. Formaldehyde was determined by the chromotropic acid method[12]. Found: 1.01 moles of formaldehyde produced per mole of **3**.

A sample of **3** (40 mg) was oxidized for 20 min with 1.07 moles of sodium metaperiodate per mole in the aqueous buffer already mentioned. Ethylene glycol was then added and, after 0.5 h, the pH of the mixture was adjusted to 5 with hydrochloric acid, and the solution was evaporated to dryness. Methanol was repeatedly added to and evaporated from the residue, and the resulting product was hydrolyzed with 0.5 M aqueous sulfuric acid for 4 h. After neutralization with barium hydroxide, the mixture was filtered, and the filtrate was passed through a column of Dowex 1 X4 anion-exchange resin. By t.l.c. on Avicel with 4:1 isopropyl alcohol–water, the eluate was shown to contain arabinose only.

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