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Note

Conformation of 1,3:4,6-di-*O*-chloroethylidenegalactitol and its conversion into [1(*R**),4(*S**)]-2,1,3:5,4,6-di-*O*-ethanylylidenegalactitol

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As reported previously, chloroacetaldehyde diethyl acetal and galactitol react under acidic conditions to give a crystalline diacetal, 1,3:4,6-di-*O*-chloroethylidenegalactitol[1]. Two conformers, **1** and **2** (R = CH_2Cl, R′ = H), having the 1,3-dioxane ring in a chair conformation and the chloromethyl group equatorially disposed, were considered the most probable. Structure **2** (R = CH_2Cl, R′ = H) was favored on the basis of 1,3-nonbonded interactions. Information presented herein establishes that structure **1** (R = CH_2Cl, R′ = H) is correct.

^{1}H-N.m.r. spectroscopy appeared to permit differentiation of conformations **1** or **2** because: (*1*) the symmetry of either conformer would halve the number of magnetically nonequivalent protons, thus decreasing the complexity of the spectrum, (*2*) the expected H-1ax–H-2 coupling-constants[2] for **1** and **2** would show a large difference, and (*3*) esterification of the hydroxyl group would result in a downfield chemical shift[3] of the attached methine proton, which could thus be identified readily.

^{1}H-N.m.r. spectroscopy of the dibenzoate (R = CH_2Cl, R′ = PhCO) revealed $J_{1,2}$ 2.0 and $J_{1',2}$ 2.0 Hz. Thus, H-2 is equatorial and **1** is the correct conformation.

Further evidence that **1** is the correct structure was found in the observation that **1** (R = CH_2Cl, R′ = H), when treated with boiling ethanolic sodium hydroxide, gave an unusual compound assigned the structure **3**. Analysis indicated the formula $C_{10}H_{14}O_6$; the compound showed no hydroxyl groups, and it exhibited an unusually high melting point of ~265°. The low solubility of **3** (less than 0.5% w/v in Me_2SO) hampered the securing of a ^{1}H-n.m.r. spectrum. The pattern could be interpreted on a first-order basis.

Mass spectroscopy revealed large peaks at *m/e* 230 (72), 171 (19), 144 (7), 115 (29), 86 (87), and 57 (100) (values in parentheses are percentages of the base

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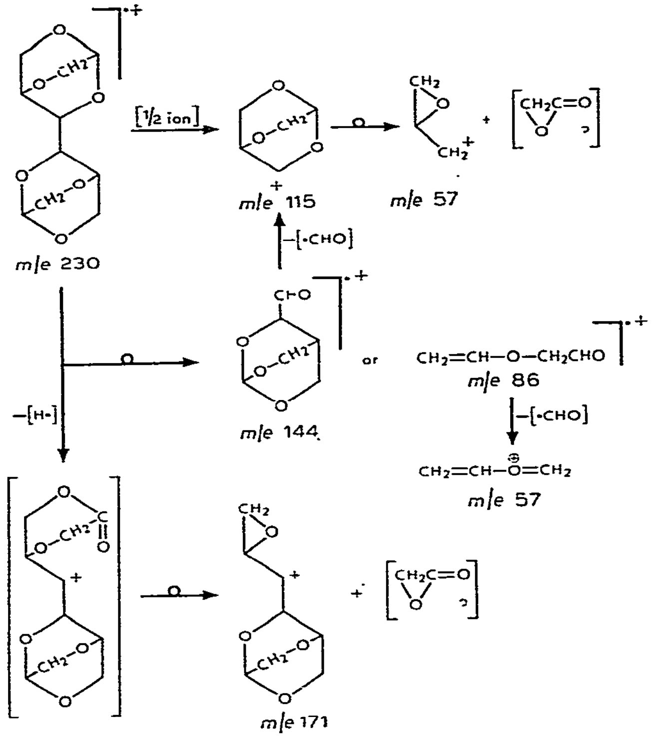


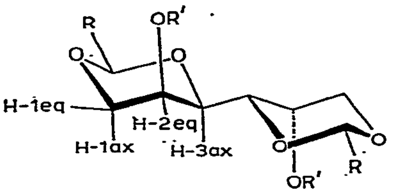
Scheme 1

peak). Although a positive assignment of structures cannot be made on the basis of low-resolution data, a plausible series of fragment ions (Scheme 1) may be postulated by using accepted fragmentation mechanisms[4].

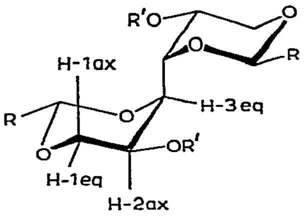
Christensen and Goodman[5] reported that carbohydrate acetals are hydrolyzed in 5–10 min when dissolved in 9:1 (v/v) trifluoroacetic acid–water at room temperature. Although **3** was altered under these conditions, the transformation was slow (after 5 days, t.l.c. indicated a sizable amount of unchanged **3** still present) and produced no identifiable product(s) (t.l.c. showed a long streak suggestive of polymerization or condensation).

Examination of molecular models shows that only **1**, in which the R = CH_2Cl and R′ = H groups are *cis* on the 1,3-dioxane ring, can form a bicyclo[2.2.2]octyl system as shown in **3**. No amount of twisting, turning, or bending of molecular models would allow the *trans*-1,3-dioxane in **2** to form a bicyclo[2.2.2]octane.

Another structure derivable from **2** and different from **3** might be possible wherein the chloroethylidene group that spans the 1,3-positions forms an ether with O-5 and correspondingly, the 4,6-chloroethylidene group with O-2. This structure is viewed as unlikely; it is not only strained, but also cannot account for the sizable half-molecular ion peak observed in the mass spectrum. Consequently, **3**, [1(*R**), 4(*S**)]-2,1,3:5,4,6-di-*O*-ethanylylidenegalactitol, is considered the correct structure.



1



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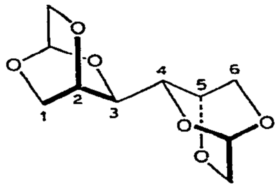

3

All of the derivatives of di-*O*-(2-chloroethylidene)galactitol previously reported[1] should be noted as possessing a [1(*R**),4(*S**)] arrangement, as shown in **1**.

EXPERIMENTAL

General methods. — T.l.c. was performed on precoated plates of Silica Gel F-254. The plates were air-equilibrated. Spots were rendered visible by spraying them with 5% ethanolic sulfuric acid and heating at 150 ± 10° until charring occurred. Spectra were recorded on a Varian HA-100 spectrometer, a Bruker WH-90 spectrometer at 90 MHz, and a DuPont 491 mass spectrometer at 70 eV using a direct-probe insertion. ^{1}H-N.m.r. data are reported as δ values against internal tetramethylsilane. Melting points are uncorrected. Analytical samples were dried at room temperature in the presence of sodium hydroxide and sulfuric acid at 10–20 torr. Solutions were evaporated *in vacuo*.

*2,5-Di-*O*-benzoyl-[1(*R**),4(*S**)]-1,3:4,6-di-*O*-(2-chloroethylidene)galactitol (1, R = CH_2Cl, R' = PhCO).* — This compound was prepared[1] previously, but the following is a much improved procedure. Compound **1** (R = CH_2Cl, R' = H) (1.00 g, 3.3 mmol) was dissolved in pyridine (15 mL) and benzoyl chloride (0.8 mL, 6.8 mmol) was added in one portion. After 18 h at room temperature, water (10 mL) was added. The solid was separated by filtration, sucked dry, and immediately recrystallized from ethanol (600 mL). Filtration gave **1** (R = CH_2Cl, R' = PhCO); yield 1.346 g (79.8%), m.p. 221–222°; ^{1}H-n.m.r. in $CDCl_3$: δ 7.3–8.2 (m, 5 H, aryl), 5.12 (unresolved multiplet, 1 H, H-2), 4.38 (1 H, dd, $J_{1,1'}$ 12.5, $J_{1,2}$ 2.0 Hz, H-1), 4.17 (1 H, unresolved multiplet, H-3), 3.95 (1 H, dd, $J_{1,1'}$ 12.5, $J_{1',2}$ 2.0 Hz, H-1'), 4.63 (1 H, t, J 4.0 Hz, 1 H, acetal-CH), and 3.45 (2 H, d, J 4.0 Hz, CH_2Cl).

*[1(*R**),4(*S**)]-2,1,3:5,4,6-Di-*O*-ethanylylidenegalactitol.* — Compound **1** (R = CH_2Cl, R' = H) (2.0 g, 6.5 mmol) was covered with ethanol (150 mL) and the mixture

was boiled under reflux. A solution of sodium hydroxide (2.0 g, 50 mmol) in 100 mL of 75% ethanol was added dropwise to the refluxing, ethanolic solution during ~3 h. When the addition had been completed, the mixture was heated for 2 h more under reflux. After cooling and diluting with water (100 mL), carbon dioxide was bubbled through the mixture for 30 min. Following storage for 18 h at 5°, filtration gave a white powder; yield 1.161 g (76.4%), m.p. 268–272°. Recrystallization of 236 mg from 100 mL of ethanol yielded an analytical sample (201 mg), m.p. 263–268°; ^{1}H-n.m.r. data δ 4.93 (s, acetal H-?), 4.37, 4.35, 4.26, 4.24 (dd, H-?), 4.16, 4.14, 4.05, 4.01, 3.99, and 3.96. The spectrum was unchanged on addition of D_2O. The m.p. varied between 262° and 272°, according to the rate of heating.

Anal. Calc. for $C_{10}H_{14}O_6$: C, 52.17; H, 6.13. Found: C, 52.24; H, 6.28.

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