REACTION OF METHYL 4,6-DICHLORO-4,6-DIDEOXY-α-D-GALACTO-PYRANOSIDE 2,3-DI(CHLOROSULFATE) WITH SODIUM AZIDE, AND WITH SODIUM BROMIDE, IN *N,N*-DIMETHYLFORMAMIDE

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ABSTRACT

Treatment of methyl 4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside 2,3-di(chlorosulfate) (**1**) with sodium azide in *N,N*-dimethylformamide at room temperature gives a mixture of four major products: methyl 4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside, its 2- and 3-(chlorosulfate) derivatives (**2** and **3**), and an azidosulfate derivative (**4**). The first compound and the derivatives **2** and **3** are also formed when **1** is treated with sodium bromide in *N,N*-dimethylformamide at room temperature.

INTRODUCTION

The synthesis and reactions of carbohydrate chlorosulfates have been the subject of several publications[1–4]. The ease of removal of a chlorosulfate group with sodium iodide to give the corresponding hydroxyl group with retention of configuration, and the ability of certain reactive chlorosulfate groups to undergo bimolecular nucleophilic displacement by chloride ion have led to facile syntheses of difficultly accessible chlorodeoxy[2,4], deoxy[5–7], and aminodeoxy[7,8] sugars. A chlorosulfated glycopyranosyl chloride has also been used in the synthesis of a disaccharide[9]. Recently, carbohydrate chlorosulfates have been converted into the corresponding fluorosulfates with silver fluoride in methanol[10]. In continuation of our studies of sugar chlorosulfates, we have now investigated the effect of azide and bromide ion on the chlorosulfate groups in methyl 4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside 2,3-di(chlorosulfate)[3] (**1**).

RESULTS AND DISCUSSION

Treatment of methyl 4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside 2,3-di(chlorosulfate)[3] (**1**) with sodium azide in *N,N*-dimethylformamide at room temperature gave a mixture of four major products which was partially resolved by chroma-

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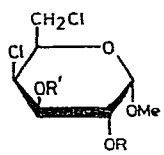
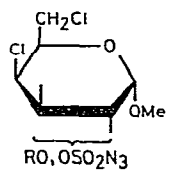
tography on silica gel. These products are methyl 4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside[3] and its 2- and 3-(chlorosulfate) derivatives (**2** and **3**), and an azidosulfate derivative (**4**). Methyl 4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside was obtained as a chromatographically (t.l.c.) homogeneous, crystalline compound, and was identified by comparison of its physical constants with those of an authentic sample prepared previously[3].

Compounds **2** and **4** were obtained as a mixture which, in our hands, could not be resolved by chromatography on silica gel; they were assigned the structures of methyl 4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside 2-(chlorosulfate) and a methyl 4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside azidosulfate, respectively, on the basis of the following experimental evidence. Treatment of the mixture with an aniline–pyridine reagent[11] afforded a characteristic orange-red color indicative of the presence of a chlorosulfate group[2,11]. The infrared spectrum of the mixture revealed, in addition to the presence of hydroxyl and chlorosulfate groups, the presence of an azido function. De-chlorosulfation of the mixture with sodium iodide gave crystalline methyl 4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside[3] and a compound that migrated on a thin-layer chromatogram at the same rate as the starting mixture, but that failed to react with the pyridine–aniline spray reagent[11].

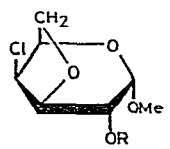
Treatment of the mixture of **2** and **4** with pyridine afforded crystalline methyl 4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside 2,3-sulfate[3] and a compound which, again, was indistinguishable by t.l.c. from the starting mixture, but which gave a negative reaction for a chlorosulfuric ester[2,11]. When the mixture was treated at 0° with acetic anhydride and sulfuric acid, a mixture of acetates **5** and **6** was obtained. The monoacetate **6**, which readily crystallized from an ether solution of the mixture, failed to react with the aniline–pyridine reagent[11]; moreover, liberation of iodine was not observed when **6** was treated with sodium iodide in acetone. The infrared spectrum of **6** showed, in addition to absorptions due to acetate and azide, strong



1 R = R′ = SO_2Cl
2 R = SO_2Cl, R′ = H
3 R = H, R′ = SO_2Cl
5 R = SO_2Cl, R′ = Ac
7 R = Ac, R′ = SO_2Cl
8 R = Ac, R′ = H
11 R = H, R′ = Ac
12 R = Me, R′ = Ac



4 R = H
6 R = Ac



9 R = H
10 R = Me

absorptions at 7.08 and 8.37 μm that are considered to be due to the presence of an azidosulfate group (OSO_2N_3). The isolation from the reaction of **6** with sodium azide in *N,N*-dimethylformamide at room temperature of a crystalline monoacetate that was identical with the monoacetate (**11**) obtained when methyl 4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside was treated with acetic anhydride (1 molar proportion) and pyridine (2 molar proportions) suggests that the azidosulfate group is attached to C-2 in compound **6**. As the possibility, during the removal of the azidosulfate group from **6** with sodium azide, of the migration of an acetyl group from O-2 to O-3 has not been excluded, this assignment must be regarded as tentative. Although there were marked similarities in the n.m.r. spectra of **5** and **6** (see Fig. 1), an unequivocal assignation of the azidosulfate group to C-2 could not be made by n.m.r. spectroscopy. The acetate **5** was obtained as a chromatographically (t.l.c.) homogeneous syrup from the mother liquor remaining after the removal of **6** (see the Experimental section). Compound **5** gave a positive reaction with the aniline–pyridine reagent[11] and afforded the acetate **11** when de-chlorosulfated with sodium iodide in acetone.

Compound **11** was shown to be methyl 3-*O*-acetyl-4,6-dichloro-4,6-dideoxy-α-

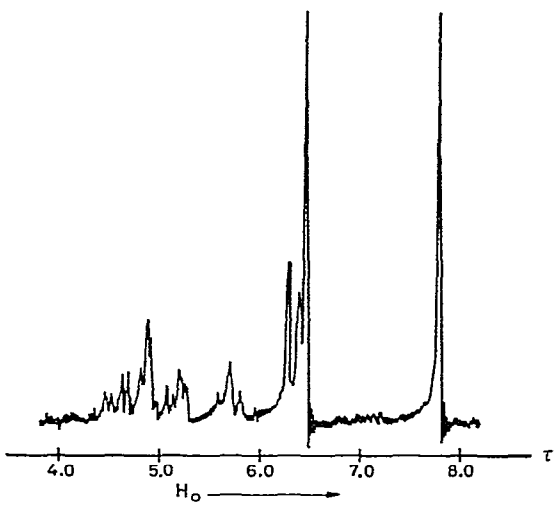


Fig. 1. The n.m.r. spectrum at 60 MHz of methyl *O*-acetyl-4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside azidosulfate (**6**) in chloroform-*d*.

D-galactopyranoside, because its 2-*O*-methyl derivative* (**12**), on treatment with sodium hydroxide, afforded a syrup that was identical with methyl 3,6-anhydro-4-chloro-4-deoxy-2-*O*-methyl-α-D-galactopyranoside (**10**). Compound **10** was synthesized in high yield from methyl 4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside[3] in the following way. Treatment of methyl 4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside with base afforded, after 7 h, a chromatographically (t.l.c.) homogeneous

*The extent of acetyl migration during the methylation of compound **11** with methyl iodide and silver oxide was examined by treatment of **11** with silver oxide in chloroform; only a trace of a component having the same mobility as the 2-acetate **8** was detected by t.l.c.

syrup to which the structure of methyl 3,6-anhydro-4-chloro-4-deoxy-α-D-galactopyranoside (**9**) was assigned on the basis of its elemental analysis, optical rotation*, and positive reaction with resorcinol[12]**. Methylation of **9** in *NN*,-dimethylformamide with silver oxide and methyl iodide afforded, after 2 h, syrupy methyl 3,6-anhydro-4-chloro-4-deoxy-2-*O*-methyl-α-D-galactopyranoside (**10**).

Compound **3** was obtained as a stable, crystalline compound and was shown to be methyl 4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside 3-(chlorosulfate) in the following way. It gave a positive reaction with aniline and pyridine[2,11], afforded methyl 4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside[3] when de-chlorosulfated, and gave methyl 4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside 2,3-sulfate[3] when treated with pyridine. The 2,3-sulfate was also obtained in an attempted methylation of **3** with methyl iodide and silver oxide. Acetylation of **3** with acetic anhydride and sulfuric acid afforded syrupy **7**, which did not give a satisfactory elemental analysis because of a slow loss of the chlorosulfate group. De-chlorosulfation of **7** afforded **8** as a syrup. Compound **8** contained a hydroxyl and an acetoxyl group, and was chromatographically distinguishable from the acetate **11**. Deacetylation of **8** afforded methyl 4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside[3]. This evidence indicates that compound **8** is methyl 2-*O*-acetyl-4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside.

T.l.c. examination of the products of the reaction of **1** with sodium bromide in *N,N*-dimethylformamide at room temperature revealed the presence of **2**, **3**, and methyl 4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside. The last compound was present in greater proportion than when **1** was similarly treated with sodium azide.

EXPERIMENTAL

General methods. — Melting points were determined on a Fisher–Johns apparatus and are uncorrected. Optical rotations were measured with a Perkin–Elmer Model 141 automatic polarimeter at 23 ±2°. Thin-layer chromatography (t.l.c.) was performed with Silica Gel G as the adsorbent and the following solvent-systems (v/v): (*a*) 6:5 ether–petroleum ether, (*b*) 19:1 chloroform–methanol, (*c*) 2:3 ether–petroleum ether, and (*d*) 1:9 ether–petroleum ether. The term "petroleum ether" refers to the fraction of b.p. 30–60°. The developed plates were air-dried, sprayed with 5% ethanolic sulfuric acid, and heated at about 150°. G.l.c. was performed on an F and M Model 402 gas chromatograph, with 14.7% (w/w) LAC-4R-886 polyester wax on acid-washed Chromosorb W (100–120 mesh) as the stationary phase, at an operating temperature of 145°. I.r. spectra were recorded on a Perkin–Elmer Model 21 spectrophotometer. N.m.r. spectra were recorded at 60 MHz for solutions in chloroform-*d*, with tetramethylsilane as the internal standard.

Reaction of methyl 4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside 2,3-di(chloro-

*The value obtained for the specific rotation of compound **9**, namely, $[\alpha]_D$ +76.8° (*c* 1.0, chloroform), is close to values listed for several derivatives of methyl 3,6-anhydro-α-D-galactopyranoside: compare, F. SMITH and R. MONTGOMERY, *The Chemistry of Plant Gums and Mucilages*, Reinhold, New York, 1959, p. 528.

**The resorcinol reagent is commonly used for a colorimetric determination of 3,6-anhydrogalactose[12].

sulfate) (**1**) *with sodium azide.* — To a solution of compound[3] **1** (12 g) in *N,N*-dimethylformamide (20 ml) was added sodium azide (7.2 g), and the mixture was kept at room temperature with occasional stirring. After 48 h, the mixture was diluted with chloroform (250 ml), and the suspension was filtered to remove inorganic salts; the filtrate was washed successively with water, saturated sodium hydrogen carbonate solution, and water, dried (sodium sulfate), and evaporated to a syrup (8.0 g); t.l.c. (solvent *a*) revealed the presence of three major components having R_F values of 0.09, 0.42, and 0.60. The syrup was applied to a column of silica gel and eluted first with chloroform to remove unreacted compound **1**; the eluant was then changed to 1:1 ether–petroleum ether, and the following fractions were obtained.

Fraction *i*, a chromatographically (t.l.c.) homogeneous syrup (2.74 g), R_F 0.60 (solvent *a*), gave a positive reaction with the aniline–pyridine spray reagent[11]; $[\alpha]_D$ +156.2°(*c* 3.68, chloroform); λ_{max}^{film} 2.88 (broad band, OH), 4.65 (N_3), 7.06, and 8.36 μm (OSO_2N_3 and OSO_2Cl). This syrup was shown to be a mixture of **2** and **4**. After being kept for a few hours at room temperature, the syrup was found to be contaminated with a small proportion of a compound chromatographically (t.l.c.) indistinguishable from methyl 4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside 2,3-sulfate[3].

Anal. Calc. for $C_7H_{11}Cl_3O_6S$ (**2**): Cl, 32.3; S, 9.7. Calc. for $C_7H_{11}Cl_2N_3O_6S$ (**4**): Cl, 21.4; S, 9.5. Found: Cl, 26.9; S, 8.9.

Fraction *ii*, a semi-crystalline mass (0.6 g), was shown (t.l.c., solvent *a*) to be a mixture of two components having R_F values of 0.60 and 0.42.

Fraction *iii*, a chromatographically (t.l.c.) homogeneous component (1.75 g), R_F 0.42 (solvent *a*), gave a positive reaction with the aniline–pyridine spray reagent[11]. The compound crystallized as needles from chloroform–petroleum ether, m.p. 132–133° (dec.), $[\alpha]_D$ +180° (*c* 0.3, chloroform); λ_{max}^{KBr} 2.90 (OH), 7.06, and 8.35 μm (OSO_2Cl). This compound was shown to be **3**.

Anal. Calc. for $C_7H_{11}Cl_3O_6S$: Cl, 32.3; S, 9.7. Found: Cl, 32.3; S, 9.9.

The column was finally eluted with ether, to yield crystalline methyl 4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside (1.02 g), whose physical constants were in agreement with those previously reported for this compound[3].

Treatment of mixture (*fraction* i) *of compounds* **2** *and* **4** *with sodium iodide.* — A portion (100 mg) of fraction *i* was treated with sodium iodide in acetone according to the method of Lawton *et al.*[6], to give a syrup which was shown by t.l.c. (solvent *a*) to be a mixture of two components having R_F values of 0.09 and 0.60; the component having R_F 0.60 failed to react with the aniline–pyridine spray reagent[11]. The syrup yielded crystals from chloroform–petroleum ether, m.p. 157–158° (not depressed on admixture with authentic methyl 4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside[3]); R_F 0.09.

Treatment of mixture (*fraction* i) *of compounds* **2** *and* **4** *with pyridine.* — A portion of fraction *i* (100 mg) was treated with dry pyridine (2 ml) at room temperature. After 30 min, t.l.c. (solvent *a*) revealed the presence of two components (R_F 0.60

and 0.67); the component having R_F 0.60 failed to react with the aniline–pyridine spray reagent[11]. The reaction mixture was processed in the usual way[3], to afford a syrup that deposited methyl 4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside 2,3-sulfate[3] as needles (35 mg) from chloroform–petroleum ether (b.p. 60–80°), m.p. 103–104°, not depressed on admixture with an authentic sample.

Methyl 3-O-acetyl-4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside 2-(chlorosulfate) (**5**) *and methyl O-acetyl-4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside azidosulfate* (**6**). — A portion of fraction *i* (900 mg) in acetic anhydride (5 ml) was treated at 0° with a 50:1 mixture (5 ml) of acetic anhydride and sulfuric acid. After 30 min at 0°, the mixture was poured into ice water, and the solid material was collected by filtration, washed with cold water, and dissolved in chloroform. The chloroform solution was dried (sodium sulfate), and evaporated to a syrup (850 mg). T.l.c. examination of the syrup revealed the presence of a single component with solvent *c* (R_F 0.76), and two components with solvent *d* (R_F 0.32 and 0.40); only the faster-moving component gave a positive reaction with the aniline–pyridine spray reagent[11]. The slower-moving compound (**6**) crystallized from ether as fine needles (250 mg), m.p. 122–123°. After recrystallization from ether, the crystals had m.p. 126–127°, $[\alpha]_D$ +206.5° (*c* 1.0, chloroform); λ_{max}^{solid} 4.65 (N_3), 5.75 (OAc), 7.08, and 8.37 μm (OSO_2N_3); the n.m.r. spectrum is shown in Fig. 1. Liberation of iodine was not observed when the crystals were treated with sodium iodide in acetone[3].

Anal. Calc. for $C_9H_{13}Cl_2N_3O_7S$: C, 28.7; H, 3.4; Cl, 18.8; N, 11.1; S, 8.5. Found: C, 28.4; H, 3.3; Cl, 18.6; N, 11.3; S, 8.6.

To compound **6** (40 mg) in *N,N*-dimethylformamide (2 ml) was added sodium azide (40 mg); the mixture was kept for 24 h at room temperature, poured into water (10 ml), and extracted with chloroform (3 × 10 ml). The extracts were combined, washed with water, dried (sodium sulfate), and evaporated to a syrup (20 mg) which crystallized on standing. Recrystallization from ether–petroleum ether** gave **11**, m.p. 117–118°, not depressed on admixture with an authentic sample prepared by selective acetylation of methyl 4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside (see later).

On concentration, the ether mother liquors from the foregoing acetylation afforded a second crop of compound **6**. Further crystalline crops of impure **6** were obtained on addition of increasing amounts of petroleum ether**; the ether was finally evaporated at room temperature, and the syrup that separated from the petroleum ether solution was removed. Concentration of the petroleum ether solution afforded a chromatographically homogeneous syrup (150 mg), R_F 0.40, solvent *a*, that gave a positive reaction with the aniline–pyridine spray reagent[11]; λ_{max}^{film} 5.71 (OAc), 7.06, and 8.37 μm (OSO_2Cl)*. De-chlorosulfation of the syrup (70 mg) in acetone (5 ml) according to the method of Lawton *et al.*[6] afforded compound **11**, yield 80%, m.p. 117–118° (not depressed on admixture with an authentic sample), $[\alpha]_D$ +209° (*c* 1.0,

*A very weak, azide absorption at 4.6 μm was also observed, so that the syrup presumably still contained a trace of compound **6**.

**B.p. 60–80°.

chloroform). Compound **11** was also obtained when the syrup was treated with sodium azide in *N,N*-dimethylformamide as described for compound **6**. The syrup is, therefore, methyl 3-*O*-acetyl-4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside 2-(chlorosulfate) (**5**).

Dechlorosulfation of methyl 4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside 3-(chlorosulfate) (**3**). — Compound **3** (50 mg) was treated with sodium iodide in acetone according to the method of Lawton *et al.*[6], to give methyl 4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside[3], yield 80%, m.p. 157–158°, not depressed on admixture with an authentic sample.

Treatment of compound 3 with pyridine. — Compound **3** (100 mg) was treated with dry pyridine (2 ml) at room temperature. After 30 min, t.l.c. (solvent *b*) revealed the absence of starting material. The reaction mixture was processed in the usual way[3], to give methyl 4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside 2,3-sulfate[3] as needles, yield 90%, m.p. 103–104°, not depressed on admixture with an authentic sample.

Attempted methylation of compound **3**. — Compound **3** (100 mg) was dissolved in methyl iodide (5 ml), silver oxide (1 g) added, and the mixture was stirred for 30 min at room temperature. Isolation of the product in the usual way afforded a chromatographically homogeneous syrup that crystallized on standing. Recrystallization from chloroform–petroleum ether (b.p. 60–80°) afforded methyl 4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside 2,3-sulfate[3] as fine, colorless needles, m.p. 103–104°, not depressed on admixture with an authentic sample.

Methyl 2-O-acetyl-4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside 3-(chlorosulfate) (**7**). — Compound **3** (150 mg) was treated with acetic anhydride and sulfuric acid, as described for the mixture (fraction *i*) of compounds **2** and **4**, to give the 2-*O*-acetyl derivative **7** as a chromatographically (t.l.c.) homogeneous syrup, yield 130 mg (79%), $[\alpha]_D$ +142.2° (*c* 1.1, chloroform); R_F 0.62 (solvent *c*); it gave a positive reaction with the aniline–pyridine spray reagent[11]. A satisfactory elemental analysis could not be obtained, because of loss of the chlorosulfate group on standing.

Methyl 2-O-acetyl-4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside (**8**). — Compound **7** (110 mg) was treated with sodium iodide in acetone according to the method of Lawton *et al.*[6], to yield a syrupy product (75 mg). T.l.c. examination (solvent *b*) of the syrup revealed the presence of a major component (**8**) having R_F 0.48 and a trace of a component having R_F 0.56 (identical with that of compound **11**). The syrup had $[\alpha]_D$ +174.7° (*c* 1.1, chloroform); λ_{max}^{film} 2.85 (OH) and 5.75 μm (OAc). Deacetylation of the syrup yielded crystalline methyl 4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside[3], m.p. 157–158°, not depressed on admixture with an authentic sample.

Methyl 3,6-anhydro-4-chloro-4-deoxy-α-D-galactopyranoside (**9**). — To a solution of methyl 4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside (1 g) in 1:1 water–ethanol (10 ml) was added 2M sodium hydroxide solution (10 ml), and the mixture was allowed to stand for 7 h at room temperature. The solution was made neutral with acetic acid, and extracted with chloroform. The extract was successively washed with sodium hydrogen carbonate solution and water, dried (sodium sulfate), and evapor-

ated, to give compound **9** as a chromatographically (t.l.c., solvent *b*) homogeneous syrup, yield 800 mg (95%); the syrup gave a positive resorcinol reaction for a 3,6-anhydro sugar[12]. An analytically pure sample was obtained by distillation at 90–95°/0.3 torr; $[\alpha]_D$ +76.8° (*c* 1.0, chloroform).

Anal. Calc. for $C_7H_{11}ClO_4$: C, 43.2; H, 5.7; Cl, 18.3. Found: C, 43.2; H, 5.8; Cl, 18.1.

Methyl 3,6-anhydro-4-chloro-4-deoxy-2-O-methyl-α-D-galactopyranoside (**10**). — Compound **9** (150 mg), *N,N*-dimethylformamide (1 ml), methyl iodide (5 ml), and silver oxide (1 g) were stirred for 2 h at room temperature. The methylated product was isolated in the usual way, to give a syrup that was purified by distillation at 68–73°/0.2 torr; yield 130 mg (81%); $[\alpha]_D$ +94.9° (*c* 2.3, chloroform); a positive resorcinol reaction for a 3,6-anhydro sugar[12] was observed.

Anal. Calc. for $C_8H_{13}ClO_4$: C, 46.1; H, 6.2; OMe, 29.7. Found: C, 45.8; H, 6.1; OMe, 29.6.

Methyl 3-O-acetyl-4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside (**11**). — Methyl 4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside[3] (2 g) in chloroform (50 ml) was treated with pyridine (1.37 g, 2 molar equivs.) and acetic anhydride (0.88 g, 1 molar equiv.), and the mixture was kept for 28 h at room temperature. The solution was then washed successively with water, dilute sulfuric acid, and water, dried (sodium sulfate), and evaporated to a syrup. T.l.c. examination of the syrup revealed the presence of two major products (R_F 0.48 and 0.56, solvent *b*). A crystalline product (**11**) was obtained from ether–petroleum ether (b.p. 60–80°), yield 1.1 g (47%), m.p. 117–118°, $[\alpha]_D$ +210.5° (*c* 1.1, chloroform); R_F 0.56 (t.l.c., solvent *b*).

Anal. Calc. for $C_9H_{14}Cl_2O_5$: C, 39.6; H, 5.1; Cl, 26.0. Found: C, 39. 8; H, 5.0; Cl, 26.1.

Methyl 3-O-acetyl-4,6-dichloro-4,6-dideoxy-2-O-methyl-α-D-galactopyranoside (**12**). — Compound **11** (100 mg) was treated with silver oxide (2.5 g) and methyl iodide (10 ml), with stirring, for 48 h at room temperature. The product was isolated as a syrup in the usual way; g.l.c. showed the presence of a 20:1 mixture of two components. Compound **12** was obtained pure by distillation at 110–115°/0.3 torr, yield 90 mg (86%), $[\alpha]_D$ +194.6° (*c* 1.8, chloroform).

Anal. Calc. for $C_{10}H_{16}Cl_2O_5$: C, 41.8; H, 5.6; OMe, 21.6. Found: C, 41.8; H, 5.8; OMe, 22.7.

The effect of silver oxide on compound **11** was investigated in the following way. Compound **11** (50 mg) in chloroform (10 ml) was stirred with silver oxide (1.25 g) for 48 h at room temperature. T.l.c. (solvent *b*) then showed the presence of starting material (R_F 0.56) and a trace of a slower-moving component (R_F 0.48). A syrup was isolated that crystallized from ether to give compound **11**, m.p. 117–118°, not depressed on admixture with an authentic sample.

Conversion of compound **12** *into methyl 3,6-anhydro-4-chloro-4-deoxy-2-O-methyl-α-D-galactopyranoside* (**10**). — Compound **12** (50 mg) in ethanol (2 ml) and 2M sodium hydroxide (2 ml) was heated for 2 h at 60°. The solution was made neutral with acetic acid, and evaporated to dryness, and the residue was extracted with

chloroform. Evaporation of the extract gave compound **10** as a syrup, yield 25 mg (70%), which was purified by distillation at 67–73°/0.3 torr; $[\alpha]_D$ +91.9° (*c* 1.0, chloroform); a positive resorcinol reaction for a 3,6-anhydro sugar[12] was observed, and the i.r. spectrum (film) was identical with that of a sample of compound **10** prepared from **9**.

Reaction of methyl 4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside 2,3-di(chlorosulfate) (**1**) *with sodium bromide.* — To a solution of compound **1** (4 g) in *N,N*-dimethylformamide (10 ml) was added sodium bromide (3.85 g), and the mixture was kept for 48 h at room temperature and then processed as described for the reaction of compound **1** with sodium azide, to give a syrup (2.4 g). T.l.c. examination (solvent *a*) of the syrup revealed the presence of **2**, **3**, and methyl 4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside. The last compound (R_F 0.09) was present in much greater proportion than when **1** was treated with sodium azide.

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