Anal. Calcd for $C_{27}H_{42}O_6$: C, 69.63; H, 9.09. Found: C, 69.59; H, 9.02.

Reaction of 12-Hydroxymethylabiet-7,8-enoic Acid with Paraformaldehyde.—12-Hydroxymethylabiet-7,8-enoic acid (10 g), paraformaldehyde (2 g), and glacial acetic acid (80 cc) were refluxed 36 hr and excess acetic acid was removed *in vacuo*. Usual work-up, addition of excess ethereal diazomethane, and concentration *in vacuo* gave a pale yellow viscous liquid (11.7 g). Glpc showed the presence of two major components at t = 3.7 and 3.8 with three minor components at t = 6.5–8.4 min.

The above mixture (7 g) was chromatographed over Alcoa alumina (50 g). Elution with *n*-hexane–ether (9:1) gave unresolved components with retention times t = 3.7 and 3.8 (**mixture A**, 6 g) followed by components with t = 6.5–8.4 min (**mixture B**, 1.0 g).

Rechromatography of mixture A on Alcoa alumina (50 g) and elution with *n*-hexane afforded **methyl 12-acetoxymethylabiet-7,8-enoate** (3.6 g): nmr signals appeared at 0.87 and 0.96 (isopropyl group, J = 6.5 cps), 0.78 (C-10 Me), 1.16 (C-4 Me), 1.95 (acetate Me), 3.57 (ester Me), and a broadened doublet at 5.33 ppm (H-7, J = 4.0 cps).[5] After eluting with hexane–ether (19:1, 150 cc), further elution with hexane–ether (9:1) gave a crystalline solid (2.0 g) which on recrystallization from aqueous EtOH gave colorless needles, mp 118–119°, identified as **methyl 12,14-methyleneoxyabiet-8,9-enoate** (**14**) (see later).

Rechromatography of mixture B (1 g) over Alcoa alumina (40 g) and elution with hexane (200 cc), hexane–ether (19:1, 200 cc), and hexane–ether (9:1, 200 cc) failed to give any material. Elution with hexane–ether (4:1) gave unresolved components with glpc retention times t = 7.5 and t = 8.4 min. Preparative glpc (T = 300°) gave a component with t = 7.5 min as a viscous liquid and was identified as **methyl 7,12-diacetoxymethylabiet-7,8-enoate** (**11**), identical (infrared and nmr spectra) with that obtained from the hydrogenation of **9** (*vide infra*).

The second component with t = 8.4 min was obtained as a pale yellow viscous liquid (0.15 g), λ_{max} 245 mμ ($E^{1\%}_{1.cm}$ 350), identified as **methyl 7-acetoxymethyl-12-methylabietate** (**13**): nmr signals at 0.93 and 1.03 (isopropyl group, J = 7.0 cps), 0.80 (C-10 Me), 1.18 (C-4 Me), 1.97 (acetate Me), 1.92 (C-7 acetate $-CH_2-$ singlet), 3.56 (ester Me), and a singlet at 5.93 ppm (H-14).

Anal. Calcd for $C_{25}H_{38}O_4$: C, 74.78; H, 9.54. Found: C, 74.56; H, 9.43.

Methyl 12,14-Methyleneoxyabiet-8,9-enoate (**14**).—A mixture of paraformaldehyde (0.45 g), glacial acetic acid (5 cc), and concentrated sulfuric acid (2 drops) was heated to 50° with stirring, then methyl 12-hydroxymethylabiet-7,8-enoate (3.5 g, 0.01 mole) in acetic acid (5 cc) was added. After heating at 90° for 4 hr, the mixture was poured into water and ether extracted. The extracts were washed with aqueous $NaHCO_3$ solution and water and then dried ($MgSO_4$). Removal of solvent and recrystallization from aqueous EtOH gave **14** (2.7 g, 74%) as colorless needles: mp 118–119°; $[\alpha]^{23}D$ +70° (c 1.21); ν_{max} 1725 cm^{-1} (ester C=O), no OH, acetate C=O or C=C bands; nmr signals ($CDCl_3$) appeared at 0.75, 0.86, 0.81 and 0.92 (isopropyl group, J = 6.0 cps), 1.02 (C-10 Me), 1.21 (C-4 Me), and 3.66 (ester Me).

Anal. Calcd for $C_{23}H_{36}O_3$: C, 76.61; H, 10.07. Found: C, 76.49; H, 10.01.

Reduction of 14.—Ester **14** (1.8 g) was refluxed 2 hr with lithium aluminum hydride (1.0 g) in ether (100 cc). Addition of water and dilute HCl (1:1) followed by ether extraction gave 1.5 g (88%) of a colorless solid: mp 220–221°; ν_{max} 3400 (OH), no C=O bands; nmr signals (pyridine) appeared at 0.78 and 0.89 (isopropyl group), 0.91 (C-10 Me), 1.09 (C-4 Me), and a quartet centered at 3.48 ppm (J = 10 cps, $-CH_2OH$).

Anal. Calcd for $C_{22}H_{36}O_2$: C, 78.90; H, 11.63. Found: C, 79.26; H, 10.92.

Acetylation of the above alcohol by refluxing 1 hr with acetic anhydride gave the corresponding acetate as a colorless viscous liquid.

Anal. Calcd for $C_{24}H_{38}O_3$: C, 77.15; H, 9.99. Found: C, 77.11; H, 9.92.

12,14-Methyleneoxyabiet-8,9-enoic acid.—Ester **14** (1.8 g) was refluxed 24 hr with KOH (3 g) in water (20 cc) and ethanol (20 cc). Sodium dihydrogen phosphate (10 g) in water (40 cc) was added, the mixture was ether extracted, and the extracts were washed with water until neutral. After drying, concentration *in vacuo* gave the **acid** as a colorless solid (1.2 g), mp 225–227° (from aqueous EtOH), $[\alpha]^{24}D$ +56° (c 1.2).

Anal. Calcd for $C_{22}H_{34}O_3$: C, 76.23; H, 9.89; neut equiv, 336. Found: C, 76.18; H, 10.08; neut equiv, 346.

Registry No.—Abietic acid, 514-10-3; paraformaldehyde, 110-88-3; **1b**, 14969-87-0; **2b**, 14909-58-1; **3**, 15038-62-7; **4**, 14909-59-2; 7,14-dihydroxymethylabietic acid, 14909-60-5; 7-hydroxymethylabietic acid, 14909-61-6; **5**, 14909-62-7; **6**, 14909-63-8; **7**, 14909-64-9; 7,12,14-trihydroxymethylabietol tetraacetate, 14909-65-0; methyl 12-hydroxymethylabietate, 14909-66-1: **8**, 14909-72-2; **9**, 14909-68-3, **10**, 14909-69-4, **11**, 14909-70-7; methyl 12-acetoxymethylabiet-7,8-enoate, 15076-91-2; **13**, 14969-84-7; **14**, 14969-85-8; alcohol of mp 220–221°, 14909-71-8; 12,14-methyleneoxyabiet-8,9-enoic acid, 14909-72-9.

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Studies in the Ganglioside Series. I. Synthesis of 4-*O*-(2-Acetamido-2-deoxy-β-D-glucopyranosyl)-D-galactopyranose[1]

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The synthesis of the 1 → 4 disaccharide XIII is reported. A new stable and reactive bromide (III) has been employed in the Koenigs–Knorr reaction. Condensation of III with 2-*O*-acetyl-1,6-anhydro-β-D-galactopyranose (VI) also led to the 1 → 3 isomer which suffered cleavage under the influence of mild alkali. The diacetyl derivative VII could be obtained by selective acetylation of VI.

In the ganglioside molecule *N*-acetylgalactosamine is connected with galactose by a 1 → 4 β linkage.[2-4] The synthesis of glycosides of this type poses a special problem owing to the unstable nature of the acylated amino sugar bromides employed in the Koenigs–Knorr reaction. Thus, Micheel[5] has shown that 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranosyl bromide easily transforms into the amine hydrobromide by an N → O acyl migration *via* the oxazoline. Other bromides in which the amine function was protected by the

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benzylsulfonyl, benzylidene, 2,4-dinitrophenyl, benzyloxycarbonyl, and diphenoxyphosphinyl groups[6-10] were found to give satisfactory results only with reactive aglucons such as methanol, benzyl alcohol, or the primary hydroxyl of sugars. In addition, most of these methods suffer from the disadvantage that the blocking groups cannot be removed under mild conditions.

The rearrangement of *N*-acylhexosamine bromides depends largely on the nature of the neighboring acyl group.[5,11] Electrophilic substituents should weaken the nucleophilic attack of the carbonyl oxygen on the anomeric center and thus minimize the tendency of oxazoline formation. On the other hand, Micheel has observed that O-benzoylated bromides impart to the anomeric carbon atom enhanced stability, compared with the acetylated derivatives.[12] The bromide III with the powerful electron-attracting dichloroacetyl group appeared to have the appropriate structure to meet the three requirements: reactivity, stability, and deblocking of the amino group under mild conditions. While this investigation was in progress, Strachan, *et al.*,[13] reported the preparation of 3,4,6-tri-*O*-acetyl-2-deoxy-2-trifluoroacetamide-α-D-glucopyranosyl bromide. However, only reactive aglucons (ethanol and phenol) have been employed by these authors.

In view of the difficulty of obtaining galactosamine in quantities, we studied the synthesis of the glucosamine derivative XIII as model compound. Treatment of glucosamine hydrochloride with dichloroacetic anhydride and sodium dichloroacetate led to a compound which was not fully acylated and had a chlorine value closely corresponding to a triester amide. Catalytic deacylation with barium methoxide gave the amide I in fairly good yield. Benzoylation, followed by treatment with hydrogen bromide in acetic acid–acetic anhydride afforded the bromide III. It reacted quickly with benzyl alcohol, both with and without a catalyst, to give pure benzyl 3,4,6-tri-*O*-benzoyl-2-deoxy-2-dichloroacetamido-β-D-glucopyranoside (IV) in a yield of 87%.

In general equatorial hydroxyls react with esterifying agents more readily than the axial groups. Aspinall and Zweifel[14] have shown that 1,6-anhydro-4-*O*-methyl-β-D-mannose, in which the 2- and the 3-hydroxyl groups are equatorial–axial, undergoes selective esterification of the equatorial C-2. On the other hand, Jeanloz observed that the selectivity depends on the nature of the reagent,[15] and it is believed that besides conformational other factors, presumably electronic, must be involved in the course of the esterification.[16] In an attempt to bring about a partial acetylation of 2-*O*-acetyl-1,6-anhydrogalactopyranose (VI) no preferential reactivity of the equatorial C-4 hydroxyl over the axial[17] C-3 hydroxyl could be observed. Careful acetylation of VI with 1 mole of acetic anhydride in pyridine yielded the 2,3-diacetate VII as the main product, along with the triacetate and some unreacted material. The structure of VII was inferred from the nuclear magnetic resonance (nmr) spectrum and was supported by the fact that it reacted with III to give a product identical with IX.

A similar result was obtained in the condensation of 2-*O*-acetyl-1,6-anhydro-β-D-galactopyranose (VI) with the bromide III. The reaction, which was carried out in dichloroethane in the presence of mercuric cyanide, led to a 47% yield of a mixture of the two isomers VIII and XIV in an approximate ratio of 3:2. After passing through a silica gel column the isomers were separated by fractional crystallization as homogeneous products. The infrared spectra of both glycosides showed, in addition of a strong band of 11.25 μ (β linkage), a minor absorption at 11.7 μ which disappeared in the subsequent steps of the synthesis and was probably due to a small amount of the α isomer. The nmr spectra of the two pairs of glycosides VIII–XIV and IX–XV showed a distinct shift of the acetate resonances in comparison with the mono- and diacetates VI and VII. The τ value of the axial acetoxyl of VI (7.88) was found to be increased in VIII to 7.94 and still higher in XIV (8.03) with the hexose unit as vicinal group. Similarly are the acetate resonances shifted in IX and XV. In triacetylgalactosan, both the axial and equatorial groups are reported to have considerably lower values.[17] These observations are probably due to a shielding effect of the bulky substituent.[18]

For introduction of the N-acetyl group, the isomeric disaccharides VIII and XIV (Scheme I) were deacylated by barium methoxide and treated at room temperature with aqueous barium hydroxide to remove the protective dichloroacetyl group. Subsequent acetylation afforded X and XVI. Their structure was proved by converting them, respectively, into the deacetylated glycosides XI and XVII. The former consumed 2 moles of periodate, whereas the latter reacted with 1 mole of the reagent.

The 1,6-anhydro ring was found to be rather resistant to the usual acidic reagents, and more drastic conditions than those described in the literature[19,20] had to be used. Under these conditions the 3-O isomer suffered partial cleavage. Another difference between the two isomers was found in their behavior to alkaline reagents. Whereas XII could be smoothly deacetylated by barium methoxide to the desired disaccharide XIII, the same treatment of XVIII caused complete rupture of the glycosidic bond. This result is in accordance with the well known alkali lability of 1 → 3 disaccharides.[21-23]

Experimental Section

Melting points were taken on a Fischer-Johns apparatus. Optical rotations were determined with a Perkin-Elmer No. 141 polarimeter. Nmr spectra were recorded in deuteriochloroform

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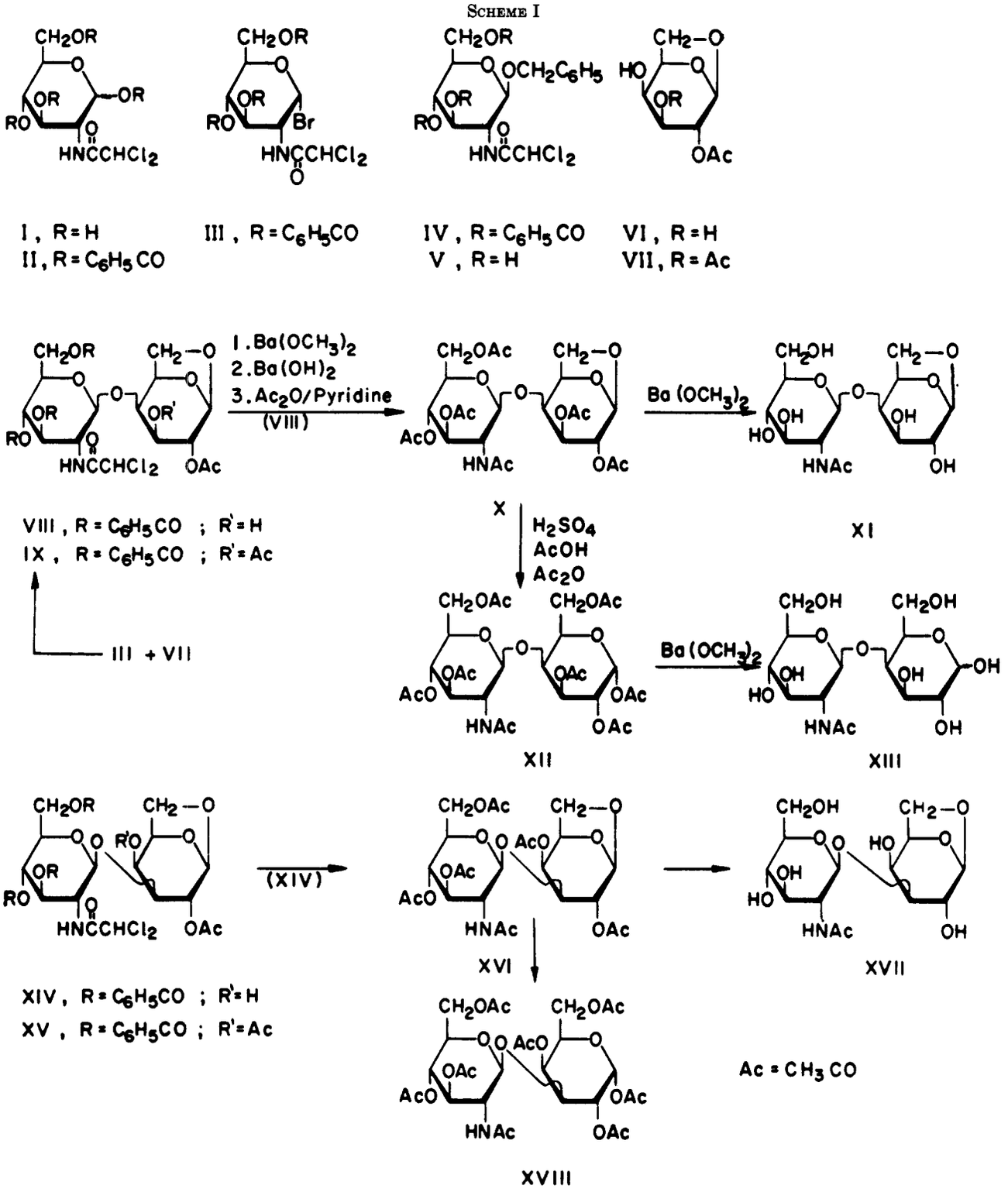
SCHEME I



with a Varian A-60 spectrometer. Thin layer chromatograms were prepared on silica gel G (Merck, Darmstadt) and developed with anisaldehyde–ethanol–concentrated sulfuric acid (18:1:1). For column chromatography 50–70 parts of silica gel Davison (grade 950, 60–200 mesh) was used without pretreatment. The fractions eluted were 4–6 ml/g of adsorbent. Pyridine (Fluka) was dried over barium oxide before use. Optical rotations were determined in chloroform, unless stated otherwise.

2-Deoxy-2-dichloroacetamido-D-glucopyranose (I).—A stirred mixture of glucosamine hydrochloride (Mann Research Laboratories, 35 g), dried sodium dichloroacetate (52.5 g), and dichloroacetic anhydride (Eastman, 126 ml) was gradually warmed within 2 hr to 70°, which temperature was maintained for 6 hr. The dark syrup was cooled to room temperature and poured into ice water (1.5 l.), and the mixture was kept in the refrigerator overnight. After decantation the semisolid was thoroughly triturated two to three times with water (1 l.), and the precipitate was filtered and washed to neutrality. The product was dissolved in hot methanol (800 ml); the solution was treated with charcoal (3 g), and filtered. After addition of distilled water (800 ml) to the filtrate, the suspension was cooled in the refrigerator overnight, washed with cold methanol–water (1:1), and dried over phosphorus pentoxide. The amido ester (55–60 g) melted at 60–70° and gave a chlorine value of about 44%. For deacylation, the product was dissolved in absolute methanol (1 l.), the solution was cooled to −10°, and a solution of 1 *N* barium methoxide (20 ml) was added. After standing at 2–5° overnight, the solvent was evaporated *in vacuo*, and the residue was recrystallized from ethanol (800 ml), giving 32 g (68%) of the amide I, melting at 203–205°, $[\alpha]^{20}D$ +27.5° (in water) after mutarota-

tion from 51.0° (8 hr). The infrared spectrum in potassium bromide showed bands at 3.0 (OH), 6.0, 6.45 (amide), and 12.3 μ (CCl). Thin layer chromatography (tlc) (benzene–methanol, 7:3) gave R_{I-NAc} 1.6.

Anal. Calcd for $C_8H_{13}Cl_2NO_6$: C, 33.12; H, 4.52; Cl, 24.44. Found: C, 33.26; H, 4.67; Cl, 24.37.

1,3,4,6-Tetra-*O*-benzoyl-2-deoxy-2-dichloroacetamido-D-glucopyranose (II).—To a stirred solution of I (10 g) in dry pyridine (250 ml) was added freshly distilled benzoyl chloride (20 ml) at −10°, and the mixture was allowed to stand at ambient temperature overnight. The reaction product was poured into ice water (100 ml); the semisolid was separated by decantation and triturated successively with 0.5 *N* hydrochloric acid and water. Crystallization from methanol–water (95:5) gave 20 g (82%) of white needles: mp 185–186°, $[\alpha]^{20}D$ +75.4°, tlc (benzene–ether, 9:1) R_{III} 0.84.

Anal. Calcd for $C_{36}H_{29}Cl_2NO_{10}$: C, 61.20; H, 4.14; Cl, 10.04. Found: C, 61.11; H, 4.12; Cl, 9.81.

3,4,6-Tri-*O*-benzoyl-2-deoxy-2-dichloroacetamido-α-D-glucopyranosyl Bromide (III).—To a stirred suspension of the benzoate II (6 g) in acetic anhydride (9 ml) cooled to −15° was added a cold 45% solution of hydrogen bromide in acetic acid (21 ml). After 15 min the temperature was allowed to rise, and the mixture was stirred at 18–20° for 5 hr. The clear solution was concentrated *in vacuo* (<1 mm) at 25–30°. For complete removal of anhydride the oily product was distilled with three portion each of 10 ml of toluene. The residue was dissolved in dry ether (15 ml), the solution was filtered, and dry hexane (5-7 ml) was added at 15–20° while crystallization was being induced by scratching. Aftr cooling overnight, the white amorphous precipitate was collected and washed with cold ether–hexane (1:1): yield 4.9 g, (85%), mp 125–127°, $[\alpha]^{20}D$ +88.6°, tlc (benzene–ether, 9:1) R_{II} 1.2.

Anal. Calcd for $C_{29}H_{24}BrCl_2NO_8$: C, 52.35; H, 3.64; Br, 12.01; Cl, 10.66; N, 2.10. Found: C, 52.30; H, 3.70; Br, 11.95; Cl, 10.66; N, 2.01.

3,4,6-Tri-*O*-benzoyl-2-deoxy-2-dichloroacetamido-D-glucopyranose.—The bromide III (665 mg) was dissolved in acetone, water (2 ml) was added, and the solution was shaken with silver carbonate (1 g) for 1 hr. The filtrate was evaporated *in vacuo* to dryness and the residue was chromatographed by a column of silica gel. The product eluted with dichloromethane–ether (8:2) crystallized from alcohol–water (9:1, 12 ml): yield 530 mg (88%), mp 168°, tlc (benzene–ether, 9:1) R_{II} 0.33.

Anal. Calcd for $C_{29}H_{25}Cl_2NO_9$: C, 57.82; H, 4.18; Cl, 11.77; N, 2.33. Found: C, 57.95; H, 4.25; Cl, 11.90; N, 2.53.

Benzyl 3,4,6-Tri-*O*-benzoyl-2-deoxy-2-dichloroacetamido-β-D-glucopyranoside (IV).—The bromide III (3.3 g) was stirred with benzyl alcohol (10 ml) at room temperature for 3 hr. The solution was then treated with hexane (20 ml) and the supernatant was decanted. This procedure was repeated nine times. The sticky residue solidified on addition of ether, and the product was filtered. Crystallization from ethanol (15 ml) gave needles (3 g, 87.5%) of mp 145°, $[\alpha]^{20}D$ −64.2°. The infrared spectrum showed a band at 11.2 μ characteristic of β-glycosides, tlc (benzene–methanol, 3:1) R_{II} 1. The same product was obtained when silver carbonate was added as catalyst.

Anal. Calcd for $C_{35}H_{31}Cl_2NO_9$: C, 62.43; H, 4.51; Cl, 10.24. Found: C, 62.61; H, 4.68; Cl, 10.17.

Benzyl 2-Deoxy-2-dichloroacetamido-β-D-glucopyranoside (V).—The glycoside IV (dried over phosphorous pentoxide, 1 g) was dissolved in chloroform (10 ml) and absolute methanol (3 ml), and treated at −10° with 1 *N* barium methoxide (10 drops). The solution was kept at 2–5° overnight, and the separated crystals were filtered and washed with chloroform and ether. Recrystallization from ethanol gave 0.5 g (90%) of needles: mp 239–240°, $[\alpha]^{20}D$ −20.3° (*c* 1, pyridine), tlc (benzene–methanol, 3:1) R_{IV} 0.5.

Anal. Calcd for $C_{15}H_{19}Cl_2NO_6$: C, 47.38; H, 5.04; Cl, 18.65; N, 3.68. Found: C, 47.13; H, 5.05; Cl, 18.34; N, 3.88.

2-*O*-Acetyl-1,6-anhydro-4-*O*-(3,4,6-tri-*O*-benzoyl-2-deoxy-2-dichloroacetamido-β-D-glucopyranosyl)-β-D-galactopyranose (VIII).—To a solution of 2-acetylgalactosan (VI,[20,24] 2.5 g, 12.25 mmoles) in dry dichloroethane (150 ml) were added mercuric cyanide (2.24 g, 8.85 mmoles) and the bromide III (11.2 g, 16.85 mmoles), and the reaction was allowed to proceed with stirring at 40–45° for 7 days. The cooled solution was then poured into a mixture of ice water (200 ml) and chloroform (250 ml), and shaken thoroughly with 5% sodium hydrogen carbonate (20 ml). The chloroform layer was washed four times with cold water, dried over sodium sulfate, and evaporated *in vacuo* to constant weight (12.65 g). Tlc (benzene–methanol, 185:15) showed, in addition to III and its debrominated derivative, four other spots. The product was dissolved in benzene (15 ml) and passed through a silica gel column, the eluates being analyzed by nmr spectra. The fraction eluted with benzene–ether (25:20) contained the two slowest moving spots and showed signals consistent with the structure of the glycosides VIII and XIV. The mixture weighing 4.65 g (47.6% based on VI) was treated with boiling methanol from which 2 g of VIII melting at 138–140° crystallized on cooling. Two further recrystallizations from methanol yielded 1.7 g of a chromatographically homogeneous product with R_f 0.41 or R_{XIV} 0.73, mp 146–148°, $[\alpha]^{20}D$ −40°. The infrared spectrum showed a strong band at 11.25 μ (β-glycoside) and a minor absorption at 11.7 μ which may be due to a small amount of the α isomer. The nmr spectrum showed signals at τ 2–2.8 (15 aromatic protons), 4.15, and 7.94 (1-dichloroacetyl and 3-acetyl protons).

Anal. Calcd for $C_{37}H_{35}Cl_2NO_{14}$: C, 56.35; H, 4.47; Cl, 8.99. Found: C, 55.99; H, 4.50; Cl, 9.11.

2-*O*-Acetyl-1,6-anhydro-3-*O*-(3,4,6-tri-*O*-benzoyl-2-deoxy-2-dichloroacetamido-β-D-glucopyranosyl)-β-D-galactopyranose (XIV).—The collected mother liquors of VIII were evaporated *in vacuo* to dryness and chromatographed by a silica gel G column. Dichloromethane–ether (20:3) eluted 1.6 g of XIV, followed by a 1:1 mixture of both glycosides (0.6 g) and finally by a further crop of VIII (0.5 g). The first fraction yielded, after recrystallization from ethanol, 1.4 g of the homogeneous 3-O isomer: mp 235–236°, $[\alpha]^{20}D$ −40.6°, R_f 0.54 or R_{VIII} 1.36. The infrared and nmr spectra of XIV were essentially identical with those of VIII, except for the acetoxy signal which appeared at τ 8.03.

Anal. Calcd for $C_{37}H_{35}Cl_2NO_{14}$: C, 56.35; H, 4.47; Cl, 8.99. Found: C, 56.54; H, 4.49; Cl, 9.29.

2,3-Di-*O*-acetyl-1,6-anhydro-4-*O*-(3,4,6-tri-*O*-benzoyl-2-deoxy-2-dichloroacetamido-β-D-glucopyranosyl)-β-D-galactopyranose (IX). A.—Acetylation of VIII (158 mg) was carried out in the usual manner. After stirring overnight with acetic anhydride (2 ml) and pyridine (4 ml), the solution was warmed to 50° for 1 hr, then concentrated *in vacuo* at this temperature and coevaporated with several portions of toluene to remove completely the pyridine. The residue was crystallized from chloroform and ether and recrystallized from ethanol: yield 140 mg (85%), mp 235–236°, $[\alpha]^{20}D$ −33.1°, R_{VIII} 1.72. The melting point was not depressed by admixture of the reaction product of III with VII. The integration of signals in the nmr spectrum showed a ratio of 15 aromatic protons to 6 of the acetoxy groups (τ 7.92 and 8.0).

Anal. Calcd for $C_{39}H_{37}Cl_2NO_{15}$: C, 56.39; H, 4.49; Cl, 8.54. Found: C, 56.65; H, 4.54; Cl, 8.54.

B.—A solution of VII (0.700 g), mercuric cyanide (0.522 g) and the bromide III (2.61 g) in dichloroethane (50 ml) was refluxed with stirring for 3 days. On working-up as described for the glycosidation of VI, the chromatographically pure product (210 mg, 9%) was eluted from a silica gel column with benzene–ether (1.5:1). After crystallization from ethanol it melted at 235–236°, $[\alpha]^{20}D$ −33.4°. The compound was identical in every respect with that obtained by acetylation of VIII.

2,3-Di-*O*-acetyl-1,6-anhydro-4-*O*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-β-D-galactopyranose (X).—A solution of VIII (1.3 g) in dry chloroform (5 ml) and absolute methanol (20 ml) was treated at −15° with 1 *N* barium methoxide (15 drops) and allowed to stand in the refrigerator overnight at about +2°. The solution was neutralized with methanolic hydrogen chloride to pH 6 and evaporated *in vacuo*. For hydrolysis of the amide group the residue was dissolved in methanol (15 ml), 1 *N* methanolic barium methoxide (12 ml) and water (3 ml) were added, and the solution was allowed to stand overnight at room temperature (17–22°). After 24 hr crystals appeared, and tlc (benzene–methanol, 2:1) indicated the completion of the reaction. The solution was neutralized with methanolic hydrogen chloride, evaporated to dryness *in vacuo*, and the moisture was removed by evaporation with isopropyl alcohol to constant weight. The amino sugar, dried over phosphorous pentoxide for 48 hr, was dissolved in pyridine (14 ml), acetic anhydride (8 ml) was added, and the mixture was stirred overnight at room temperature. After warming at 50° for 1 hr, the solution was concentrated and coevaporated several times with toluene. The residue was taken up with chloroform (100 ml) and the solu-

(24) G. H. Colemann, *Ind. Eng. Chem.*, **36**, 1040 (1944).

tion was washed with four portions of water (50 ml). The residue obtained after evaporation of the dried solution was crystallized from acetone–ether and recrystallized from ethanol. The fully acetylated compound X was obtained in 86.5% yield (820 mg): mp 238–239°, $[\alpha]^{20}D$ −29.3°, infrared spectrum (KBr) 6.0 and 6.45 μ (amide). The nmr spectrum showed signals of six 3-acetyl protons at τ 7.91, 7.95, 7.95, 8.01, 8.01, and 8.02; tlc (ethyl acetate) R_{XVI} 0.9.

Anal. Calcd for $C_{24}H_{33}NO_{15}$: C, 50.08; H, 5.78. Found: C, 49.91; H, 5.71.

Periodate Oxidation of XI and XVII.—Deacylation of X and XVI was effected with barium methoxide as described above. The residue obtained after evaporation of the methanol *in vacuo* at room temperature was dissolved in water (10 ml) and the solution was immediately passed through a column (10 × 120 mm) of Dowex 50-X8, 50–100 mesh, H^+ form. The eluate (100 ml) was concentrated *in vacuo;* the residue was coevaporated several times with isopropyl alcohol, and dried over phosphorous pentoxide for 48 hr. The products obtained in theoretical yield were homogeneous on tlc and subjected to periodate oxidation by the spectrophotometric method.[25] The reaction was performed in the dark at 35° until the concentration of periodate remained constant for 48 hr. Compound XVII consumed 1.17 moles/mole, whereas the consumption of XI was 2.14 moles of the reagent.

1,2,3,6-Tetra-*O*-acetyl-4-*O*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-α-D-galactopyranose (XII).—The ring opening in X was effected by the method of Hudson,[19] modified with respect to temperature and the quantity of sulfuric acid. The disaccharide (800 mg) was stirred for 2.5 hr at 55° with a 7:3 mixture (32 ml) of acetic anhydride–acetic acid and concentrated sulfuric acid (0.4 ml). The cooled reaction product was poured into ice water (200 ml) containing 5% sodium hydrogen carbonate (40 ml) and extracted with four 50-ml portions of chloroform. The combined extract was washed three times with water and concentrated *in vacuo*. The residue was taken up several times with isopropyl alcohol and evaporated to constant weight (880 mg). The product obtained by elution from a silica gel G column with 1,1-dichloromethane–ether (1:1) was crystallized from ether and then from ethanol: yield 600 mg (63.5%), mp 178–179°, $[\alpha]^{20}D$ +55.5°, tlc (ethyl acetate) R_X 1.1. The nmr spectrum showed signals of eight 3-acetyl protons at τ 7.84, 7.92, 7.97, 7.97, 7.97, 8.00, 8.00, and 8.05).

Anal. Calcd for $C_{28}H_{39}NO_{18}$: C, 49.63; H, 5.80; N, 2.07. Found: C, 49.62; H, 6.00; N, 2.30.

4-*O*-(2-Acetamido-2-deoxy-β-D-glucopyranosyl)-D-galactopyranose (XIII).—A solution of the octaacetyl derivative XII (135 mg) in absolute methanol (10 ml) was deacetylated as described above. The residue resulting from evaporation of the methanol was dissolved in water (10 ml) and the solution was immediately passed through a column (10 × 120 mm) of Dowex 50-X8, 50–100 mesh, H^+ form. The eluate (200 ml) was evaporated *in vacuo*, and the residue was collected by treatment with ether and crystallized by dissolving in a few drops of water and adding methanol–ether (approximately 3:1). The hygroscopic disaccharide (55 mg, 72%) was homogeneous on tlc (1-butanol–acetone–water, 4:5:1): $R_{lactose}$ 1, mp 162–165° dec, $[\alpha]^{20}D$ +8.0° (*c* 1, water). The infrared spectrum showed 11.2 (β-glycoside) and 11.45 μ (galactopyranose).

(25) G. O. Aspinall and R. J. Ferrier, *Chem. Ind.* (London), 1216 (1957).

Anal. Calcd for $C_{14}H_{25}NO_{11}$: C, 43.86; H, 6.57; N, 3.65. Found: C, 43.81; H, 6.70; N, 3.64.

The compounds derived from XIV were prepared in the same manner as that described for the 4 isomers.

2,4-Di-*O*-acetyl-1,6-anhydro-3-*O*-(3,4,6-tri-*O*-benzoyl-2-deoxy-dichloroacetamido-β-D-glucopyranosyl)-β-D-galactopyranose (XV) was prepared as described for IX, but could not be induced to crystallize. The oily product was homogeneous by tlc and identical with IX by infrared and nmr spectra (the two acetoxy protons appeared at τ 7.96 and 8.05).

2,4-Di-*O*-acetyl-1,6-anhydro-3-*O*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-β-D-galactopyranose (XVI) was obtained in 76% yield. The infrared and nmr spectra were identical with those of X; XVI had mp 202–204°, $[\alpha]^{20}D$ −77.7°, tlc (ethyl acetate) R_f 0.344 and R_X 1.15.

Anal. Calcd for $C_{24}H_{33}NO_{15}$: C, 50.08; H, 5.78. Found: C, 49.76; H, 5.83.

1,2,4,6-Tetra-*O*-acetyl-3-*O*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-α-D-galactopyranose (XVIII).—The ring opening of XVI was accompanied by scission of the disaccharide, and the reaction time was, therefore, limited to 1 hr. Even so, spots of pentaacetylgalactose and a glucosamine derivative were identified by tlc (ethyl acetate), which reduced the yield to 44% (after crystallization); XVIII had mp 212–213°, $[\alpha]^{20}D$ +79.5°, R_f 0.325 and R_{XVI} 0.95.

Anal. Calcd for $C_{28}H_{39}HO_{18}$: C, 49.63; H, 5.80; N, 2.07. Found: C, 49.70; H, 5.84; N, 2.09.

2,3-Di-*O*-acetyl-1,6-anhydro-β-D-galactopyranose (VII). A. By Acetylation of VI.—The acetylgalactosan (0.612 g, 3 mmoles), dissolved in pyridine (6 ml), was treated overnight at room temperature with acetic anhydride (0.31 ml, 3.3 mmoles). After warming the solution at 50° for 1 hr, the excess of acylating agents was removed *in vacuo*, and the remainder was coevaporated several times with toluene. Tlc (ethyl acetate) showed unreacted material (R_f 0.44), triacetylgalactosan (R_{VI} 1.56), and two spots moving together (R_{VI} 1.3). The mixture was chromatographed by a silica gel column from which the triacetate was removed by benzene–ether (5:3), whereupon 400 mg of the diacetate were eluted with benzene–ether (1:1). The pure product (250 mg, 54%) was obtained after crystallization from ether and recrystallization from isopropyl alcohol, in both cases with the addition of a few drops of hexane: mp 113–115°, $[\alpha]^{20}D$ −0.8°. The nmr spectrum of the diacetate showed two axial groups at τ 7.88 and 7.91, in contrast to the triacetate[17] in which the equatorial group at C-4 appeared at 7.98 and the two axial groups had τ 7.86.

Anal. Calcd for $C_{10}H_{14}O_7$: C, 44.78; H, 5.73. Found: C, 44.87; H, 5.73.

B. By Direct Acetylation of Galactosan.—Treatment of 1,6-anhydro-β-D-galactopyranose (0.324 g, 2 mmoles) with acetic anhydride (0.47 ml, 5 mmoles) as above yielded 200 mg (41%) of VII.

Registry No.—I, 14213-34-4; II, 14213-35-5; III; 14213-36-6; IV, 14213-37-7; V, 14213-38-8; VII, 14213-39-9; VIII, 14213-40-2; IX, 14213-41-3; X, 14213-42-4, XII, 14362-46-0; XIII, 14213-43-5; XIV, 14213-44-6; XV, 14213-45-7; XVI, 14409-82-6; XVIII, 14213-46-8; 3,4,6-tri-*O*-benzoyl-2-deoxy-2-dichloroacetamido-D-glucopyranose, 14213-47-9.