from the above chromatogram of the hydrogenation product was recrystallized three times from chloroform–hexane to yield 32 mg. of pure methyl 3,11-diketobisnorallocholanate, m.p. 202–203.5°, $[\alpha]^{23}D$ +55° (*c* 0.762 in acetone). The infrared spectrum was in agreement with the structure suggested above.

Anal. Calcd. for $C_{23}H_{34}O_4$: C, 73.76; H, 9.15. Found: C, 74.08; H, 9.38.

3,11-Diketobisnorallocholanic acid (XI) was formed when compound X (60.5 mg.) was refluxed in 10 ml. of methanolic 1 *N* potassium hydroxide for 4 hours. Separation of the product into acidic and neutral components yielded 10 mg. of starting material and 49.2 mg. of the desired acid which was recrystallized twice from ether, m.p. 256–258°, $[\alpha]^{23}D$ +60° (*c* 0.391 in acetone).

Anal. Calcd. for $C_{22}H_{32}O_4$: C, 73.30; H, 8.95. Found: C, 73.03; H, 8.95.

D. Structure Proof of 6β,11α,22-Trihydroxybisnor-4-cholen-3-one. Bioconversion of 11α,22-Dihydroxybisnor-4-cholen-3-one (II) to 6β,11α,22-Trihydroxybisnor-4-cholen-3-one (III) by *Cunninghamella blakesleeana* (A.T.C.C. 8688a).—To 12 l. of medium H was added a vegetative inoculum of *Cunninghamella blakesleeana* and the acetone solution (50 ml.) of 1 g. of substrate (II). After 72 hours of incubation, extraction with methylene dichloride gave 10.32 g. of solids. Papergram analysis indicated that, besides a multitude of very minor components, 6β,11α,22-trihydroxybisnor-4-cholen-3-one was the preponderant metabolite. The extract was dissolved in 100 ml. of benzene and chromatographed over 250 g. of alumina. Acetone–5% methanol and acetone–10% methanol eluted 466.6 mg. of an oil which was shown by papergram to contain about 20% of compound III. This fraction was allowed to crystallize from acetone–ether 1:1 by slow evaporation of the solvents at room temperature to give 38.5 mg. of crystals, m.p. 222–228°. The ultraviolet spectrum [λ_{max}^{alc} 239 mμ (*E* 12,400)] and the infrared spectrum established the identity of this compound with 6β,11α,22-trihydroxybisnor-4-cholen-3-one (III) as isolated from bioconversions with *Rhizopus*.

Rearrangement of III to 11α,22-Dihydroxybisnorallocholane-3,6-dione (XII).—Compound III (185 mg.) was suspended in 35 ml. of freshly distilled *t*-butyl alcohol and 10 ml. of 10% sulfuric acid. The suspension was heated on the steam-bath to complete solution. The reaction mixture was allowed to stand at room temperature overnight and then heated under reflux for 1.5 hours. After dilution with water, the steroids were extracted with ether–chloroform 5:1. The extracts were washed twice with 5% sodium carbonate and twice with water. Evaporation of the solvents yielded 224 mg. of an oily residue which was chromatographed in benzene solution (10 ml.) over 11 g. of alumina. Chloroform–10% acetone, chloroform–30% acetone, chloroform–50% acetone and acetone eluted 145 mg. of a saturated compound which was recrystallized twice from methanol–ether to give 71.5 mg. of crystals, m.p. 191–193°, $[\alpha]^{23}D$ −27° (*c* 0.363 in methanol). The infrared spectrum showed absorption bands for hydroxyl groups (3500 cm.$^{-1}$) and for non-conjugated ketones (1704 cm.$^{-1}$).

Anal. Calcd. for $C_{22}H_{34}O_4$: C, 72.89; H, 9.45. Found: C, 73.14; H, 9.42.

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KALAMAZOO, MICHIGAN

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4-*O*-Methyl-D-galactosamine Hydrochloride (2-Amino-2-deoxy-4-*O*-methyl-D-galactose Hydrochloride)[1,2]

BY ROGER W. JEANLOZ AND PIERRE J. STOFFYN[3]

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4-*O*-Methyl-D-galactosamine hydrochloride (2-amino-2-deoxy-4-*O*-methyl-D-galactose hydrochloride) has been prepared in crystalline form from 1,6:2,3-dianhydro-β-D-talopyranose and has been characterized through the following crystalline derivatives: *N*-(2′-hydroxynaphthylidene), methyl *N*-acetyl-α-D-glycoside and methyl *N*-acetyl-3,6-di-*O*-acetyl-α-D-glycoside.

In recent papers from this Laboratory,[4] syntheses of methylated galactosamines and methods for their identification and separation have been reported. The present paper describes the preparation of a new monomethylgalactosamine, 4-*O*-methyl-α-D-galactosamine hydrochloride (2-amino-2-deoxy-4-*O*-methyl-α-D-galactose hydrochloride) (VI) by the method shown in the accompanying diagram.

It is inconvenient to use D-galactosamine as a starting material because of the length of time involved in its preparation, and also because the route leading to the 4-methyl derivative requires a large number of intermediates as is analogously shown in the synthesis of 4-*O*-methyl-D-glucosamine.[5]

Hann and Hudson[6] and James, *et al.*,[7] describe a convenient route for the synthesis in quantity of 1,6:2,3-dianhydro-β-D-talose (I), from lactose.

The course of the reaction of alkaline reagents on epoxy sugars is well known and the results can be predicted with a high degree of certainty.[8] James, *et al.*,[7] treating I with ammonia were able to obtain the 2-amino-2-deoxy-D-galactose derivative in a 56% yield, whereas the 3-amino-3-deoxy-D-idose

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(2) Presented before the Division of Carbohydrate Chemistry at the 126th Meeting of the American Chemical Society, New York, N. Y., September 1954.

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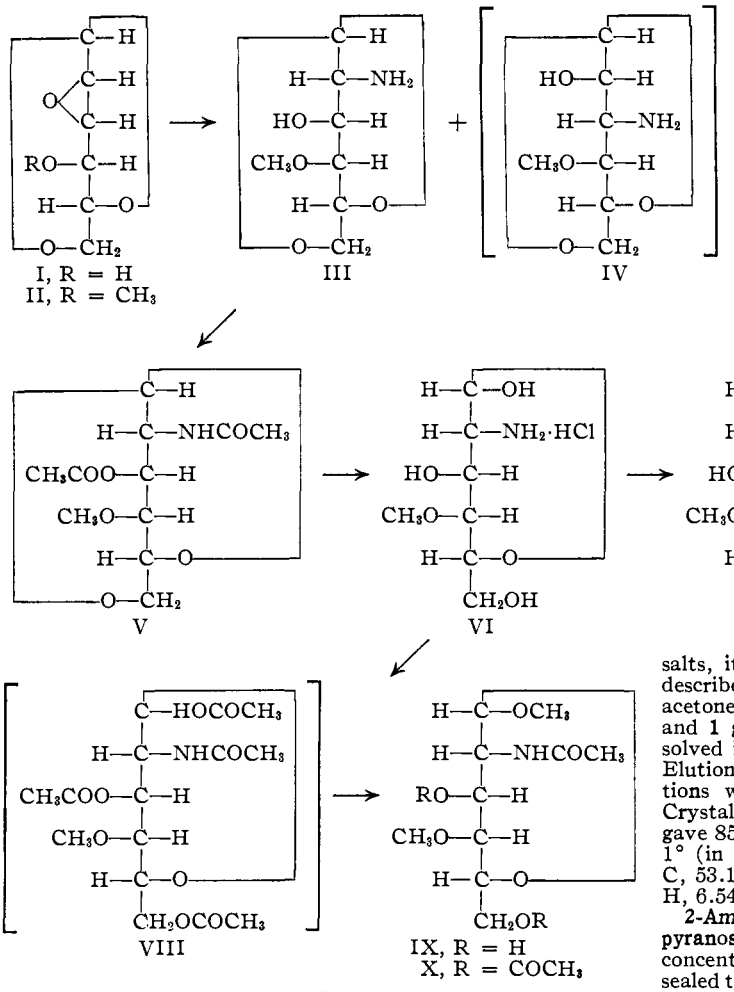
(4) P. J. Stoffyn and R. W. Jeanloz, THIS JOURNAL, **76**, 561, 563 (1954).

(5) C. T. Bothner-By and R. W. Jeanloz, unpublished.

(6) R. M. Hann and C. S. Hudson, THIS JOURNAL, **64**, 2435 (1942).

(7) S. P. James, F. Smith, M. Stacey and L. F. Wiggins, *J. Chem. Soc.*, 625 (1946).

(8) A. K. Bose, D. K. R. Chaudhuri and A. K. Bhattacharyya, *Chem. Ind.*, 869 (1953); F. H. Newth, *ibid.*, 1257 (1953).



derivative was found only in very small yield. In the present work, the preparation of 4-*O*-methyl-D-galactosamine proceeded along similar lines, starting from the 4-*O*-methyl derivative of I.

Methylation of I with methyl iodide and silver oxide gave the 4-methyl derivative II in good yield. When the epoxy ring was opened with ammonia, a galactosamine derivative III and a 3-aminoidose (IV) derivative were obtained and, as was the case in the non-methylated series, the predominant product was the galactosamine derivative. Complete separation of the 2-aminogalactose compound from the 3-aminoidose compound was achieved by chromatography of the *N*-acetyl-*O*-acetyl derivatives of these two. Investigation of the idose derivative will be reported later.

Hydrolysis of the 2-acetamido-3-*O*-acetyl-1,6-anhydro-2-deoxy-4-*O*-methyl-β-D-galactopyranose (V) with hot dilute hydrochloric acid led simultaneously to the opening of the 1,6-ring and deacetylation, giving crystalline 2-amino-2-deoxy-4-*O* methyl-α-D-galactose hydrochloride (VI), which was characterized by its crystalline *N*-(2′-hydroxynaphthylidene) derivative (VII).

Crystalline methyl 2-acetamido-2-deoxy-4-*O*-methyl-α-D-galactopyranoside (IX) and methyl 2-acetamido-3,6-di-*O*-acetyl-2-deoxy-4-*O*-methyl-α-D-galactopyranoside (X) were prepared so that the products here obtained could be compared with known methylated galactosamine derivatives.

There is little doubt that the methyl group is attached at C_4, since known 4-*O*-methyl-D-galactose and 2,4-di-*O*-methyl-D-galactose[9] were prepared from the same starting material, and the nature of the reactions here used is such that a shift of this methyl group is not to be expected.

Experimental[10]

1,6:2,3-Dianhydro-4-*O*-methyl-β-D-talopyranose (II).—To a solution of 1.0 g. of 1,6:2,3-dianhydro-β-D-talopyranose[7] in 5 ml. of acetone were added 25 ml. of methyl iodide and 1 g. of silver oxide. The mixture was refluxed overnight with stirring in the absence of moisture. After cooling the solution and filtering to remove the silver salts, it was concentrated to a sirup. (The procedure described above was repeated without the addition of acetone after a second addition of 25 ml. of methyl iodide and 1 g. of silver oxide.) The residual sirup was dissolved in benzene and chromatographed on silicic acid. Elution with mixtures of benzene and ether gave fractions which crystallized after being cooled to −60°. Crystallizations from a mixture of ether and pentane gave 855 mg. (78%) of prisms, m.p. 51°, $[\alpha]^{27}D$ −104 ± 1° (in methanol, *c* 4.70). *Anal.* Calcd. for $C_7H_{10}O_4$: C, 53.18; H, 6.37; OCH_3, 19.62. Found: C, 53.10; H, 6.54; OCH_3, 19.81.

2-Amino-1,6-anhydro-2-deoxy-4-*O*-methyl-β-D-galactopyranose (III).—A solution of 1.67 g. of II in 150 ml. of concentrated ammonia was heated at 100° for 30 hours in sealed tubes. After cooling, the solution was concentrated *in vacuo* after flushing the vessel with nitrogen. The partially crystalline residual sirup was recrystallized from a mixture of acetone and ether, giving 365 mg. of III; m.p. 95–96°, $[\alpha]^{22}D$ −37 ± 1° (in water, *c* 0.92). *Anal.* Calcd. for $C_7H_{13}O_4N$: C, 48.01; H, 7.48; N, 8.00. Found: C, 48.09; H, 7.63; N, 8.07.

2-Acetamido-3-*O*-acetyl-1,6-anhydro-2-deoxy-4-*O*-methyl-β-D-galactopyranose (V).—The residual mother liquors of the preparation of III were evaporated to dryness and the residue acetylated with 30 ml. of anhydrous pyridine and 6 ml. of acetic anhydride at room temperature for 24 hours. The solvents were evaporated *in vacuo* below 40°, the last traces being removed by codistillation with absolute toluene. The crystalline residue was recrystallized from ethanol, after filtration through charcoal, to give 720 mg. of V, m.p. 231–233°, $[\alpha]^{23}D$ −57 ± 1° (in chloroform, *c* 1.12). *Anal.* Calcd. for $C_{11}H_{17}O_6N$: C, 50.95; H, 6.61; OCH_3, 11.97. Found: C, 50.87; H, 6.53; OCH_3, 12.02.

The residual mother liquors of V were evaporated, the residue was dissolved in chloroform and chromatographed on silicic acid. A mixture of ethyl acetate and acetone 2:1 eluted 500 mg. of crystalline fractions. Recrystallization from a mixture of ethanol and ether gave an additional crop of 400 mg. of V. The total yield of galactosamine derivatives (III and V) was 52%, calculated on the basis of II. A mixture of ethyl acetate and acetone 1:1 eluted 700 mg. (25%) of crude crystalline fractions, probably 3-acetamido-2-*O*-acetyl-1,6-anhydro-3-deoxy-4-*O*-methyl-β-D-idopyranose.

4-*O*-Methyl-α-D-galactopyranosamine Hydrochloride (2-Amino-2-deoxy-4-*O*-methyl-α-D-galactopyranose Hydrochloride) (VI).—A solution of 300 mg. of V in 15 ml. of 2.5 *N* hydrochloric acid was heated for 24 hours in a sealed tube

(9) R. W. Jeanloz, THIS JOURNAL, **76**, 5684 (1954).
(10) R. W. Jeanloz, *ibid.*, **76**, 555 (1954).

at 100°. The solution was filtered through charcoal, concentrated to dryness *in vacuo* and the last traces of water were removed by codistillation with absolute ethanol. After standing for one month, the residual sirup crystallized. Recrystallization from a mixture of methanol and acetone gave 140 mg. (53%) of VI, decomposing above 178°. The product showed mutarotation, from $[\alpha]^{24}_{D}$ + 125° (after 10 minutes) to $[\alpha]^{26}_{D}$ +100 ± 1° (after 17 hours, in water, *c*, 1.09). *Anal.* Calcd. for $C_7H_{15}O_5NCl$: C, 36.61; H, 7.02; OCH_3, 13.51. Found: C, 36.93; H, 7.22; OCH_3, 13.23.

2-Deoxy-2-(2′-hydroxynaphthylidenamino)-4-*O*-methyl-α-D-galactopyranose (VII).—A solution of 37 mg. of VI in 1.0 ml. of water was treated as previously described[11] with 70 mg. of 2-hydroxynaphthaldehyde and 50 mg. of sodium acetate. The product was purified by chromatography on silicic acid. Forty-eight milligrams (87%) of crystalline fractions was eluted with pure acetone and mixtures of acetone and methanol. Recrystallization from a mixture of methanol and ether gave 43 mg. (77%) of yellow prismatic needles (VII), m.p. 207–209° (with decomposition). The product showed mutarotation from $[\alpha]^{27}_{5461}$ +187° (after 7 minutes) to $[\alpha]^{27}_{5461}$ +168 ± 2° (after 20 hours, in methanol, *c* 1.40). *Anal.* Calcd. for $C_{18}H_{21}O_6N$: C, 62.24; H, 6.09. Found: C, 62.27; H, 6.18.

Methyl 2-Acetamido-3,6-di-*O*-acetyl-2-deoxy-4-*O*-methyl-α-D-galactopyranoside (IX).—Sixty milligrams of VI was treated with 1.0 ml. of dry pyridine and 0.6 ml. of acetic anhydride for two days at room temperature. After addition of two drops at methanol the solution was evaporated *in vacuo* and dried overnight in a desiccator over sulfuric acid and soda lime to give the crude sirupy 2-acetamido-1,3,6-tri-*O*-acetyl-2-deoxy-4-*O*-methyl-D-galactopyranose (VIII). The sirup was refluxed for two hours with 5 ml. of 2% hydrochloric acid in methanol. After cooling, the solution was treated with an excess of silver carbonate and the silver salts were filtered. The remaining soluble silver ions were precipitated with hydrogen sulfide, the solution was filtered over a double layer of charcoal and Celite and evaporated *in vacuo* to give 69 mg. of crude crystalline methyl 2-acetamido-2-deoxy-4-*O*-methyl-D-galactopyranoside. The dry crystalline residue was acetylated by standing with a mixture of 0.5 ml. of dry pyridine and 0.3 ml. of acetic anhydride for two days at room temperature. After evaporation *in vacuo* and elimination of the last traces of solvent by codistillation with dry toluene, the sirupy residue was dissolved in benzene and chromatographed on silicic acid. Elution with mixtures of ether and ethyl acetate gave 52 mg. of crystalline fractions. Recrystallization from ether supersaturated with pentane gave 30 mg. of prismatic needles, m.p. 114–115°, $[\alpha]^{25}_{D}$ +82 ± 2° (in chloroform, *c* 1.30). *Anal.* Calcd. for $C_{14}H_{23}O_8N$: C, 50.44; H, 6.95; OCH_3, 18.62. Found: C, 50.42; H, 6.85; OCH_3, 18.76.

The crystallization of IX was difficult and the partially crystalline residues were directly transformed to X (see below).

Methyl 2-Acetamido-2-deoxy-4-*O*-methyl-α-D-galactopyranoside (X).—A solution of 16.0 mg. of IX in methanol was treated with 0.5 ml. of a solution of 0.2 *N* barium methoxide in methanol. After standing overnight at 0°, the solution was filtered through a column of Dowex 50 in the H form. The solution was evaporated *in vacuo* and the crystalline residue was recrystallized from a mixture of methanol and ether to give 11.5 mg. (95%) of needles, m.p. 241–242°, $[\alpha]^{20}_{D}$ +147 ± 6° (in methanol, *c* 0.52). *Anal.* Calcd. for $C_{10}H_{19}O_6N$: C, 48.18; H, 7.68. Found: C, 48.13; H, 7.62.

Twenty-two milligrams of mother liquors from the preparation of IX was similarly transformed to X. The product was purified by chromatography on silicic acid. Mixtures of acetone and methanol eluted crystalline fractions. Recrystallization from a mixture of methanol and ether gave 8.5 mg. of X. The total yield of X, calculated on the basis of VI, was 46%.

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BOSTON, MASS.

(11) R. W. Jeanloz, THIS JOURNAL, **74**, 4597 (1952).

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Syntheses of 4-*O*-Methyl-β-D-galactopyranose and 2,4-Di-*O*-methyl-α-D-galactopyranose[1,2]

BY ROGER W. JEANLOZ

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4-*O*-Methyl-β-D-galactopyranose and 2,4-di-*O*-methyl-α-D-galactopyranose have been prepared from 1,6:2,3-dianhydro-4-*O*-methyl-β-D-talopyranose by the action of aqueous potassium hydroxide and sodium methoxide, respectively, with subsequent hydrolysis in each case.

Although 4-*O*-methyl-β-D-galactopyranose (VI) and more often 2,4-di-*O*-methyl-α-D-galactopyranose (IX) have been isolated many times in the study of the structure of galactose-containing polysaccharides, their syntheses have not yet been reported.[3] The opening of the epoxy ring of 1,6:2,3-dianhydro-β-D-talopyranose by the action of basic reagents has been reported[4] to yield the 2-amino-2-deoxy derivative of galactose on treatment with ammonia, and the 2-*O*-methyl derivative of galactose on treatment with sodium methoxide.

In the preceding paper,[5] the preparation of crystalline 1,6:2,3-dianhydro-4-*O*-methyl-β-D-talopyranose (III) and its reaction with ammonia has been described. The further investigation of the reactions of the readily accessible III with alkaline reagents appeared to provide an attractive route to the synthesis of VI and IX, and was followed through as described below.

Treatment of III with aqueous potassium hydroxide for 40 hours gave 1,6-anhydro-4-*O*-methyl-β-D-galactopyranose (I), which was purified through its 2,3-di-*O*-acetyl derivative II, in 87% yield (calculated on the basis of a theoretical yield from III). No idose derivative was obtained. Hydrolysis of the 1,6-anhydro ring gave crystalline 4-*O*-methyl-

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(2) Presented before the Division of Carbohydrate Chemistry at the 126th Meeting of the American Chemical Society, New York, N. Y., September 1954.

(3) D. J. Bell, *Adv. Carbohydrate Chem.*, **6**, 11 (1951).

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