Paper chromatograms developed in irrigants A and B and sprayed with indicator C revealed monoacetone D-glucose as the only sugar derivative; yield, 100%; m.p. 159–160°, undepressed when admixed with authentic sample; $[\alpha]^{25}D$ −12.3 (*c* 6.5, in water).

Pure monoacetone D-glucose was obtained by dissolving the undried crystalline mass obtained above in 100 ml. of warm ethyl acetate. Incompletely dried monoacetone D-glucose preparations dissolve rapidly in a minimum of ethyl acetate, whereas thoroughly dried preparations are difficult to solvate. Cooling the ethyl acetate solution to 0° gave a pure white crystalline product in 90% yield; m.p. 161°; $[\alpha]^{25}D$ −11.6 (*c* 2.5, in water).

3,4,6-Tri-*O*-acetyl-2-amino-2-deoxy-α-D-galactopyranosyl Bromide Hydrobromide[1]

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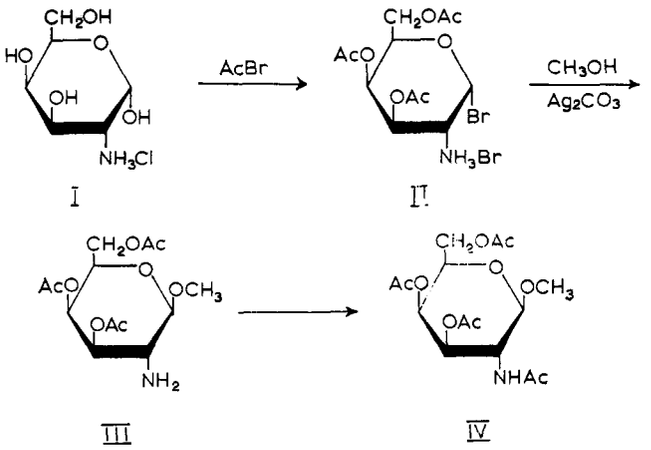
Received May 6, 1963

Peracylated glycosyl halides are valuable intermediates in a wide range of syntheses,[2] but such derivatives of the 2-amino-2-deoxy sugars suffer from two important limitations as general intermediates in synthesis. It is difficult or impossible to remove the *N*-acyl blocking group after a coupling reaction has been effected, with, for example, the peracetylated or perbenzoylated derivatives, and a 2-acetamido or 2-benzamido derivative results. Even labile *N*-substituents may be difficult to remove when sensitive functions are introduced at C-1.[3] The second complicating factor arises from the readiness with which a 2-acylamido group interacts with the C-1 glycosyl halide function, to give oxazoline[4] or oxazolidine[5] type derivatives.[6]

In the 2-amino-2-deoxy-D-galactose series, the fully acetylated halides, 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-galactopyranosyl bromide,[7] and chloride[8] have been reported; the present work describes the synthesis of 3,4,6-tri-*O*-acetyl-2-amino-2-deoxy-α-D-galactopyranosyl bromide hydrobromide (II), a glycosyl halide derivative in which the amino group is unsubstituted. By analogy with the corresponding known[9] D-glucose derivative, compound II should undergo a wide range of reactions leading to β-D-galactopyranosyl derivatives with an unsubstituted amino group at C-2.

The D-glucose analog of II is prepared[9] by heating 2-amino-2-deoxy-D-glucose hydrochloride with acetyl bromide at 70°, a procedure which is an adaptation of



the seldom-used[3,4] method of Colley[10] for preparation of 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl chloride. The reaction is capricious, but under carefully controlled conditions[11] good yields of the aminoglycosyl halide are obtainable. When applied to 2-amino-2-deoxy-α-D-galactose hydrochloride (I) under the conditions of Wolfrom and Shen Han[11] for the D-glucose analog, a dark red crystalline product, exhibiting a poor analysis for II, was obtained in modest yield; at lower temperatures reaction was incomplete, even at extended reaction times. Conditions were established, with heating at 55°, where about 60% of the starting material underwent reaction, to give the desired glycosyl bromide II as a crystalline product with acceptable purity without further recrystallization. The yields based upon material reacted, varied between 65 and 90%, the run described (76%) being typical. The unchanged starting material could be recovered by filtration and recycled in the reaction. Product II appeared stable for at least several weeks, if stored in a desiccator, and the stored material showed no change in its infrared spectrum. The observed molecular rotation value of +71,200° is indicative of the α-D anomeric configuration.

Compound II was treated with methanol in the presence of silver carbonate to give methyl 3,4,6-tri-*O*-acetyl-2-amino-2-deoxy-β-D-galactopyranoside (III) as a sirup. Acetylation of III hydrobromide gave the known[7] crystalline methyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-galactopyranoside (IV); this establishes that II reacts with alcohols to give glycosides of the β-D configuration.

Experimental[12]

3,4,6-Tri-*O*-acetyl-2-amino-2-deoxy-α-D-galactopyranosyl Bromide Hydrobromide (II).—A modification of the procedure

(1) Supported by Contract No. DA-49-193-MD-2143 (Research Foundation Project 1187) from the Walter Reed Army Institute of Research, Washington, D. C. The opinions expressed in this article are those of the authors, and not necessarily those of the sponsoring agency.

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(11) M. L. Wolfrom and T. M. Shen Han, *J. Org. Chem.*, **26**, 2145 (1961).

(12) Melting points were determined with a Fisher-Johns apparatus and correspond to corrected melting point. Specific rotations were determined with a 4-dm. polarimeter tube, and optical rotatory dispersion measurements were taken with a Rudolph Model 260/655/850/810-614 recording spectropolarimeter. Infrared spectra were determined with a Perkin-Elmer Infracord infrared spectrophotometer. The potassium bromide pellets were pressed from a finely ground mixture of the dried sample with dry analytical grade potassium bromide. Elemental microanalyses were made by W. N. Rond. X-Ray powder diffraction data: interplanar spacing, Å., CuKα radiation; relative intensity, estimated visually: s, strong; m, medium; w, weak; v, very. Strongest lines are numbered in order of intensity (1, strongest); double numbers indicate approximately equal intensities. Thin layer chromatographic data refer to separations made with silica gel G (E. Merck, Darmstadt, Germany) activated at 100°. Zones were detected with concentrated sulfuric acid.

used for the D-*gluco* analog[9,11] was used. 2-Amino-2-deoxy-α-D-galactose hydrochloride[13] (I, 1.00 g.) was placed in a 25-ml. Erlenmeyer flask equipped with a Teflon-covered stirring bar and a drying tube, acetyl bromide (2.5 g., 5 mole equiv.) was added, and the vigorously stirred mixture was heated slowly during 30 min. to 55° (oil bath temperature). This temperature was maintained for 1 hr., during which time the mixture became red and slowly solidified. At this point the flask was cooled and was connected to a water pump aspirator through a series of four 8-in. U-tubes containing soda lime. After all the acid vapors were absorbed (about 3 hr.), the residue was extracted with dry methylene chloride, the undissolved residue removed by filtration, and the filtrate decolorized with activated carbon. Dry ether was added to the solution to the point of incipient crystallization, and the mixture was refrigerated overnight to give II as pink plates, yield 900 mg. or 76% (range 65–90%) based on the amount of I which had undergone reaction, m.p. 144–148° dec., $[\alpha]^{23}D$ +160 ± 2° (*c* 0.7, chloroform); specific optical rotatory dispersion curve (*c* 0.34, 26°) +100 (700), +157 (600), +231 (500), +403 (400), +574° (350 mμ); λ_{max}^{KBr} 5.74 vs (OAc), 6.11 w, 6.70 m (NH_3^+), 7.34 m (CH_3C), 11.80 w (equatorial H at C-1), 13.45 μ w (C–Br?); X-ray powder diffraction data[12]: 12.96 vs (2), 8.76 w, 8.04 w, 6.03 vs (1,1), 5.31 w, 4.33 vs (1,1), 4.15 m, 4.04 s, 3.93 s, 3.58 w, 3.02 vs (3), 2.87 s. Recrystallization from methylene chloride and ether gave a less colored product, but the melting point and specific rotation did not change significantly.

Anal. Calcd. for $C_{12}H_{19}Br_2NO_7$: C, 32.09; H, 4.26; Br, 35.56; N, 3.12. Found: C, 32.01; H, 4.44; Br, 35.37; N, 3.12.

The methylene chloride-insoluble material was dissolved in aqueous ethanol (decolorizing carbon), and recovered by evaporation; yield, 400 mg. This material was treated with acetyl bromide as already described, and a further quantity of II was isolated, in similar yield.

When higher reaction temperatures were employed, the amount of methylene chloride-insoluble material remaining diminished, and was negligible when the reaction temperature was raised to 70°. However, under these more vigorous conditions, the product was deep red in color, and required several recrystallizations for acceptable purity. Reaction at room temperature for extended periods gave very little product. Efficient stirring was essential for success of the reaction.

The bromo sugar II underwent no decomposition when stored in a desiccator for 6 weeks. The infrared spectrum of II was very similar to that exhibited by the D-*gluco* analog.

A crude product, m.p. 161°, considered to contain II, has been prepared by another route,[14] but no analytical or other physical data were given.

Methyl 3,4,6-Tri-*O*-acetyl-2-amino-2-deoxy-β-D-galactopyranoside (III).—A solution of the bromo sugar II (500 mg.) in dry methanol (5 ml.) was shaken overnight with an excess of dry silver carbonate and finely ground Drierite.[15] The mixture was filtered through Celite,[16] and the filtrate evaporated to a colorless sirup which failed to crystallize. The product gave a positive ninhydrin reaction, migrated as a single zone (R_f = 0.75) on thin layer chromatograms with 8:1:1 benzene–methanol–pyridine as developer, and did not reduce Fehling solution.

Conversion of the product to the hydrobromide salt with an equivalent of hydrogen bromide in methanol, followed by evaporation, gave a hygroscopic sirup, λ_{max}^{KBr} 2.97 s (NH), 5.73 vs (OAc), 6.12 w, 6.63 μ w (NH_3^+). The product was not obtained crystalline.

Methyl 2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-galactopyranoside (IV).—The sirupy hydrobromide product from the preceding preparation was dissolved in a cold mixture of dry pyridine (5 ml.) and acetic anhydride (2.5 ml.), and left for 3 hr. at room temperature. The mixture was poured into water, and the product was extracted with chloroform. The extract was washed with water, and the final traces of pyridine were removed by shaking the extract with aqueous cadmium chloride solution. The cadmium chloride–pyridine complex was filtered, and the dried extract evaporated to a crystalline residue. Recrystallization from methanol gave IV as large prisms; yield 200 mg. (55% calculated on II), m.p. 212–216°. A further recrystallization gave analytically pure product; m.p. 215–217°, $[\alpha]^{23}D$ −15 ± 1° (*c* 1.5, chloroform); λ_{max}^{KBr} 3.03 m (NH), 5.70 s (OAc), 6.03 s, 6.40 m (NHAc), 7.28 m (CH_3C), 11.13 μ w (axial H at C-1); X-ray powder diffraction data[12]: 13.27 s, 7.97 vs (1,1), 7.38 vs (3), 6.92 m, 6.15 vs (2), 5.5 w, 4.93 s, 4.57 m, 4.37 m, 4.15 m, 3.95 vs (1,1), 3.75 s.

Anal. Calcd. for $C_{15}H_{23}NO_8$: C, 49.84; H, 6.42; N, 3.87. Found: C, 50.09; H, 6.44; N, 3.91.

The following constants have been recorded[7] for this compound, prepared by a different procedure: m.p. 216–217°, $[\alpha]^{23}D$ −17 ± 1° (*c* 1.84, chloroform).

(13) A product of Pfanstiehl Laboratories, Waukegan, Ill. The authors thank Dr. D. G. Doherty, of Oak Ridge National Laboratory, Oak Ridge, Tenn., for a gift of this material.

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(15) Anhydrous calcium sulfate, a product of W. A. Hammond Drierite Co., Xenia, Ohio.

(16) Celite, a siliceous filter-aid, product of the Johns-Manville Co., N. Y.

The Chromous Chloride Reduction of Ergosterol Epidioxide[1]

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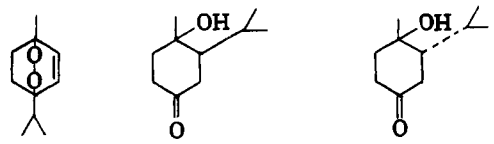
Received June 24, 1963

The reduction of ascaridole (I) with ferrous ion is reported to yield,[2] besides ascaridole glycol, a mixture of two stereoisomeric hydroxy ketones II and III.



I II III

Formation of the isomeric ketones is thought to arise by one electron transfer from ferrous ion to the oxide bridge, generating a tertiary alkoxy radical. The alkoxy radical fragments to an α,β-unsaturated cyclohexenone and an isopropyl radical, followed by isopropyl radical attack on the β-carbon of the cyclohexenone. Further electron and proton acquisitions yield the observed products II and III.

To establish whether one-electron reduction by a metal ion on ergosteryl acetate epidioxide (IV) would follow a similar reaction course and generate a steroidal *t*-alkoxy radical, the reduction of IV was studied.

Treatment of epidioxide IV with chromous chloride[3] in ethanolic hydrochloric acid resulted in rapid reduction. Chromatography of the materials formed yielded ergosteryl acetate (V), a dimeric substance, $C_{60}H_{90}O_4$ (VI), and the hydroxy acetate (VII), all formed in equal yields of about 30%.

The structures are assigned as follows. The dimer VI showed no selective ultraviolet absorption. Saponification of the dimer diacetate yielded a diol which differed from the well known bisergostatrienol (IX),[4] the product of photodimerization of ergosterol. The n.m.r. spectrum of the dimer VI indicated vinyl proton absorp-

(1) This work was supported by Public Health Service Research Grant AM-05183 from the National Institute of Arthritis and Metabolic Diseases.

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