Anal. Calcd. for $C_{17}H_{22}N_2O_6$: C, 58.28; H, 6.28; N, 8.00. Found: C, 58.17; H, 6.36; N, 8.11.

1,2-Diacetamido-3-*O*-acetyl-4,6-*O*-benzylidene-1,2-dideoxy-β-D-glucopyranose (IV).—A solution of 0.12 g. of II in a mixture of 0.6 ml. of pyridine and 0.2 ml. of acetic anhydride was allowed to stand for 24 hr. at room temperature. Water (2 drops) was added, the mixture was allowed to stand a further 5 min., and it was then poured into ice–water (70 ml.). The precipitate was filtered, washed with much water, and dissolved in chloroform. The solution, after drying, was treated with Darco G-60 and Celite and concentrated. The product (0.027 g.) crystallized into needles, and was recrystallized from a mixture of methanol and chloroform. The sample did not melt below 365°, though some decomposition took place above 300°.

Anal. Calcd. for $C_{19}H_{24}N_2O_7$: C, 58.15; H, 6.17; N, 7.14. Found: C, 58.06; H, 6.23; N, 7.40.

2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl Azide (VI).—A freshly prepared, dried solution of 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranosyl bromide, prepared from 2-acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-D-glucopyranose according to Inouye, *et al.*,[14] (*ca.* 1 g.), in 20 ml. of chloroform was added to a suspension of silver azide in chloroform. The suspension had been prepared by mixing aqueous solutions of sodium azide (0.45 g.) and silver nitrate (1.1 g.) and washing the precipitate by decantation with water, ethanol, ether, and chloroform. The mixture was refluxed for 30 min., then it was filtered and the filtrate concentrated to dryness. The residue crystallized readily, and recrystallization from a mixture of chloroform and ether afforded 0.62 g. (68%) of needles with the same properties as those described by Micheel and Wulff.[12]

2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosylamine (V).—A solution of 2.87 g. of azide VI in 25 ml. of ethanol was hydrogenated at room temperature and atmospheric pressure for 4 hr. in the presence of 0.28 g. of Adams' platinum oxide catalyst. After removal of the catalyst by filtration through a Darco G-60 Celite pad, the filtrate was concentrated to dryness. The residue was crystallized from a mixture of ethyl acetate and pentane, yielding 0.8 g. (30%) of needles, m.p. 225–230° dec.; $[\alpha]^{28}D$ −5.2° (*c* 1.27, in chloroform).

Anal. Calcd. for $C_{14}H_{22}N_2O_8$: C, 48.55; H, 6.40; N, 8.09. Found: C, 48.52; H, 6.51; N, 7.97.

2-Acetamido-3,4,6-tri-*O*-acetyl-1-benzamido-1,2-dideoxy-β-D-glucopyranose (VII).—A solution of 0.5 g. of V in 3 ml. of pyridine containing 0.3 ml. of benzoyl chloride was allowed to stand at room temperature for 3 days. After the addition of 1 drop of water, the mixture was left for a short time, and then it was poured into ice–water (75 ml.) and extracted with chloroform. The extract was washed with cold dilute hydrochloric acid, then with aqueous cadmium chloride, aqueous sodium bicarbonate, and water. The solution was dried over sodium sulfate and was concentrated to dryness. The residue was crystallized from a mixture of ethyl acetate and pentane yielding 0.173 g. (27%), m.p. 250.5–251.5°; $[\alpha]^{26}D$ −14° (*c* 1.10, in chloroform).

Anal. Calcd. for $C_{21}H_{26}N_2O_9$: C, 55.99; H, 5.82; N, 6.22. Found: C, 55.98; H, 5.89; N, 6.36.

Benzyl N^2-Carbobenzyloxy-*N*-(2-acetamido-3,4,6-tri-*O*-acetyl 2-deoxy-β-D-glucopyranosyl)-L-asparaginate (VIII).—1-Benzyl-*N* carbobenzyloxy-L-aspartyl chloride was prepared according to the method of Bergmann, *et al.*,[17] after purification of 1-benzyl *N*-carbobenzyloxy-L-aspartate according to LeQuesne and Young.[19,22]

The glucosylamine V (0.57 g.) was added to a solution of 0.76 g. of the acid chloride in 5 ml. of dry pyridine and the mixture was allowed to stand at room temperature for 3 days. The mixture was diluted with chloroform, and the resulting solution was washed with cold *N* sulfuric acid and water, then dried over sodium sulfate, and concentrated to dryness. The residue, dissolved in benzene, was purified by chromatography on silica gel. Elution with a mixture of ether and ethyl acetate (1:1) afforded VIII as a colorless sirup (0.32 g., 28.5%), which crystallized in fine needles from a mixture of chloroform and ether, m.p. 214–217° dec.; $[\alpha]^{25}D$ +28° (*c* 1.41, in chloroform).

Anal. Calcd. for $C_{33}H_{39}N_3O_{13}$: C, 57.80; H, 5.73; N, 6.13. Found: C, 57.89; H, 5.87; N, 6.19.

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A Convenient Preparation of 1,2-Mono-*O*-isopropylidene-α-D-glucofuranose[1]

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Received May 10, 1963

In connection with a series of reactions to introduce new heteroatoms into the D-glucose ring, a convenient method was developed for the preparation of monoacetone D-glucose, 1,2-mono-*O*-isopropylidene-α-D-glucofuranose.

Monoacetone D-glucose is a useful compound for the preparation of numerous D-glucose derivatives. It is usually prepared from diacetone D-glucose, 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose, by preferential hydrolysis of the more acid labile 5,6-isopropylidene group. Previous methods[2-8] have been rather long and require pH control, neutralization, filtration, and evaporation of large quantities of solvent before the first crop of crude crystals are obtained. The present method is shorter and avoids some of the manipulations required in other procedures.

The 5,6-isopropylidene group of diacetone D-glucose is hydrolyzed in 77% aqueous acetic acid and the solution completely evaporated to produce a quantitative yield of monoacetone D-glucose, free of D-glucose and diacetone D-glucose. It is suitable for direct use in many sugar reactions but may be purified by one crystallization from ethyl acetate. Isolation of almost pure crystalline monoacetone D-glucose from the hydrolysis mixture is attributed to its insolubility in 77% aqueous acetic acid. Scale-up of the preparation from 5 g. to 500 g. can be done without reduction in yield or loss of purity.

Experimental

Purity of monoacetone D-glucose preparations was determined by thin layer chromatography on 1 × 3 in. silica gel G-coated[9] microscope slides, irrigated with ethyl acetate and chloroform. Plates were sprayed with a dilute solution of sulfuric acid in ethanol and charred at 100° until permanent spots appeared. Further chromatographic identification of the components was performed on Whatman No. 1 filter paper at 25° with irrigants (A) ethyl acetate–pyridine–water (10:4:3 v./v.) and (B) 1-butanol–ethanol–water (40:11:19 v./v.). The spray indicator was (C) permanganate-periodate.

Preparation of 1,2-Mono-*O*-isopropylidene-α-D-glucofuranose.—Diacetone D-glucose (5 g.) was dissolved at 25° in a solution containing 10 ml. of acetic acid and 3 ml. of water. This solution was poured into a shallow evaporating dish and allowed to evaporate slowly in a hood at 25°. Within a few hours the entire mixture crystallized as a mass of crystalline monoacetone D-glucose. This was broken up with a spatula and recrystallized or allowed to air dry. Thin layer chromatography revealed no contamination from either the starting material or from D-glucose.

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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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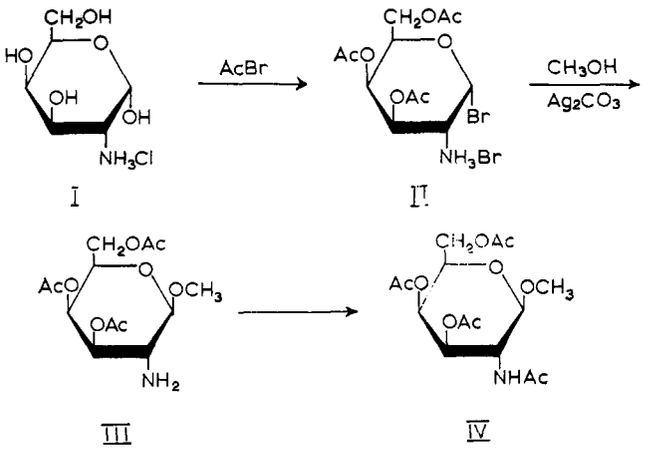
Received May 6, 1963

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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(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.