Glycosyl Halide Derivatives of 3-Amino-3-deoxy-D-mannose[1]

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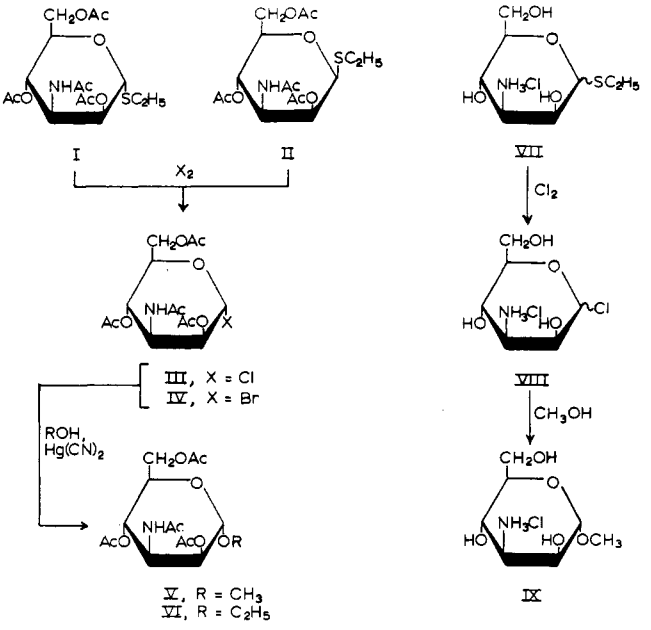
1-Thioglycoside derivatives of 3-acetamido-2,4,6-tri-*O*-acetyl-3-deoxy-D-mannopyranose react with chlorine or bromine to give 3-acetamido-2,4,6-tri-*O*-acetyl-3-deoxy-α-D-mannopyranosyl chloride or bromide, and the reaction provides a facile route to a versatile synthetic intermediate from readily available starting materials. Nonacetylated 1-thioglycoside derivatives of 3-amino-3-deoxy-D-mannose react with chlorine to give a novel glycosyl halide derivative in which the amino and hydroxyl groups are not acylated. This substance reacts with alcohols to give glycosides of the α-D configuration.

The work of Bonner[2] and of Weygand and associates[3] has opened a new route to the poly-*O*-acylglycosyl bromides, useful in the synthesis of nucleosides.[4] The method consists in the replacement of the ethylthio group of acylated 1-thioglycosides with bromine. In this laboratory we have been especially concerned with the extension of this reaction to the corresponding chlorides.[5] The glycosyl halide derivatives formed retain the ring form of their 1-thioglycoside precursor, and the anomeric disposition of the product is dependent on conformational, polar, steric hindrance, and neighboring group participation effects in the derivative considered.[2,3]

The present work describes the application of this procedure to amino sugar derivatives, for preparation of 3-acetamido-2,4,6-tri-*O*-acetyl-3-deoxy-α-D-mannopyranosyl bromide (IV) and the analogous chloride (III). Acetylated glycosyl halides are versatile synthetic intermediates and this work enables preparation of the stable crystalline III, with the rare 3-amino-3-deoxy-D-mannose structure,[6] in 15% yield from methyl α-D-glucopyranoside, with only two isolated intermediate stages.[7,8] The reaction of the nonacetylated 1-thioglycosides with chlorine also was found to give a chloride derivative, and some reactions of this novel nonacetylated glycosyl halide are discussed.

Mercaptolysis of methyl 3-amino-3-deoxy-α-D-mannopyranoside hydrochloride (IX) with ethanethiol and hydrochloric acid has been shown[8] to give ethyl 3-amino-3-deoxy-1-thio-α(and β)-D-mannopyranoside as a mixture which is readily resolved, after acetylation to the corresponding tetraacetyl derivatives I and II.[8] Either anomeric form I or II reacted readily with chlorine, under appropriate conditions, to yield the same crystalline 3-acetamido-2,4,6-tri-*O*-acetyl-3-deoxy-α-D-mannopyranosyl chloride (III) in nearly quantitative yield. The acetylated glycosyl chloride III is stable and suffers no apparent decomposition on storage over several weeks. With alcohols in the presence of mercuric cyanide[9] III gives glycosides with the α-D configuration, and no ortho ester type derivatives were observed in the products under these reaction conditions. In the case of the reaction with methanol, the structure of the product, methyl 3-acetamido-2,4,6-tri-*O*-acetyl-3-deoxy-α-D-mannopyranoside (V), was directly verified by comparison with a known sample prepared by acetylation of methyl 3-amino-3-deoxy-α-D-mannopyranoside hydrochloride, the anomeric configuration of which is known with certainty since it is synthesized from methyl α-D-glucopyranoside.[6]



The positive specific rotation of the acetylated glycosyl chloride III would indicate that it possesses the α-D configuration, and this assignment is supported by the optical rotatory data listed in Table I for III and related derivatives.

The anomeric 1-thioglycosides I and II also underwent reaction with bromine under conditions similar to those used in the reaction with chlorine, to give a product formulated as 3-acetamido-2,4,6-tri-*O*-acetyl-3-deoxy-α-D-mannopyranosyl bromide (IV). This product was relatively stable and could be stored for several weeks, but, in contrast to the analogous chloride, it was difficult to purify, and acceptable analytical data were not obtained. However, it underwent conversion to the known acetylated methyl α-D-glycoside

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(2) W. A. Bonner, *J. Am. Chem. Soc.*, **70**, 3491 (1948).

(3) F. Weygand, H. Ziemann, and H. J. Bestmann, *Ber.*, **91**, 2534 (1958); F. Weygand and H. Ziemann, *Ann.*, **657**, 179 (1962); see also H. Zinner, A. Koine, and H. Nimz, *Ber.*, **93**, 2705 (1960).

(4) M. L. Wolfrom, P. McWain, and A. Thompson, Abstracts, 142nd National Meeting of the American Chemical Society, Atlantic City, N. J., September, 1962, p. 7D.

(5) M. L. Wolfrom and W. Groebke, *J. Org. Chem.*, **28**, 2986 (1963).

(6) H. H. Baer and H. O. L. Fischer, *J. Am. Chem. Soc.*, **82**, 3709 (1960).

(7) A. C. Richardson, *J. Chem. Soc.*, 373 (1962).

(8) M. L. Wolfrom, D. Horton, and H. G. Garg, *J. Org. Chem.*, **28**, 1569 (1963).

(9) B. Helferich and K. F. Wedemeyer, *Ann.*, **563**, 139 (1949); R. Kuhn and W. Kirschenlohr, *Ber.*, **86**, 1331 (1953).

TABLE I

OPTICAL ROTATORY DATA

Compound	$[\alpha]_D$, deg. ($CHCl_3$)	$[M]_D$, deg.	Ref.
3-Acetamido-2,4,6-tri-*O*-acetyl-3-deoxy-α-D-mannopyranosyl chloride (III)	+55	+10,100	*a*
2,3,4,6-Tetra-*O*-acetyl-α-D-mannopyranosyl chloride	+90	+32,850	*b*
Methyl 3-acetamido-2,4,6-tri-*O*-acetyl-3-deoxy-α-D-mannopyranoside (V)	+40	+14,500	*a, c*
Methyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside	+49	+17,800	*d, e*
Methyl 3-acetamido-3-deoxy-α-D-mannopyranoside	+44[f]	+10,350	*a, c*
Methyl α-D-mannopyranoside	+79[f]	+18,700	*g*
2,3,4,6-Tetra-*O*-acetyl-β-D-mannopyranosyl chloride	−34	−12,500	*h*
Methyl 2,3,4,6-tetra-*O*-acetyl-β-D-mannopyranoside	−48	−17,300	*i, j*
Methyl β-D-mannopyranoside	−70[f,k]	−16,500	*j*

[a] See Experimental. [b] D. H. Brauns, *J. Am. Chem. Soc.*, **44**, 401 (1922); E. Pacsu, *Ber.*, **61**, 1508 (1928). [c] See ref. 6. [d] J. K. Dale, *J. Am. Chem. Soc.*, **46**, 1046 (1924). [e] T. L. Harris, E. L. Hirst, and C. E. Wood, *J. Chem. Soc.*, 2108 (1932). [f] In water. [g] E. Fischer and L. Beensch, *Ber.*, **29**, 2927 (1896); J. E. Cadotte, F. Smith, and D. Spriestersbach, *J. Am. Chem. Soc.*, **74**, 1501 (1952). [h] W. Korytnyk and J. A. Mills, *J. Chem. Soc.*, 636 (1959). [i] H. G. Bott, W. N. Haworth, and E. L. Hirst, *ibid.*, 2653 (1930). [j] H. S. Isbell and Harriet L. Frush, *J. Res. Natl. Bur. Std.*, **24**, 125 (1940). [k] Calculated for the unsolvated glycoside.

V under the same conditions as were used for the analogous reaction of the chloride III. This clearly establishes the structure of the glycosyl bromide precursor IV.

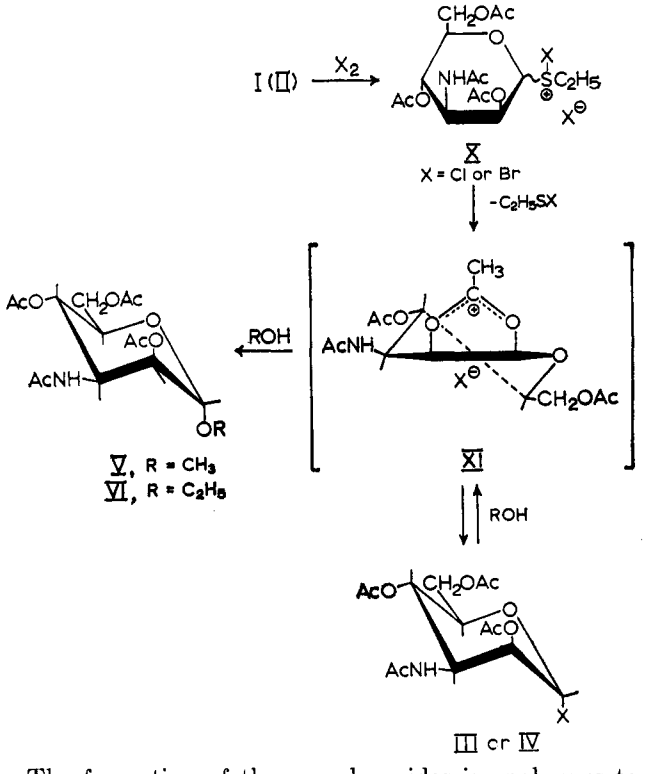
In contrast to the extensive investigations made on the poly-*O*-acetylglycosyl halides, the free glycosyl halides have received little study, and most of the reports have involved the glycosyl fluoride structure,[10] where the stability of the C–F bond permits saponification of the poly-*O*-acyl derivatives. Other glycosyl halides might be expected to be quite unstable in view of the reactivity of the halogen atom at the anomeric center toward hydroxyl groups. Ethyl 3-amino-3-deoxy-1-thio-α(and β)-D-mannopyranoside (VII), suspended in absolute chloroform, underwent reaction with chlorine heterogeneously, under the conditions that were described, to yield a crystalline product which was the unacetylated chloride VIII. A suitable recrystallizing solvent could not be found for this substance and its anomeric nature was not established. It was rapidly converted by water into 3-amino-3-deoxy-D-mannose, and chromatography indicated that this was essentially the sole reaction product. Methanol reacted readily with VIII, and the product, isolated in high yield, was identical with the known methyl 3-amino-3-deoxy-α-D-mannopyranoside (IX). Weygand and Ziemann[3] prepared methyl α-D-glucopyranoside by treating a methanolic solution of ethyl 1-thio-α-D-glucopyranoside with bromine; a nonacylated glycosyl halide is a probable intermediate in this reaction. Under similar conditions sugar diethyl dithioacetals also give glycosides.[11]

(10) F. Micheel and Almuth Klemer, *Advan. Carbohydrate Chem.*, **16**, 85 (1961).

(11) R. Kuhn, W. Baschang-Bister, and W. Dafeldecker, *Ann.*, **641**, 160 (1961).

An example of a crystalline, nonacylated highly reactive sugar derivative, 1-deoxy-1-diazo-D-*galacto*-heptulose has been reported.[12] Such derivatives can normally be isolated only as the acylated forms.

The steric course of the reactions leading to formation of the acetylated glycosyl halide derivatives III and IV, and their subsequent conversion into the glycosides V and VI with the α-D configuration, would suggest the involvement in each reaction of a common closed-ion intermediate XI, as proposed by Weygand and Ziemann[3] and mentioned by Wolfrom and Groebke.[5] The intermediate XI, probably distorted toward the half-chair form, would open by attack at C-1 from below the plane of the ring to give the observed products III, IV with the favored axial disposition of the halogen substituent. In this orientation, the interaction of the C-1–X dipole with the dipole formed from the unshared electron pairs of the ring oxygen is at a minimum,[13] and the halogen atom is *trans* to the C-5 substituent.[14] A reversal of the step III(IV) → XI may be regarded as the first step in the conversion of the glycosyl halide derivatives into α-D glycosides V, VI.



The formation of the α-D-glycosides is analogous to the reaction, with alcohols, of other 1,2-*trans* related poly-*O*-acetylglycosyl halides, first noted by Levene and Wolfrom[15] in the D-lyxose structure. In this case, as in others found later, the yield of the α-D-glycoside has been low owing to the operation of other pathways leading to ortho ester and β-D-glycoside formation.[16,17] In the present work, the use of mercuric cyanide[9] in a homogeneous medium afforded the α-D-gly-

(12) M. L. Wolfrom, R. L. Brown, and E. F. Evans, *J. Am. Chem. Soc.*, **65**, 1021 (1943).

(13) J. T. Edward, *Chem. Ind.* (London), 1102 (1955).

(14) O. Hassel and B. Ottar, *Acta Chem. Scand.*, **1**, 929 (1947).

(15) P. A. Levene and M. L. Wolfrom, *J. Biol. Chem.*, **78**, 525 (1928).

(16) E. Pacsu, *Advan. Carbohydrate Chem.*, **1**, 77 (1945); R. U. Lemieux *ibid.*, **9**, 1 (1954); L. J. Haynes and F. H. Newth, *ibid.*, **10**, 207 (1955).

(17) H. S. Isbell and Harriet L. Frush, *J. Res. Natl. Bur. Std.*, **43**, 161 (1949).

cosides in high yield, and no other products were isolated.

The intermediate XI is pictured as being stabilized by acetate participation. It is not immediately apparent how this would apply to the unacetylated reaction series VII → VIII → IX wherein the α-D-glycoside was likewise obtained in high yield. As noted, the anomeric nature of VIII could not be established and indeed it may have been an anomeric mixture.

Experimental[18]

3-Acetamido-2,4,6-tri-*O*-acetyl-3-deoxy-α-D-mannopyranosyl Chloride (III). A. From Ethyl 3-Acetamido-2,4,6-tri-*O*-acetyl-3-deoxy-1-thio-β-D-mannopyranoside (II).—Dry chlorine was passed[5] for 5 min. through a chilled solution of II[8] (0.50 g.) in dichloromethane (20 ml.). After 10 min. at room temperature the solution was evaporated, and the residue twice evaporated from dry ether (30 ml.). The colorless sirup crystallized on trituration with petroleum ether; yield, 0.42 g. (90%). Recrystallization from anhydrous ether gave III as plates; m.p. 131–133°; $[\alpha]^{22}D$ +55 ± 2° (*c* 0.4, absolute chloroform[18]); λ_{max}^{KBr} 3.0 (NH), 5.70 (OAc), 6.05, 6.50 (NHAc), 13.40 μ (C–Cl[19]); X-ray powder diffraction data[20]: 11.87 w, 10.78 vw, 9.26 w, 8.51 w, 7.28 s (1), 5.45 m, 4.45 m (2), 4.07 m (3,3), 3.84 vw, 3.63 vw, 3.41 m (3), 3.17 w, 2.97 vw.

Anal. Calcd. for $C_{14}H_{20}ClNO_8$: C, 45.96; H, 5.47; Cl, 9.71, N, 3.83. Found: C, 45.80; H, 5.92; Cl, 10.05; N, 3.93.

B. From Ethyl 3-Acetamido-2,4,6-tri-*O*-acetyl-3-deoxy-1-thio-α-D-mannopyranoside (I).—A solution of I[8] (0.20 g.) in anhydrous ether (60 ml.) was treated with chlorine and processed as in A, to give crystalline III; yield, 0.18 g. (96%); X-ray powder diffraction data and other physical constants identical with those recorded for III prepared from II.

The product could be stored in a desiccator for several weeks without decomposition.

Methyl 3-Acetamido-2,4,6-tri-*O*-acetyl-3-deoxy-α-D-mannopyranoside (V). A. From 3-Acetamido-2,4,6-tri-*O*-acetyl-3-deoxy-α-D-mannopyranosyl Chloride (III).—Five hundred milligrams of II was converted into III by treatment with chlorine, and to the product was added mercuric cyanide (0.50 g.), benzene (3 ml.), and anhydrous methanol (1 ml.). The mixture was stirred for 3 hr. at room temperature, diluted with chloroform (30 ml.), and washed with five 20-ml. portions of water until the washings gave no precipitate with silver nitrate solution. The solution was dried (magnesium sulfate) and evaporated, and the crystalline residue was recrystallized from ethanol–petroleum ether to give V; yield, 0.25 g. (46% on basis II); m.p. 151–152°, $[\alpha]^{20}D$ +40.2 ± 1.2° (*c* 0.4, water); λ_{max}^{KBr} 3.05 (NH), 5.70 (OAc), 6.02, 6.45 μ (NHAc); X-ray powder diffraction data[20] identical with that of an authentic specimen: 11.12 vw, 8.42 vw, 7.73 m, 6.73 s (1), 6.11 w, 5.85 s (2), 5.05 s (2,2), 4.81 vw, 4.56 vw, 4.43 m (3), 4.25 m (3,3), 4.06 w.

Anal. Calcd. for $C_{15}H_{23}NO_9$: C, 49.86; H, 6.37; N, 3.87. Found: C, 50.29; H, 6.85; N, 3.87.

Richardson[7] quotes m.p. 153°, $[\alpha]D$ +41° (water), for this compound.

B. From 3-Acetamido-2,4,6-tri-*O*-acetyl-3-deoxy-α-D-mannopyranosyl Bromide (IV).—To a chilled solution of ethyl 3-acetamido-2,4,6-tri-*O*-acetyl-3-deoxy-1-thio-α-D-mannopyranoside[8] (I) (0.20 g.) in anhydrous ether (60 ml.), was added bromine (0.08 g.) dissolved in a small amount of ether. The well stirred mixture was evaporated after 10 min. at room temperature, the sirup re-evaporated with ether (twice), and the residue triturated with petroleum ether to give a pale yellow, amorphous product [yield, 0.18 g. (86%); m.p. 60°] to a viscous liquid which became mobile at 125°, $[\alpha]^{20}D$ +58.7 ± 0.8° (0.5 hr., *c* 0.63, pure chloroform); λ_{max}^{KBr} 2.95 (NH), 5.70 (OAc), 6.00, 6.45 μ (NHAc).

The same product was formed, in 81% yield, when ethyl 3-acetamido-2,4,6-tri-*O*-acetyl-3-deoxy-1-thio-β-D-mannopyranoside (II) was used as the starting material.

The compound could be stored in a desiccator for 2 weeks without apparent decomposition.

Treatment of IV (0.10 g.) with methanol in the presence of mercuric cyanide as in A gave V [yield, 0.05 g. (57%)] with physical constants identical to those of the product from A and to those of a sample prepared by acetylation of methyl 3-amino-3-deoxy-α-D-mannopyranoside hydrochloride (IX).

Methyl 3-Acetamido-3-deoxy-α-D-mannopyranoside—Methyl 3-acetamido-2,4,6-tri-*O*-acetyl-3-deoxy-α-D-mannopyranoside (V) was de-*O*-acetylated with methanolic ammonia at 0° to give the known methyl 3-acetamido-3-deoxy-α-D-mannopyranoside in 70% yield; m.p. 241–243°; $[\alpha]^{22}D$ +42.8 ± 0.8° (*c* 1.35, water). For this compound Richardson[7] records the corresponding constants 241–242° and +44°.

Ethyl 3-Acetamido-2,4,6-tri-*O*-acetyl-3-deoxy-α-D-mannopyranoside (VI).—To 3-acetamido-2,4,6-tri-*O*-acetyl-3-deoxy-α-D-mannopyranosyl chloride (III) prepared by the action of chlorine on I (1.00 g.) was added benzene (6 ml.), mercuric cyanide (1.0 g.), and anhydrous ethanol (2 ml.). The mixture was stirred for 3 hr. at room temperature, processed by the procedure used for V, and recrystallized from ethanol–petroleum ether as needles; yield, 0.65 g. (69% based on I); m.p. 162–163°; $[\alpha]^{20}D$ +32.7 ± 0.9° (*c* 0.6, methanol); λ_{max}^{KBr} 3.05 (NH), 5.70 (OAc), 6.05, 6.50 μ (NHAc); X-ray powder diffraction data[20]: 8.93 w, 7.83 m (3), 6.78 vw, 5.85 m (2), 4.62 vw, 4.45 m, 4.27 vw, 3.96 s (1), 3.70 vw, 3.56 vw, 3.44 vw, 3.36 vw.

Anal. Calcd. for $C_{16}H_{25}NO_9$: C, 51.20; H, 6.66; N, 3.73. Found: C, 51.14; H, 6.89; N, 3.78.

Ethyl 3-Acetamido-3-deoxy-α-D-mannopyranoside.—Dry ammonia was passed for 30 min. through a solution of ethyl 3-acetamido-2,4,6-tri-*O*-acetyl-3-deoxy-α-D-mannopyranoside (VI) (0.30 g.) in methanol (15 ml.) at 0°. After 1 hr. at room temperature the solution was evaporated and the residue was recrystallized from ethanol–ether; yield, 0.095 g. (52%); m.p. 209–210°, softening at 189°; $[\alpha]^{20}D$ +42.2 ± 1.2° (*c* 0.44, methanol); λ_{max}^{KBr} 2.95 (OH, NH), 6.02, 6.48 μ (NHAc); X-ray powder diffraction data[20]: 8.67 m (3), 7.94 m, 7.41 vw, 6.26 m (3,3), 5.97 s (1), 4.75 w, 4.15 vw, 3.93 s (2), 3.63 m, 3.41 vw, 3.24 vw, 3.12 w.

Anal. Calcd. for $C_{10}H_{19}NO_6$: C, 48.19; H, 7.63; N, 5.62 Found: C, 48.32; H, 7.69; N, 5.72.

3-Amino-3-deoxy-D-mannopyranosyl Chloride Hydrochloride (VIII).—A mixture (0.50 g.) containing approximately equal amounts of ethyl 3-amino-3-deoxy-1-thio-α- and β-D-mannopyranosides (VII), as isolated by mercaptolysis of methyl 3-amino-3-deoxy-α-D-mannopyranoside hydrochloride (IX),[8] was suspended in chloroform (50 ml.). Chlorine was passed for 10 min. through the chilled suspension, which was then stirred for 3 hr. and filtered. The crystalline solid was washed well with chloroform and dry ether; yield, 0.45 g. (100%). The crude product was insoluble in all nonhydroxylic solvents tried, and a suitable recrystallization solvent could not be found; m.p. 165–175° (preliminary browning at 160°); $[\alpha]^{21}D$ +34.8 ± 0.5° (*c* 0.9, *N*,*N*-dimethylformamide); λ_{max}^{KBr} (μ) 3.05 (OH), 6.25, 6.55 (NH_3^+), 13.65 (C–Cl[26]); X-ray powder diffraction data[20]: 10.59 w, 7.28 s (2), 5.17 vw, 4.86 vw, 4.32 vs (1), 4.08 vw, 3.28 w, 3.60 w, 3.39 m (3), 3.08 m (3,3), 2.98 w, 2.67 w.

Anal. Calcd. for $C_6H_{13}Cl_2NO_4$: C, 30.76; H, 5.55; Cl, 30.34; N, 5.98. Found: C, 30.65; H, 5.78; Cl, 30.30; N, 5.96.

Reaction of 3-Amino-3-deoxy-D-mannopyranosyl Chloride Hydrochloride (VIII) A. With Water.—A few milligrams of VIII was dissolved in water and the solution was examined by paper chromatography. A single major zone, R_m 1.0, indistinguishable from 3-amino-3-deoxy-D-mannose hydrochloride, was observed, together with a very weak zone, R_m 1.8.

B. Methanol.—A solution of VIII (0.20 g.) in anhydrous

(18) Melting points were taken with a Hershberg apparatus. Evaporations were performed under reduced pressure below 40°. Specific rotations were determined in a 2-dm. tube. Infrared spectra were obtained on a Perkin-Elmer Infracord infrared spectrophotometer. Paper chromatography was effected by the descending technique with the upper layer of a 4:1:5 1-butanol–ethanol–water system; R_m refers to mobility relative to that of 3-amino-3-deoxy-D-mannose hydrochloride. Zones were detected by the silver nitrate–sodium hydroxide procedure of W. E. Trevelyan, D. P. Proctor, and J. S. Harrison, *Nature*, **166**, 444 (1950). Ethanol-free chloroform was purified by washing successively with sulfuric acid, aqueous sodium bicarbonate, and water, and was dried with magnesium sulfate. Microanalyses were performed by W. N. Rond.

(19) W. A. Skinner, A. P. Martinez, H. F. Gram, L. Goodman, and B. R. Baker, *J. Org. Chem.*, **26**, 148 (1961); A. P. Martinez, W. A. Skinner, W. W. Lee, L. Goodman, and B. R. Baker, *J. Am. Chem. Soc.*, **82**, 6050 (1960).

(20) Interplanar spacing, Å., CuKα radiation. Relative intensity, estimated visually, s, strong; m, medium; w, weak; v, very. First few lines are numbered (1, strongest), doubled numbers indicate approximately equal intensities.

methanol (2 ml.) was refluxed for 1 min. and left 1 day at room temperature. Addition of ether to the solution gave crystalline methyl 3 - amino - 3 - deoxy - α - D - mannopyranoside hydrochloride (IX); yield, 0.16 g. (82%); physical constants identical to those of an authentic sample; X-ray powder diffraction data[20]: 10.98 m (3), 7.53 s (1), 6.03 vw, 5.45 vw, 5.23 vw, 4.46 s (2), 4.07 m, 3.79 m, 3.45 s (2,2), 3.14 w, 2.83 vw, 2.73 vw.

Examinations of the reaction mixture by paper chromatography revealed a major zone, R_m 1.66, corresponding to IX, with weak zones at R_m 1.0 and 2.7.

Conversion of 2-Amino-2-deoxy-1-thio-D-glucose Derivatives into Glycosyl Halide Derivatives. A Tetra-*O*-acetylglycosylsulfenyl Bromide[1]

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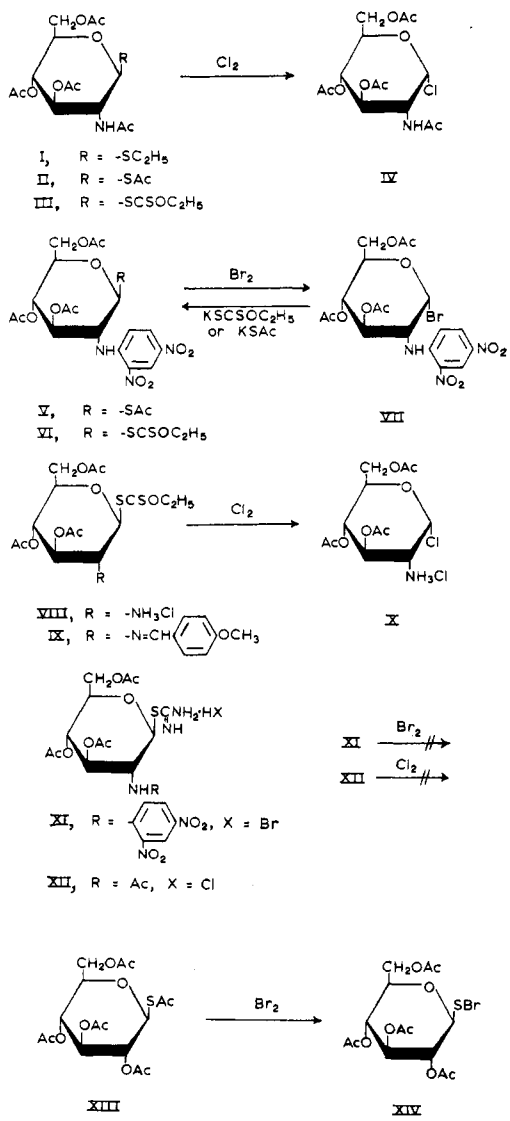
The *N*- and *S*-substituted derivatives I, II, III, V, VI, and VIII of 3,4,6-tri-*O*-acetyl-2-amino-2-deoxy-1-thio-D-glucose react with chlorine or bromine to give the corresponding *N*-substituted 3,4,6-tri-*O*-acetyl-2-amino-2-deoxy-α-D-glucopyranosyl chlorides (IV, X) or bromides (VII). 3,4,6-Tri-*O*-acetyl-2-amino-2-deoxy-α-D-glucopyranosyl chloride hydrochloride (X) is also formed on chlorination of 3,4,6-tri-*O*-acetyl-2-anisylidene-amino-2-deoxy-β-D-glucopyranosyl ethylxanthate (IX). Bromination of 2,3,4,6-tetra-*O*-acetyl-1-*S*-acetyl-1-thio-β-D-glucopyranose (XIII) in carbon tetrachloride solution gives crystalline 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosylsulfenyl bromide (XIV), a novel derivative in the carbohydrate field with potential value as a synthetic intermediate. The *N*-substituted 2-(3,4,6-tri-*O*-acetyl-2-amino-2-deoxy-β-D-glucopyranosyl)-2-thiopseudourea salt derivatives XI and XII were found to be unreactive under the halogenation conditions. The mechanism of these reactions is discussed from a common standpoint.

The conversion of acetylated phenyl 1-thioglycosides to poly-*O*-acetylglycosyl bromides by bromine treatment in an inert solvent was first described by Bonner,[2] and extended by Weygand and associates,[3] and others,[4] with the ethyl analogs. Chlorination to the corresponding glycosyl chlorides was described by Wolfrom and Groebke,[5] and the reaction was extended in this laboratory[6] to the synthesis of amino sugar glycosyl halides in the 3-amino-3-deoxy-D-mannose series.[6] The present work describes the conversion of a range of *N*- and *S*-substituted derivatives of 3,4,6-tri-*O*-acetyl-2-amino-2-deoxy-1-thio-β-D-glucose into *N*-substituted 3,4,6-tri-*O*-acetyl-2-amino-2-deoxy-α-D-glucopyranosyl bromides or chlorides, and the behavior of related derivatives which do not react to give products of this type.

Most of the compounds utilized were prepared by the procedures described by Horton and Wolfrom.[7] 3,4,6-Tri - *O* - acetyl - 2 - deoxy - 2 - (2,4 - dinitroanilino)-β-D-glucopyranosyl ethylxanthate (VI) was prepared by treatment of 3,4,6-tri-*O*-acetyl-2-deoxy-2-(2,4-dinitroanilino)-α-D-glucopyranosyl bromide (VII) with potassium ethylxanthate in acetone–ethanol solution, followed by chromatography of the product on silica gel.

Ethyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-1-thio-β-D-glucopyranoside[8] (I), 2-acetamido-3,4,6-tri-*O*-acetyl 1-*S*-acetyl-2-deoxy-1-thio-β-D-glucopyranose[7] (II), and



2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl ethylxanthate[7] (III), all reacted rapidly in

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