Addition Reactions of Glycals. I. Addition Reaction of D-Glucal Triacetate with Thiocyanogen. The Syntheses of Methyl 2-Thio-β-D-glucopyranoside and Methyl 2-Thio-β-D-mannopyranoside Derivatives

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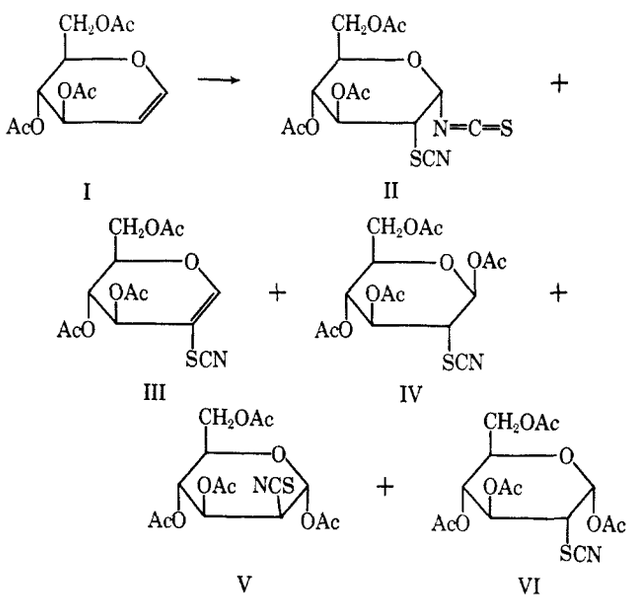
Addition reaction of D-glucal triacetate with thiocyanogen in a mixture of acetic acid, acetic anhydride, and carbon tetrachloride gave 3,4,6-tri-*O*-acetyl-2-deoxy-2-thiocyanato-α-D-glucopyranosyl isothiocyanate (II), 2-thiocyanato-D-glucal triacetate (III), 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-thiocyanato-β-D-glucopyranose (IV), and 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-thiocyanato-α-D-mannopyranose (V). The structures of these compounds were assigned from the results based on the nmr and infrared spectra. Compounds IV and V were converted to the corresponding methyl glycosides (VIII, XII, and XIII) through the glycosyl chlorides (VII and XI). Desulfurization of the methyl glycosides gave the known methyl 2-deoxy-α- and -β-D-glucoside derivatives, respectively. Treatment of the methyl glycosides (VIII and XII) with thiolacetic acid gave methyl 3,4,6-tri-*O*-acetyl-2-*S*-(*N*-acetylthiocarbamoyl)-2-thio-D-glycosides (XXV and XXVIII) and the *S*-thiocarbamoyl derivatives (XXVI and XXIX) in good yield. Hydrolysis of XXV, XXVI, XXVIII, and XXIX with methanolic ammonia and acylations of the products gave methyl 2-thio-D-glycoside disulfides (XXVII and XXX). Reductions of the disulfides (XXVII and XXX) with sodium in liquid ammonia and acylations of the products gave methyl 2-thio-β-D-glucopyranoside and methyl 2-thio-α-D-mannopyranoside derivatives, respectively.

In 1920, Fischer, Bergmann, and Schotte[1] reported the chlorination and the bromination of D-glucal triacetate. Recently, Lefar, and Weill[2] reinvestigated the chlorination of D-glucal triacetate and isolated 3,4,6-tri-*O*-acetyl-2-chloro-2-deoxy-α-D-glucopyranosyl chloride and 3,4,6-tri-*O*-acetyl-2-chloro-2-deoxy-α-D-mannopyranosyl chloride in a 4:1 ratio using preparative thin layer chromatography technique. Lemieux and Fraser-Reid studied the chlorination[3] and the bromination[4] of D-glucal triacetate. The nmr analyses of the products showed that 3,4,6-tri-*O*-acetyl-2-chloro-2-deoxy-α-D-glucopyranosyl chloride was obtained in >80% yield in the chlorination and a mixture of 3,4,6-tri-*O*-acetyl-2-bromo-2-deoxy-α-D-glucopyranosyl bromide and 3,4,6-tri-*O*-acetyl-2-bromo-2-deoxy-α-D-mannopyranosyl bromide in a 2:1 ratio was obtained in 95% yield in the bromination. Kent, Robson, and Welch[5] investigated the addition reaction of D-glucal triacetate with *N*-bromosuccinimide and hydrogen fluoride and isolated 3,4,6-tri-*O*-acetyl-2-bromo-2-deoxy-β-D-mannosyl fluoride and 3,4,6-tri-*O*-acetyl-2-bromo-2-deoxy-α-D-glucosyl fluoride. There are very few reports concerning the addition reaction of D-glycal with sulfur-containing compounds. Maki, Nakamura, Tejima, and Akagi[6] reported that the reaction of D-glucal triacetate with thiolacetic acid at 140° gave 4,6-di-*O*-acetyl-1-*S*-acetyl-2,3-dideoxy-2,3-didehydro-1-thio-α-D-erythrohexose. We wish herein to report the addition reaction of D-glucal triacetate with thiocyanogen (see Scheme I). Thiocyanogen is often classified as a pseudo-halogen[7] or a halogenoid[8] because of its resemblance to halogens in chemical behavior and it is known that the chemical reactivity of thiocyanogen lies between bromine and iodine. It is also known that thiocyanogen can add to olefins and acetylenes.[9]

SCHEME I



Results and Discussion

The addition reaction of D-glucal triacetate with thiocyanogen, which was prepared from plumbous thiocyanate and bromine,[10] did not proceed and starting material was recovered when ether or carbon tetrachloride was used as a solvent. When D-glucal triacetate was allowed to stand overnight with excess of thiocyanogen in a mixture of acetic acid, acetic anhydride, and carbon tetrachloride in the dark at ~10°, D-glucal triacetate disappeared completely; three new spots appeared on a silica gel thin layer plate using a mixture of benzene and ether (1:1) as developer. The product was fractionated by column chromatography on silica gel using the same solvent system. The general character of the nmr spectra of the products isolated suggested that they have pyranose structures.

From the first fraction, a crystalline compound was obtained in 3% yield, the elemental analysis

(1) E. Fischer, M. Bergmann, and H. Schotte, *Ber.*, **53**, 509 (1920).
(2) M. S. Lefar and C. E. Weill, *J. Org. Chem.*, **30**, 954 (1965).
(3) R. U. Lemieux and B. Fraser-Reid, *Can. J. Chem.*, **43**, 1460 (1965).
(4) R. U. Lemieux and B. Fraser-Reid, *ibid.*, **42**, 532 (1964).
(5) P. W. Kent, F. O. Robson, and V. A. Welch, *J. Chem. Soc.*, 3273 (1963).
(6) T. Maki, H. Nakamura, S. Tejima, and M. Akagi, *Chem. Pharm. Bull.* (Tokyo), **13**, 764 (1965).
(7) E. Söderbäck, *Ann.*, **419**, 217 (1919); L. Birckenbach and K. Kellermann, *Ber.*, **58**, 786 (1925).
(8) P. Walden and L. F. Audrieth, *Chem. Rev.*, **5**, 339 (1928).
(9) H. P. Kaufmann, *Angew. Chem.*, **54**, 195 (1941); J. L. Wood, *Org. Reactions*, **3**, 240 (1946).
(10) W. H. Gardner and H. Weinberger, *Inorg. Syn.*, **1**, 84 (1939).

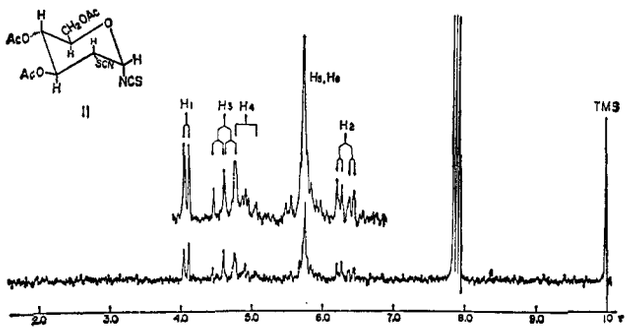


Figure 1.—The nmr spectra of II.

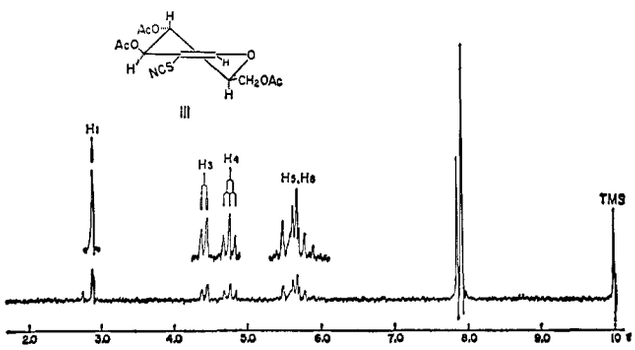


Figure 2.—The nmr spectra of III.

of which was in accord with the empirical formula $C_{14}H_{16}N_2O_7S_2$ and whose infrared spectrum showed the existence of a thiocyanato group[11] at 2160 cm^{-1} and an isothiocyanato group[11] at 1992 cm^{-1}. In the nmr spectrum (Figure 1), the anomeric proton signal appeared at τ 4.10 as a doublet ($J_{1,2}$ = 4.0 cps) and the H_2 appeared at τ 6.35 as a quartet ($J_{1,2}$ = 4.0 cps, $J_{2,3}$ = 10.5 cps). This clearly indicated[12-14] that this compound has an α-D-gluco configuration. On the basis of these results and the reaction mechanism expected, which involves first attack by a thiocyanato ion on the C_2 as an electrophile and second attack by an isothiocyanato ion which was produced by resonance in the ion involved ($\bar{S}C{\equiv}N \leftrightarrow S{=}C{=}\bar{N}$)[15] on C_1 as a nucleophile, the structure of this compound was assigned as 3,4,6-tri-*O*-acetyl-2-deoxy-2-thiocyanato-α-D-glucopyranosyl isothiocyanate (II).

From the second fraction, a colorless crystalline compound was obtained in 30% yield. Preparative thin layer chromatography of the mother liquor produced another syrupy product in 3.8% yield and additional amounts of the above colorless crystalline compound in 8% yield. The infrared spectrum of the syrupy product showed the existence of a thiocyanato group at 2175 cm^{-1} and a double bond at 1627 cm^{-1}. In the nmr spectrum (Figure 2), the H_1 signal appeared at τ 2.87 as a doublet ($J_{1,3}$ = 0.6 cps). From these results, the structure of this syrup was assigned as 2-thiocyanato-D-glucal triacetate (III). The structure elucidation of the crystalline compound (IV) was as fol-

(11) E. Lieber, C. N. R. Rao, and J. Ramachandran, *Spectrochim. Acta*, **13**, 296 (1959); G. L. Caldow and H. W. Thompson, *ibid.*, **13**, 212 (1958).

(12) R. U. Lemieux, R. K. Kullnig, H. J. Bernstein, and W. G. Schmider, *J. Am. Chem. Soc.*, **79**, 1005 (1957).

(13) M. Karplus, *J. Chem. Phys.*, **30**, 11 (1959); *J. Am. Chem. Soc.*, **85**, 2870 (1963).

(14) L. D. Hall, *Advan. Carbohydrate Chem.*, **19**, 51 (1964).

(15) N. Kharasch, "Organic Sulfur Compounds," Vol. 1, Pergamon Press Inc., New York, N. Y., 1961, pp 306, 326.

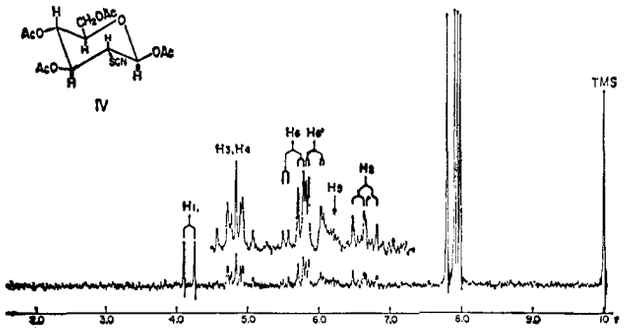


Figure 3.—The nmr spectra of IV.

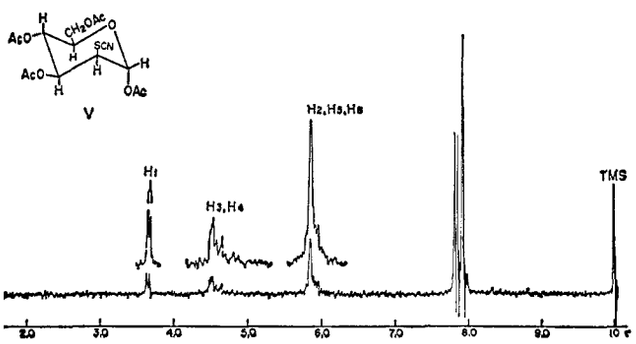


Figure 4.—The nmr spectra of V.

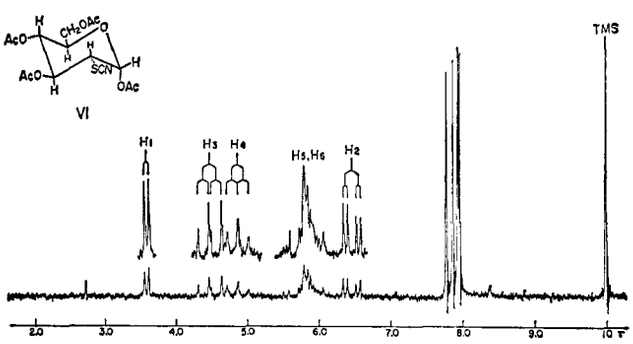


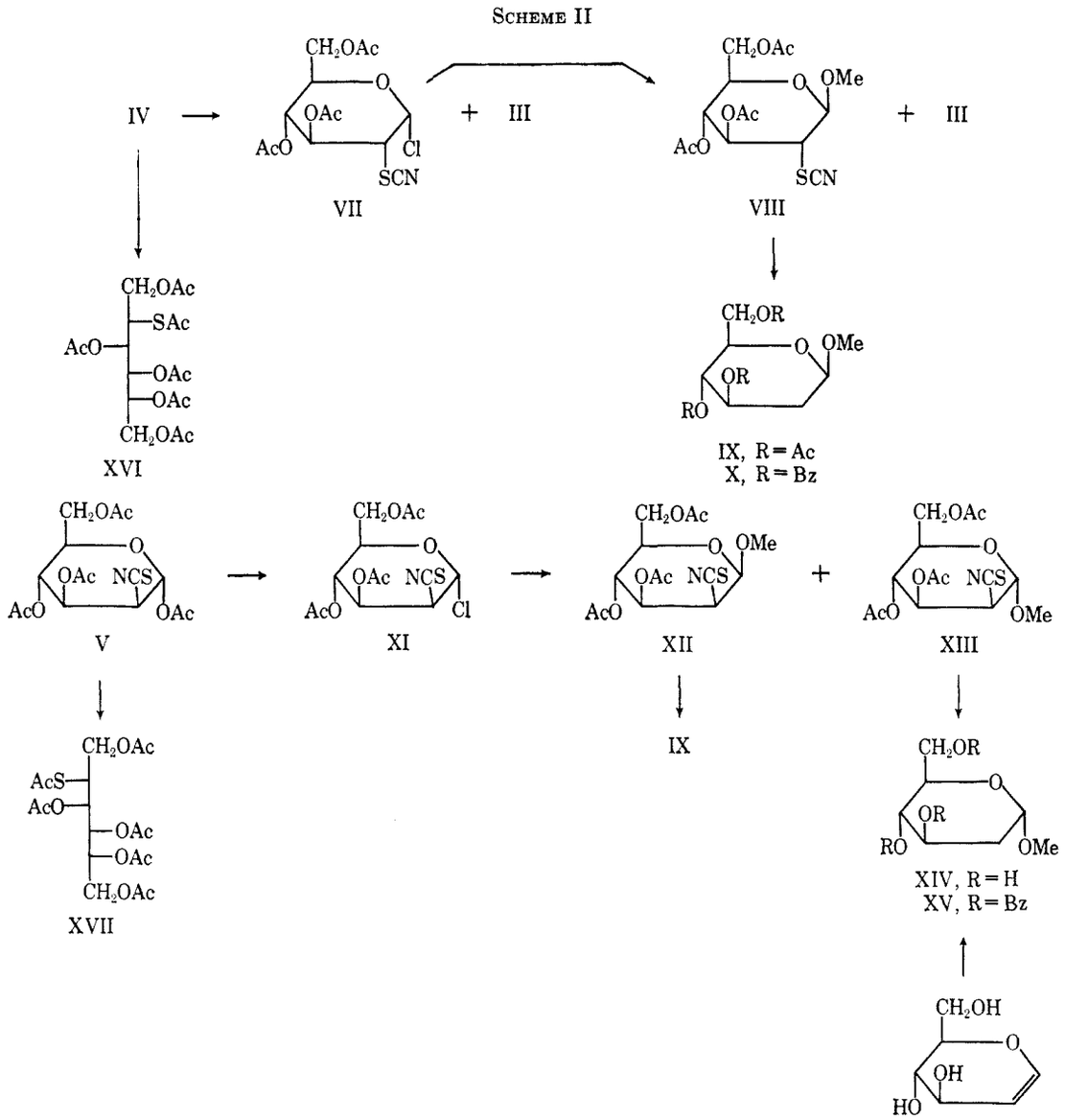
Figure 5.—The nmr spectra of VI.

lows. The elemental analysis agreed with the empirical formula $C_{15}H_{19}NO_9S$ and the infrared spectrum showed the existence of a thiocyanato group at 2163 cm^{-1} and acetates at 1759 cm^{-1}. In the nmr spectrum (Figure 3), the H_1 signal appeared at τ 4.17 as a doublet ($J_{1,2}$ = 9.0 cps) and the H_2 signal appeared at τ 6.64 as a quartet ($J_{2,3}$ = 11 cps.) These facts indicated that all of the H_1, H_2 and H_3 were axially oriented. The signals for four acetoxy groups appeared at τ 7.79, 7.89, 7.93, and 7.97, respectively. From these results the structure of IV was assigned as 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-thiocyanato-β-D-glucopyranose. The nmr spectrum of the mother liquor indicated that it contained a mixture of IV and the α-D anomer (VI) in equal amounts, but the pure VI could not be isolated from the mixture.

From the third fraction, a syrup (V) was obtained in 25% yield. The infrared spectrum of this syrup showed the existence of a thiocyanato group at 2185 cm^{-1} and *O*-acetates at 1752 cm^{-1}. In the nmr spectrum (Figure 4), the H_1 signal appeared at τ 3.65 as a doublet ($J_{1,2}$ = 1.8 cps), the H_2 signal appeared at τ ~5.85,[16] overlapping with the H_6 and H_5, and the

(16) In the case of complex, overlapping, or incompletely resolved multiplet, the chemical shifts given may be approximate (~) values.

SCHEME II



signals for four acetoxy groups appeared at τ 7.82, 7.86, and 7.93 (two). From these results the structure of V was assigned[4,17] as 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-thiocyanato-D-mannose. Furthermore, on comparison of the chemical shifts of the H_5 in IV, V, and VI (see Experimental Section), V and VI had the H_5 signals at τ ~5.95 and ~5.96, respectively, whereas IV had the H_5 signal at τ 6.15. This fact apparently showed that V has an α configuration.[17,18] Compounds II and III were not investigated further because of the small quantities. In this addition reaction, dithiocyanato derivative could not be obtained.

In order to reconfirm the above assignments chemically, the following reactions were investigated. Anomerization of IV with sulfuric acid in acetic acid and acetic anhydride at room temperature gave VI in 79% yield, whose nmr spectrum (Figure 5) showed the H_1 signal at τ 3.58 as a doublet ($J_{1,2}$ = 3.5 cps), indicating that VI has an α-D-gluco configuration. Conversion of IV to the glucosyl bromide with hydrogen bromide in acetic acid was unsuccessful because the reagent attacked to the thiocyanato group also. Treatment of IV with titanium tetrachloride in chloroform gave the crystalline 3,4,6-tri-*O*-acetyl-2-deoxy-2-thiocyanato-D-glucopyranosyl chloride (VII) together with 2-thiocyanato-D-glucal triacetate (III) (see Scheme II). The nmr spectrum of VII showed the H_1 signal at τ 3.63 as a doublet ($J_{1,2}$ = 4.0 cps), suggesting that VII has an α configuration. Treatment of VII with diethylamine[19] in anhydrous benzene at room temperature gave III in 76% yield. Methanolysis of VII in the presence of silver perchlorate and silver carbonate gave a syrupy methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-thiocyanato-D-glucopyranoside (VIII) in 83.5% yield together with III in 11% yield. Compound VIII was also obtained from IV in 70% yield without isolation of VII. Desulfurization of VIII with Raney nickel gave known methyl 3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranoside (IX)[20] in 56.5% yield and this fact showed that VIII has a β configuration.

In contrast to IV, treatment of V with titanium tetrachloride gave only syrupy 3,4,6-tri-*O*-acetyl-2-deoxy-2-thiocyanato-D-mannosyl chloride (XI) in 61.8% yield. The α configuration was assigned from

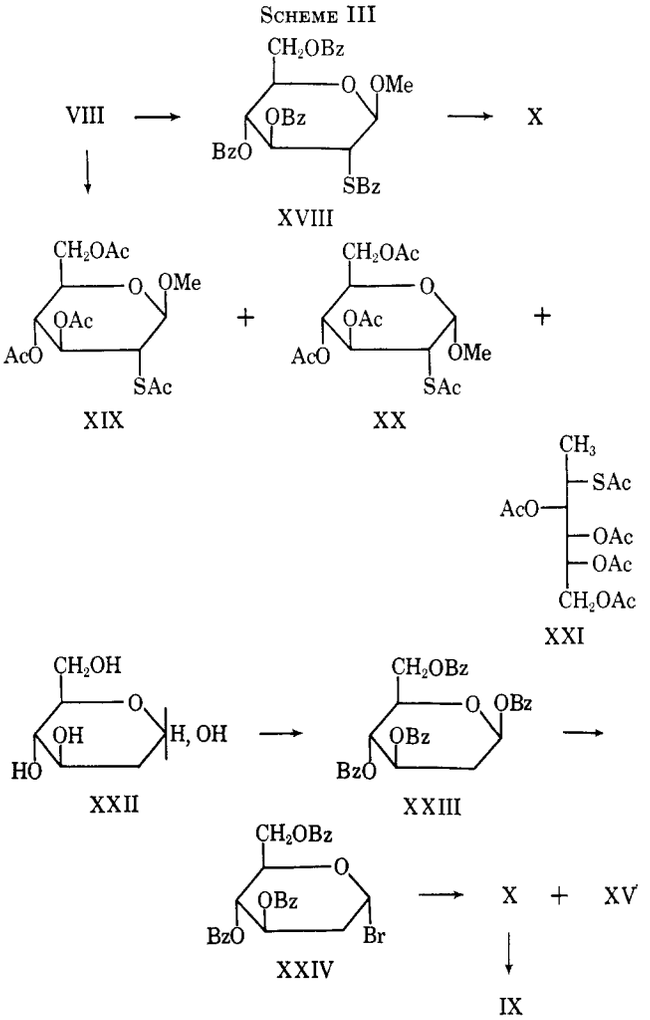
(17) R. U. Lemieux and J. D. Stevens, *Can. J. Chem.*, **43**, 2059 (1965).
(18) T. D. Inch, J. R. Plimmer, and H. G. Fletcher, Jr., *J. Org Chem.*, **31**, 1825 (1966).
(19) M. G. Blair, "Methods in Carbohydrate Chemistry," Vol. II, Academic Press Inc., New York, N. Y., 1963, p 411, and references cited therein.
(20) M. Bergmann, H. Schotte, and W. Leschinsky, *Ber.*, **56**, 1052 (1923)

the nmr data. The H_1 and H_3 signals appeared at τ 3.67 and 4.22, respectively, and had chemical shifts similar to those in VII at τ 3.63 and 4.35. Methanolysis of XI gave two methyl mannosides. Desulfurization of the crystalline methyl mannoside (XII) obtained in 51.3% yield with Raney nickel gave IX; hence XII was methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-thiocyanato-β-D-mannopyranoside. Desulfurization of the syrupy methyl mannoside (XIII) obtained in 22.8% yield and hydrolysis of the product gave known methyl 2-deoxy-α-D-glucopyranoside (XIV);[21] hence XIII was methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-thiocyanato-α-D-mannopyranoside.

The above results clearly showed that the structure assignments of III, IV, and V were correct. It can now be easily understood that III was obtained in the chlorination of IV and the methanolysis of VII, but not in the chlorination of V and the methanolysis of XI, since in VII H_2 and C_1–Cl have the diaxial *trans* configuration and H_2 can be easily abstracted owing to the anion-stabilizing effect of the sulfur atom attached to the same carbon atom, whereas in XI H_2 and C_1–Cl have *cis* configuration. The results of the methanolysis of VII and XI may also be used to support the above assignments since the methanolyses of VII proceeded normally, whereas that of XI gave a mixture of XII and XIII, probably owing to the so-called "Δ^2 effect,"[22] which reduced the formation of XII and increased the formation of XIII.

We now describe some transformations of the thiocyanato group to a thiol function. It is well known[23] that lithium aluminum hydride reduction of thiocyanato gives thiol. Lithium aluminum hydride reductions of IV and V and acetylations of the products gave the expected 1,3,4,5,6-penta-*O*-acetyl-2-*S*-acetyl-2-thio-D-glucitol (XVI) and -D-mannitol (XVII) in low yields, respectively. When VIII was reduced with lithium aluminum hydride in refluxing anhydrous tetrahydrofuran for 3 hr and the product was benzoylated, crystalline methyl 3,4,6-tri-*O*-benzoyl-2-*S*-benzoyl-2-thio-β-D-glucopyranoside (XVIII) was obtained in 34.7% yield (see Scheme III). The elemental analysis and the spectral findings supported this structure. In contrast to VIII, lithium aluminum hydride reduction of XI and benzoylation of the product gave a syrupy mixture, which showed many spots on a thin layer plate. Desulfurization of XVIII gave methyl 3,4,6-tri-*O*-benzoyl-2-deoxy-β-D-glucopyranoside (X), mp 96–97°, $[\alpha]^{21}D$ −49.2° (in $CHCl_2CHCl_2$), which was identical with an authentic sample of X prepared by Bergmann's method.[20] Bergmann reported mp 88°, $[\alpha]^{19}D$ −34.3° (in $CHCl_2CHCl_2$) for X. We reinvestigated this reaction under the same condition and obtained two crystalline compounds, which were isolated by preparative thin layer chromatography. The main product (84.0%) showed mp 96–98°, $[\alpha]^{22}D$ −53.1° (in $CHCl_2CHCl_2$), and the minor product (10.0%) showed mp 110–110.5°, $[\alpha]^{23}D$ +49.4° (in $CHCl_2CHCl_2$). Both elemental analyses agreed with the empirical formula $C_{28}H_{26}O_8$. The nmr spectra

SCHEME III



showed that the H_1 signal in the former compound appeared at τ 5.31 as a quartet ($J_{1,2a}$ = 10.0 cps, $J_{1,2e}$ = 2.0 cps) and the H_1 signal in the latter appeared at τ 5.06 as a quartet ($J_{1,2a}$ = 3.5 cps, $J_{1,2e}$ = 1.5 cps). From these results it was proved that the former was methyl 3,4,6-tri-*O*-benzoyl-2-deoxy-β-D-glucopyranoside (X) and the latter was the α anomer (XV). Hydrolysis followed by acetylation of the former compound gave IX. It is probable that Bergmann's compound was a mixture of X and XV.

When VIII was reduced with lithium aluminum hydride in refluxing anhydrous tetrahydrofuran for 3 hr and the product was acetylated, two crystalline compounds were obtained by preparative thin layer chromatography. The main product (45.3%) showed mp 83–95°, $[\alpha]^{22}D$ +10.0°, but could not be purified by recrystallization or chromatography. The nmr spectrum showed that this was a mixture of methyl 3,4,6-tri-*O*-acetyl-2-*S*-acetyl-2-thio-β-D-glucopyranoside (XIX) and the α anomer (XX). When the main product was hydrolyzed with sodium methoxide and the product was benzoylated, only XVIII was obtained as a crystalline form. The minor product (5.35%), $[\alpha]^{22}D$ +10.4°, was assigned as 3,4,5,6-tetra-*O*-acetyl-2-*S*-acetyl-1-deoxy-2-thio-D-glucitol (XXI) from the following data. The elemental analysis agreed with the empirical formula $C_{16}H_{24}O_9S$. The infrared spectrum showed the existence of *O*-acetyl groups at 1748 cm^{-1} and *S*-acetyl group at 1692 cm^{-1}. The nmr spectrum showed that a *C*-methyl signal appeared at τ 8.66 as a doublet

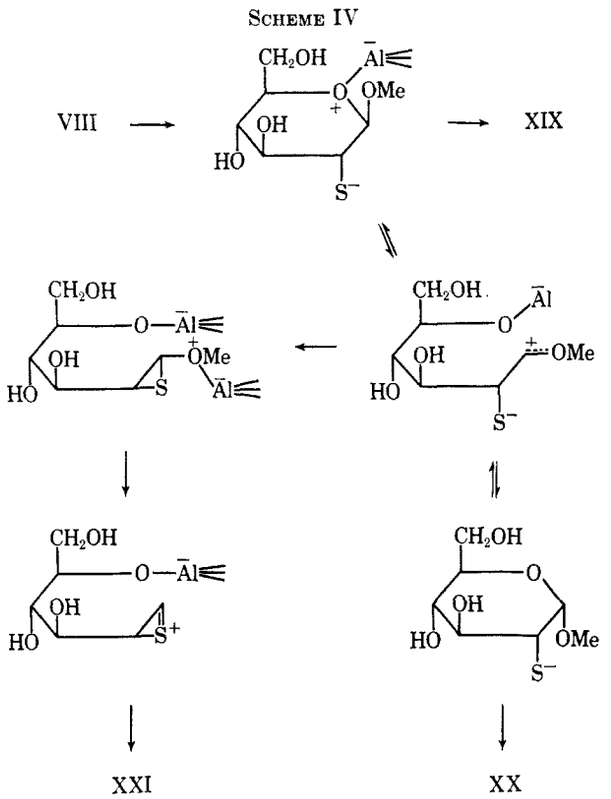
(21) I. W. Hughes W. G. Overend, and M. Stacey, *J. Chem. Soc.*, 2846 (1949).

(22) R. E. Reeves, *J. Am. Chem. Soc.*, **72**, 1499 (1950); *Advan. Carbohydrate Chem.*, **6**, 107 (1951).

(23) For example, M. Mousseron, R. Jacquier, M. Mousseron-Canet, and R. Zagdoun, *Bull. Soc. Chim. France*, 1042 (1952).

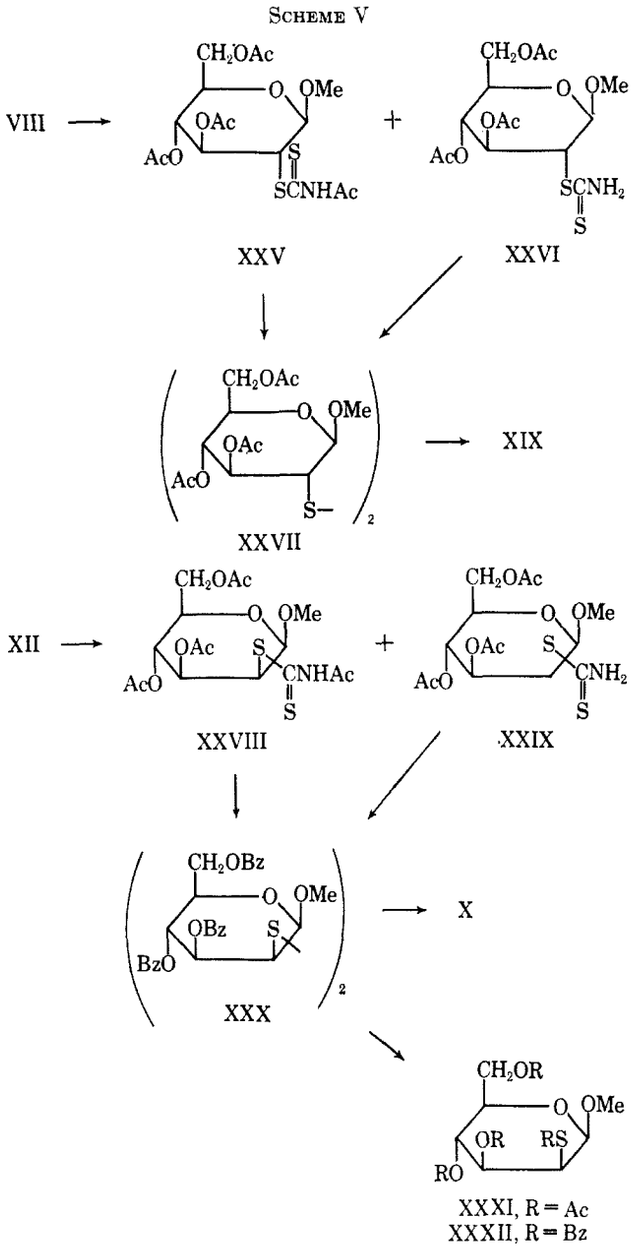
($J_{1,2}$ = 7 cps), the H_2 signal appeared at τ 6.21 as a quintet (all of J = 7 cps), and the signals for a *S*-acetyl and four *O*-acetyl groups appeared at τ 7.68, 7.88, 7.96, and 7.97 (two), respectively. Eliel, *et al.*,[24] studied the reduction of acetals, ketals, hemithioacetal, and hemithioketal with a mixture of lithium aluminum hydride and aluminum chloride and obtained ethers and thioethers, respectively, by cleavage of one of C–O bonds. It is possible to assume that XXI was produced by the similar mechanism through the episulfide intermediate (see Scheme IV).

SCHEME IV



As above, lithium aluminum hydride reduction of VIII was very complicated and the yield was unsatisfactory. Another route to XIX was therefore investigated. Chanlaroff[25] and Wheeler[26] reported that the thiocyanato group reacted with thiol acids to give *N*-acyldithiocarbamate derivatives. When VIII was refluxed with thiolacetic acid in anhydrous benzene for 6 hr and the product was fractionated by thin layer chromatography, a yellow powder and a colorless crystalline compound were obtained in 75 and 14% yields, respectively. The structure of the main product was assigned as methyl 3,4,6-tri-*O*-acetyl-2-*S*-(*N*-acetylthiocarbamoyl)-2-thio-β-D-glucopyranoside (XXV) (see Scheme V) from the following data. The nmr spectrum showed the existence of the signals for an *O*-methyl, an *N*-acetyl, and three *O*-acetyl groups at τ 6.47, 7.77, 7.91, 7.98, and 8.02, respectively. The infrared and ultraviolet spectra were similar to the spectra of ethyl *N*-acetyldithiocarbamate and 3α,9α-epoxy-3β-methoxy-11α-(*N*-acetyldithiocarbamato)-5β-androstan-17-one[27]

SCHEME V



as shown in Table I. The structure of the minor product was assigned as methyl 3,4,6-tri-*O*-acetyl-2-thio-2-*S*-thiocarbamoyl-β-D-glucopyranoside (XXVI) from the following data. The elemental analyses agreed with the empirical formula $C_{14}H_{21}NO_9S_2$, the nmr spectrum showed that the signals for an *O*-methyl and three acetoxy groups appeared at τ 6.41, 7.92, 7.95, and 7.99, respectively, the infrared spectrum showed the existence of an NH_2 group with the intramolecular hydrogen bonding, and the ultraviolet spectrum showed two peaks at 239.5 mμ (ϵ 7027) and 279 mμ (ϵ 9405). The ultraviolet spectra of *N*-unsubstituted dithiocarbamate are unreported, but the ultraviolet spectra[28] of methyl *N*,*N*-dimethyldithiocarbamate and methyl *N*,*N*-diethyldithiocarbamate each showed two maxima at 248 mμ (ϵ 8500) and 274 mμ (ϵ 9000) and 252 mμ (ϵ 9000) and 276 mμ (ϵ 11,000), respectively. The absorption band at a lower frequency is associated with the basic character of the amino group and the absorption band of the less

(24) E. L. Eliel, V. G. Badding, and M. N. Rerick, *J. Am. Chem. Soc.*, **84**, 2371 (1962); E. L. Eliel, L. A. Pilats, and V. G. Badding, *ibid.*, **84**, 2377 (1962); E. L. Eliel, B. E. Nowak, R. A. Daignault, and V. G. Badding, *J. Org. Chem.*, **30**, 2441 (1965).

(25) M. Chanlaroff, *Ber.*, **15**, 1987 (1882).

(26) H. L. Wheeler and H. F. Merrian, *J. Am. Chem. Soc.*, **23**, 283 (1901).

(27) Y. Ueda and E. Mosettig, *Steroids*, **1**, 361 (1963).

(28) H. P. Koch, *J. Chem. Soc.*, 401 (1949); G. N. Lewis, *J. Am. Chem. Soc.*, **67**, 771 (1945).

TABLE I

INFRARED AND ULTRAVIOLET SPECTRA OF SOME *N*-ACETYLDITHIOCARBAMATE DERIVATIVES

Compound	Infrared spectra, cm^{-1} NH	Infrared spectra, cm^{-1} S ‖ -SCNHAc	Ultraviolet spectra, mμ, in EtOH (ε)
Ethyl *N*-acetyldithiocarbamate	3145	1692, 1515[a]	258.5 (11,290) 309 (9710) 402 (38)
3α,9α-Epoxy-3β-methoxy-11β-(*N*-acetyldithiocarbamato)-5β-androstan-17-one	3185	1730, 1502[a]	266 (15,670) 316 (11,060) 402 (78)
XXV	3420	1727,[d] 1493[b]	257 (12,804)
	3395		311 (9094)
	3365	1753,[e] 1468[c]	410 (6.4)
XXVIII	3420	1729,[d] 1493[b]	258.5 (15,380)
	3260		312 (11,150)
	3365	1749,[e] 1468[c]	405 (51.7)

[a] Infrared spectra were measured in Nujol mull. [b] Infrared spectra were measured in KBr pellet. [c] Infrared spectra were measured in chloroform solution. [d] Shoulder. [e] Overlapped with *O*-acetate band.

basic dimethyl derivative occurs at lower frequency than that of diethyl derivative. The existence of dithiocarbamato group in XXVI, which was considered to be less basic than dimethyldithiocarbamato, was supported by applying this rule.

Similarly, treatment of XII with thiolacetic acid in anhydrous benzene gave the yellow amorphous methyl 3,4,6-tri-*O*-acetyl-2-*S*-(*N*-acetylthiocarbamoyl)-2-thio-β-D-mannopyranoside (XXVIII) and the colorless crystalline methyl 3,4,6-tri-*O*-acetyl-2-thio-2-*S*-thiocarbamoyl-β-D-mannopyranoside (XXIX) in 87.5 and 12% yields, respectively. The spectral properties of XXVIII and XXIX were in good agreement with those of XXV and XXVI, respectively.

Hydrolysis of XXV or XXVI with ammonia in methanol and acetylation of the product gave the same syrupy product in 70% yield. The product gave a positive test for sulfur and its infrared spectrum showed no *S*-acetyl group, but only *O*-acetyl groups at 1760 cm^{-1}. The circular dichroism curve showed a broad, weak, positive Cotton effect, which indicated the existence of disulfide group in XXVII.[29] From these results, the structure of XXVII was proved to be methyl 3,4,6-tri-*O*-acetyl-2-thio-β-D-glucopyranoside disulfide. Reduction of XXVII with sodium in liquid ammonia and acetylation of the product gave the pure methyl 3,4,6-tri-*O*-acetyl-2-*S*-acetyl-2-thio-β-D-glucopyranoside (XIX). Compound XIX was also obtained in 68% yield from XXV without isolation of XXVII. The infrared spectrum of XIX showed the existence of *O*-acetates at 1758 cm^{-1} and *S*-acetate at 1713 and 1697 cm^{-1}. In the nmr spectrum, the H_1 signal appeared at τ 5.43 as a doublet ($J_{1,2}$ = 9 cps) and the signal for a *S*-acetyl group appeared at τ 7.67.

Hydrolysis of XXVIII or XXIX with ammonia in methanol and benzoylation of the product gave the same crystalline product in 70% yield, which was proved to be methyl 3,4,6-tri-*O*-benzoyl-2-thio-β-D-mannopyranoside disulfide (XXX) from the following data. There was no *S*-benzoyl group in the infrared spectrum, the sulfur test was positive, and the molecular weight determination was in good agreement with the disulfide. Desulfurization of XXX with Raney nickel gave X. Reduction of XXX with sodium in liquid ammonia and acylation of the product gave methyl 2-thio-β-D-mannopyranoside derivatives (XXXI and XXXII). The infrared spectrum of the triacetate XXXI showed the existence of *O*-acetates at 1756 cm^{-1} and *S*-acetate at 1701 cm^{-1}. The nmr spectrum showed that the H_1 signal appeared at τ 5.30 as a doublet ($J_{1,2}$ = 1.7 cps), the H_2 signal appeared at τ 5.60 as a quartet ($J_{2,3}$ = 4 cps), and the signals for an *O*-methyl, an *S*-acetyl, and *O*-acetyl groups appeared at τ 6.48, 7.63, 7.92, 7.96, and 8.04.

Experimental Section

Melting points were measured on a Monoscope (H. Boch, Frankfurt am Main) and were uncorrected. The nmr spectra were measured, unless otherwise stated, in deuteriochloroform using a Varian A-60 spectrometer using tetramethylsilane as an internal reference, the infrared spectra were measured using a Koken Model D.S.-301 infrared double-monochromatic spectrophotometer, and the ultraviolet spectra were measured using a Hitachi Model E.P.S.-2 UV spectrometer in ethanol solution. The rotations were measured using an O.C. Rudolph & Sons No. 462 polarimeter in chloroform solution unless otherwise stated. The solvents were evaporated under reduced pressure below 40° using a rotatory evaporator. Preparative thin layer chromatographies were performed using silica gel G for thin layer chromatography (E. Merck AG, Darmstadt, Germany), in which the zones were detected in ultraviolet light as bright yellow after 0.01% morin solution in methanol was sprayed, collected, and extracted with dichloromethane or ethyl acetate (method A), or using silica gel GF_{254} for thin layer chromatography (E. Merck AG), in which the zones were detected in ultraviolet light, collected, and extracted with dichloromethane (method B).[30]

Addition Reaction of D-Glucal Triacetate with Thiocyanogen.—To a suspension of 13 g (40.2 mmoles) of plumbous thiocyanate in 12 ml of acetic acid containing 10% acetic anhydride was added 5.6 g (35 mmoles) of bromine dissolved in 10 ml of carbon tetrachloride at about 10° dropwise with stirring, after which the stirring was continued further for 5 min. The insoluble salts were filtered off and washed with 20 ml of carbon tetrachloride to give 26 ml of the filtrate. The filtrate (2 ml) was pipetted, diluted with acetic acid to 20 ml, and titrated with sodium thiosulfate after adding potassium iodide.[8,9] The concentration of thiocyanogen was 2.56 *N*. To 22 ml of the filtrate, in which 27.0 mmoles of thiocyanogen was contained, was added 2.45 g (9.0 mmoles) of D-glucal triacetate at 0° and the solution was allowed to stand in the dark overnight at 10°, after which D-glucal triacetate disappeared completely and three new spots appeared at R_f 0.65, 0.55, and 0.42 on a silica gel thin layer plate using a mixture of benzene and ether (1:1) as developer. The solution was poured onto ice and the mixture was stirred for 2 hr to decompose the excess of acetic anhydride and thiocyanogen. The yellow precipitate that appeared was filtered off and the filtrate was extracted with dichloromethane. The dichloromethane solution was washed with water, 10% sodium carbonate solution, and water, dried over sodium sulfate, and evaporated to a syrup. The syrup (3.66 g) was chromatographed on 366 g of silica gel using Toyo SF-200A fraction collector with a mixture of benzene and ether (1:1) as solvent. Each eluate was regulated to 10 g of weight. The residue from fractions 3–10 (R_f 0.65) (150 mg) was crystallized and recrystallized from ether and petroleum ether (bp 30–50°) to give 105 mg (3%) of 3,4,6-tri-*O*-acetyl-2-deoxy-2-thiocyanato-α-D-glucopyranosyl isothiocyanate (II) as needles: mp 94.5–96°; $[\alpha]^{22}D$ +249.0 ± 2° (*c* 1.015); $\lambda_{max}^{CCl_4}$ 2160 (SCN), 1992 (N=C=S), 1769 cm^{-1} (OAc); nmr, τ 4.10 (one-proton doublet, $J_{1,2}$ = 4 cps, H_1), 4.73 (one-proton quartet, $J_{2,3}$ = 10.5 cps, $J_{3,4}$ = 9 cps, H_3), 4.93 (one-proton multiplet, H_4), 5.63 (one-proton quartet, $J_{5,6}$ = 4.5 cps, H_5), 5.89 (one-proton quartet, $J_{5,6'}$ = 2 cps, $J_{6,6'}$ = 12

(29) K. Kuriyama, private communication. In the steroid field, many disulfides exhibited similar Cotton effects.

(30) V. Černý, J. Joska, and L. Labler, *Collection Czech. Chem. Commun.*, **26**, 1658 (1961).

cps, $H_{6'}$), 5.95 (one-proton multiplet, H_5), 6.35 (one-proton quartet, $J_{2,3}$ = 10.5 cps, H_2), 7.88, 7.91, 7.95 (three-proton singlets, OAc).

Anal. Calcd for $C_{14}H_{16}N_2O_7S_2$: C, 43.29; H, 4.15; N, 7.21; S, 16.51. Found: C, 43.57; H, 4.38; N, 7.20; S, 16.45.

The residue from fractions 12–18 (R_f 0.55) (1.750 g) was crystallized and was then recrystallized from ether and petroleum ether to give 1.050 g (30%) of 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-thiocyanato-β-D-glucopyranose (IV) as prisms: mp 99–101°; $[\alpha]^{23}D$ +72.5 ± 2° (*c* 1.045); $\lambda_{max}^{CHCl_3}$ 2163 (SCN), 1759 cm^{-1} (OAc); nmr, τ 4.17 (one-proton doublet, $J_{1,2}$ = 9 cps, H_1), ~4.72 and ~4.92 (two-proton multiplet, H_3 and H_4), 5.63 (one-proton quartet, $J_{5,6}$ = 4.5 cps, $J_{6,6'}$ = 12 cps, H_6), 5.93 (one-proton quartet, $J_{5,6'}$ = 2 cps, $H_{6'}$), 6.15 (one-proton multiplet, H_5), 6.64 (one-proton quartet, $J_{2,3}$ = 11 cps, H_2), 7.79, 7.89, 7.93, 7.97 (three-proton singlets, OAc).

Anal. Calcd for $C_{15}H_{19}NO_9S$: C, 46.27; H, 4.92; N, 3.60; S, 8.24. Found: C, 46.26; H, 4.88; N, 3.35; S, 8.39.

The mother liquor (700 mg) was again fractionated by preparative thin layer chromatography by method A using a mixture of *n*-hexane, benzene, and methanol (5:14:1). From a zone (R_f 0.54), 112 mg (3.8%) of a syrup (compound III) was obtained: $[\alpha]^{22}D$ +20.2 ± 1° (*c* 1.095); $\lambda_{max}^{CCl_4}$ 2175 (SCN), 1760 (acetate), 1627 cm^{-1} (C=C); nmr, τ 2.87 (one-proton doublet, $J_{1,3}$ = 0.6 cps, H_1), 4.39 (one-proton quartet, $J_{3,4}$ = 4.8 cps, H_3), 4.74 (one-proton triplet, $J_{4,5}$ = 4.8 cps, H_4), 7.86, 7.92 (singlets, three protons, six protons, OAc). From a zone (R_f 0.48), 270 mg of compound IV was obtained. The nmr spectrum of the mother liquor (210 mg, 6%) showed that the H_1 of VI appeared at τ 3.85 as a doublet ($J_{1,2}$ = 3.5 cps) and the H_1 of IV appeared at τ 4.17 as a doublet ($J_{1,2}$ = 9 cps). The relative intensities of these signals were 1:1.

The residue from fractions 22–50 (R_f 0.42) gave an 875-mg amount (25%) of 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-thiocyanato-α-D-mannopyranose (V) as a syrup: $[\alpha]^{22}D$ +83.5 ±4° (*c* 0.612); $\lambda_{max}^{CHCl_3}$ 2185 (SCN), 1752 cm^{-1} (OAc); nmr, τ 3.65 (one-proton doublet, $J_{1,2}$ = 1.8 cps, H_1), ~4.56 (two-proton multiplet, H_3 and H_4), ~5.85 and ~5.95 (four-proton multiplet, H_2, H_5, and 2 H_6), 7.82, 7.86, 7.93 (singlets, three protons, three protons, six protons, OAc).

Conversion of 1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-thiocyanato-β-D-glucopyranose (IV) into the α Anomer (VI).—Compound IV (200 mg) was dissolved in a mixture of 5 ml of acetic anhydride, 5 ml of acetic acid, and 0.3 ml of concentrated sulfuric acid and the solution was allowed to stand at room temperature for 7 hr. The solution was poured onto ice and the mixture was extracted with dichloromethane. The dichloromethane solution was washed with water, 10% sodium carbonate solution, and water, dried, and evaporated to a syrup. The syrup was crystallized and recrystallized from ether and petroleum ether to give 158 mg (79%) of silky needles (VI): mp 100–101°; $[\alpha]^{23}D$ +144.9 ± 2° (*c* 1.077); $\lambda_{max}^{CHCl_3}$ 2180 (SCN), 1761 cm^{-1} (OAc); nmr, τ 3.58 (one-proton doublet, $J_{1,2}$ = 3.5 cps, H_1), 4.47 (one-proton quartet, $J_{3,4}$ = 9 cps, H_3), 4.85 (one-proton triplet, $J_{4,5}$ = 9 cps, H_4), ~5.63 and ~5.96 (three-proton multiplet, H_5 and 2 H_6), 6.46 (one-proton quartet, $J_{2,3}$ = 10.5 cps, H_2), 7.78, 7.86, 7.94, 7.95 (three-proton singlets, OAc). The mixture melting point of VI with IV was depressed to 70–90°.

Anal. Calcd for $C_{15}H_{19}NO_9S$: C, 46.27; H, 4.92; N, 3.60; S, 8.24. Found: C, 46.53; H, 4.89; N, 3.76; S, 8.49.

From the mother liquor of IV described above, VI was also obtained in 60% yield by similar treatment.

Reaction of IV with Titanium Tetrachloride.—To a solution of 354 mg (0.91 mmole) of IV in 3 ml of anhydrous chloroform was added 266 mg (1.4 mmoles) of titanium tetrachloride in 3 ml of anhydrous chloroform. The mixture was refluxed on a water bath for 3 hr and poured onto ice after cooling to room temperature. The mixture was extracted with dichloromethane. The dichloromethane solution was washed with water, sodium bicarbonate solution, and water, dried, and evaporated to a syrup. The syrup was fractionated by method A using a mixture of benzene and ether (1:1) as developer. From the R_f 0.6 portion, 257 mg of a syrup was obtained and was crystallized from ether and petroleum ether by allowing it to stand at −20° overnight. 3,4,6-Tri-*O*-acetyl-2-deoxy-2-thiocyanato-α-D-glucopyranosyl chloride (VII), 96 mg (28.8%), was obtained as long needles: mp 93–95°; $[\alpha]^{22}D$ +120.6 ± 2° (*c* 1.055); $\lambda_{max}^{CCl_4}$ 2180 (SCN), 1769 cm^{-1} (OAc); nmr, τ 3.63 (one-proton doublet, $J_{1,2}$ = 4 cps, H_1), 4.35 (one-proton quartet, $J_{2,3}$ = 10.5 cps and $J_{3,4}$ = 9 cps, H_3), 4.80 (one-proton triplet, $J_{4,5}$ = 9 cps, H_4), ~5.58 and ~5.70 (three-proton multiplet, H_5 and 2 H_6), 6.10 (one-proton quartet, H_2), 7.82, 7.90, 7.94 (three-proton singlets, OAc).

Anal. Calcd for $C_{12}H_{16}NO_7SCl$: C, 42.68; H, 4.41; N, 3.83; S, 8.77; Cl, 9.69. Found: C, 42.91; H, 4.55; N, 3.79; S, 8.77; Cl, 9.71.

From the R_f 0.5 portion, 26 mg (8.68% yield) of a syrup was obtained. This syrup was identical with 2-thiocyanato-D-glucal triacetate (III) by comparison of their infrared spectra and chromatographic behavior. Compound III was also formed during the thin layer chromatography because III was detected on the thin layer chromatogram of pure VII. In another run, VII was obtained in 31.9% yield by direct crystallization of the product with seeding. The mother liquor contained further VII and was used to the methanolysis.

3,4,6-Tri-*O*-acetyl-2-deoxy-2-thiocyanato-α-D-mannopyranosyl Chloride (XI).—To a solution of 2.359 g (6.05 mmoles) of V in 15 ml of anhydrous chloroform was added 2.30 g (12.1 mmoles) of titanium tetrachloride in 3 ml of anhydrous chloroform. The solution was refluxed on a water bath for 4.5 hr and poured onto ice. The mixture was extracted with dichloromethane. The dichloromethane solution was washed with water, sodium bicarbonate solution, and water, dried, and evaporated to a syrup. The syrup was fractionated by method A using a mixture of benzene and ether (1:1) as developer. A syrup obtained from the R_f 0.61 portion was purified by rechromatography to give 1.366 g (61.7% yield) of XI as colorless syrup: $[\alpha]^{23}D$ +98.4 ± 2° (*c* 1.048); $\lambda_{max}^{CCl_4}$ 2163 (SCN), 1761 cm^{-1} (OAc); nmr, τ 3.67 (one-proton doublet, $J_{1,2}$ = 1.0 cps, H_1), 4.22 (one-proton quartet, $J_{2,3}$ = 4 cps, $J_{3,4}$ = 9.5 cps, H_3), 4.65 (one-proton triplet, $J_{4,5}$ = 9.5 cps, H_4), 5.65 (one-proton quartet, H_2), ~5.70 and ~5.78 (three-proton multiplet, H_5 and 2 H_6), 7.86, 7.93 (singlets, three protons, six protons, OAc). From the R_f 0.38 portion, 223 mg (9.47%) of the starting material was recovered.

2-Thiocyanato-D-glucal Triacetate (III) from VII.—To a solution of 42 mg (0.574 mmole) of freshly distilled diethylamine in 0.7 ml of anhydrous benzene was added 140 mg (0.383 mmole) of VII, mp 93–95°, at room temperature. The mixture was stirred at room temperature for 16 hr. The solvent and the excess diethylamine were evaporated to dryness and the residue was extracted with chloroform. The chloroform solution was filtered to remove the insoluble diethylamine hydrochloride and the filtrate was evaporated to a syrup. The syrup was purified by method A using benzene and ether (1:1) as developer. From the R_f 0.53 portion, 96 mg (76.1% yield) of syrup III was obtained: $[\alpha]^{25}D$ +20.1 ±0.4° (*c* 1.071); $\lambda_{max}^{CCl_4}$ 2175 (SCN), 1760 (acetate), 1627 cm^{-1} (C=C).

Methyl 3,4,6-Tri-*O*-acetyl-2-deoxy-2-thiocyanato-β-D-glucopyranoside (VIII). A. From Pure VII.—To a solution of 613 mg (1.68 mmoles) of VII, mp 93–95°, in 6.6 ml of anhydrous methanol was added 2.0 g of Drierite,[31] 320 mg (1.16 mmoles) of silver carbonate, and 62 mg (0.3 mmole) of silver perchlorate. The mixture was stirred in the dark (foil-covered flask) at room temperature for 4 hr. The insoluble salts were filtered off and washed with methanol. The combined filtrate and washings were evaporated to a syrup. The syrup was fractionated by method A using a mixture of benzene and ether (1:1) as developer. From the R_f 0.5 portion, 63 mg (11.4% yield) of III was obtained. From the R_f 0.45 portion, 505 mg (83.5% yield) of VIII was obtained as a syrup. For measurements of the physical constants, the syrup was purified by rechromatography: $[\alpha]^{22}D$ +99.9 ± 2° (*c* 1.011); $\lambda_{max}^{CHCl_3}$ 2180 (SCN), 1759 cm^{-1} (OAc); nmr, τ ~4.82 (two-proton multiplet, H_3 and H_4), 5.46 (one-proton doublet, $J_{1,2}$ = 8.5 cps, H_1), 5.62 (one-proton quartet, $J_{5,6}$ = 4.5 cps, H_6), 5.90 (one-proton quartet, $J_{5,6'}$ = 2.5 cps, $J_{6,6'}$ = 12 cps, $H_{6'}$), ~6.23 (one-proton multiplet, H_5), 6.38 (three-proton singlet, OCH_3), 6.92 (one-proton quartet, $J_{2,3}$ = 10.5 cps, H_2), 7.91, 7.92, 7.96 (three-proton singlets, OAc).

B. From the Mother Liquor of VII.—The mother liquor of VII (1.443 g) described above was treated as in A. Compound VIII was obtained in 58% yield together with III in 11.7% yield.

C. From IV without Isolation of VII.—Compound IV (2.0 g) was treated with titanium tetrachloride followed by methanolysis as described above to give 1.261 g (67.8%) of VIII and 136 mg (8.05%) of III.

Methanolysis of XI.—To a solution of 1.366 g (3.74 mmoles) of XI in 15 ml of anhydrous methanol was added 4.7 g of pul-

(31) Anhydrous calcium sulfate as soluble anhydrite, W. A. Hammond Drierite Co., Xenia, Ohio.

verized Drierite,[31] 683 mg (2.48 mmoles) of silver carbonate, and 137 mg (0.66 mmole) of silver perchlorate. The mixture was stirred in the dark (foil-covered flask) at room temperature for 3 hr and the insoluble salts were filtered off and washed with dichloromethane. The combined filtrate and washings were evaporated to a syrup. The syrup was dissolved in ether and the ethereal solution was decolorized with charcoal and evaporated to a syrup. The syrup was recrystallized from ether and petroleum ether to give 555 mg (41%) of methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-thiocyanato-β-D-mannopyranoside (XII) as needles, which melted at 126–127° and resolidified to prisms: mp 130–131°; $[\alpha]^{22}D$ +1.3 ± 2° (*c* 1.094); $\lambda_{max}^{CHCl_3}$ 2170 (SCN), 1753 cm^{-1} (OAc); nmr, τ ~4.74 (two-proton multiplet, H_3 and H_4), 5.26 (one-proton doublet, $J_{1,2}$ = 1.8 cps, H_1), ~5.81 (three-proton multiplet, H_2 and 2 H_6), ~6.28 (one-proton multiplet, H_5), 6.45 (three-proton singlet, OCH_3) 7.84, 7.92, 7.93 (three-proton singlets OAc).

Anal. Calcd for $C_{14}H_{19}NO_8S$: C, 46.53; H, 5.30; N, 3.88; S, 8.87. Found: C, 46.73; H, 5.35; N, 4.07; S, 9.01.

The mother liquor was fractionated by method A using a mixture of benzene and ether (1:1) as developer. From the R_f 0.70 portion, 121 mg of a syrup was obtained but it was not investigated further. A syrup which was obtained from the R_f 0.60 portion was purified by rechromatography to give 307 mg (22.8%) of methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-thiocyanato-α-D-mannopyranoside (XIII): $[\alpha]^{22}D$ +79.3 ± 2° (*c* 1.044); λ_{max}^{film} 2160 (SCN), 1753 cm^{-1} (OAc); nmr, τ 4.45 (one-proton quartet, $J_{2,3}$ = 3.5 cps, $J_{3,4}$ = 9 cps, H_3), 4.72 (one-proton triplet, $J_{4,5}$ = 9 cps, H_4), 5.02 (one-proton doublet, $J_{1,2}$ = 1.5 cps, H_1), ~5.85 (four-proton multiplet, H_2, H_5, and 2 H_6), 6.56 (three-proton singlet, OCH_3), 7.88, 7.91, 7.95 (three-proton singlets, OAc). From the R_f 0.34 portion, 122 mg (9.05%) of XII was obtained.

Desulfurization of VIII.—A mixture of 285 mg (0.79 mmole) of VIII and 4 ml of Raney nickel in 20 ml of methanol was refluxed for 1 hr. The catalyst was filtered off and washed with methanol. The combined filtrate and washings were evaporated to a syrup, which was crystallized from ether and petroleum ether to give 129 mg (53.8%) of methyl 3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranoside (IX), mp 87–98°. This was recrystallized from the same solvents to give the pure sample: mp 98–100.5°; $[\alpha]^{22}D$ −31.2 ± 2° (*c* 0.938, $CHCl_2CHCl_2$); λ_{max}^{Nujol} 1736 cm^{-1} (OAc); nmr, τ 5.53 (one-proton quartet, $J_{1,2e}$ = 2 cps, $J_{1,2a}$ = 9.0 cps, H_1), 6.50 (three-proton singlet, OCH_3), 7.90, 7.97 (singlets, three protons, six protons, OAc).

Anal. Calcd for $C_{13}H_{20}O_8$: C, 51.31; H, 6.63. Found: C, 51.44; H, 6.70.

This was identical with an authentic sample of IX prepared by Bergmann's method (see below).

Desulfurization of XII.—To a solution of 490 mg of XII in 30 ml of mehtaonl was added 10 ml of Raney nickel. The mixture was refluxed on a water bath for 1 hr and the catalyst was filtered off. The filtrate was evaporated to a syrup, which was fractionated by method A using a mixture of benzene and ether (1:1) as developer. From the R_f 0.40 portion, 90 mg (21.7%) of methyl 3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranoside (IX) was obtained after recrystallization from ether and petroleum ether: mp 100–100.5°; $[\alpha]^{22}D$ −29.4 ± 2° (*c* 1.023); λ_{max}^{Nujol} 1757 cm^{-1} (OAc). This was identical with an authentic sample of IX (see below).

Methyl 2-Deoxy-α-D-glucopyranoside (XIV) and Its Tri-*O*-benzoate (XV) from XIII.—To a solution of 466 mg (1.29 mmoles) of XIII in 10 ml of anhydrous methanol was added 9 ml of Raney nickel. The mixture was refluxed on a water bath for 1 hr. After cooling, the catalyst was filtered off and washed with methanol. The combined filtrate and washings were evaporated to a syrup. The syrup was dissolved in 15 ml of anhydrous methanol and to the solution ammonia gas was saturated under cooling with a mixture of ice and salt. The solution was allowed to stand at room temperature overnight and evaporated to dryness. The residue was fractionated by method A using *n*-butyl alcohol as developer. From the R_f 0.50 portion, 210 mg of crude crystals were obtained. Those were recrystallized three times from ethyl acetate to give 85 mg (37.0%) of XIV as prisms: mp 92–94°; $[\alpha]^{23}D$ +133.1 ± 2° (*c* 1.017, water); λ_{max}^{Nujol} 3370 cm^{-1} (OH).

Anal. Calcd for $C_7H_{14}O_5$: C, 47.18; H, 7.92. Found: C, 47.16; H, 7.93.

This was identical with an authentic sample of XIV prepared by Stacey's method[21] from D-glucal: mp 93–95°; $[\alpha]^{22}D$ +132.8 ± 2° (*c* 1.090, water) [lit.[21] mp 90–92°; $[\alpha]^{20}D$ +135° (in water)]. Compound XIV (41 mg) obtained from XIII was benzoylated with 0.42 ml of benzoyl chloride and 5 ml of pyridine at room temperature for 24 hr. The product obtained was fractionated by column chromatography using 30 g of silica gel. The eluates with a mixture of benzene and petroleum ether were discarded and the eluate with ether was crystallized after evaporation of the solvent. This was recrystallized from ether and petroleum ether to give 89.5 mg (78.8%) of methyl 3,4,6-tri-*O*-benzoyl-2-deoxy-α-D-glucopyranoside (XV): mp 110.5–111°; $[\alpha]^{23}D$ +62.1 ± 2° (*c* 1.065); $\lambda_{max}^{CHCl_3}$ 1727 (OBz), 1605, 1586, 1493 cm^{-1} (benzene). Compound XIV (35 mg) obtained from D-glucal was similarly benzoylated: mp 110–111°; $[\alpha]^{22}D$ +61.3 ± 2° (*c* 1.054); $\lambda_{max}^{CHCl_3}$ 1727 (OBz), 1605, 1585, 1493 cm^{-1} (benzene). Both compounds were identical with an authentic sample of XV prepared by Bergmann's method (see below).

1,3,4,5,6-Penta-*O*-acetyl-2-*S*-acetyl-2-thio-D-glucitol (XVI).—To a suspension of 800 mg of lithium aluminum hydride in anhydrous tetrahydrofuran was added a solution of 816 mg of IV in anhydrous tetrahydrofuran with cooling. The mixture was refluxed on a water bath for 3 hr. After cooling with ice water, the excess of lithium aluminum hydride was decomposed with ethyl acetate and ice was added to the mixture. The insoluble salts which precipitated were filtered off and washed with cold water. The combined filtrate and washings were evaporated to dryness. The residue was acetylated with 2 ml of acetic anhydride and 10 ml of pyridine at 10° for 16 hr. The mixture was poured onto ice and extracted with dichloromethane. The dichloromethane solution was washed with water, diluted hydrochloric acid, water, saturated sodium bicarbonate solution, and water, successively, dried over sodium sulfate, and evaporated to a syrup. The syrup was recrystallized from ether and petroleum ether to give 131 mg (13.5%) of prisms (XVI): mp 101–102°; $[\alpha]^{23}D$ +13.7 ± 2° (*c* 1.140); λ_{max}^{Nujol} 1742 (OAc) 1687 cm^{-1} (SAc); nmr, τ 7.59 (three-proton singlet, SAc), 7.87, 7.89, 7.92, 7.94 (singlets, three protons, three protons, three protons, six protons, OAc).

Anal. Calcd for $C_{18}H_{26}O_{11}S$: C, 47.99; H, 5.82; S, 7.12. Found: C, 48.06; H, 5.73; S, 7.41.

1,3,4,5,6-Penta-*O*-acetyl-2-*S*-acetyl-2-thio-D-mannitol (XVII).—To a suspension of 300 mg (7.89 mmoles) of lithium aluminum hydride in 5 ml of anhydrous tetrahydrofuran was added a solution of 361 mg (0.93 mmole) of V in 6 ml of anhydrous tetrahydrofuran dropwise. The mixture was stirred at room temperature for 4 hr and the excess lithium aluminum hydride was decomposed with ethyl acetate. Ice was added to the mixture and the precipitate was filtered off and washed with water. The combined filtrate and washings were evaporated to dryness and the residue was acetylated with 2 ml of acetic anhydride and 10 ml of pyridine. The mixture was poured onto ice and extracted with dichloromethane. The dichloromethane solution was washed with water, diluted hydrochloric acid, water, sodium bicarbonate solution, and water, dried, and evaporated to a syrup. The syrup was recrystallized from ether and petroleum ether to give 62 mg (14.8%) of XVII as needles: mp 132–134°; $[\alpha]^{22}D$ +15.3 ± 2° (*c* 1.070); λ_{max}^{Nujol} 1740 (OAc), 1696 cm^{-1} (SAc); nmr, τ 7.67 (three-proton singlet, SAc), 7.90, 7.93, 7.97 (singlets, three protons, three protons, nine protons, OAc).

Anal. Calcd for $C_{18}H_{26}O_{11}S$: C, 47.99; H, 5.82; S, 7.12. Found: C, 48.20; H, 5.99; S, 7.24.

The mother liquor was fractionated by method A using a mixture of benzene and ether (1:1) as developer. From the R_f 0.59 portion, 18 mg (4.3%) of XVII, mp 132–134°, was obtained.

Lithium Aluminum Hydride Reduction of VIII. A. Methyl 3,4,6-Tri-*O*-benzoyl-2-*S*-benzoyl-2-thio-β-D-glucopyranoside (XVIII).—To a suspension of 900 mg of lithium aluminum hydride in 14 ml of anhydrous tetrahydrofuran was added dropwise 977 mg (2.7 mmoles) of VIII in 14 ml of anhydrous tetrahydrofuran. The mixture was refluxed on a water bath for 3 hr, after which the excess lithium aluminum hydride was decomposed with ethyl acetate under cooling with ice. Ice was added to the mixture and the precipitate which appeared was filtered off and washed with water. The combined filtrate and washings were evaporated to dryness and to the residue was added 20 ml of pyridine and 6 ml of benzoyl chloride. After standing overnight at room temperature, the mixture was poured onto ice and extracted with dichloromethane. The dichloromethane solution was washed with water, diluted hydrochloric acid, water, sodium bicarbonate solution, and water, successively, dried, and evaporated to a syrup. The syrup was chromatographed on 50 g of silica gel to remove benzoic anhydride which was produced during

the reaction. The eluates with a mixture of benzene and petroleum ether (2:8 to 1:1) were discarded and the eluate with benzene was collected and crystallized from ether and petroleum ether to give 586 mg (34.7%) of needles. Recrystallization from acetone and *n*-hexane gave the pure methyl 3,4,6-tri-*O*-benzoyl-2-*S*-benzoyl-2-thio-β-D-glucopyranoside (XVIII): mp 162–163°; $[\alpha]^{22}D$ −6.5 ± 2° (*c* 1.022); $\lambda_{max}^{CCl_4}$ 3068 (benzene), 1737 (OBz), 1684 (SBz), 1604, 1585, 1493 cm^{-1} (benzene); nmr, τ 4.09 (one-proton quartet, $J_{2,3}$ = 10 cps, $J_{3,4}$ = 9 cps, H_3), 4.41 (one-proton triplet, $J_{4,5}$ = 9 cps, H_4), 5.16 (one-proton doublet, $J_{1,2}$ = 9 cps, H_1), ~5.45 (two-proton multiplet, 2 H_6), 5.87 (one-proton quartet, H_2), ~5.90 (one-proton multiplet, H_5), 6.48 (three-proton singlet, OCH_3).

Anal. Calcd for $C_{35}H_{30}O_9S$: C, 67.08; H, 4.83; S, 5.12. Found: C, 67.35; H, 4.89; S, 5.23.

B.—Compound VIII (691 mg, 1.915 mmoles) was reduced with 690 mg of lithium aluminum hydride as described in A. The syrup obtained was acetylated with 10 ml of acetic anhydride and 20 ml of pyridine at room temperature for 16 hr. The mixture was poured onto ice and extracted with dichloromethane. The dichloromethane solution was washed with water, diluted hydrochloric acid, water, sodium bicarbonate solution, and water, successively, dried, and evaporated to a syrup. The residue was fractionated by method A using a mixture of benzene and ether (1:1) as developer. The product (164 mg) from the R_f 0.6 portion was recrystallized from ether and petroleum ether to give 40 mg (5.35%) of 3,4,5,6-tetra-*O*-acetyl-2-*S*-acetyl-1-deoxy-2-thio-D-glucitol (XXI) as prisms: mp 98–99°; $[\alpha]^{22}D$ +10.4 ± 2° (*c* 1.038); $\lambda_{max}^{CHCl_3}$ 1748 (OAc), 1692 cm^{-1} (SAc); nmr τ 6.21 (one-proton quintet, *J* = 7 cps, H_2), 7.68 (three-proton singlet, SAc), 7.88, 7.96, 7.97 (singlets, three protons, three protons, six protons, OAc), 8.66 (three-proton doublet, *J* = 7 cps, 3 H_1).

Anal. Calcd for $C_{16}H_{24}O_9S$: C, 48.72; H, 6.13; S, 8.13. Found: C, 48.75; H, 6.24; S, 8.20.

The product from the R_f 0.52 portion was crystallized from ether and petroleum ether to give 314 mg (43.2% yield) of a mixture of needles and prisms: mp 83–95°; $[\alpha]^{22}D$ +10.0 ± 2° (*c* 1.033). This could not be purified by recrystallization or thin layer chromatography technique. The nmr spectrum showed that the *O*-methyl signals appeared at τ 6.50 and 6.66 in the ratio of 2:1 and the *S*-acetyl signals appeared at τ 7.63 and 7.67 in the ratio of 1:2. From this result this compound was assumed to be a mixture of methyl 3,4,6-tri-*O*-acetyl-2-*S*-acetyl-2-thio-β-D-glucopyranoside (XIX) and the α anomer (XX) in the ratio of 2:1. When this mixture was hydrolyzed with sodium methoxide in methanol and the product was benzoylated, only XVIII was obtained in 27.6% yield as a crystalline compound.

Desulfurization of XVIII.—To a solution of 190 mg (0.33 mmole) of XVIII in 13 ml of methanol was added 2.7 ml of Raney nickel and the mixture was refluxed for 1 hr. The catalyst was filtered off and washed with methanol. The combined filtrate and washings were evaporated to a syrup, which was recrystallized from methanol to give 72 mg (48.3%) of methyl 3,4,6-tri-*O*-benzoyl-2-deoxy-β-D-glucopyranoside (X): mp 95.5–97.5°; $[\alpha]^{21}D$ −49.2 ± 4° (*c* 0.531, $CHCl_2CHCl_2$); silky needles; $\lambda_{max}^{CCl_4}$ 3080 (benzene), 1731 (OBz), 1603, 1585, 1493 cm^{-1} (benzene); nmr, τ 5.31 (one-proton quartet, $J_{1,2e}$ = 2.0 cps, $J_{1,2a}$ = 10 cps, H_1), 6.46 (three-proton singlet, OCH_3).

Anal. Calcd for $C_{28}H_{26}O_8$: C, 68.56; H, 5.34. Found: C, 68.52; H, 5.43.

This was identical with an authentic sample of X prepared by Bergmann's method (see below).

Preparations of IX and X from 2-Deoxy-D-glucose.[20]—3,4,6-Tri-*O*-benzoyl-2-deoxy-α-D-glucopyranosyl bromide (XXIV), mp 132–133°, $[\alpha]^{21}D$ +105.5 ± 2° (*c* 1.068, $CHCl_2CHCl_2$) [lit.[20] mp 139°, $[\alpha]^{16}D$ +121.4° (in $CHCl_2CHCl_3$)], which was obtained from 2-deoxy-D-glucose,[32] mp 151.5–153.5°, $[\alpha]^{22}D$ +46.3 ± 2° (*c* 1.107, H_2O), was treated with silver carbonate in methanol for 1 hr as described in the literature.[20] The product was fractionated by method B using a mixture of benzene and ethyl acetate (9:1) as developer. The product from the R_f 0.57 portion was recrystallized from ether and petroleum ether to give 102 mg (10.0%) of methyl 3,4,6-tri-*O*-benzoyl-2-deoxy-α-D-glucopyranoside (XV) as long needles: mp 110–110.5°; $[\alpha]^{22}D$ +49.4 ± 2° (*c* 1.019, $CHCl_2CHCl_2$); $[\alpha]^{23}D$ +60.9 ± 2° (*c* 1.085); $\lambda_{max}^{CHCl_3}$ 3070 (benzene), 1727 (OBz), 1605, 1585, 1493 cm^{-1} (benzene); nmr, τ 5.06 (one-proton quartet, $J_{1,2e}$ = 1.5 cps, $J_{1,2a}$ = 3.5 cps, H_1), 6.57 (three-proton singlet, OCH_3).

Anal. Calcd for $C_{28}H_{26}O_8$: C, 68.56; H, 5.34. Found: C, 68.56; H, 5.47.

The product from the R_f 0.5 portion was recrystallized from methanol to give 861 mg (84.1% yield) of X: mp 96–98°; $[\alpha]^{22}D$ −53.1 ± 2° (*c* 1.031, $CHCl_2CHCl_2$) [lit.[20] mp 88°; $[\alpha]^{19}D$ −34.31° (in $CHCl_2CHCl_2$)].

Anal. Calcd for $C_{28}H_{26}O_8$: C, 68.56; H, 5.34. Found: C, 68.43; H, 5.49.

This was identical with X prepared from XVIII. This was hydrolyzed with ammonia in methanol and the product was acetylated with acetic anhydride and pyridine to give IX: mp 100–100.5°; $[\alpha]^{22}D$ −30.0 ± 2° (*c* 1.001, $CHCl_2CHCl_2$) [lit.[20] mp 96–97°; $[\alpha]D$ −30.3° (in $CHCl_2CHCl_2$)].

Reaction of VIII with Thiolacetic Acid.—A mixture of 553 mg (1.53 mmoles) of VIII and 274 mg (3.52 mmoles) of thiolacetic acid in 13 ml of anhydrous benzene was refluxed for 6 hr. The solvent and the excess thiolacetic acid were evaporated to a yellow amorphous powder. The residue was fractionated by method B using a mixture of benzene and ether (1:1) as developer. Methyl 3,4,6-tri-*O*-acetyl-2-*S*-(*N*-acetylthiocarbamoyl)-2-thio-β-D-glucopyranoside (XXV) (502 mg, 75% yield) was obtained from the R_f 0.26 portion as a yellow amorphous powder, which resisted crystallization: $[\alpha]^{22}D$ −46.9 ± 2° (*c* 1.019); λ_{max}^{KBr} 3420, 3395 (NH), 1756, 1727, 1493 cm^{-1} (OAc and SC(=S)NHAc); $\lambda_{max}^{CHCl_3}$ 3365 (NH), 1753, 1468 cm^{-1} (OAc and SC(=S)NHAc); λ_{max} 257 mμ (ε 12,804), 311 mμ (ε 9094), 410 mμ (ε 46.4); nmr, τ 6.50 (three-proton singlet, OCH_3), 7.77 (three-proton singlet, NAc), 7.91, 7.98, 8.02 (three-proton singlets, OAc).

Colorless needles (134 mg), mp 163–166°, were obtained from R_f 0.20 portion. Those were recrystallized from ether and petroleum ether to give 85 mg (14%) of pure methyl 3,4,6-tri-*O*-acetyl-2-thio-2-*S*-thiocarbamoyl-β-D-glucopyranoside (XXVI): mp 165–166°; $[\alpha]^{22}D$ −21.3 ± 2° (*c* 1.069); λ_{max}^{Nujol} 3370, 3275, 3187 (NH_2), 1738 (OAc), 1628 cm^{-1} (NH_2); $\lambda_{max}^{CHCl_3}$ 3435, 3392, 3367, 3301, 3180 (NH_2) (in 5-mm cell), 1753 (OAc), 1605, 1597 cm^{-1} (NH_2) (in 1-mm cell); λ_{max} 239.5 mμ (ε 7027), 279 mμ (ε 9405); nmr, τ 5.48 (one-proton doublet, $J_{1,2}$ = 8.7 cps, H_1), 6.41 (three-proton singlet, OCH_3), 7.92, 7.95, 7.99 (three-proton singlets, OAc).

Anal. Calcd for $C_{14}H_{21}NO_8S_2$: C, 42.52; H, 5.35; N, 3.54; S, 16.22. Found: C, 42.75; H, 5.43; N, 3.46; S, 16.16.

Reaction of XII with Thiolacetic Acid.—To a solution of 400 mg (1.11 mmoles) of XII in 10 ml of anhydrous benzene was added 194 mg (2.55 mmoles) of thiolacetic acid in 5 ml of anhydrous benzene. The solution was refluxed on an oil bath for 6 hr and concentrated to dryness. The residue (542 mg) was fractionated by method B using a mixture of benzene and methanol (9:1) as developer. From the R_f 0.25 portion a yellow amorphous powder was obtained. This was purified by rechromatography to give 424 mg (87.7%) of methyl 3,4,6-tri-*O*-acetyl-2-*S*-(*N*-acetylthiocarbamoyl)-2-thio-β-D-mannopyranoside (XXVIII): $[\alpha]^{22}D$ +28.1 ± 2° (*c* 1.016); λ_{max}^{KBr} 3420, 3260 (NH), 1749, 1729, 1493 cm^{-1} (OAc and SC(=S)NHAc); $\lambda_{max}^{CHCl_3}$ 3365 (NH), 1749, 1468 cm^{-1} (OAc and SC(=S)NHAc); λ_{max} 258.5 mμ (ε 15,380), 312 mμ (ε 11,150), 405 mμ (ε 51.7); nmr, τ 5.19 (one-proton doublet, $J_{1,2}$ = 2 cps, H_1), 6.50 (three-proton singlet, OCH_3), 7.77 (three-proton singlet, NAc), 7.90, 7.94, 7.97 (three-proton singlets, OAc).

From the R_f 0.20 portion, 63 mg (14.5% yield) of crystals were obtained after evaporation of the solvent. Those were recrystallized from dichloromethane and petroleum ether to give 31 mg (7.2%) of pure methyl 3,4,6-tri-*O*-acetyl-2-thio-2-*S*-thiocarbamoyl-β-D-mannopyranoside (XXIX) as colorless needles: mp 154.5–156.5°; $[\alpha]^{22}D$ +2.5 ± 2° (*c* 1.044); λ_{max}^{Nujol} 3424, 3295, 3180 (NH_2), 1749 (OAc), 1615, 1600 cm^{-1} (NH_2); $\lambda_{max}^{CHCl_3}$ 3473, 3365 (NH_2), 1752 (OAc), 1580 cm^{-1} (NH_2); λ_{max} 242.5 mμ (ε 8086), 277 mμ (ε 9883).

Anal. Calcd for $C_{14}H_{21}NO_8S_2$: C, 42.52; H, 5.35; N, 3.54; S, 16.22. Found: C, 42.50; H, 5.37; N, 3.71; S, 15.93.

Methyl 3,4,6-Tri-*O*-acetyl-2-thio-β-D-glucopyranoside Disulfide (XXVII). A. From XXV.—To a solution of 200 mg (0.46 mmole) of XXV in 6 ml of anhydrous methanol was saturated ammonia gas under cooling with a mixture of ice and salt. The solution was allowed to stand overnight at room temperature and concentrated to a syrup. The residue was acetylated with 1 ml of acetic anhydride and 5 ml of pyridine. This mixture was poured onto ice and extracted with dichloromethane. The dichloro-

(32) Available from Nutritional Biochemical Corp., Cleveland, Ohio.

methane solution was washed with water, diluted hydrochloric acid, water, sodium carbonate solution, and water, successively, dried, and evaporated. The residue was dissolved in ether and the ethereal solution was decolorized with charcoal and evaporated. The residue was fractionated by method B using a mixture of benzene and methanol (9:1) as developer. From the R_f 0.48 portion, 108 mg (70.4% yield) of colorless syrupy XXVII was obtained: $[\alpha]^{22}D$ +140 ± 2° (*c* 0.912); $\lambda_{max}^{CCl_4}$ 1760 cm^{-1} (OAc); CD curve, $[\theta]_{300}$ 0, $[\theta]_{242}$ +2730, $[\theta]_{225}$ +560, $[\theta]_{215}$ +4498 (in MeOH).

B. From XXVI.—Compound XXVI was treated as described above and XXVII was obtained in 70% yield.

Methyl 3,4,6-Tri-*O*-benzoyl-2-thio-β-D-mannopyranoside Disulfide (XXX). A. From XXVIII.—To a solution of 261 mg (0.6 mmole) of XXVIII in 6 ml of anhydrous methanol was saturated ammonia gas under cooling with a mixture of ice and salt. The solution was allowed to stand at room temperature for 24 hr and concentrated to dryness. The residue was benzoylated with 1 ml of benzoyl chloride and 5 ml of pyridine. This mixture was poured onto ice and extracted with dichloromethane. The dichloromethane solution was washed with water, diluted hydrochloric acid, water, sodium carbonate solution, and water, dried, and evaporated to a syrup. The syrup was fractionated by column chromatography using 10 g of silica gel. The eluates with benzene were discarded and the eluates with dichloromethane were collected and evaporated to a syrup. The syrup was crystallized and recrystallized from dichloromethane and methanol to give 238 mg (76.4%) of XXX as colorless needles: mp 209.5–210.5°; $[\alpha]^{22}D$ +60.9 ± 2° (*c* 1.015); $\lambda_{max}^{CHCl_3}$ 1728 (OBz), 1605, 1588 cm^{-1} (benzene); nmr, τ 5.23 (one-proton doublet, $J_{1,2}$ = 2 cps, H_1), 6.48 (three-proton singlet, OCH_3); mol wt 1113 (calcd for $C_{56}H_{50}O_{16}S_2$, 1043.092), (using a vapor pressure osmometer, Mechrolab Model 301 A, Mountain View, Calif.).

Anal. Calcd for $C_{56}H_{50}O_{16}S_2$: C, 64.48; H, 4.83; S, 6.15. Found: C, 64.27; H, 4.74; S, 6.15.

B. From XXIX.—By similar treatment of XXIX, XXX was obtained in 75% yield.

Desulfurization of XXX.—To a solution of 103 mg (0.1 mmole) of XXX in a mixture of 3 ml of anhydrous dioxane and 7 ml of anydrous methanol was added 2 ml of Raney nickel. The mixture was refluxed on an oil bath for 1 hr. The catalyst was filtered off and washed with dioxane and the combined filtrate and washings were evaporated to a syrup. The syrup was dissolved in ether and the ethereal solution was filtered to remove the insoluble material. The filtrate was evaporated to a syrup, which was recrystallized from methanol to give 50 mg (51.7%) of methyl 3,4,6-tri-*O*-benzoyl-2-deoxy-β-D-glucopyranoside (X) as silky needles: mp 95.5–97.5°; $[\alpha]^{22}D$ −45.3 ± 2° (*c* 1.053, $CHCl_2CHCl_2$). This was identical with an authentic sample of X described above.

Methyl 3,4,6-Tri-*O*-acetyl-2-*S*-acetyl-2-thio-β-D-glucopyranoside (XIX). A. From XXVII.—To about 10 ml of redistilled liquid ammonia was added a solution of 89 mg (0.13 mmole) of XXVII dissolved in 2 ml of anhydrous ether at −78°. To the solution were added small pieces of sodium metal with stirring at −78° until the blue color of sodium was persisted. After 20 min the excess of sodium metal was decomposed by adding ammonium chloride and the ammonia was evaporated to dryness. The residue was acetylated with 7 ml of acetic anhydride and 15 ml of pyridine. This mixture was poured onto ice and extracted with dichloromethane. The dichloromethane solution was washed with water, diluted hydrochloric acid, water, sodium carbonate solution, and water, dried, and evaporated to a syrup. The syrup was fractionated by method A using a mixture of benzene and ether (1:1) as developer. Syrup (56 mg) was obtained from the R_f 0.47 portion. This syrup was recrystallized from ether and petroleum ether to give 41 mg (41%) of pure methyl 3,4,6-tri-*O*-acetyl-2-*S*-acetyl-2-thio-β-D-glucopyranoside (XIX) as colorless long needles: mp 96.5–97°; $[\alpha]^{22}D$ −8.9 ± 2° (*c* 1.052); $\lambda_{max}^{CCl_4}$ 1758 (OAc), 1713, 1697 cm^{-1} (SAc); nmr, τ ~4.83 (two-proton multiplet, H_3 and H_4), 5.43 (one-proton doublet, $J_{1,2}$ = 9 cps, H_1), 5.65 (one-proton quartet, $J_{5,6}$ = 4 cps, H_5), 5.91 (one-proton quartet $J_{5,6'}$ = 2 cps, $J_{6,6'}$ = 12 cps, $H_{6'}$), ~6.28 (two-proton multiplet, H_2 and H_5), 6.50 (three-proton singlet, OCH_3), 7.67 (three-proton singlet, SAc), 7.92, 8.00 (singlets, three protons, six protons, OAc).

Anal. Calcd for $C_{15}H_{22}O_9S$: C, 47.61; H, 5.86; S, 8.47. Found: C, 47.83; H, 5.91; S, 8.22.

B. From XXV.—Compound XIX was obtained in 68% yield from XXV without isolation of XXVII by the above-mentioned method.

Methyl 3,4,6-Tri-*O*-acetyl-2-*S*-acetyl-2-thio-β-D-mannopyranoside (XXXI) and Methyl 3,4,6-Tri-*O*-benzoyl-2-*S*-benzoyl-2-thio-β-D-mannopyranoside (XXXII) from XII.—A mixture of 540 mg (1.5 mmoles) of XII, 250 mg (3.3 mmoles) of thiolacetic acid, and 15 ml of anhydrous benzene was refluxed on an oil bath for 6 hr. Thin layer chromatography on silica gel showed that the starting material disappeared completely. The benzene and the excess thiolacetic acid were evaporated. The residue was dissolved in 15 ml of anhydrous methanol and to the solution ammonia gas was saturated under cooling with a mixture of ice and salt. The solution was allowed to stand at room temperature for 36 hr and concentrated to a syrup. About 30 ml of redistilled liquid ammonia was collected to the flask, in which the syrup was placed, at −78° under cooling with Dry Ice and acetone. To the mixture small pieces of sodium metal were added until the blue color of sodium persisted with stirring. After 20 min the excess sodium was decomposed by adding ammonium chloride and the ammonia was evaporated to dryness. The residue (1.081 g) was divided into two parts. One part (681 mg) was acetylated with 2 ml of acetic anhydride and 10 ml of pyridine at room temperature for 24 hr. The mixture was poured onto ice and extracted with dichloromethane. The dichloromethane solution was washed with water, diluted hydrochloric acid, water, sodium carbonate solution, and water, dried, and evaporated to a syrup. The residue was dissolved in acetone and the acetone solution was decolorized with charcoal and concentrated to dryness. The residual solid was recrystallized from acetone and *n*-hexane to give 267 mg of methyl 3,4,6-tri-*O*-acetyl-2-*S*-acetyl-2-thio-β-D-mannopyranoside (XXXI) as leaflets: mp 151–153° (sintered at 149°); $[\alpha]^{23}D$ −22.4 ± 2° (*c* 1.102); $\lambda_{max}^{CCl_4}$ 1756 (OAc), 1701 cm^{-1} (SAc); nmr, τ ~4.75 and ~4.92 (two-proton multiplet, H_3 and H_4), 5.30 (one-proton doublet, $J_{1,2}$ = 1.7 cps, H_1), 5.60 (one-proton quartet, $J_{2,3}$ = 4.0 cps, H_2), 5.96 (two-proton doublet, J = 4 cps, 2 H_6), ~6.33 (one-proton multiplet, H_5), 6.48 (three-proton singlet, OCH_3), 7.63 (three-proton singlet, SAc), 7.92, 7.96, 8.04 (three-proton singlets, OAc).

Anal. Calcd for $C_{15}H_{22}O_9S$: C, 47.61; H, 5.86; S, 8.22. Found: C, 47.34; H, 5.85; S, 8.35.

Another part (400 mg) of the residue was benzoylated with 2 ml of benzoyl chloride and 10 ml of pyridine at room temperature for 16 hr. The mixture was poured onto ice and extracted with dichloromethane. The dichloromethane solution was washed with water, diluted hydrochloric acid, water, sodium carbonate solution, and water, dried, and evaporated. The residue was fractionated by method B using a mixture of benzene and ethyl acetate (9:1). The R_f 0.51 portion was crystallized and was then recrystallized from methanol and acetone to give the product from the same solvent gave pure methyl 3,4,6-tri-*O*-benzoyl-2-*S*-benzoyl-2-thio-β-D-mannopyranoside (XXXII): mp 155.5–156.5°; $[\alpha]^{23}D$ −80.3 ± 2° (*c* 1.022); $\lambda_{max}^{CCl_4}$ 1735 (OBz), 1676 (SBz), 1605, 1582 cm^{-1} (benzene).

Anal. Calcd for $C_{35}H_{30}O_9S$: C, 67.08; H, 4.83; S, 5.12. Found: C, 66.94; H, 4.89; S, 5.23.

Registry No.—I, 2873-29-2; II, 13145-11-4; III, 13145-12-5; IV, 13131-71-0; V, 13145-13-6; VI, 13145-14-7; VII, 13145-15-8; VIII, 13145-16-9; IX, 6087-41-8; X, 13145-18-1; XI, 13145-19-2; XII, 13145-20-5; XIII, 13145-21-6; XIV, 13145-22-7; XV, 13145-23-8; XVI, 13131-72-1; XVII, 13145-24-9; XVIII, 13145-25-0; XIX, 13145-26-1; XXI, 13145-27-2; XXV, 13145-28-3; XXVI, 13145-29-4; XXVII, 13145-30-7; XXVIII, 13137-32-1; XXIX, 13145-31-8; XXX, 13145-32-9; XXXI, 13145-33-0; XXXII, 13145-34-1; thiocyanogen, 505-14-6.