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92. Hiroshi Nakamura, Setsuzo Tejima, and Masuo Akagi: Thiosugars. Ⅷ.*1 Synthesis of 1,2-Dithio-β-D-mannopyranose.*2

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In the recent few years there has been marked interest in the synthesis of thiosugars.[1] According to literature, replacement of an anomeric hydroxyl by mercapto is easily performed using the method which starts from acylated halogeno sugars, *via* intermediates obtainable by reaction of nucleophiles having sulfur, followed by degradation with alkaline. A primary hydroxyl is replaceable without so much difficulty,[2] because a sulfonic ester of a primary alcohol is directly replaced by potassium thiolacetate[3] or sodium iodide, and, by way of the deoxyiodo derivative, by other nucleophiles having sulfur.

While a halogen substituted for a secondary hydroxyl of sugars or a secondary sulfonyloxy group makes resistance to nucleophilic substitution.[4] Therefore, previous investigations on thiosugars involving a secondary mercapto in furanose or pyranose ring have dealt with few data.[5] A noted method introducing a secondary mercapto in sugar lactol ring, first established by Jamieson and Brown, is a ring-opening of methyl 2,3-anhydro-4,6-O-benzylidene-α-D-manno or allo-pyranoside with sodium benzylmercaptide, followed by reduction with sodium in liquid ammonia.

The authors have been interested in the bromine addition products of 3,4,6-tri-O-acetyl-D-glucal (I)[6] as a starting material of thiosugar synthesis, and, during the course of the investigation on D-glucal derivative, we noticed unexpectedly that an interesting reaction occurred when potassium thiolacetate had been reacted on sugar bromides having a bromine or mesyl at C2. Further investigation confirmed that the bromine or the mesyl at C2 was easily replaceable by thioacetyl when ethylxanthate or thioacetyl group had been situated at C1 in D-glucopyranose.

In this paper the authors wish to describe the preparation of the title compound by the method mentioned above. We assume that the method provides a simple but a valuable procedure introducing a secondary mercapto in sugars. As the title compound has vicinal mercapto groups in the pyranose ring, it might be interesting, from the therapeutic point of view, as a sugar analogue of BAL, 2,3-dimercapto-1-propanol.

Reaction of bromine upon I in carbon tetrachloride[7] afforded a sirupy dibromide mixture (Ⅱ) after evaporation of the solvent. Treatment of Ⅱ with potassium ethylxanthate in dry ethanol gave 2-bromo-2-deoxy-3,4,6-tri-O-acetyl-β-D-glucopyranosyl ethylxanthate (Ⅲ), m.p.128~129°, $[\alpha]_D^{17}$ −10.8°, in 27% yield. The product was also obtain-

*1 Part Ⅷ. T. Maki, H. Nakamura, S. Tejima, M. Akagi: This Bulletin, **13**, 764 (1965).
*2 Preliminary communication of this paper: *Ibid.*, **13**, 1478 (1965).
*3 Kita 15-jo, Nishi-7-chome, Sapporo, Hokkaido (中村 博, 手島節三, 赤木満洲雄).
1) D. Horton, D.H. Hutson: "Advances in Carbohydrate Chemistry," Vol. 18, 123 (1963), Academic Press Inc., New York and London.
2) M. Akagi, S. Tejima, M. Haga: This Bulletin, **10**, 562 (1962), **11**, 58 (1963); R.L. Whistler, R.M. Rowell: J. Org. Chem., **29**, 1259 (1964); K. Tokuyama, M. Kiyokawa: *Ibid.*, **29**, 1475 (1964); D.H. Hutson: Chem. & Ind. (London), **1964**, 740.
3) J.H. Chapman, L.N. Owen: J. Chem. Soc., **1950**, 579.
4) A.C. Maehly, T. Reichstein: Helv. Chem. Acta, **30**, 496 (1947).
5) N.C. Jamieson, R.K.Brown: Can. J. Chem., **39**, 1765 (1961); J.E. Christensen, L. Goodman: J. Org. Chem., **28**, 158, 2610, 2995 (1963); R.L. Whistler, W.E. Dick, T.P. Ingle, R.M. Rowell, B. Urbas: *Ibid.*, **29**, 3723 (1964).
6) H. Nakamura, S. Tejima, M. Akagi: This Bulletin, **12**, 1302 (1964).
7) E. Fischer: Ber., **47**, 196 (1914); B. Helferich, E.N. Mulcahy, H. Ziegler: Chem. Ber., **87**, 233 (1954).

able in good yield (86%) by heating 2-bromo-2-deoxy-3,4,6-tri-O-acetyl-α-D-glucopyranosyl bromide (IV)[6] with potassium ethylxanthate in dry acetone. 2-O-Mesyl-3,4,6-tri-O-acetyl-β-D-glucopyranosyl ethylxanthate (VII), m.p. 98~100°, $[\alpha]_D^{21}$ +9.52°, was prepared in 70% yield by warming sirupy 2-O-mesyl-3,4,6-tri-O-acetyl-α-D-glucopyranosyl bromide (VI), prepared from 2-O-mesyl-1,3,4,6-tetra-O-acetyl-α-D-glucopyranose (V) according to the method of Helferich and Zirner,[8] and potassium ethylxanthate in dry ethanol. The nuclear magnetic resonance spectra of III and VII were measured at 60 and 100 Mc. At 60 Mc. the anomeric protons of III and VII showed a doublet at τ 4.45 and 4.53, respectively, with the same coupling constant ($J_{1,2}$=11.0 c.p.s.). The comparatively large coupling constant value was in agreement with an axial-axial orientation at C1 and C2[9] which clearly confirmed the β-configuration of their structure.

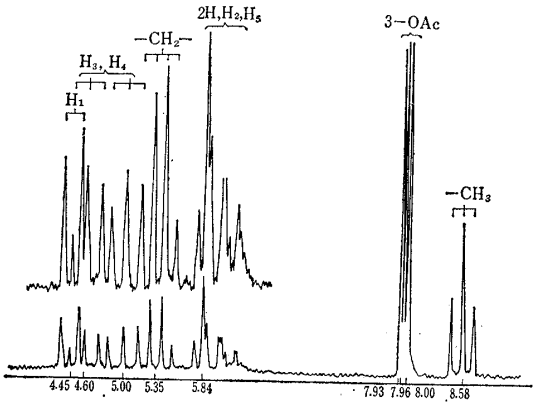


Fig. 1a. Nuclear Magnetic Resonance Spectrum of 2-Bromo-2-deoxy-3,4,6-tri-O-acetyl-β-D-glucopyranosyl Ethylxanthate (III), at 60 Mc.

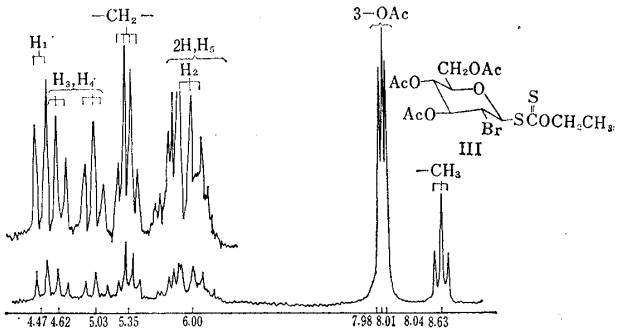


Fig. 1b. Nuclear Magnetic Resonance Spectrum of 2-Bromo-2-deoxy-3,4,6-tri-O-acetyl-β-D-glucopyranosyl Ethylxanthate (III), at 100 Mc.

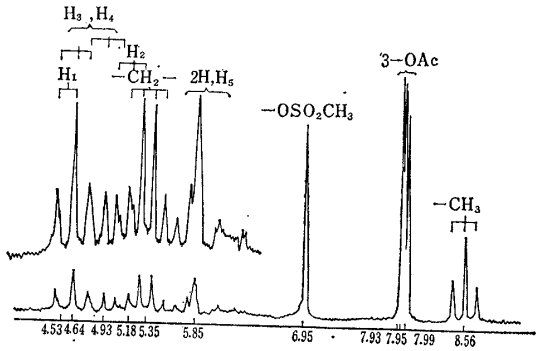


Fig. 1c. Nuclear Magnetic Resonance Spectrum of 2-O-Mesyl-3,4,6-tri-O-acetyl-β-D-glucopyranosyl Ethylxanthate (VII), at 60 Mc.

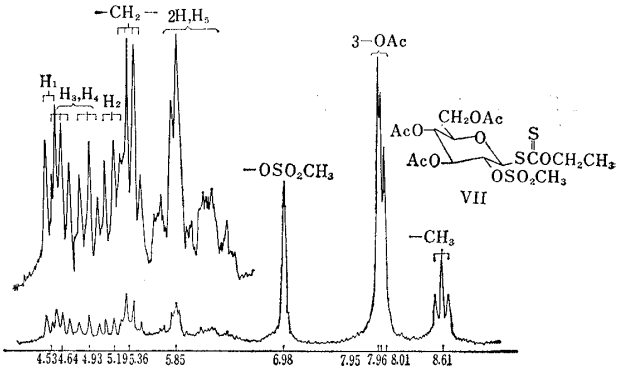


Fig. 1d. Nuclear Magnetic Resonance Spectrum of 2-O-Mesyl-3,4,6-tri-O-acetyl-β-D-glucopyranosyl Ethylxanthate (VII), at 100 Mc.

An approximately equal amounts of two crystalline products (VIII and IX) were obtained when one mole of the bromide (VI) and 1.5 moles of potassium thiolacetate were refluxed in acetone for five minutes, followed by silica gel chromatography. The product, m.p. 155~156°, $[\alpha]_D^{22}$ +33.3°, separated from the earlier part of elution, was assigned to be 1,2-di-*S*-acetyl-1,2-dithio-3,4,6-tri-O-acetyl-β-D-mannopyranose (IX) from the data mentioned below. The elementary analysis was in agreement with a $C_{16}H_{22}O_9S_2$, and the

8) B. Helferich, J. Zirner : *Ibid.*, **95**, 2604 (1962).
9) R.U. Lemieux, R.K. Kullnig, H.J. Bernstein, W.G. Schneider : J. Am. Chem. Soc., **80**, 6098 (1958); L.D. Hall : "Advances in Carbohydrate Chemistry," Vol. 19, 51 (1964), Academic Press Inc., New York and London.

infrared spectrum showed thioacetyl at 1710, while the absence of sulfonyloxy near 1170 and 1335 cm.$^{-1}$ Reductive desulfrization with Raney nickel gave 3,4,6-tri-O-acetyl-D-hydroglucal (X), colorless oil, $[\alpha]_D^{22}$ +33.3°, in 93% yield, which was induced to crystalline D-hydroglucal (XI), m.p. 86~87°, $[\alpha]_D^{22}$ +20°, after deacetylation with methanolic ammonia.

The nuclear magnetic resonance spectrum of IX at 60 Mc. showed a singlet at τ 7.59 and 7.62 corresponding to the two thioacetyl groups. The anomeric proton appeared as a doublet at τ 4.04 with a coupling constant ($J_{1,2}$=2.5 c.p.s.) which indicated an axially oriented C1 proton having a projected valence angle of 60° with a C2 proton.[10]

Another crystal, m.p. 170~171°, $[\alpha]_D^{21}$ +16.5°, separated from the later part of elution, was assigned to be 1-*S*-acetyl-1-thio-2-O-mesyl-3,4,6-tri-O-acetyl-β-D-glucopyranose (VIII): the structure was supported by the satisfactory elemental analysis and the infrared spectrum, ν_{max}^{Nujol} 1170, 1335 (-SO_2-O-), 1710 cm^{-1} (-SAc). The nuclear magnetic resonance spectrum of VIII at 60 Mc. showed a singlet at τ 6.97 and 7.58 corresponding to mesyl and thioacetyl groups, respectively. The anomeric proton appeared as a doublet at τ 4.69 with a coupling constant ($J_{1,2}$=11.0 c.p.s.).

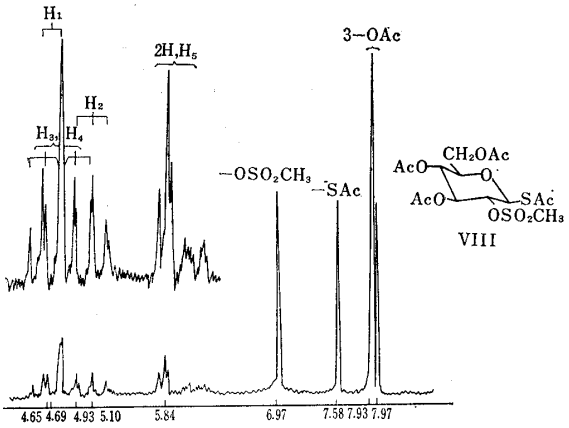


Fig. 2a. Nuclear Magnetic Resonance Spectrum of 1-*S*-Acetyl-1-thio-2-O-mesyl-3,4,6-tri-O-acetyl-β-D-glucopyranose (VIII), at 60 Mc.

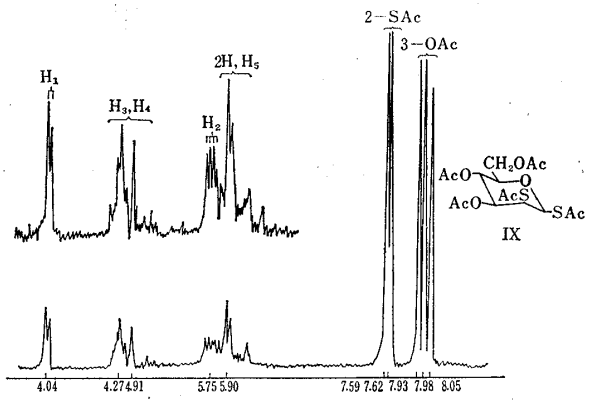


Fig. 2b. Nuclear Magnetic Resonance Spectrum of 1,2-Di-*S*-acetyl-1,2-dithio-3,4,6-tri-O-acetyl-β-D-mannopyranose (IX), at 60 Mc.

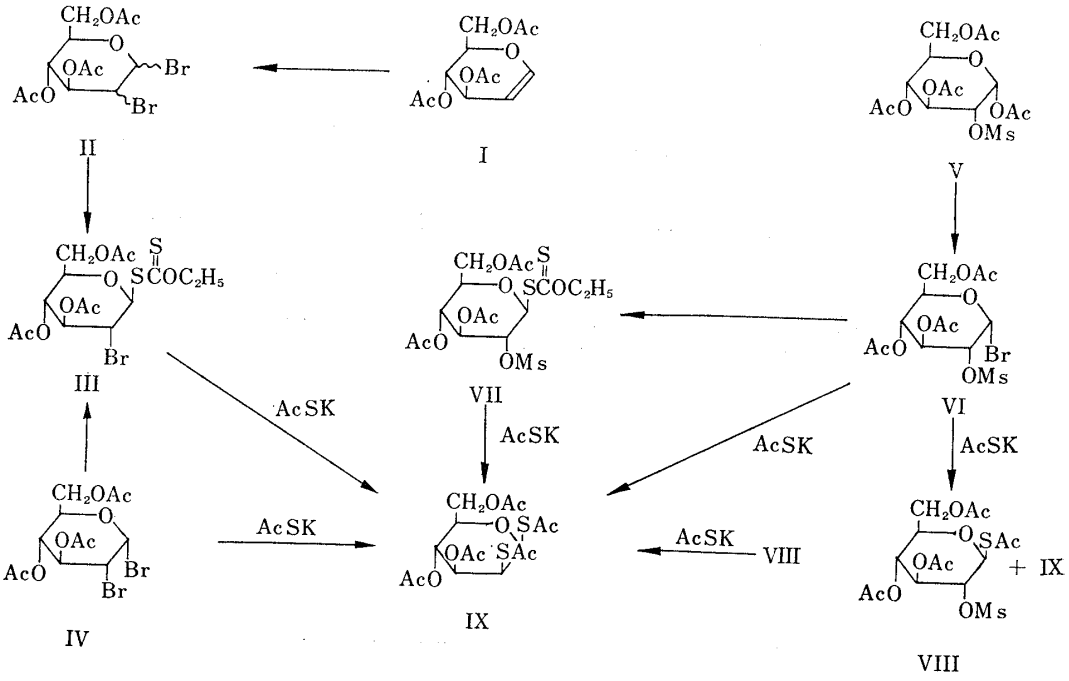
When either a mixture of III (or IV, VII, VIII) and potassium thiolacetate, or an excess potassium thiolacetate (2.5 moles) and one mole of VI was refluxed in acetone-ethanol for five minutes, only one product (IX) was obtained in 70% yield.

As mentioned in the earlier part of this paper, a secondary halogen or a sulfonyloxy group of sugars makes resistance to nucleophilic substitution by nucleophiles as potassium thiolacetate. Thus, the authors assume that the substitution, which occurred under very mild condition as mentioned above, might be one of characteristic reactions in thiosugars having a thioketone or thiocarbonyl at C1. We speculate the mechanism as chart 2.

Another unexpected substitution of carbohydrate mesyl to ethers has been reported recently by Ball, Eades and Long.[11]

Deacetylation of IX with methanolic ammonia afforded the title compound (XIII) as a slight yellow, hygroscopic sirup. The product gave a positive nitroprusside test, reduced hot Benedict's reagent, and the aqueous solution showed a mutarotation, −109.3° (10 min.) → −34° (24 hr.). Acetylation of XIII returned to IX and reaction of phenylhydrazine in acetic acid gave D-glucose phenylosazone (XIV).

10) M. Karplus : J. Chem. Phys., **30**, 11 (1959).
11) D.H. Ball, E.D. Eades, L. Long, Jr. : J. Am. Chem. Soc., **86**, 3579 (1964).



Ms=Methanesulfonyl

Chart 1.

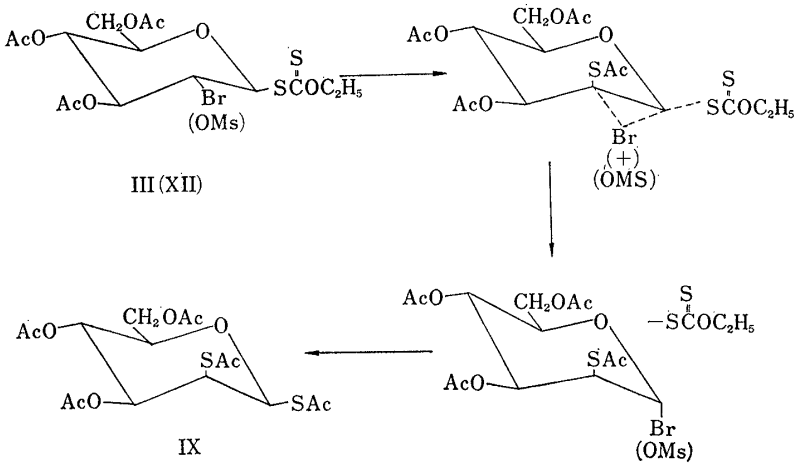


Chart 2.

Prior to the preparation of the title compound some attempts, which might be expected to yield methyl 2-deoxy-2-thio-α-D-mannopyranoside, were made starting from 2-bromo-xanthate (III) or 2-O-mesyl-xanthate (VII), *via* 1,2-dideoxy-1,2-epithio-β-D-mannopyranose (XV), and thence, by acidic hydrolysis of XV.

Contrary to our expectation, alkaline degradation of III or VII did not afford episulfide (XV) but gave amorphous powders (XVI), m.p. 108~113°, $[\alpha]_D^{23}$ +77.8°, after acetylation. The product did not show bromine test and its infrared spectrum revealed the absence of thioacetyl or mesyl group. It gave a satisfactory elementary analysis on the basis of the acetate of XV and reductive desulfurization followed by deacetylation with sodium methoxide gave D-hydroglucal (XI). While, the product showed a marked resistance against acid hydrolysis and did not afford trithiocarbonate when heated with carbon

disulfide and alkali, which is a characteristic reaction of episulfide.[12]

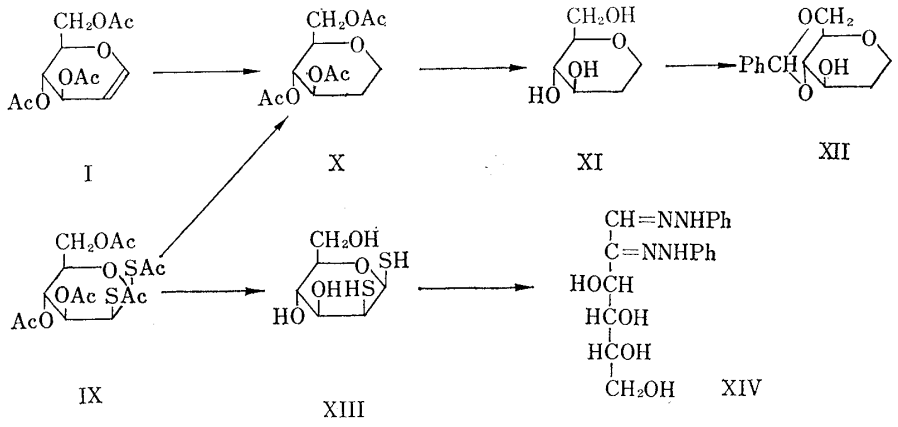


Chart 3.

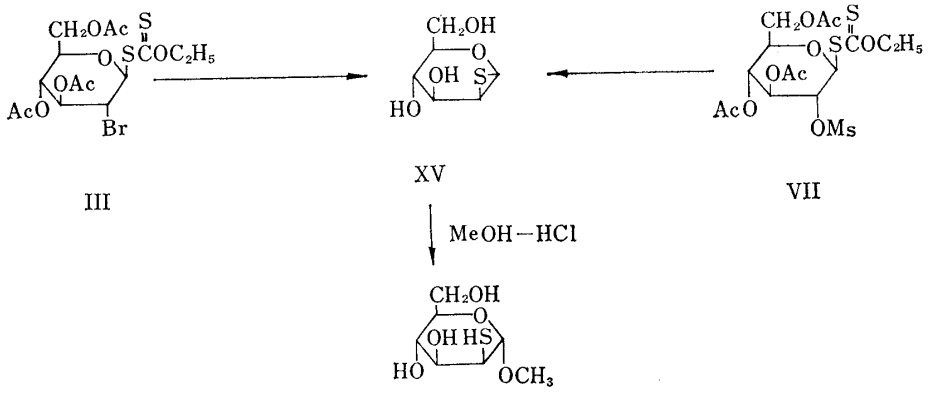


Chart 4.

From these data the authors speculated the structure of XVI as polymeric products involving various degrees of polymerization. The thin-layer chromatography showed, at least, seven spots, which supported our speculation on the mixture.

2-Bromo-2-deoxy-4,6-O-benzylidene-β-D-glucopyranosyl ethylxanthate (XVIII) and 2-O-mesyl-4,6-O-benzylidene-β-D-glucopyranosyl ethylxanthate (XX) were prepared starting from III and VII, *via* 2-bromo-2-deoxy-β-D-glucopyranosyl ethylxanthate (XVII) and 2-O-mesyl-β-D-glucopyranosyl ethylxanthate (XIX).

Similarly, alkaline degradation of XVIII or XX gave polymeric products (XXI), amorphous powders, $[\alpha]_D^{23}$ +111°, which showed only one spot by thin-layer chromatography. Acetylation of XXI gave the acetate (XXII), white powder, $[\alpha]_D^{18}$ +80°.

In 1961, Christensen and Goodman[13] reported the formation of polymeric products containing amino and mercapto groups when methyl 2,3-dideoxy-2,3-epithio-4,6-O-benzylidene-α-D-glucopyranoside had been treated with ammonia in a sealed tube. Further, Hall, Hough and Pritchard[14] reported the formation of sulfur containing polymer when 1,2-O-isopropylidene-5,6-dideoxy-5,6-epithiohexofuranoses had been treated with dilute sodium hydroxide at room temperature. From these data, if we consider the higher reactivity of an anomeric position than that of others in sugars, our consideration on the formation of polymeric products as XVI or XXI might be not so unreasonable.

12) A.M. Creighton, L.N. Owen : J. Chem. Soc., **1960**, 1024; S.M. Iqbal, L.N. Owen : *Ibid.*, **1960**, 1030.
13) J.E. Christensen, L. Goodman : J. Am. Chem. Soc., **83**, 3827 (1961).
14) L.D. Hall, L. Hough, R.A. Pritchard : J. Chem. Soc., **1961**, 1537.

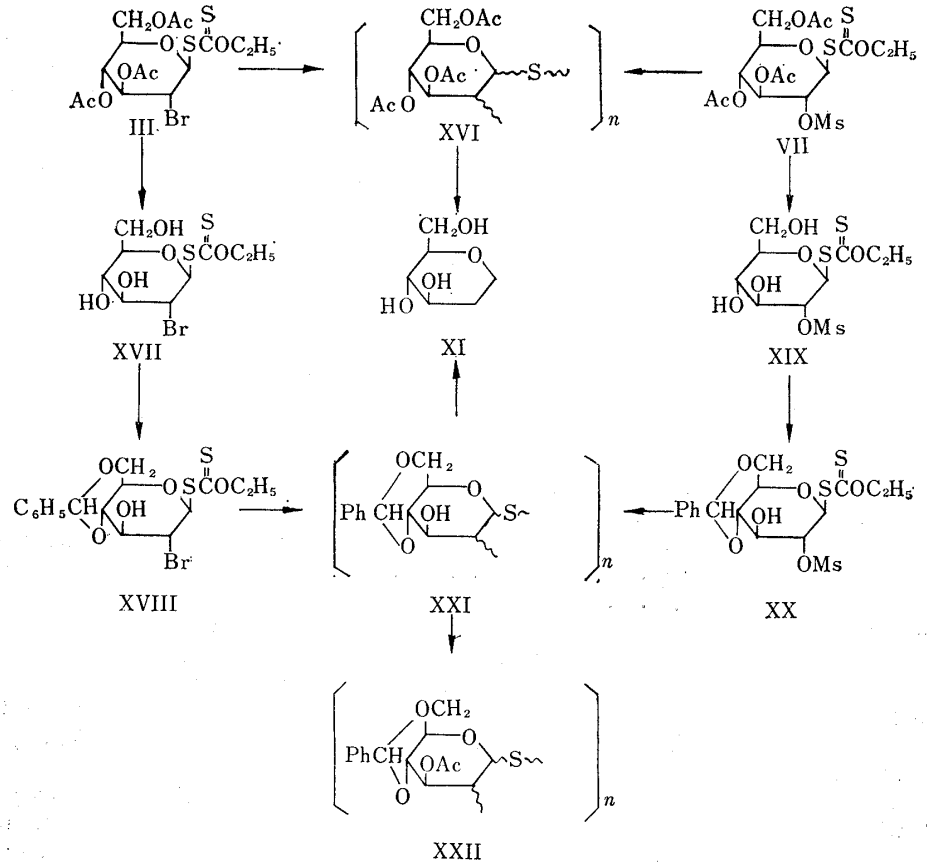


Chart 5.

Experimental

Unless stated otherwise, solvents were evaporated *in vacuo* at a bath temperature of 40° in a rotatory evaporator. Thin-layer chromatography was carried out by Wakogel B-5 using 50% H_2SO_4 as spray reagent. The NMR spectra were measured by JNM-3H-60- or JNM-4H-100-spectrometer (Japan Electron Optics Laboratory Co., Ltd.) in $CDCl_3$ at 60 or 100 Mc., respectively, with Me_4Si as internal standard. Chemical schifts were given in τ values and coupling constants (J) in c.p.s. A double resonance experiment at 60 Mc. was employed to confiirm the chemical shift of C2 proton.

2-Bromo-2-deoxy-3,4,6-tri-O-acetyl-β-D-glucopyranosyl Ethylxanthate (III)——a) From 3,4,6-Tri-O-acetyl-D-glucal (I): A solution of Br_2 (3.5 g.) in CCl_4 (15 ml.) was added gradually, under ice-cooling and stirring, to a solution of I (5 g.) in CCl_4 (15 ml.). The mixture was protected from moisture and left in a refrigerator overnight, evaporated to dryness and the residue (II) dissolved in warm abs. EtOH (80 ml.). Potassium ethylxanthate (4 g.) was added to the solution and the mixture was refluxed for 5 min. After cooling at room temperature, filtred, the filtrate was concentrated to about 50 ml. and allowed to stand in a refrigerator overnight. The resulting crystals were collected by filtration (3.1 g., 27.3%), and several recrystallizations from abs. EtOH gave a pure material, m.p. 128~129°, $[\alpha]_D^{17}$ −10.8°(c=1.20, $CHCl_3$). *Anal.* Calcd. for $C_{15}H_{20}O_8S_2Br$: C, 38.14; H, 4.27. Found: C, 38.08; H, 4.27.

b) From 2-bromo-2-deoxy-3,4,6-tri-O-acetyl-α-D-glucopyranosyl bromide (IV): The bromide (IV) was available from previous work.[6] A mixture of IV (12.3 g.) and potassium ethylxanthate (5.5 g.) in acetone (100 ml.) was refluxed for 5 min., cooled, and poured into ice water. The resulting precipitates were collected by filtration and recrystallized twice from abs. EtOH to give a pure material (11.5 g., 86%), m.p. 128~129°. The IR spectrum was identical with that of the product prepared by method a), and did not show mixed melting point depression. The anomeric proton of III showed a doublet at τ 4.45 with a coupling constant ($J_{1,2}$=11.0 c.p.s.).

2-O-Mesyl-3,4,6-tri-O-acetyl-β-D-glucopyranosyl Ethylxanthate (VII)——2-O-Mesyl-1,3,4,6-tetra-O-acetyl-α-D-glucopyranose (V) was prepared by the method of Helferich, *et al.*[8] Twice recrystallizations from abs. EtOH gave a pure material, m.p. 104.5~107.5°, $[\alpha]_D^{19}$ +95°(c=2.2, $CHCl_3$). *Anal.* Calcd. for $C_{15}H_{22}O_{12}S$: C, 42.25; H, 5.21. Found: C, 42.16; H, 5.32. Helferich, *et al.* report m.p. 80~84°, $[\alpha]_D^{21}$ +92.1°(c=2.2, $CHCl_3$), after recrystallization from ether.

A mixture of sirupy 2-O-mesyl-3,4,6-tri-O-acetyl-α-D-glucopyranosyl bromide (VI) (20 g.), prepared from V by the method of Helferich, *et al.*[8] and potassium ethylxanthate (7.5 g.) in abs. EtOH (150 ml.) was refluxad for 5 min., cooled, and poured into ice water. It was extracted with $CHCl_3$ (150 ml.×3), the $CHCl_3$-layer was washed with H_2O and dried over $CaCl_2$. The filtrate was concentrated to a light yellow sirup which was dissolved in ether (120 ml.) and left in a rafrigerator. The resulting crystals were collected by filtration and recrystallized twice from abs. EtOH to yield a pure material (16 g., 70%), m.p. 98~100°, $[\alpha]_D^{21}$ +9.52° (c=1.05, $CHCl_3$). *Anal.* Calcd. for $C_{16}H_{24}O_{11}S_3$: C, 39.35; H, 4.95. Found: C, 39.50; H, 4.98. The anomeric proton showed a doublet at τ 4.53 with a coupling constant ($J_{1,2}$=11.0 c.p.s.).

1,2-Di-*S*-acetyl-1,2-dithio-3,4,6-tri-O-actyl-β-D-mannopyranose (IX)——a) From 2-bromo-2-deoxy-3,4,6-tri-O-acetyl-β-D-glucopyranosyl ethylxanthate (III): To a solution of III (2 g.) in acetone (30 ml.) was added a hot solution of AcSK (0.8 g.) in abs. EtOH (15 ml.) and the mixture was refluxed for 10 min. After cooling, the mixture was diluted with H_2O (200 ml.), and extracted with $CHCl_3$. The $CHCl_3$-layer was washed with H_2O, dried over $CaCl_2$ and concentrated to a light yellow sirup which was dissolved in a small amount of ether. After treatment with activated carbon the solution was cooled to yield colorless crystals. Several recrystallizations from abs. EtOH gave a pure material (1.1 g., 62%), m.p. 155~156°, $[\alpha]_D^{22}$ +33.3° (c=0.60, $CHCl_3$). *Anal.* Calcd. for $C_{16}H_{22}O_9S_2$: C, 45.48; H, 5.25; S, 15.18. Found: C, 45.67; H, 5.45; S, 14.98.

b) From 2-bromo-2-deoxy-3,4,6-tri-O-acetyl-α-D-glucopyranosyl bromide (IV): A mixture of IV (1.2 g.) in dry acetone (20 ml.) and AcSK (1.2 g.) in abs. EtOH (15 ml.) was refluxed for 10 min; during the time a pale yellow solution became slight turbid. After cooling, it was poured into ice water, the resulting precipitates were collected by filtration, washed with H_2O and dried in a desiccator. The product was recrystallized from abs. EtOH to yield colorless crystals (0.9 g., 73%), m.p. 155.5~156°, $[\alpha]_D^{22}$ +30.5°(c=0.82, $CHCl_3$). *Anal.* Calcd. for $C_{16}H_{22}O_9S_2$: C, 45.48; H, 5.25. Found: C, 45.29; H, 5.08.

c) From 2-O-mesyl-3,4,6-tri-O-acetyl-α-D-glucopyranosyl bromide (VI): A mixture of VI (4.8 g.) and AcSK (1.8 g.) in acetone (70 ml.) was refluxed for 5 min.; the mixture became turbid and potassium methane sulfonate precipitated. It was poured into ice H_2O and triturated until crystallization and precipitation occurred. The supernatant light crystals were collected by decantation and recrystallized twice from EtOH to give a pure material (0.6 g.), m.p. 155~156°, $[\alpha]_D^{22}$ +32°(c=0.64, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 1710 (-SAc). The product was assigned to be IX.

The remained gummy precipitates were recrystallized three times from EtOH to give a product (2.1 g.), m.p. 135~139°, which showed two spots by thin-layer chromatography over silica gel with MeOH-benzene (3:97). The product (2 g.) was dissolved in benzene (40 ml.) and chromatographed on silica gel (150 g.). From the eluate of MeOH-benzene (3:97) (800 ml.), crystals (0.7 g.), m.p. 155~156°, were obtained after evaporation of the solvent and assigned to be IX. From the successive eluate (200 ml.), crystals (1 g.), m.p. 170~171°, $[\alpha]_D^{21}$ +16.5°(c=0.37, $CHCl_3$), IR ν_{max}^{Nujol} cm^{-1}: 1170, 1335 (-SO_2-O-), 1710 (-SAc), were obtained, followed by evaporation of the solvent and recrystallization of the residue from EtOH. The elementary analysis was in agreement with that of 1-*S*-acetyl-1-thio-2-O-mesyl-3,4,6-tri-O-acetyl-β-D-glucopyranose (VIII). *Anal.* Calcd. for $C_{15}H_{22}O_{11}S_2$: C, 40.72; H, 5.01; S, 14.49. Found: C, 40.58; H, 4.97; S, 15.00.

Only one product (IX) was obtained when excess AcSK (2.5 mole) had been reacted upon VI (1 mole); a mixture of VI (8.1 g.) in Me_2CO (100 ml.) and AcSK (5.2 g.) in abs. EtOH (70 ml.) was treated as described in b) to yield the product (6.0 g.), m.p. 155~156°, $[\alpha]_D^{22}$ +33°(c=0.65, $CHCl_3$).

d) From 2-O-mesyl-3,4,6-tri-O-acetyl-β-D-glucopyranosyl ethylxanthate (VII): A mixture of VII (1 g.) in Me_2CO (50 ml.) and AcSK (0.35 g.) in abs. EtOH (30 ml.) was treated with the similar procedure as mentioned in a), to afford crystals (0.5 g.), m.p. 155~156°. *Anal.* Calcd. for $C_{16}H_{22}O_9S_2$: C, 45.48; H, 5.25. Found: C, 45.35; H, 5.36.

e) From 1-*S*-acetyl-1-thio-2-O-mesyl-3,4,6-tri-O-acetyl-β-D-glucopyranose (VIII): A mixture of VIII (70 mg.) in Me_2CO (10 ml.) and AcSK (50 mg.) in abs. EtOH (5 ml.) was treated with the similar procedure to yield crystals (58 mg.), m.p. 155~156°.

The NMR spectrum of VIII at 60 Mc. showed a doublet at τ 4.69 (anomeric proton) with a coupling constant ($J_{1,2}$=11.0 c.p.s.), a singlet at τ 6.97 (-OMs) and a singlet at τ 7.58 (-SAc). That of IX showed singlets at τ 7.59 and 7.62 corresponding to the two -SAc. The anomeric proton of IX appeared as a doublet at τ 4.04 with a coupling constant ($J_{1,2}$=2.5 c.p.s.) which indicated an axially oriented C1 proton having a projected valence angle of 60° with a C2 proton.[10]

D-Hydroglucal (XI)——a) From 3,4,6-tri-O-acetyl-D-glucal (I): Fifteen grams of I dissolved in abs. EtOH (250 ml.) was treated with an approximately 70 g. of freshly prepared Raney Ni suspended in abs. EtOH. The mixture was refluxed gently for 6 hr. The supernatant solution was removed, the Ni washed with abs. EtOH and the combined solution and washings concentrated to a sirup which was distilled under high vacuum to give a colorless oil (12.5 g.), b.$p_{0.01}$ 115~125°, $[\alpha]_D^{19}$ +33.3°(c=1.95, EtOH), $[\alpha]_D^{19}$ +32°(c=7.78, EtOH). Fischer[7] reports $[\alpha]_D$ +35.55°(c=8.41, EtOH) for 3,4,6-tri-O-acetyl-D-hydroglucal (X).

A mixture of the sirup (12 g.) and MeONa in abs. MeOH (80 ml.) containing Na (0.5 g.) was left at room temperature overnight. The solvent was removed to a sirup which was dissolved in H_2O (50 ml.) and the solution passed through a column of Amberlite IR-120 (H^+). Concentration of the eluate afforded a colorless sirup which was turned to a hygroscopic crystalline mass after storage in a desiccator overnight. Recrystallization from abs. EtOH-petr. ether gave a hygroscopic pure material (6 g., 92%), m.p. 86~87°, $[\alpha]_D^{21}$ +21.1°(c=0.95,

H_2O). *Anal.* Calcd. for $C_6H_{12}O_4$: C, 48.65; H, 8.16. Found: C, 48.64; H, 8.12. Fischer[7] reports m.p. 86~87°, $[\alpha]_D^{19}$ +16.37°(c=10.14, H_2O) for D-hydroglucal.

b) Desulfurization of 1,2-di-*S*-acetyl-1,2-dithio-3,4,6-tri-O-acetyl-β-D-mannopyranose (IX): A mixture of IX (2.5 g.) and Raney Ni (50 g.) was refluxed for 8 hr., filtered, and removal of the solvent afforded a colorless sirup (1.5 g., 93%), $[\alpha]_D^{22}$ +33.3°(c=1.26, EtOH). A mixture of the sirup (1.3 g.) in dry MeOH (20 ml.), saturated with dry NH_3 at 0°, was allowed to stand at 0° overnight. The solvent was removed to give a colorless sirup which was dissolved in a small amount of EtOH. Crystalline mass appeared after addition of petr. ether, followed by seeding. The product was separated by filtration (0.5 g.) and recrystallized from EtOH-petr. ether to give a pure material, m.p. 86~87°, $[\alpha]_D^{22}$ +20°(c=0.90, H_2O). *Anal.* Calcd. for $C_6H_{12}O_4$: C, 48.65; H, 8.16. Found: C, 48.59; H, 8.20.

4,6-O-Benzylidene-D-hydroglucal (XII)——A mixture of anhyd. $ZnCl_2$ (2 g.), XI (2.5 g.) and PhCHO (6 ml.) was stirred for 40 hr. at room temperature. The mixture was diluted with a small amount of H_2O, followed by addition of a large amount of petr. ether. Crystallization was induced spontaneously, filtered, and washed with H_2O, finally with petr. ether. Recrystallization from AcOEt-petr. ether gave a pure material (0.9 g., 23%), m.p. 104°, $[\alpha]_D^{21}$ −43.4°(c=0.88, EtOH). *Anal.* Calcd. for $C_{13}H_{16}O_4$: C, 66.09; H, 6.38. Found: C, 66.04; H, 6.80.

1,2-Dithio-β-D-mannopyranose (XIII)——A mixture of acetate (IX) (0.3 g.) in dry MeOH (10 ml.), saturated with dry NH_3 at 0°, was allowed to stand for 8 hr. in a refrigerator. The solvent was removed to give a slight yellow, hygroscopic residue. It was triturated with abs. EtOH until crystallization occurred, filtered, and washed with ether. The product was dissolved in a small amount of H_2O and treated with active carbon. On removal of H_2O, a hygroscopic sirup (XIII) was obtained, which gave a positive nitroprusside test and reduced hot Benedict's reagent. The aqueous solution (c=0.32) showed mutarotation as follows: $[\alpha]_D^{22}$ −109.3°(10 min.), −87.5°(30 min.), −53.1°(2 hr.), −34°(24 hr.).

The sirup (0.1 g.) was added to an ice cold mixture of Ac_2O (0.5 ml.) and pyridine (0.5 ml.). After 24 hr., it was poured into ice water, and the resulting precipitates were collected by filtration. Recrystallization from EtOH gave a pure material (0.12 g., 60%), m.p. 155~156°, which showed no depression of the melting point on admixture with IX.

A mixture of XIII (0.12 g.), $PhNHNH_2 \cdot HCl$ (0.3 g.) and $AcONa \cdot 3H_2O$ (0.45 g.) in H_2O (4 ml.) was heated on a steam-bath for 1.5 hr. The resulting yellow crystalline mass was collected by filtration and washed with H_2O. Recrystallization from EtOH gave yellow crystals (XIV) (0.1 g.), m.p. 208~210°, which were identical with that of authentic D-glucose phenylosazone.

Alkaline Degradation of 2-Bromo-2-deoxy-3,4,6-tri-O-acetyl-β-D-glucopyranosyl Ethylxanthate (III)——A solution of III (1.48 g.) in $CHCl_3$ (5 ml.) was treated, under stirring and cooling at 0°, with a cold methanolic solution (40 ml.) of MeONa containing Na (0.3 g.); it was turbid as the reaction took place. After 10 min., the mixture was concentrated to give a pale yellow crystalline mass. A mixture of Ac_2O (15 ml.) and pyridine (15 ml.) was added gradually under ice cooling and stirring, the mixture left at room temperature overnight, then poured into H_2O (300 ml.). The resulting precipitates were collected by filtration, washed with H_2O and air-dried (0.9 g.). Several recrystallizations from abs. EtOH gave an amorphous powder (XVI), m.p. 108~113°, $[\alpha]_D^{23}$ +77.8°(c=0.54, $CHCl_3$). *Anal.* Calcd. for $(C_{12}H_{16}O_7S)_n$: C, 47.37; H, 5.26; S, 10.53. Found: C, 47.17; H, 5.26; S, 10.25.

The product gave negative thiol nor Br test and did not reduce hot Benedict's reagent. The IR spectrum in Nujol did not show any absorption at about 1700 cm^{-1} (-SAc). Thin-layer chromatography by double developing method over silica gel with MeOH-benzene (3:97 or 5:95) gave more than 7 spots.

A mixture of XVI (0.55 g.), CS_2 (4.5 ml.) and KOH (2.0 g.) in MeOH (18 ml.) was refluxed for 4.5 hr. in a steam-bath. The residue, obtained after evaporation of the solvent, was acetylated with Ac_2O (15 ml.) and pyridine (15 ml.) for 24 hr. The separated material (0.4 g.) was the starting material (XVI).

A mixture of XVI (0.5 g.) in 1% methanolic HCl (10 ml.) was refluxed for 11 hr. The residue, obtained after evaporation of the solvent, was acetylated as described above. The separated material (0.5 g.) was the starting material. Boiling of XVI (0.35 g.) in 7% methanolic HCl for 2.5 hr., during the time H_2S evolved, still recovered the starting material (0.15 g.) after evaporation of the solvent and acetylation of the residue.

Alkaline Degradation of 2-O-Mesyl-3,4,6-tri-O-acetyl-β-D-glucopyranosyl Ethylxanthate (VII)——Treatment of VII (14.7 g.) with the similar procedure described in the degradation of III afforded an amorphous material (8.2 g.), m.p. 109~113.5°, $[\alpha]_D^{23}$ +78.9°(c=0.57, $CHCl_3$). The physical constants were almost similar to that of XVI. The IR spectrum in Nujol did not show any absorption at 1175 and 1330 cm^{-1} (-O-SO_2-). *Anal.* Calcd. for $(C_{12}H_{16}O_7S)_n$: C, 47.37; H, 5.26; S, 10.53. Found: C, 47.47; H, 5.31; S, 10.65.

Determination of Acetyl Contents in XVI——A mixture of XVI (80 mg.) in 0.1*N* EtOH-KOH (20 ml.) was stirred for 10 min., added H_2O (20 ml.), then left for 18 hr. at room temperature. Excess KOH was back-titrated with 0.1*N* HCl, using phenolphthaleine as an indicator. *Anal.* Calcd. for $(C_6H_7O_4Ac_3S)_n$: CH_3CO, 42.43. Found: CH_3CO, 43.14.

Reductive Desulfurization of XVI——A solution of XVI (3 g.) in abs. EtOH (150 ml.) was treated with Raney Ni (45 g.) by the similar procedure described in XI a) to give a colorless oil (1.7 g., 63%), $[\alpha]_D^{22}$ +33° (c=2.15, EtOH). The sirup was deacetylated with methanolic MeONa (30 ml.) having Na (50 mg.), as mentioned in XI a), to yield crystals (0.24 g.), m.p. 85~87°, which showed no depression of the melting point on

admixture with XI.

2-Bromo-2-deoxy-β-D-glucopyranosyl Ethylxanthate (XVII)——To a solution of acetate (III) (1.2 g.) in dry MeOH (10 ml.) was added methanolic solution of HCl (5 ml.), saturated with dry HCl at 0°, and left for 15 hr. in a refrigerator. The mixture was concentrated to a light yellow sirup. The distillation was repeated several times by addtion of dry benzene to remove the solvent completely. The residual sirup was dissolved in a small amount of AcOEt, then a large amount of benzene was added to near turbidity to precipitate colorless crystals. Recrystallization from AcOEt-benzene gave a pure material (0.9 g., 95%), m.p. 131~132°, $[\alpha]_D^{19}$ −92°(c=1.20, EtOH). *Anal.* Calcd. for $C_9H_{15}O_5S_2Br$: C, 31.13; H, 4.48. Found: C, 31.28; H, 4.43.

2-Bromo-2-deoxy-4,6-O-benzylidene-β-D-glucopyranosyl Ethylxanthate (XVIII)——A mixture of XVII (1.2 g.), anhyd. $ZnCl_2$ (1 g.) and freshly distilled PhCHO (4 ml.) was stirred vigorously for 25 min. At the end of the time, the mixture turned to a hard mass. Treatment of it with the similar procedure as in XII afforded white needles. Recrystallization from abs. EtOH gave a pure material (1.4 g., 95%), m.p. 164~165°, $[\alpha]_D^{19}$ −20°(c=0.5, $CHCl_3$). *Anal.* Calcd. for $C_{16}H_{19}O_5S_2Br$: C, 44.14; H, 4.40; S, 14.73. Found: C, 43.77; H, 4.41; S, 14.57.

2-O-Mesyl-β-D-glucopyranosyl Ethylxanthate (XIX)——Deacetylation of acetate (VII) (3.7 g.) was performed by the method mentioned in XVII. Recrystallization from AcOEt-benzene gave a pure material (2.4 g., 87%), m.p. 127~128°, $[\alpha]_D^{21}$ −24.3° (c=1.15, EtOH). *Anal.* Calcd. for $C_{10}H_{18}O_8S_3$: C, 33.14; H, 5.01. Found: C, 33.18; H, 5.14.

2-O-Mesyl-4,6-O-benzylidene-β-D-glucopyranosyl Ethylxanthate (XX)——Treatment of XIX (0.2 g.), anhyd. $ZnCl_2$ (0.15 g.) and PhCHO (0.5 ml.) with the procedure, mentioned in XVIII, yielded a white crystalline mass. Several recrystallizations from EtOH-petr. ether gave a pure material (0.23 g., 95%) having a constant m.p. 95.5~96.5°(decomp.), $[\alpha]_D^{21}$ +35.6°(c=0.90, $CHCl_3$). *Anal.* Calcd. for $C_{17}H_{22}O_8S_3$: C, 45.32; H, 4.92. Found: C, 45.23; H, 5.05.

Alkaline Degradation of 2-Bromo-2-deoxy-4,6-O-benzylidene-β-D-glucopyranosyl Ethylxanthate (XVIII)——A solution of XVIII (1 g.) in $CHCl_3$ (8 ml.) was treated, under stirring and cooling, with a cold methanolic solution (20 ml.) of MeONa containing Na (0.16 g.). After 5 min. the mixture was concentrated to dryness, H_2O (20 ml.) was added and insoluble part collected by filtration. Twice recrystallizations from $CHCl_3$-petr. ether gave amorphous powders (XXI) (0.7 g.), $[\alpha]_D^{23}$ +111°(c=0.53, $CHCl_3$), giving negative thiol nor Br test. The product began to decompose gradually at about 210° and did not show sharp melting point. Thin-layer chromatography over silica gel employing AcOEt-iso-PrOH-H_2O (18:1:1) as developer, afforded one single spot. An attempt to determine mol. wt. by Barger's method[15] using azobenzene as a standard showed over 5330. *Anal.* Calcd. for $(C_{13}H_{14}O_4S)_n$: C, 58.63; H, 5.30; S, 12.04. Found: C, 58.53; H, 5.37; S, 11.75.

The product (0.5 g.) was added to an ice-cold mixture of Ac_2O (5 ml.) and pyridine (5 ml.). After 24 hr., it was poured into ice water and the resulting solid materials were collected by filtration (0.5 g.). Recrystallization from AcOEt-petr. ether gave white powders (XXII), $[\alpha]_D^{18}$ +80°(c=0.88, $CHCl_3$), decompose gradually at about 200°. *Anal.* Calcd. for $(C_{15}H_{17}O_5S)_n$: C, 58.56; H, 5.24; S, 10.42. Found: C, 58.24; H, 5.40; S, 10.23.

Alkaline Degradation of 2-O-Mesyl-4,6-O-benzylidene-β-D-glucopyranosyl Ethylxanthate (XX)——Treatment of XX (1 g.) with the method, described in the degradation of XVIII, afforded amorphous powders (XXI) (0.7 g.), $[\alpha]_D^{18}$ +106° (c=0.52, $CHCl_3$). *Anal.* Calcd. for $(C_{13}H_{14}O_4S)_n$: C, 58.63; H, 5.30; S, 12.04. Found: C, 58.67; H, 5.31; S, 11.80.

The IR spectrum did not show any absorption at 1175 and 1330 cm^{-1} (-O-SO_2-). Acetylation of the product (0.5 g.) with Ac_2O (94 ml.) and pyridine (4 ml.) as described above gave white powders (XXII) (0.5 g.), $[\alpha]_D^{17}$ +77.7°(c=0.88, $CHCl_3$). *Anal.* Calcd. for $(C_{15}H_{17}O_5S)_n$: C, 58.56; H, 5.24; S, 10.42. Found: C, 58.35; H, 5.36; S, 10.22.

Reductive Desulfurization of XXI——A solution of XXI (8 g.) in dioxane-EtOH (5:1) (150 ml.) was treated with Raney Ni (75 g.) and refluxed for 7 hr. Thin-layer chromatography using AcOEt-iso-PrOH-H_2O (18:1:1) gave a main spot (D-hydroglucal) and three minor spots.

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Summary

1,2-Di-*S*-acetyl-1,2-dithio-3,4,6-tri-O-acetyl-β-D-mannopyranose (IX) was obtained when a mixture of potassium thiolacetate and one of the 2-bromo-2-deoxy-3,4,6-tri-

15) S. Akiya: Yakugaku Zasshi, **57**, 967 (1937).

O-acetyl-β-D-glucopyranosyl ethylxanthate (Ⅲ), 2-bromo-2-deoxy-3,4,6-tri-O-acetyl-α-D-glucopyranosyl bromide (Ⅳ), 2-O-mesyl-3,4,6-tri-O-acetyl-β-D-glucopyranosyl ethylxanthate (Ⅶ) or 1-*S*-acetyl-1-thio-2-O-mesyl-3,4,6-tri-O-acetyl-β-D-glucopyranose (Ⅷ) in acetone-ethanol was refluxed for five minutes. The title compound, hygroscopic sirup, $[\alpha]_D^{22}$ −109.3° →−34° (H_2O), was prepared by deacetylation of Ⅸ.

Alkaline degradation of Ⅲ or Ⅶ did not afford 1,2-dideoxy-1,2-epithio-β-D-mannopyranose, but gave amorphous powders (XⅥ), m.p. 108~113°, $[\alpha]_D^{23}$ +77.8° ($CHCl_3$) after acetylation of the degradation product. Similarly, 4,6-O-benzylidene compound of Ⅲ or Ⅶ (XⅧ or XX) afforded amorphous powders (XXⅠ), $[\alpha]_D^{23}$ +111° ($CHCl_3$). The structures of XⅥ and XXⅠ were discussed and considered as polymeric products.

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