Chem. Pharm. Bull. 16(8)1567—1572(1968)

UDC 547.458.07

Thiosugars. XIII.[1] An Attempt at Thiosugar Synthesis having a Vicinal *cis*-Dimercapto Group in the Pyranose Ring

Susumu Ishiguro and Setsuzo Tejima

Faculty of Pharmaceutical Sciences, Hokkaido University[2]

(Received November 9, 1967)

Methyl 2,3-dideoxy-2,3-dimercapto-α-D-mannopyranoside, isolated as sirupy tetraacetate (XIII), was synthesized in 13% yield by reduction of methyl 2,3-dithio-4,6-O-benzylidene-α-D-mannopyranoside 2,3-S-carbonate (IX) with sodium in liquid ammonia. The product was also obtainable in the same yield by alkaline treatment of methyl 2,3-dithio-4,6-di-O-acetyl-α-D-mannopyranoside 2,3-S-carbonate (XII).

Dithiocarbonate (IX), a key intermediate of the synthesis was obtained by the following route: epoxide opening in methyl 2,3-anhydro-4,6-O-benzylidene-α-D-allopyranoside (II) with sodium N,N-dimethyldithiocarbamate (I) to give methyl 2-deoxy-2(N,N-dimethyl dithiocarbamoyl)-4,6-O-benzylidene-α-D-altropyranoside (III), sulfonation of III, and successive intramolecular ring formation in the pyranose ring involving *trans*-diaxial elimination by treatment of the sulfonate (VII or VIII) with potassium acetate.

Recently much interest has been shown in the syntheses of sugars or nucleosides having a vicinal *cis*-diamino[3] or *cis*-amino-mercapto group[4] in the pyranose or furanose ring. Concerning sugars having a *cis*-dimercapto group which might be interest as potential antiarsenicals[5] or antitumor agents,[6] the literature contains only a few reports. Thus, the synthesis of 1,2-dithio-β-D-mannopyranose which has been reported from our laboratory[7] might presumably be the first example of the compound having the title group. Incidentally Adley and Owen[8] have reported the synthesis of 1,2-O-isopropylidene-5,6-dideoxy-5,6-dimercapto-β-L-idofuranose which contains a vicinal dimercapto group out of the furanose ring.

In the course of progressive studies on thiosugars syntheses we projected the synthesis of the compound having the title group at C_2 and C_3 of methyl α-D-mannopyranoside, and succeeded in obtaining the compound. Although the yield, in the present stage, is not so satisfactory, some new intermediates, which might have utility for further studies on thiosugars, have been prepared in the route. The present paper describes full detail of this work.

In 1961, methyl 2-deoxy-2-thio-α-D-altropyranoside and corresponding 3-thio derivative were successfully synthesized by reduction of 2- or 3-thiobenzyl derivative with sodium in liquid ammonia, which is a facile synthetic route of thiosugars having a secondary mercapto group in the pyranose ring.[9] In the same year, Christensen and Goodman[10] also reported the synthesis of the former with a similar way. On the one hand, previous papers from our laboratory[1,11] have shown the syntheses and activities on glycosyl dithiocarbamates having

1) Part XII: S. Ishiguro and S. Tejima, *Chem. Pharm. Bull.* (Tokyo), **15**, 1478 (1967).
2) Location: *Kita-15-jo, Nishi-7-chome, Sapporo.*
3) B.R. Baker and T.L. Hullar, *J. Org. Chem.*, **30**, 4038, 4045, 4049, 4053 (1965); R.D. Guthrie and D. Murphy, *J. Chem. Soc.*, **1965**, 6956; Y. Ali and A.C. Richardson, *Chem. Commun.*, **1967**, 554.
4) T. Sekiya and T. Ukita, *Chem. Pharm. Bull.* (Tokyo), **15**, 542 (1967).
5) A.K.M. Anisuzzaman and L.N. Owen, *J. Chem. Soc.*, **1967**, 1021.
6) M. Akagi, S. Tejima, M. Haga, Y. Hirokawa, M. Yamada, M. Ishiguro, and D. Mizuno, *Yakugaku Zasshi*, **87**, 287 (1967).
7) H. Nakamura, S. Tejima, and M. Akagi, *Chem. Pharm. Bull.* (Tokyo), **14**, 648 (1966).
8) T.J. Adley and L.N. Owen, *J. Chem. Soc.*, **1966**, 1287.
9) N.C. Jamieson and R.K. Brown, *Can. J. Chem.*, **39**, 1765 (1961).
10) J.E. Christensen and L. Goodman, *J. Am. Chem. Soc.*, **83**, 3827 (1961).
11) S. Tejima and S. Ishiguro, *Chem. Pharm. Bull.* (Tokyo), **15**, 255 (1967).

NII-Electronic Library Service

N,N-dialkyldithiocarbamoyl radical in the place of the anomeric or the primary hydroxyl in sugars and pointed out that alkaline treatment of the carbamates gave thiosugars. As we have learned that the carbamates are easily crystallizable compounds having potential activities, in the earlier stage of this paper, we investigated the synthesis of glycosyl dithiocarbamate having the carbamoyl radical in the pyranose ring.

Reflux of two molar equivalents of sodium N,N-dimethyldithiocarbamate (I) with one molar of methyl 2,3-anhydro-4,6-O-benzylidene-α-D-allopyranoside (II) in acetone for twenty minutes afforded methyl 2-deoxy-2-N,N-dimethyldithiocarbamoyl-4,6-O-benzylidene-α-D-altropyranoside (III) in 78% yield. It is noteworthy to describe that the opening of the epoxide completes in such a short time. Substitution of the solvent from acetone to methanol required a longer reaction time (4 hours) with a lower yield (48%).

An ethanolic solution of III showed the ultraviolet (UV) absorptions at 245 and 277 mμ which appear to be characteristic of dithiocarbamates.[11] The infrared (IR) spectrum of III in nujol suggested the presence of dithiocarbamoyl along with hydroxyl.

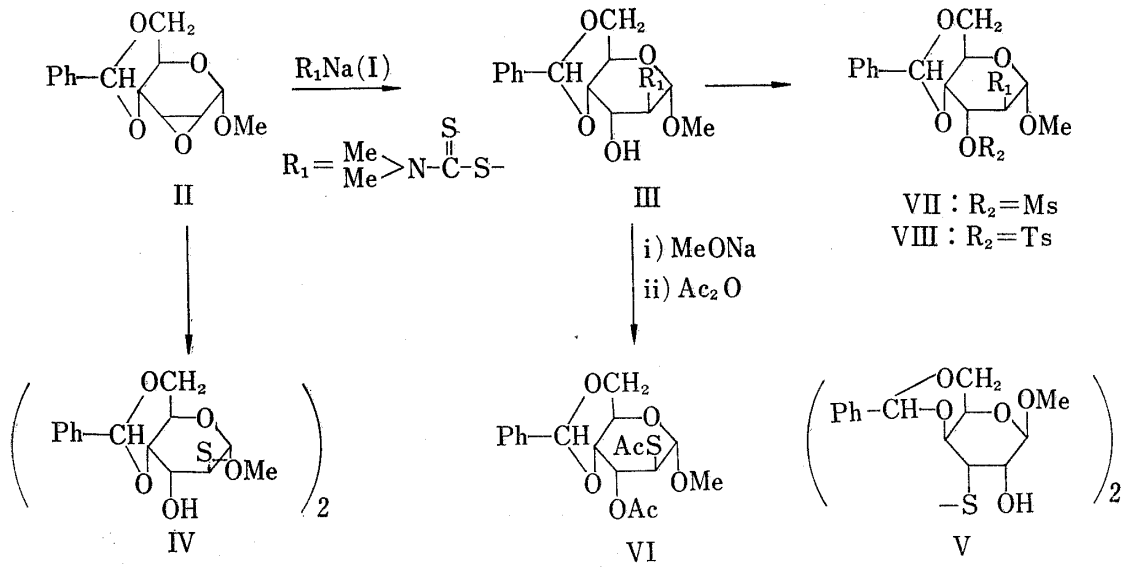

Chart 1

It has been well known as the Frust-Plattner rule that when pyranose epoxide is opened by the attack of nucleophilic reagents, it opens to give mainly the products with *trans* diaxial substitutions with minor amounts of the *trans* diequatorial products.[12] Thus, by analogy with the ring opening rule, the configuration of III was tentatively assigned to be D-altrose type.

Further proof of the structure was presented by determination of the nuclear magnetic resonance (NMR) spectra of III and two reference compounds. Namely, the signal of the anomeric proton of III or that of methyl 2-deoxy-2-thiobenzyl-4,6-O-benzylidene-α-D-altropyranoside was observed as a sharp singlet at τ 5.12 or τ 5.38, respectively, while that of methyl 2,3-di-O-tosyl-4,6-O-benzylidene-α-D-glucopyranoside appeared as a doublet ($J_{1,2}$=3.5 cps) at τ 5.47.

In the foregoing synthetic route of III, when equimolars of I and II were refluxed in methanol for four hours, another crystals, mp 222—226°, $[\alpha]_D^{20}$ +57.7°, were separated in 59% yield contaminating with a lower yield (10%) of III. The product was assigned to be bis (methyl 2-deoxy-4,6-O-benzylidene-α-D-altropyranoside)-2,2'-sulfide (IV) by the fact mentioned below. The elementary analyses were in agreement with that of $C_{28}H_{34}O_{10}S$; the

12) R.D. Guthrie and J. Honeyman, "An Introduction to the Chemistry of Carbohydrates," Clarendon Press, Oxford, 1964, p. 69.

NII-Electronic Library Service

ethanolic solution showed negative UV absorption in the range of 250 to 270 mμ, instead the presence of hydroxyl and phenyl was suggested by IR spectrum in nujol; reductive desulfurization with Raney nickel gave a similar sirupy product which was obtainable from III by the same procedure; the product (IV) was also obtainable by treatment with a mixture of II and III under the presence of sodium methoxide.

The mechanisms of the formation of (IV) have not yet been elucidated completely, it is of interest to note that the carbamoyl group in sugars so easily decomposed to give diglycosyl sulfides.

According to the literature, the stereoisomer of IV, bis(methyl 3-deoxy-4,6-O-benzylidene-β-D-gulopyranoside)-3,3'-sulfide (V), has been reported by Dahlgard.[13] Further, Horton and Turner[14] have reported the formation of an unidentified side product, mp 222—224°, when a mixture of methyl 2,3-anhydro-4,6-O-benzylidene-α-D-allopyranoside and potassium ethylxanthate was refluxed in butanol, which might presumably be identical with IV.

Treatment of III with excess sodium methoxide in methanol gave methyl 4,6-O-benzylidene-2-deoxy-2-mercapto-α-D-altropyranoside which was isolated as its acetate (VI). It was homogeneous by thin-layer chromatography (TLC) and gave an NMR spectrum in agreement with the assigned structure.

Sulfonation of III with mesyl or tosyl chloride in pyridine afforded crystalline methyl 2-deoxy-2-(N,N-dimethyldithiocarbamoyl)-3-O-mesyl-4,6-O-benzylidene-α-D-altropyranoside (VII) or corresponding 3-O-tosylate (VIII), respectively.

Reflux of VII with an excess potassium acetate in ethanol-acetone, which, on treatment with silica gel chromatography, afforded crystals, mp 177—179°, $[\alpha]_D^{20}$ −119°, in 33% yield. The product was also obtainable from VIII with a similar procedure and assigned to be methyl 2,3-dithio-4,6-O-benzylidene-α-D-mannopyranoside 2,3-S-carbonate (IX). The structure was characterized by the satisfactory elementary analyses, the IR or NMR spectrum in agreement with the assigned structure, and negative UV absorption near 270 mμ. Details of the data have been recorded in the experimental section.

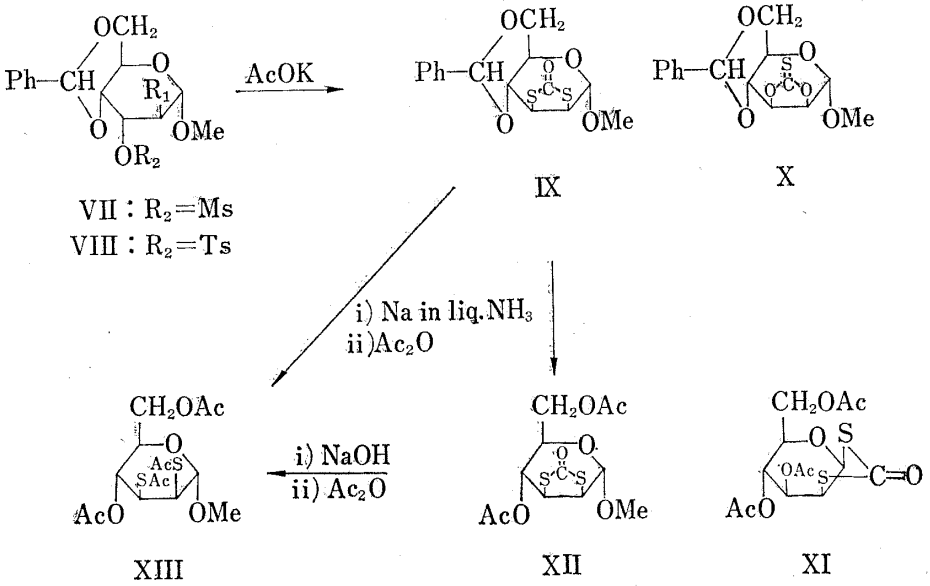

Chart 2

Recently, Horton, *et al.*[15] have reported the synthesis of methyl 4,6-O-benzylidene-α-D-mannopyranoside 2,3-thionocarbonate (X), in which they described that the signal of the anomeric proton was observed as a singlet ($J_{1,2}=0$) at τ 4.97. In IX, the anomeric proton

13) M. Dahlgard, *J. Org. Chem.*, **30**, 4352 (1965).
14) D. Horton and W.N. Turner, *Tetrahedron Letters*, **1964**, 2531.

NII-Electronic Library Service

signal was observed as a singlet at τ 5.05. When we consider the structural analogy between IX and X these data might be quite reasonable result.

In the formation of IX the carbamoyl group at C_2 in VII or VIII undergoes ring closure to form five-membered ring. The facility of the reaction is believed due to the *trans*-diaxial disposition of the attacking and departing groups. The fact is in an analogy with the experiment, previously reported from our laboratory,[16] on the formation of 1,2-dithio-3,4,6-tri-O-acetyl-β-D-mannopyranose 1,2-S-carbonate (XI) from glucosyl xanthate having mesyloxy group at C_2. In the case of XI, the ring formation might proceeds *via trans*-diaxial form in the transition state.

It is remarkable to notice that, in spite of the both compounds (IX and X) belong to the α-D-configuration, they show large levorotatory values which look like out of the isorotation rule.

Acetolysis of IX with acetic anhydride-acetic acid containig hydrogen bromide gave crystals, mp 130—131°, $[\alpha]_D^{20}$ −5.7°, in 55% yield. The structure was assigned to be methyl 2,3-dithio-4,6-di-O-acetyl-α-D-mannopyranoside 2,3-S-carbonate (XII). The NMR spectrum was in agreement with the assigned structure.

Reduction of IX with sodium in liquid ammonia using the procedure which has been reported by Jamieson and Brown[9] on the preparation of methyl 2-deoxy-2-thio-α-D-altropyranoside gave methyl 2,3-dideoxy-2,3-dimercapto-α-D-mannopyranoside, and isolated as its tetraacetate (XIII). The product, $[\alpha]_D^{20}$ +55.6°, was homogeneous by TLC and gave NMR spectrum in agreement with the assigned structure.

Treatment of an ethanolic solution of XII with sodium hydroxide solution, which, on treatment with ion-exchanger and on acetylation of the evaporated effluent, also afforded XIII in 13% yield along with a similar amount of unidentified side product.

The low yield (13%) of XIII might have to be attributed to oxidation or polymerization which occurs through the procedure.

Experimental

Unless otherwise stated, solvents were evaporated *in vacuo* at a bath temperature of 40° in a rotatory evaporator. IR spectra were taken in Nujol mulls, and NMR spectra were measured by H-6013 (Hitachi Ltd., Tokyo) in $CDCl_3$ at 60 Mc using TMS as the internal standard. Chemical shifts were given in τ values and coupling constants (J) cps. TLC was performed on Silica Gel G (E. Merck, Darmstadt, Germany) with UV lamp or 50% H_2SO_4 as the indicator, and benzene—ether (8:2 or 7:3, v/v) as the developer. Sodium N,N-dimethyldithiocarbamate (I) was prepared by the method of Kulka.[17]

Methyl 2-Deoxy-2-(N,N-dimethyldithiocarbamoyl)-4,6-O-benzylidene-α-D-altropyranoside (III)——A mixture of I (4.4 g, 2 equiv.) and methyl 2,3-anhydro-4,6-O-benzylidene-α-D-allopyranoside (II)[18] (4 g, 1 equiv.) in dry acetone (60 ml) was refluxed for 20 min, cooled, and evaporated to give a sirupy residue. It was dissolved completely in $CHCl_3$ (40 ml), followed by addition of H_2O (200 ml). The H_2O-layer was extracted with $CHCl_3$ (2×40 ml), the combined organic phases were washed twice with aq. $NaHCO_3$ (200 ml), dried over Na_2SO_4, and then evaporated to give a sirup which crystallized on trituration with a small amount of ether. Crystals (4.5 g, 78%) were collected by filtration and recrystallized from ether to give pure material, mp 132—133°, $[\alpha]_D^{20}$ +7.2° (c=1.8, $CHCl_3$), UV λ_{max}^{EtOH} mμ (ε): 245 (7600), 277 (8500); IR λ_{max}^{Nujol} cm^{-1}: 3500 (OH), 1500 (dithiocarbamoyl,[11] 760, 700 (phenyl); NMR: τ 4.38 (1H, singlet, C_6H_5-C<u>H</u>), 5.12 (1H, singlet, anomeric H), 6.50 (9H, multiplet, O<u>CH</u>$_3$+N(<u>CH</u>$_3$)$_2$). *Anal.* Calcd. for $C_{17}H_{23}O_5NS_2$: C, 52.97; H, 6.01; N, 3.68; S, 16.64. Found: C, 53.13; H, 6.06; N, 3.39; S, 16.63.

The product (2.8 g, 48%) was also prepared by reflux of a mixture of I (4.4 g, 2 equiv.) and II (4 g, 1 equiv.) in MeOH (60 ml) for 4 hr. Recrystallization of the crude product from EtOH gave crystals contaminating with 3—4% of the starting material (II), but allowed to use to the next steps.

15) E. Albano, D. Horton, and T. Tsuchiya, *Carbohydrate Res.*, 2, 349 (1966).
16) K. Araki and S. Tejima, *Chem. Pharm. Bull.* (Tokyo), **14**, 1303 (1966).
17) M. Kulka, *Can. J. Chem.*, **34**, 1093 (1956).
18) L.F. Wiggins, "Methods in Carbohydrate Chemistry," Vol. II, Academic Press Inc., New York and London, 1964, p. 189.

NII-Electronic Library Service

NMR Data of Methyl 2-Deoxy-2-thiobenzyl-4,6-O-benzylidene-α-D-altropyranoside——The material was prepared by the method of Jamieson and Brown[9]; mp 134—135°, $[\alpha]_D^{26}$ +98.3° (c=0.9, $CHCl_3$); NMR data: τ 2.50—2.75 (5H, multiplet, $C_6\underline{H}_5$), 4.38 (1H, singlet, C_6H_5–C$\underline{H}$), 5.38 (1H, singlet, anomeric H), 6.14 (2H, singlet, C_6H_5–C$\underline{H}_2$), 6.64 (3H, singlet, C$\underline{H}_3$).

NMR Data of Methyl 2,3-Di-O-tosyl-4,6-O-benzylidene-α-D-glucopyranoside——The material was prepared by the method of Richtmyer and Hudson[19]; mp 148—149°, $[\alpha]_D^{20}$ +13° (c=1.5, $CHCl_3$); NMR data: τ 2.1—3.1 (13H, multiplet, $C_6\underline{H}_5$+2$C_6\underline{H}_4$), 4.69 (1H, singlet, C_6H_5–C$\underline{H}$), 5.47 (1H, doublet, $J_{1,2}$=3.5 cps), anomeric H), 6.56 (3H, singlet, C$\underline{H}_3$), 7.51—7.70 (6H, doublet, C$\underline{H}_3$–C_6H_4).

Bis(Methyl 2-Deoxy-4,6-O-benzylidene-α-D-altropyranoside)-2,2′-sulfide (IV)——(a) A mixture of I (2 g, 0.92 equiv.) and II (4 g, 1 equiv.) in MeOH (40 ml) was heated under reflux for 4 hr, cooled and stored in a refrigerator for 2 hr to precipitate unreacted II, which removed by filtration (0.24 g, 6%). The solvent was evaporated to dryness and the residue was treated with a similar way as described in the preparation of III. The crude crystals (3.5 g) were treated with ether, and the ether–insoluble parts (2.5 g, 59%) were recrystallized from EtOH to give pure product (IV), mp 222—226°, $[\alpha]_D^{20}$ +57.7° (c=0.78, $CHCl_3$), IR λ_{max}^{Nujol} cm^{-1}: 3500 (OH), 760, 700 (phenyl); negative UV absorption in the range of 250 to 270 mμ. *Anal.* Calcd. for $C_{28}H_{34}O_{10}S$: C, 59.77; H, 6.09; S, 5.70. Found: C, 60.02; H, 6.31; S, 5.76.

From the etherial solution, from which crude IV had been separated, crystals (0.58 g, 10%) precipitated after standing in room temperature. The product was indistinguishable with III by IR and mixed mp.

(b) A mixture of II (0.09 g, 1 equiv.) and III (0.13 g, 1 equiv.) in dry MeOH (5 ml) containing Na (0.01 g, 1.26 equiv.) was refluxed for 5.5 hr, cooled and left in a refrigerator to precipitate unreacted II, which removed by filtration (0.06 g). The filtrate was treated with a similar way as described in (a) to afford III (0.06 g) and IV (0.05 g, 40%).

Desulfurization of III or IV——A mixture of approximately 20 g of activated Raney Ni and III or IV (1 g), respectively, in EtOH (50 ml) was refluxed for 8 hr. After cooling, the mixture was filtered through Celite and evaporated to give a pale green sirup (0.5 g) which showed neither absorption of phenyl nor dithiocarbamoyl by IR, nor sulfur test. The ethanolic solution, however, showed the Dische test[20] for 2-deoxysugars.

Methyl 2-Deoxy-2-S-acetyl-3-O-acetyl-4,6-O-benzylidene-α-D-altropyranoside (VI)——A mixture of III (1 g) and MeONa in dry MeOH (25 ml) containing Na (0.6 g, 10 equiv.) was refluxed for 12 hr, cooled, and then evaporated to give a sirup which acetylated with Ac_2O (10 ml) in pyridine (10 ml). After standing for 2 days at room temperature, the mixture was poured into ice–H_2O (200 ml) and extracted with $CHCl_3$ (3×20 ml). The organic phases were washed with 3 N H_2SO_4, aq. $NaHCO_3$, and H_2O, respectively, dried over Na_2SO_4. Evaporation of the solvent gave a sirup (0.7 g) which dissolved in benzene and chromatographied on silica gel (20 g) column (Kieselgel 7734, E. Merck). Elution was performed using benzene and 5% ether–benzene (v/v). From the effluent a sirup (VI) (0.3 g, 30%), $[\alpha]_D^{20}$ +57° (0.47, $CHCl_3$) was obtained after removal of the solvent. The ethanolic solution of VI showed a single spot by TLC and negative UV absorption near 270 mμ. IR λ_{max}^{Nujol} cm^{-1}: 1760 (OAc), 1710 (SAc), 760, 700 (phenyl); NMR: τ 4.40 (1H, singlet, C_6H_5–C$\underline{H}$), 5.37 (1H, singlet, anomeric H), 6.55 (3H, singlet, OC$\underline{H}_3$), 7.57 (3H, singlet, SCOC$\underline{H}_3$), 7.83 (3H, singlet, OCOC$\underline{H}_3$).

Methyl 2-Deoxy-2-(N,N-dimethyldithiocarbamoyl)-3-O-mesyl-4,6-O-benzylidene-α-D-altropyranoside (VII)——To a chilled, stirred solution of III (2 g, 1 equiv.) in dry pyridine (20 ml) was added dropwise mesyl chloride (1 ml, 2 equiv.). The mixture stirred for further 1 hr, then left to stand overnight at room temperature with the exclusion of moisture. It was poured into ice–H_2O (200 ml) and extracted with $CHCl_3$ (2×40 ml). The combined organic phases were washed with 3 N HCl, aq. $NaHCO_3$ and H_2O, decolorized with charcoal, dried over Na_2SO_4, and then evaporated to give a pale yellow sirup which crystallized on trituration with EtOH. Recrystallization from EtOH gave pure material (2 g, 83%), mp 142—143°, $[\alpha]_D^{20}$ +65.5° (c=0.59, $CHCl_3$), UV λ_{max}^{EtOH} mμ (ε): 244 (8000), 277 (8500); IR λ_{max}^{Nujol} cm^{-1}: 1500 (dithiocarbamoyl), 1340, 1250 (OMs), 760, 700 (phenyl). *Anal.* Calcd. for $C_{18}H_{25}O_7NS_3$: C, 46.64; H, 5.43; N, 3.03; S, 20.75. Found: C, 46.78; H, 5.49; N, 2.97; S, 20.21.

Methyl 2-Deoxy-2-N,N-dimethyldithiocarbamoyl-3-O-tosyl-4,6-O-benzylidene-α-D-altropyranoside (VIII)——A mixture of III (2.6 g, 1 equiv.) and TsCl (3 g, 21. equiv.) in pyridine (26 ml) was stirred for 1 hr at 0°, then left for 3 days at room temperature. The mixture was treated as described in VII to give pure material, mp 155—156°, $[\alpha]_D^{20}$ +60° (c=0.66, $CHCl_3$), UV λ_{max}^{Nujol} mμ (ε): 276 (8700); IR λ_{max}^{Nujol} cm^{-1}: 1500 (dithiocarbamoyl), 1340, 1250 (OTs), 750, 700 (phenyl). *Anal.* Calcd. for $C_{24}H_{29}O_7NS_3$: C, 53.41; H, 5.41; N, 2.59; S, 17.81. Found: C, 53.25; H, 5.48; N, 2.52; S, 17.54.

Methyl 2,3-Dithio-4,6-O-benzylidene-α-D-mannopyranoside 2,3-S-Carbonate (IX)——(a) A mixture of VII (8 g, 1 equiv.) and AcOK (17 g, 10 equiv.) in EtOH–acetone (1:1, 160 ml) was heated under reflux for 18 hr. After addition of $CHCl_3$ (100 ml), the mixture was poured into ice–H_2O (500 ml). The aqueous layer was extracted with $CHCl_3$ (2×50 ml), the combined organic phases were washed with H_2O, dried over Na_2SO_4,

19) N.K. Richtmyer and C.S. Hudson, *J. Am. Chem. Soc.*, **63**, 1727 (1941).
20) R.E. Deriaz, M. Stacey, E.G. Teece, and L.F. Wiggins, *J. Chem. Soc.*, **1949**, 1222.

NII-Electronic Library Service

and evaporated to give a sirup (8 g) which dissolved in benzene and chromatographed on silica gel (80 g). The benzene–effluent was evaporated to give a sirup which solidified by trituration with ether. Recrystallization from EtOH gave a pure material (IX) (1.95 g, 33%), mp 177—179°, $[\alpha]_D^{16}$ −119° (c=0.93, $CHCl_3$), IR λ_{max}^{Nujol} cm^{-1}: 1650 (dithiocarbonyl), 760, 700 (phenyl); NMR: τ 2.60 (5H, multiplet, $C_6\underline{H}_5$), 4.38 (1H, singlet, C_6H_5–C$\underline{H}$), 5.05 (1H, singlet, anomeric H), 6.51 (3H, singlet, OC$\underline{H}_3$); negative UV absorption near 270 mμ. *Anal.* Calcd. for $C_{15}H_{16}O_5S_2$: C, 52.92; H, 4.74; S, 18.84. Found: C, 52.65; H, 4.70; S, 18.60.

(b) A mixture of VIII (5.2 g, 1 equiv.) and AcOK (9.5 g, 10 equiv) in a mixture of $CHCl_3$ (20 ml)—EtOH (50 ml)—acetone (50 ml) was refluxed for 30 hr, then treated with a similar way as described in (a) to give pure material (IX) (1.1 g, 33%).

Methyl 2,3-Dithio-4,6-di-O-acetyl-α-D-mannopyranoside 2,3-Dithiocarbonate (XII)——To a solution of IX (2.7 g) in $CHCl_3$ (27 ml) was added glacial AcOH (14 ml) containing 35% HBr, and Ac_2O (14 ml). The mixture stirred for 1 hr at 0°, kept overnight at room temperature, and then poured into ice–H_2O (200 ml). It was extracted with $CHCl_3$ (2×20 ml), the combined extracts were washed with aq. $NaHCO_3$, dried over Na_2SO_4, decolorized with charcoal, and evaporated to give a crystalline residue. Twice recrystallizations from EtOH gave pure material (XII) (1.45 g, 55%), mp 130—131°, $[\alpha]_D^{20}$ −5.7° (c=0.53, $CHCl_3$), IR λ_{max}^{Nujol} cm^{-1}: 1740 (OAc), 1650 (dithiocarbonyl), negative absorption near 760 nor 700; NMR: τ 5.00 (1H, singlet, anomeric H), 6.50 (3H, singlet, OC$\underline{H}_3$), 7.86 (6H, singlet, 2×OCOC$\underline{H}_3$). *Anal.* Calcd. for $C_{12}H_{16}O_7S_2$: C, 42.84; H, 4.79; S, 19.06. Found: C, 42.75; H, 4.78; S, 19.08.

Methyl 2,3-Di-S-acetyl-2,3-dideoxy-4,6-di-O-acetyl-α-D-mannopyranoside (XIII)——(a) Finely powdered IX (2.2 g) was added to liquid NH_3 (70 ml) which had been preserved in a round flask previously chilled with dry ice–acetone. Small pieces of Na were added to the solution under constant stirring until the blue color persisted for 10 min. At the end of the time, NH_4Cl was added until the blue color discharged, from which the ammonia was allowed to evaporate under nitrogen to prevent oxidation of the mercaptan. The residue was acetylated by stirring for 1 hr at 0° with Ac_2O (20 ml) in pyridine (20 ml), and left for 3 hr at room temperature. The mixture was poured into ice–H_2O (300 ml), and the resultant solution was extracted with $CHCl_3$ (3×30 ml). The combined extracts were washed with dil. HCl, aq. $NaHCO_3$ and H_2O, dried over Na_2SO_4, and evaporated to give a sirup (1 g) which was dissolved in benzene and chromatographied on silica gel (30 g). Elution was performed using benzene, 5% ether—benzene (v/v) and 10% ether—benzene. From the last effluent a yellow sirup (0.33 g, 13%), $[\alpha]_D^{20}$ +55.6° (c=0.45, $CHCl_3$), was obtained after removal of the solvent. IR λ_{max}^{Nujol} cm^{-1}: 1750 (OAc), 1700 (SAc); NMR: τ 6.53 (3H, singlet, OC$\underline{H}_3$), 7.57 (3H, singlet, SCOC$\underline{H}_3$ at C_2), 7.63 (3H, singlet, SCOC$\underline{H}_3$ at C_3), 7.86 (3H, singlet, OCHC$\underline{H}_3$ at C_4), 7.94 (3H, singlet, OCOC$\underline{H}_3$ at C_6).

(b) To a solution of XII (0.9 g) in warm EtOH (20 ml) was added dropwise 1 N NaOH (10 ml). The mixture was warmed in a water bath to dissolve the solid materials completely, then it was passed through Amberlite IR-120 (H^+). The effluent was evaporated to give a sirup (0.5 g), $[\alpha]_D^{20}$ +72.6° (c=0.62, MeOH), which acetylated with Ac_2O (10 ml) in pyridine (10 ml) overnight. It was treated as described in (a) to give two kinds of sirup; from the forthcoming effluent of the 10% ether—benzene, a colorless sirup (0.15 g), $[\alpha]_D^{20}$ +95.2° (c=1.45, $CHCl_3$), no structure could be assigned to this product. An another sirup (0.14 g, 13%) $[\alpha]_D^{20}$+34° (c=1.2, $CHCl_3$) was obtained after evaporation of the successive effluent. The product was the identical with one prepared by (a) in IR and NMR.

Acknowledgement The authors are indebted to Miss. Y. Kishio of this Faculty for NMR measurements. Thanks are also due to the Tokyo Laboratory, Kowa Co., Ltd. for a part of elementary analyses.

NII-Electronic Library Service