

*Anal.* Calcd for  $C_{18}H_{26}NO_9$ : C, 53.59; H, 7.25; N, 3.49. Found: C, 53.70; H, 7.02; N, 3.69.

**Registry No.**—1, 604-68-2; 2, 7784-54-5; 3, 10026-53-6; 4, 3068-34-6; 5, 7772-75-0; 6, 7772-76-1; 7, 7784-55-6; 8, 3068-36-8; 9, 10028-44-1; 10, 10026-54-7; 11, 10026-55-8; 12, 604-69-3; 13, 7772-79-4; 14, 7772-80-7; 15, 7772-81-8; 16, 7772-82-9; 17, 10043-45-5; 18, 7597-81-1; 19, 10022-13-6; 20, 10060-23-8;

21, 7772-85-2; 22, 7772-86-3; 23, 10028-45-2; 24, 7772-87-4; 25, 10043-46-6; 26, 10036-64-3; 27, 7772-881-5; 2-*d*<sub>1</sub>, 7772-89-6; 29, 7772-90-9; 30, 4539-83-7; 31, 7772-92-1; 32, 6730-10-5; 33, 7772-93-2; 34, 7772-94-3; 10-*d*<sub>1</sub>, 7772-95-4.

**Acknowledgment.**—The authors thank Mrs. S. J. Gelb for valued experimental assistance.

## Anomalous Rearrangement of Oxidized Xanthate Derivatives of D-Mannose and D-Mannitol<sup>1a</sup>

W. M. DOANE, B. S. SHASHA, C. R. RUSSELL, AND C. E. RIST

Northern Regional Research Laboratory,<sup>1b</sup> Peoria, Illinois 61604

Received November 3, 1966

Xanthation of 2,3:5,6-di-*O*-isopropylidene-D-mannose followed by coupling with iodine at 0° gave crystalline bis(1-*S*-carbonyl-2,3:5,6-di-*O*-isopropylidene-1-thio-D-mannofuranose) disulfide (II) while none of the expected bis(*O*-thiocarbonyl) disulfide derivative could be isolated. Compound II decomposed on standing in different organic solvents to carbonyl sulfide and crystalline bis(2,3:5,6-di-*O*-isopropylidene- $\alpha$ -D-mannofuranosyl) disulfide (IV). The structure of IV was proved by its independent synthesis and by its conversion to 1,4-anhydro-D-mannitol. Xanthation of 2,3:5,6-di-*O*-isopropylidene-D-mannitol (VI) followed by coupling with iodine gave the corresponding bis(*O*-thiocarbonyl) disulfide derivative (VII). On standing in pyridine, VII decomposed to elemental sulfur, carbon disulfide, VI, and a high-melting, crystalline compound which was shown to be bis(2,3:5,6-di-*O*-isopropylidene-D-mannitol) orthocarbonate (VIII).

The synthesis of bis(*O*-thiocarbonyl) disulfide derivatives of sugars<sup>2</sup> and simple alkanediols<sup>3</sup> was reported recently. Under the proper conditions, these derivatives undergo rearrangement-fragmentation to give either thionocarbonates or *S*-alkyl dithiocarbonates. The rearrangement appears to be a good method for preparing certain thionocarbonates and *S*-alkyl dithiocarbonates otherwise difficult to obtain. Because such derivatives of sugars have utility as intermediates in the preparation of unsaturated<sup>4</sup> and deoxy sugars,<sup>5</sup> further studies of these rearrangements with carbohydrates seemed warranted. In determining the nature of the rearrangement of the bis(*O*-thiocarbonyl) disulfide derivative at position C-1 of D-mannose and D-mannitol, the anomalous behavior of these derivatives was established.

When 2,3:5,6-di-*O*-isopropylidene-D-mannose (I) was treated with carbon disulfide and sodium hydroxide at 25° and then treated with iodine, the expected bis(*O*-thiocarbonyl) disulfide derivative was formed in low yield. Attempts to improve the yield by modification of the xanthation conditions failed. Interestingly, when the xanthation was carried out at 25° and then allowed to stand at 0° for 1 hr, followed by oxidative coupling, none of the expected product formed. In-

stead, a rearrangement occurred between the thiocarbonyl sulfur atom and the oxygen atom at C-1 to give the crystalline bis(1-*S*-carbonyl-2,3:5,6-di-*O*-isopropylidene-1-thio-D-mannofuranose) disulfide (II) as the only sugar derivative which contained sulfur (Scheme I). Product II was isolated in about 13% yield while most of the remaining I was recovered unchanged. In an attempt to prepare the corresponding 1-*S*-carbonyl-*S*-methyl derivative, no rearrangement occurred and only the *S*-methyl dithiocarbonate product was isolated.

A rearrangement of sulfur and oxygen in a sugar derivative was reported previously by Freudenberg and Wolf,<sup>6</sup> who found that on pyrolysis of 1,2:5,6-di-*O*-isopropylidene-3-*O*-[(methylthio)thiocarbonyl]- $\alpha$ -D-glucofuranose, isomerization occurred to give the *S*-carbonyl-3-thio derivative.

The structure of II was formulated on the basis of experimental evidence. Elemental and molecular weight analyses agreed with the proposed structure. The infrared spectrum showed carbonyl absorption at 5.85 and 6.15  $\mu$ . The ultraviolet spectrum had an absorption maximum at 235, whereas compounds containing the bis(*O*-thiocarbonyl) disulfide group have maxima near 240 and 285  $\mu$ .<sup>7</sup> Reductive desulfurization of II with Raney nickel gave 1,4-anhydro-2,3:5,6-di-*O*-isopropylidene-D-mannitol which on acid hydrolysis gave the known, crystalline 1,4-anhydro-D-mannitol (III). It was thought that alkali treatment of II would form the corresponding mercaptide which on oxidation should yield bis(2,3:5,6-di-*O*-isopropylidene- $\alpha$ -D-mannofuranosyl) disulfide (IV). Indeed, IV resulted when II was refluxed in aqueous acetone containing barium hydroxide, but no oxidant was required. Also, II gave IV on warming for a short time or even on standing at 25° in different organic solvents. In

(1) (a) Presented before Division of Carbohydrate Chemistry, Winter Meeting of the American Chemical Society, Phoenix, Ariz., Jan 1966. (b) This is a laboratory of the Northern Utilization Research and Development Division, Agricultural Research Service, U. S. Department of Agriculture. Article is not copyrighted.

(2) (a) W. M. Doane, B. S. Shasha, C. R. Russell, and C. E. Rist, *J. Org. Chem.*, **30**, 162 (1965); (b) B. S. Shasha, W. M. Doane, C. R. Russell, and C. E. Rist, *Carbohydrate Res.*, in press; (c) E. I. Stout, W. M. Doane, B. S. Shasha, C. R. Russell, and C. E. Rist, *ibid.*, in press.

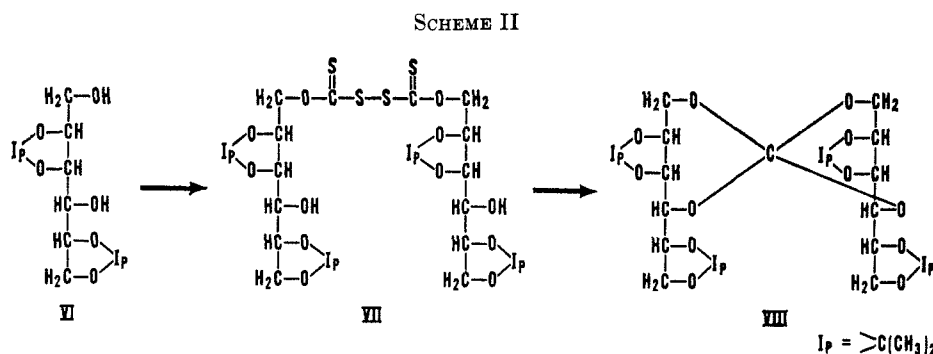
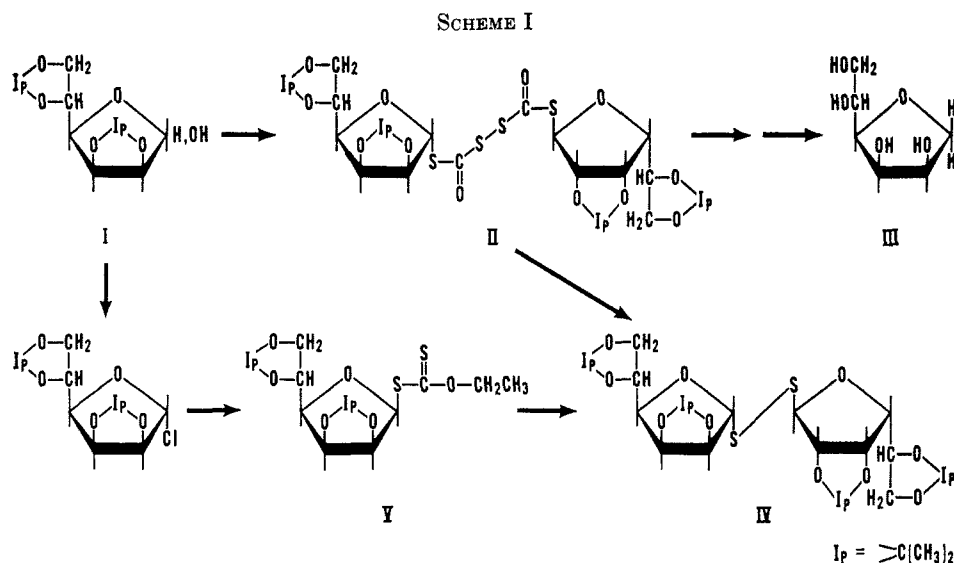
(3) B. S. Shasha, W. M. Doane, C. R. Russell, and C. E. Rist, *Nature*, **211**, 965 (1966).

(4) (a) D. Horton and W. N. Turner, *Tetrahedron Letters*, No. 25, 31 (1964); (b) D. Horton, Abstracts, 150th National Meeting of the American Chemical Society, Atlantic City, N. J., 1965, p 21D; (c) A. H. Haines, *Carbohydrate Res.*, **1**, 214 (1965).

(5) D. Horton and D. H. Hutson, *Advan. Carbohydrate Chem.*, **18**, 124 (1963).

(6) K. Freudenberg and A. Wolf, *Ber.*, **60**, 232 (1927).

(7) W. M. Doane, B. S. Shasha, C. R. Russell, and C. E. Rist, *J. Org. Chem.*, **30**, 3071 (1965).



either case the crystalline disulfide was isolated in nearly quantitative yield. When II came in contact with pyridine, the gas that immediately formed was collected and identified as carbonyl sulfide. That the free 1-thio sugar is not an intermediate in the formation of IV is apparent since IV was recovered in nearly quantitative yield from the treatment of II with anhydrous sodium methoxide. The sodium salt of the 1-thio sugar is not formed since, as will be seen later, this derivative is reasonably stable.

The structure of IV followed from elemental analysis, molecular weight determination, ultraviolet spectrum, and the amount of oxidant consumed on bromine oxidation. Reduction of IV with zinc in the presence of acetic anhydride gave, as expected,<sup>8</sup> the corresponding 1-*S*-acetyl derivative. This product was identified by sulfur analysis and by infrared and nmr spectra, which showed peaks at 5.85  $\mu^9$  and 2.4 ppm,<sup>10</sup> respectively, for the *S*-acetyl group.

Furthermore, IV was independently synthesized by treating the known 2,3:5,6-di-*O*-isopropylidene- $\alpha$ -D-mannofuranosyl chloride with ethylxanthate to give crystalline 2,3:5,6-di-*O*-isopropylidene- $\beta$ -D-mannofuranosyl ethylxanthate (V). Treatment of V with anhydrous sodium methoxide in methanol formed the sodium salt of the 1-thio sugar which on oxidation with iodine gave IV in over 90% yield.

The anomeric assignments to II, IV, V, and the 1-*S*-acetyl derivative were made on the basis of nmr spectra.

(8) F. Wrede, *Z. Physiol. Chem.*, **119**, 46 (1922).

(9) D. Horton and M. L. Wolfrom, *J. Org. Chem.*, **27**, 1794 (1962).

(10) C. V. Holland, D. Horton, M. J. Miller, and W. N. Turner, Abstracts, 149th National Meeting of the American Chemical Society, Detroit, Mich., 1966, p 1C.

In a nonrigid mannofuranose ring the  $\alpha$  anomer, which has a *trans* relationship between protons  $H_1$  and  $H_2$ , should show a low-field singlet ( $J < 1$  cps), whereas the  $\beta$  anomer, where  $H_1$  and  $H_2$  are *cis*, should show a low-field doublet with a coupling constant of approximately 4 cps.<sup>11</sup> Compounds II, IV, and the *S*-acetyl derivative gave low-field singlets at 6.02, 5.43, and 5.94 ppm, respectively, whereas V gave a low-field doublet centered at 5.66 ppm with an apparent coupling constant of 3.5 cps.

When a dioxane solution of 2,3:5,6-di-*O*-isopropylidene-D-mannitol (VI, scheme II) was treated with carbon disulfide and sodium hydroxide and then oxidatively coupled with iodine, a bis(*O*-thiocarbonyl) disulfide derivative (VII) was recovered as an amorphous powder in good yield. Its tlc with different organic solvents exhibited one major component and traces of another. Since its nmr spectrum revealed a doublet at 2.52 ppm for one hydrogen which corresponds to the presence of a secondary alcohol, the bis(*O*-thiocarbonyl) disulfide group must occupy the C-1 position in the D-mannitol moiety. Upon shaking the sample with deuterium oxide the doublet disappeared.

When compound VII was allowed to stand in anhydrous pyridine for several hours, it decomposed with rearrangement to give elemental sulfur, carbon disulfide, 2,3:5,6-di-*O*-isopropylidene-D-mannitol (VI), and bis(2,3:5,6-di-*O*-isopropylidene-D-mannitol) orthocarbonate (VIII). A crude syrup remained whose infrared spectrum contained a strong carbonyl peak at 5.7  $\mu$ .

(11) K. N. Rinehart, Jr., W. S. Chilton, and M. Hichens, *J. Am. Chem. Soc.*, **84**, 3216 (1962), and references cited therein.

The structure of VIII was formulated on the basis of experimental evidence. Elemental analysis gave the empirical formula  $C_{25}H_{40}O_{12}$ , formula weight being 532. Molecular weight determination by the Rast method gave 520. The mass spectrum of VIII, which was reported in a preliminary communication,<sup>12</sup> had a high mass peak at 532 and was consistent with the proposed structure. The infrared spectrum revealed no hydroxyl absorption. As predicted for such an orthocarbonate structure, VIII was stable to alkali. Attempts were made to convert VIII into VI and the corresponding 1,4-carbonate of VI by preferential acid hydrolysis. These attempts were not completely successful since both the orthocarbonate and isopropylidene groups hydrolyzed rapidly. However, when the hydrolysis was stopped after a short time, the presence of VI was detected by tlc. In another experiment the acid hydrolysis was followed polarimetrically and stopped after the reading approached a constant value. The infrared spectrum of the hydrolysate exhibited strong carbonyl absorption at  $5.75 \mu$ , owing presumably to the presence of the 1,4-carbonate derivative of D-mannitol and no absorption at  $8.6 \mu$  for the isopropylidene groups. Paper chromatography of the hydrolysate revealed D-mannitol along with other components. When the hydrolyzate was allowed to stand for a few hours, a second carbonyl peak appeared at  $5.6 \mu$ , owing probably to the carbonyl group wandering to form a more stable, five-membered ring. Saponification of the hydrolysate with excess barium hydroxide and back titration with acid showed 0.92 mole of the carbonate derivative per mole of VIII hydrolyzed.

Although the precise mechanism of the rearrangement of VII to form VIII cannot be formulated at present, an unstable 1,4-cyclic thionocarbonate is probably formed as an intermediate. This proposal is based on the reaction of VI with thiophosgene, which produced no thionocarbonate derivative and from which only VIII could be isolated. A similar reaction of thiophosgene with D-glucose derivatives<sup>2a</sup> and 2,2-dimethyl-1,3-propanediol<sup>3</sup> gave the corresponding thionocarbonates. Also, the presence of a carbonyl peak in the infrared spectrum of the rearrangement mixture might be explained by the formation of a carbonate derivative via an unstable thionocarbonate.

### Experimental Section

Melting points were taken in a calibrated Thomas-Koffler<sup>13</sup> melting point apparatus. Optical rotations were measured at 5893 Å with a Rudolph polarimeter. Molecular weights were determined by the Rast method in camphor or in a vapor pressure osmometer (Mechrolab, Inc., Mountain View, Calif.) in acetone as specified. Ultraviolet spectra were determined with a Perkin-Elmer Model 202 spectrophotometer. Infrared spectra were recorded by a Perkin-Elmer Model 137 spectrophotometer with silver chloride optics as Nujol mulls or films. Nmr spectra were recorded in deuterated chloroform by a Varian A-60 nmr spectrometer with tetramethylsilane as internal reference.

**Bis(2,3:5,6-di-O-isopropylidene-1-O-thiocarbonyl-D-mannofuranose) Disulfide.**—2,3:5,6-Di-O-isopropylidene-D-mannose (I) was prepared by a procedure similar to that used for preparation of 1,2:5,6-di-O-isopropylidene-D-glucose with concentrated sulfuric acid and anhydrous cupric sulfate. Compound I was

recovered in 78% yield with mp 122–123°. A solution of I (5 g) in dioxane (20 ml) was treated with 2 ml of carbon disulfide and 5 ml of sodium hydroxide (5 N) at 25° for 30 min. The reaction mixture was neutralized with acetic acid (5 N), treated with iodine solution, and diluted with 250 ml of cold water. The precipitate which formed was collected, dissolved in ether, and dried over anhydrous sodium sulfate. After filtration, the ethereal solution was evaporated to yield a crystalline mass. Extraction of the mass with a few milliliters of carbon disulfide left I. Evaporation of the carbon disulfide extract gave the title compound (0.1 g) as a crude mass contaminated with I. The ultraviolet spectrum exhibited maxima at 235 and 280 m $\mu$  connoting the bis(O-thiocarbonyl) disulfide group. Attempts to increase the yield by use of higher ratios of sodium hydroxide or carbon disulfide or both, to I, or by extending the reaction time, failed.

**Bis(1-S-carbonyl-2,3:5,6-di-O-isopropylidene-1-thio- $\alpha$ -D-mannofuranose) Disulfide (II).**—A solution of I (5 g) in dioxane (20 ml) was treated with 2 ml of carbon disulfide and 5 ml of sodium hydroxide (5 N) at 25° for 30 min. The reaction mixture was allowed to stand in an ice bath for 60 min and then neutralized with acetic acid (5 N) before oxidatively coupling the xanthate by addition of iodine solution. The precipitate formed was collected, dissolved in ether, and dried over anhydrous magnesium sulfate. After filtration, the ethereal solution was evaporated to yield a crystalline mass. Extraction of the mass with a few milliliters of carbon disulfide left I (4 g). Evaporation of the carbon disulfide extract gave 0.8 g of crude II which was recrystallized from dioxane-hexane: mp 175°,  $\lambda_{\text{max}}^{\text{ether}}$  235 m $\mu$  ( $\epsilon$  12,500).

*Anal.* Calcd for  $C_{26}H_{38}O_{12}S_4$ : C, 46.6; H, 5.7; S, 19.1. Found: C, 46.3; H, 5.9; S, 18.2.

**2,3:5,6-Di-O-isopropylidene-1-O-[(methylthio)thiocarbonyl]-D-mannofuranose.**—To a solution of I (1 g) in dioxane (4 ml), carbon disulfide (1 ml) and sodium hydroxide (5 N, 2 ml) were added. The solution was stirred for 12 min and then placed at 0° for 25 min. The pH was adjusted to about 6 and methyl iodide (2 ml) was added. After 1 hr, water (5 ml) was added and the mixture was extracted with ether. The ether extract was evaporated to a semicrystalline mass. The mass was dissolved in hexane from which I rapidly separated. After filtration to remove I, the filtrate was stored at 0°. The crystals, which soon deposited in the flask, gave mp 81–82°;  $\lambda_{\text{max}}^{\text{MeOH}}$  280 m $\mu$  ( $\epsilon$  11,700) and 223 m $\mu$  ( $\epsilon$  7900). Freudenberg and Wolf<sup>6</sup> reported mp 80–81° for 2,3:5,6-di-O-isopropylidene-1-O-[(methylthio)thiocarbonyl]-D-mannofuranose.

**1,4-Anhydro-D-mannitol (III).**—A solution of 300 mg of II in 6 ml of dioxane and 60 ml of ethanol was refluxed for 1 hr with excess Raney nickel. The Raney nickel was removed by filtration, and the filtrate was evaporated to a syrup whose elemental analysis corresponded to 1,4-anhydro-2,3:5,6-di-O-isopropylidene-D-mannitol. A solution of this anhydro derivative (200 mg) in 10 ml of methanol and 2 ml of hydrochloric acid (1 N) was heated on a steam bath for 1 hr and then neutralized with silver carbonate. Evaporation of the filtrate gave a syrup which crystallized on standing. The product, identified as 1,4-anhydro-D-mannitol (III), was recrystallized from methanol, mp 145–147°,  $[\alpha]_{\text{D}}^{25} -24^\circ$  ( $c$  1.0, water). Other workers reported<sup>14</sup> for III mp 146–147°,  $[\alpha]_{\text{D}}^{20} -23.7^\circ$  (water). An authentic sample supplied by Dr. J. W. LeMaistre gave mp 143–144°, which was undepressed on admixture with III.

**Bis(2,3:5,6-di-O-isopropylidene- $\alpha$ -D-mannofuranosyl) Disulfide (IV).** **A. From II.**—One gram of II was treated with 0.2 ml of anhydrous pyridine at 25°. On contact with pyridine an immediate evolution of gas was observed which continued for a few minutes. After 15 min no carbonyl absorption was recorded in the infrared. Ether (3 ml) was added and the solution was transferred to a crystallizing dish. When the solvents were allowed to evaporate in a hood, a crystalline residue remained (0.8 g) which showed one major component by tlc with silica gel G as adsorbent and several solvents as developers. Recrystallization from methanol gave IV as white needles: mp 118–120°,  $\lambda_{\text{max}}^{\text{MeOH}}$  250 m $\mu$  ( $\epsilon$  383). [Diethyl disulfide was reported to have an absorption maximum at 250 m $\mu$  ( $\epsilon$  380).]<sup>15</sup>

*Anal.* Calcd for  $C_{24}H_{38}O_{10}S_2$ : C, 52.3; H, 6.9; S, 11.6; mol wt, 550. Found: C, 51.9; H, 7.3; S, 11.6; mol wt, 518 (vapor pressure osmometry in chloroform).

(12) B. S. Shasha, W. M. Doane, and W. K. Rohwedder, *Tetrahedron Letters*, No. 14, 1479 (1966).

(13) Mention of firm names or trade products does not imply that they are endorsed or recommended by the U. S. Department of Agriculture over other firms or similar products not named.

(14) R. C. Hockett, H. G. Fletcher, Jr., E. L. Sheffield, R. M. Goepf, Jr., and S. Soltzberg, *J. Am. Chem. Soc.*, **68**, 930 (1946).

(15) H. Mohler and J. Sorge, *Helv. Chim. Acta*, **23**, 1200 (1940).

When treated with bromine,<sup>16</sup> IV consumed 5.5 moles of the oxidant per mole (requires 5.0 moles per mole).

The gas evolved on treatment of II with pyridine was trapped in methanol containing 0.4% diethylamine. The ultraviolet spectrum of the solution showed the characteristic absorption maximum at 227 m $\mu$  for the diethylamine-carbonyl sulfide complex. No maxima were observed near 260 or 290 m $\mu$  where the diethylamine-carbon disulfide complex absorbs.

Compound IV was obtained also on treatment of a solution of II (100 mg) in a dioxane-methanol mixture with metallic sodium. Evaporation of the solvents gave crude IV (80 mg, 98%).

Treatment of IV with zinc and acetic anhydride according to the procedure of Wrede<sup>9</sup> gave the corresponding 1-*S*-acetyl derivative as revealed by sulfur analysis and by the characteristic peak for an *S*-acetyl group in the infrared spectrum at 5.85  $\mu^9$  and in the nmr spectrum at 2.4 ppm.<sup>10</sup>

**B. From 2,3:5,6-Di-*O*-isopropylidene- $\beta$ -D-mannofuranosyl Ethylxanthate (V).**—Treatment of I with phosphorous pentachloride according to the procedure of Allison and Hixon<sup>17</sup> gave the known<sup>6</sup> 2,3:5,6-di-*O*-isopropylidene- $\alpha$ -D-mannofuranosyl chloride. The method described by Horton<sup>18</sup> was adopted to convert the 1-chloro compound to the corresponding 1-ethylxanthate derivative (V). Compound V, obtained crystalline in about 50% yield, was recrystallized from hexane: mp 91–92°, [ $\alpha$ ]<sub>D</sub><sup>25</sup> –37° (c 3, chloroform).

*Anal.* Calcd for C<sub>15</sub>H<sub>24</sub>O<sub>8</sub>S<sub>2</sub>: C, 49.5; H, 6.8; S, 17.6. Found: C, 49.6; H, 6.9; S, 17.4.

Deesterification of V (1 g) was accomplished by treatment with sodium methoxide (0.1 g of sodium in 10 ml of methanol) at 40° for 10 min. The clear solution was cooled to 25°, neutralized with dilute acetic acid, and oxidatively coupled by iodine (0.1 N). When the slightly turbid solution was allowed to stand, IV crystallized after a few minutes and was recovered in over 90% yield. Recrystallization from methanol gave mp 118–119°, [ $\alpha$ ]<sub>D</sub><sup>25</sup> +93° (c 2.5, chloroform). On admixture with the compound prepared by route A the melting point was 115–117°.

The ultraviolet, infrared, and nmr spectra and the X-ray diffraction patterns confirmed the identity of the two disulfide preparations.

**2,3:5,6-Di-*O*-isopropylidene-D-mannitol (VI).** **A.**—To a solution of I (5 g) in 20 ml of dioxane, 15 ml of water was added. A solution of 1 g of potassium borohydride in 10 ml of water was added dropwise over a period of 5 min. The temperature increased to 40° during this addition. After the solution was stirred for an additional 25 min, Rexyn RG 51 (H) (carboxylic-type resin) was slowly added to destroy excess borohydride. The resin was filtered and the solution was evaporated to dryness and extracted three times with ether (100-ml portions). Evaporation of the ether gave VI as a syrup, which crystallized on long standing, mp 47–48°. Yields of 60–88% were obtained.

*Anal.* Calcd. for C<sub>12</sub>H<sub>22</sub>O<sub>6</sub>: C, 55.0; H, 8.4. Found: C, 54.9; H, 8.6.

**B.**—To a solution of I (30 g) in 100 ml tetrahydrofuran, 5 g of lithium aluminumhydride was added portionwise during 10 min. The suspension was refluxed for 20 min, and then allowed to cool to room temperature. After destruction of the excess hydride, the suspension was filtered and the precipitate was washed with an excess of water. The combined filtrate was evaporated to dryness, redissolved in water, and refiltered. Compound VI was obtained in 81% yield on evaporation of the water.

**Bis(2,3:5,6-di-*O*-isopropylidene-1-*O*-thiocarbonyl-D-mannitol) Disulfide (VII).**—To a solution of VI (4 g) in 20 ml of dioxane and 2 ml of carbon disulfide, 2 ml of sodium hydroxide (5 N) was added. The reaction mixture was stirred at 25° for 5 min and excess base was neutralized with acetic acid. The resulting xanthate was oxidatively coupled with iodine solution and the disulfide product was collected as a syrup on partial evaporation. After the syrup was washed with water, it was dissolved in ether and dried over anhydrous sodium sulfate. Evaporation of the filtrate gave 3.2 g of VII (70% yield) as an amorphous powder:  $\lambda_{\max}^{\text{MeOH}}$  236 m $\mu$  ( $\epsilon$  15,800) and 290 m $\mu$  ( $\epsilon$  6600).

*Anal.* Calcd for C<sub>26</sub>H<sub>42</sub>O<sub>12</sub>S<sub>4</sub>: C, 46.3; H, 6.2; S, 19.0. Found: C, 46.3; H, 6.6; S, 19.3.

**Bis(2,3:5,6-di-*O*-isopropylidene-D-mannitol) Orthocarbonate (VIII).** **A.** From VII.—A solution of VII (3.8 g) in 5 ml of pyridine was allowed to stand at 25° for 12 hr. Evaporation of the pyridine gave a syrup (3.1 g) which was extracted with water. Evaporation of the extract left a syrup identified by elemental analysis and infrared as VI. The water-insoluble part was washed with methanol and extracted with a few milliliters of carbon disulfide. Evaporation of the carbon disulfide extract gave 190 mg of free sulfur. The infrared spectrum of the crude syrup left after extraction with carbon disulfide showed a carbonyl peak at 5.7  $\mu$  owing probably to the presence of 2,3:5,6-di-*O*-isopropylidene-D-mannitol 1,4-carbonate. Crystallization of the syrup from ethanol-water gave crude VIII which after recrystallization from dioxane-water had mp 246–247°, [ $\alpha$ ]<sub>D</sub><sup>25</sup> +91° (c 0.7, chloroform).

*Anal.* Calcd for C<sub>26</sub>H<sub>40</sub>O<sub>12</sub>: C, 56.4; H, 7.5; mol wt, 532. Found: C, 56.6; H, 7.6; mol wt, 520 (Rast in camphor) and 532 (mass spectrometry).

The carbon disulfide formed during the rearrangement of VIII was collected and determined by a procedure described previously.<sup>8</sup> The formation of carbon disulfide was complete after 5 hr, during which 1 mole was produced per mole of VII.

**B. From VI.**—One gram of VI was dissolved in 20 ml of anhydrous ether and treated with an excess of sodium metal for 20 hr at 25°. The ether solution was decanted and 0.5 ml of thiophosgene was added. The formation of sodium chloride was immediate and the resulting suspension was shaken with potassium hydroxide (1 N) for 30 min to destroy the excess thiophosgene. The ether layer was evaporated to dryness and crystallized twice from dioxane-water to give 150 mg of VIII, mp 246–247°. The product also was prepared, but in lower yield by treating VI in dioxane with thiophosgene and pyridine by a method reported earlier.<sup>2a</sup>

**Barium Hydroxide Treatment of VIII.**—A solution of VIII (50 mg) in dioxane (5 ml) was treated with 1% barium hydroxide solution (1 ml). The mixture was refluxed for 3 hr and neutralized by addition of solid carbon dioxide. The barium carbonate formed was filtered and the solution was concentrated to give VIII unchanged.

**Acid Hydrolysis of VIII.**—A solution of VIII (50 mg) in acetone (3 ml) and ethanol (3 ml) was treated with hydrochloric acid solution (1 N, 0.6 ml). After standing for 12 min the solution was neutralized with silver carbonate and concentrated to dryness. A water extract (1 ml) of the hydrolyzate revealed VI by tlc.

In another experiment, VIII (128 mg) in a mixture of dioxane (10 ml) and ethanol (5 ml) was treated with hydrochloric acid (5 N, 0.2 ml). The mixture was allowed to stand at 25° and the change of optical rotation ( $\alpha$ ) in degrees with time in minutes (in parentheses) was as follows: +66 (4), +53 (8), +28 (21), +18 (35), +10 (60), and +8 (80). After 80 min the solution was neutralized and concentrated. Strong carbonyl absorption was observed at 5.75 with an additional peak at 5.6  $\mu$  when the solution was allowed to stand for a few hours. Paper chromatography of the hydrolysate with *n*-butyl alcohol-ethanol-water (40:11:19, v/v) or ethyl acetate-acetate acid-formic acid-water (18:3:1:4, v/v) revealed D-mannitol along with other components.

Treatment of the hydrolysate with barium hydroxide (0.5%) followed by acid titration of the excess base showed 0.92 mole of carbonate per mole of VIII. Paper chromatography at this state disclosed only D-mannitol.

**Registry No.**—Bis(2,3:5,6-di-*O*-isopropylidene-1-*O*-thiocarbonyl-D-mannofuranose) disulfide, 7734-00-1; I, 7757-38-2; II, 7734-01-2; 2,3:5,6-di-*O*-isopropylidene-1-*O*-[(methylthio)thiocarbonyl]-D-mannofuranose, 7726-96-7; III, 7726-97-8; IV, 7726-98-9; V, 7726-99-0; VI, 3969-61-7; VII, 7727-01-7; VIII, 7727-02-8.

**Acknowledgment.**—We are grateful to C. A. Glass and L. W. Tjarks for nmr analysis, to Mrs. Margaret Hinkle for X-ray patterns, to Mrs. Clara McGrew and Mrs. Bonita Heaton for microanalysis and the molecular weight determination by vapor pressure osmometry, and to Miss Mabel Swanson for technical assistance.

(16) S. Siggia and R. L. Edesberg, *Anal. Chem.*, **20**, 938 (1948).

(17) J. N. Allison and R. M. Hixon, *J. Am. Chem. Soc.*, **48**, 406 (1926).

(18) D. Horton, *Methods Carbohydrate Chem.*, **2**, 434 (1963).