**Note**

# Monothiocarbonate derivatives of 1,2.5,6-di-*O*-isopropylidene-α-D-glucofuranose

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Reports from this Laboratory revealed that oxidized xanthate ($RO\overset{S}{\overset{\|}{C}}SS\overset{S}{\overset{\|}{C}}OR$) readily underwent fragmentation by the action of base[1], heat[2], or u v light[3] to provide thionocarbonate or thio sugar derivatives, together with other products Cruz[4] reported that stability of oxidatively coupled starch xanthate improved following conversion of the xanthate into the monothiocarbonate ($RO\overset{O}{\overset{\|}{C}}SS\overset{O}{\overset{\|}{C}}OR$) by chlorine dioxide Our latest research was undertaken to prepare monothiocarbonate derivatives of 1,2 5,6-di-*O*-isopropylidene-α-D-glucofuranose and to compare their behavior with analogous dithiocarbonate compounds

Reaction of the sodium alcoholate of 1,2 5,6-di-*O*-isopropylidene-α-D-glucofuranose in ether gave the monothiocarbonate salt (**1**)

$$RONa + COS \longrightarrow RO\overset{O}{\overset{\|}{C}}SNa$$

The i r spectrum of the product showed a strong absorption at 1600 cm$^{-1}$, presumably due to–$O\overset{O}{\overset{\|}{C}}SNa$, but, as expected, the product was unstable and decomposed on acidification to the parent sugar

Oxidation of **1** with iodine gave bis(1,2 5,6-di-*O*-isopropylidene-α-D-glucofuranose) 3,3′-[dithiobis(formate)] (**2**), isolated as a white solid and characterized by elemental analysis and i r spectrum Selective hydrolysis of the 5,6-*O*-isopropylidene group by mild acid treatment led to the monoacetal **3**, which underwent rearrangement–fragmentation in presence of pyridine to 1,2-*O*-isopropylidene-α-D-

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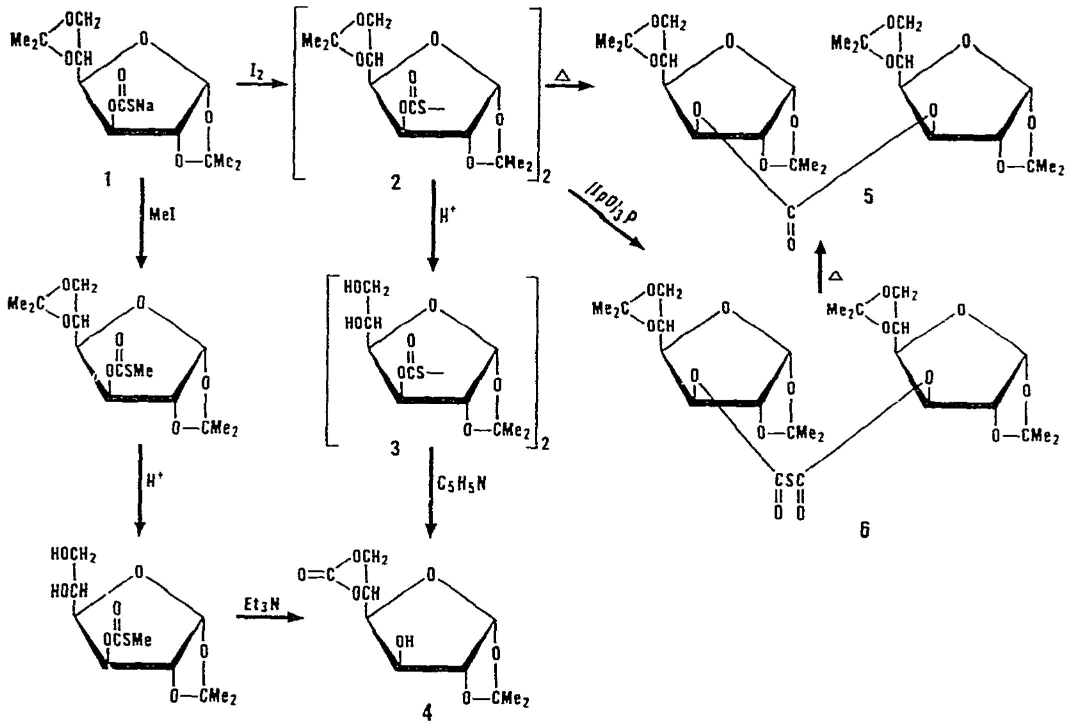

glucofuranose, carbonyl sulfide, elemental sulfur, and 1,2-*O*-isopropylidene-α-D-glucofuranose 5,6-carbonate (**4**) The carbonate was characterized by elemental analysis and by comparison with an authentic sample This reaction is analogous to the rearrangement–fragmentation reported earlier of bis(1,2-*O*-isopropylidene-α-D-glucofuranose) 3,3′-[dithiobis(thioformate)] Products from decomposition of the dithiobis(thioformate) derivative were 1,2-*O*-isopropylidene-α-D-glucofuranose, carbon disulfide, elemental sulfur, and 1,2-*O*-isopropylidene-α-D-glucofuranose 5,6-thionocarbonate[1]

Compound **4** was also prepared from **1** as follows Reaction of methyl iodide with **1** gave the corresponding *S*-methyl ester, 1,2 5,6-di-*O*-isopropylidene-3-*O*-[methylthio(carbonyl)]-α-D-glucofuranose, which was characterized by elemental analysis and i r spectrum Selective acid hydrolysis of the 5,6-*O*-isopropylidene group followed by treatment with triethylamine gave **4**

Compound **2** on heating for 2 h at 180–200° decomposed to a multicomponent mixture (t l c ), but after heating at 120° in the presence of pyridine, the mixture showed (t l c ) one major component that was isolated crystalline and characterized as bis(3-deoxy-1,2 5,6-di-*O*-isopropylidene-α-D-glucofuranos-3-yl)3,3′-carbonate (**5**) The dithiobis(thioformate)analogue (**7**) gave, upon heating under similar conditions, only a trace amount (t l c ) of a compound having the same mobility as the corresponding 3,3′-thionocarbonate (**9**) On the other hand, with the D-galactose analogue, the corresponding 6,6′-thionocarbonate was isolated in good yield These decompositions are somewhat analogous to thermal decomposition of mixed carbonic anhydrides to their corresponding esters and symmetrical anhydrides[5]

$$R\overset{O}{\overset{\|}{C}}O\overset{O}{\overset{\|}{C}}OR' \xrightarrow{\Delta} R\overset{O}{\overset{\|}{C}}OR' + R\overset{O}{\overset{\|}{C}}O\overset{O}{\overset{\|}{C}}R + CO_2$$

Isopropyl phosphite reacted with **2** and with **7** to give the monosulfide derivatives bis(3-*O*-carbonyl-1,2 5,6-di-*O*-isopropylidene-α-D-glucofuranose) monosulfide (**6**) and bis(1,2 5,6-di-*O*-isopropylidene-α-D-glucofuranose-3-*O*-thiocarbonyl) monosulfide (**8**) The structure **6** assigned was consistent with elemental analysis and the i r spectrum, and the structure of **8** was confirmed by comparison with an authentic sample Pyrolysis of **6** and **8** gave the carbonate **5** and thionocarbonate **9**, respectively.

## EXPERIMENTAL

*General* — Melting points were determined with a Fisher–Johns apparatus and are uncorrected Optical rotations were measured in a 1-dm tube with a Rudolph polarimeter I r spectra were recorded with a Perkin–Elmer Model 137 spectrometer having silver chloride optics by using Nujol mulls or films U v spectra were recorded with a Perkin–Elmer Model 202 spectrometer For t l c Silica Gel G was used as the adsorbent, 9 1 (*v*/*v*) carbon disulfide–ethyl acetate as the solvent, and 19.1 (*v*/*v*) methanol–sulfuric acid as the spray reagent Triisopropyl phosphite was obtained from Mobil Chemical Co , Richmond, Virginia For reference purposes, 1,2-*O*-isopropylidene-α-D-glucofuranose 5,6-carbonate[6], bis(1,2 5,6-di-*O*-isopropylidene-α-D-glucofuranose) 3,3′-dithiobis(thioformate)[7], and bis(1,2 3,4-di-*O*-isopropylidene-α-D-galactopyranose) 6,6′-dithiobis(thioformate)[8] were prepared as described previously

*Monothiocarbonate salt of 1,2 5,6-di-O-isopropylidene-α-D-glucofuranose* (**1**) — Metallic sodium (1,5 g) was added to a solution of 5 g of 1,2 5,6-di-*O*-isopropylidene-α-D-glucofuranose in 50 ml of anhydrous ethyl ether After 12 h at 25° the solution was filtered, cooled to 5°, and saturated with carbonyl sulfide After the mixture had been kept for 15 min, the i r spectrum showed strong absorption at 1600 $cm^{-1}$, presumably due to $-O\overset{O}{\overset{\|}{C}}SNa$ Conversion into the monothiocarbonate was not complete, as evidenced by absorption for the hydroxyl group As expected, the monothiocarbonate salt decomposed on acidification to give the parent sugar

*Bis (1,2 5,6-di-O-isopropylidene-α-D-glucofuranose) 3,3′-[dithiobis(formate)]* (**2**) — The monothiocarbonate salt prepared from 5 g of 1,2 5,6-di-*O*-isopropylidene-α-D-glucofuranose in 50 ml of diethyl ether was cooled to 5° and crosslinked by the action of iodine solution (~0 1 N) that contained crushed ice. After evaporation, of the ether, a thin syrup precipitated, which was collected and dissolved in ethanol (20 ml) The title compound was precipitated from the ethanol solution by 200 ml of water and was, filtered off, and dried to yield 3.5 g of **2**, m p. 54–58°. $[\alpha]_D^{25}$ −32° (*c*, 1 acetone), $\lambda_{max}$ 1760 $cm^{-1}$ (C=O); the u v spectrum revealed no major maximum (ε 1,000 or more) in the range of 190–390 nm

*Anal* Calc for $C_{26}H_{38}O_{14}S_2$ C, 48 9, H, 6 0, S, 10 0 Found C, 49 4, H, 6 3, S, 9 8

*1,2 5,6-di-O-isopropylidene-3-O-[methylthio(carbonyl)]-α-D-glucofuranose* —The monothiocarbonate salt obtained from 5 g of 1,2 5,6-di-*O*-isopropylidene-α-D-glucofuranose in 50 ml of ether was mixed with methyl sulfoxide (10 ml) and methyl iodide (5 ml) The mixture turned turbid immediately, and after a few min, a solid (sodium iodide) settled from the solution The mixture was extracted with ether and the extract washed with water and dried Evaporation of the ether gave a syrup that solidified on standing and crystallized from ethanol–water to yield 3 g of the title compound, m p 77–78°, $[\alpha]^{25}_{D}$ −35° (*c* 3, acetone); $\lambda_{max}$ 1750 cm$^{-1}$ (strong)

*Anal* Calc for $C_{14}H_{22}O_7S$ C, 50 3, H, 6 6, S, 9 6 Found C, 50 4, H, 6 8, S, 9.5.

*1,2-O-Isopropylidene-α-D-glucofuranose 5,6-carbonate* (**4**) — (*A*) A solution of **2** (0 8 g) in glacial acetic acid (40 ml) was diluted with water (10 ml) The mixture was kept for 1 h at 45–50° for during which time complete hydrolysis of the 5,6-*O*-isopropylidene group was achieved (t l c ) Excess solvent was evaporated at 40–45° to give a thick syrup, which was dissolved in pyridine After a few min, the pyridine was evaporated to yield a white crystalline mass that was washed with carbon disulfide to remove elemental sulfur (characterized by elemental analysis) and then washed with water (25 ml) The residue (222 mg) was recrystallized from alcohol and identified as **4** by elemental analysis and by comparison with an authentic sample (m p , i r and t l c ,) The water extract was evaporated to give a crystalline product which, after recrystallization from ethyl acetate, gave 150 mg of 1,2-*O*-isopropylidene-α-D-glucofuranose, identified by comparison with an authentic sample (i r and m p )

(*B*) A solution of 1,2 5,6-di-*O*-isopropylidene-3-*O*-[methylthio(carbonyl)]-α-D-glucofuranose (300 mg) was treated with acetic acid as in part *A* After evaporation of the solvent, the product was treated with triethylamine (1 ml) On being kept for 6 h (an obnoxious odor developed), a crystalline product precipitated, which was washed with water and dried, yield 95 mg The product was recrystallized from ethanol to give the title compound, identified by m p and i r spectrum Previously **4** had been conveniently prepared in high yield by treatment of 1,2-*O*-isopropylidene-α-D-glucofuranose in methyl sulfoxide–triethylamine with *O,O'*-diethyl dithiobis(thio formate)[6]

*Bis(3-O-carbonyl-1,2 5,6-di-O-isopropylidene-α-D-glucofuranose) monosulfide* (**6**) — To a solution of **2** (1 1 g) in diethyl ether (33 ml), isopropyl phosphite (630 mg) was added dropwise with stirring After 30 min, excess reagent and solvent were evaporated in a hood to give **6** as a colorless syrup which crystallized on scratching the surface of the flask The yield was 650 mg after recrystallization from ethanol, m p 128–129°, $[\alpha]^{25}_{D}$ −52° (*c* 1, chloroform), $\lambda_{max}$ 1740, 1765, and 1810 cm$^{-1}$ (C=O), $\lambda^{KBr}_{max}$ (1765 and 1810 cm$^{-1}$)

*Anal* Calc for $C_{26}H_{38}O_{14}S$ C, 51 5, H, 6 3, S, 5 3 Found C, 51 8, H, 6 2, S, 5 3

Under conditions similar to those used for **2**, the thiocarbonyl analogue **7** reacted with triisopropyl phosphite to give the corresponding xanthoanhydride **8** in 70% yield The product (110 mg), which was characterized by comparison with an authentic sample, gave on heating for 15 min at 170° 55 mg of the corresponding known thionocarbonate (**9**)

*Bis(3-deoxy-1,2 5,6-di-O-isopropylidene-α-D-glucofuranos-3-yl)3,3′-carbonate* (**5**) — Compound **2** (800 mg) was kept for 30 min at 120° in the presence of pyridine (0 3 ml) The mixture was cooled and excess pyridine was evaporated off T l c showed a major component corresponding to **5** together with a minor one that corresponded to the parent sugar alcohol Crystallization of the mixture from ethanol–water gave **5** (350 mg), characterized by elemental analysis and by comparison with an authentic sample (t l c and i r )

Previously **5** had been prepared by reaction of 1,2 5,6-di-*O*-isopropylidene-α-D-glucofuranose with phosgene or by oxidation of the thinocarbonate analogue of **5** with lead tetraacetate[8]

Heating **2** in a sealed ampule for 2 h at 180–210° led to a mixture of several products, one of which corresponded (t l c ) to **5** On the other hand, heating **6** (110 mg) under similar conditions led to **5** in high yield (90 mg)

*Decomposition of dithiobis(thioformates) of 1,2 5,6-di-O-isopropylidene-α-D-glucofuranose and of 1,2 3,4-di-O-isopropylidene-α-D-galactopyranose* — Heating bis(1,2 5,6-di-*O*-isopropylidene-α-D-glucofuranose)3,3′-[dithiobis(thioformate)] (**7**) without pyridine (up to 200°) or with pyridine (up to 130°) for 2 h gave a mixture of products that contained only a trace amount of the dimeric thionocarbonate **9** Heating bis(1,2 3,4-di-*O*-isopropylidene-α-D-galactopyranose) 6,6′-[dithiobis(thioformate)] (270 mg) for 1 h at 190-210° gave the corresponding thionocarbonate (45 mg), characterized by comparison with an authentic sample (m p , u v , i r , and t l c ) A higher yield of this thionocarbonate resulted when the 6,6′-[dithiobis(thioformate)] (1 5 g) was heated for 30 min at 180° in the presence of pyridine (0 1 ml) After cooling, the product was extracted with 3 ml of acetone (to remove elemental sulfur), and the extract was concentrated to a syrup that crystallized from alcohol to yield 730 mg of the thionocarbonate Previously, this thionocarbonate had been prepared by reaction of thiophosgene with 1,2 3,4-di-*O*-isopropylidene-α-D-galactopyranose[9]

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