Note

# Reactions of a sugar chlorothioformate*

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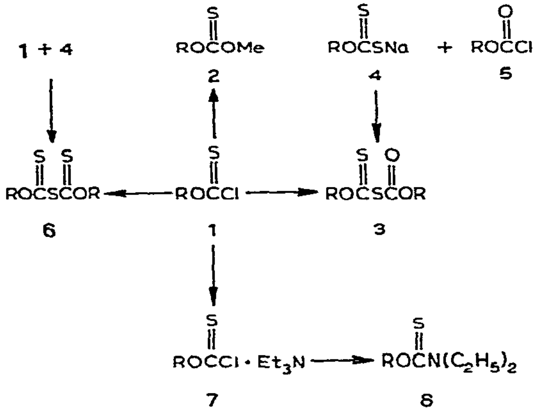
Recently[1] we described a method for the preparation of chlorothioformic esters of sugars, by treating a sugar dithiobis(thioformate) with chlorine to give the corresponding bis(*O*-chloromethylsulfenyl chloride) and then treating the latter with sodium iodide to afford the chlorothioformate. Now we report some reactions tha 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose 3-chlorothioformate (**1**) undergoest



R = 3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose-3-yl

## RESULTS

*With methanol.* — Treatment of **1** with methanol in presence of pyridine as catalyst gave the corresponding 3-*O*-methoxythiocarbonyl derivative (**2**) in high yield. Previously[1,2], **2** had been prepared by treating bis[(3-*O*-chloromethylsulfenyl chloride)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose] disulfide or bis(1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose) 3,3′-[dithiobis(thioformate)] with methanol in the presence of pyridine.

*With pyridine.* — Compound **1** decomposed in the presence of pyridine to give different products depending on the ratio of pyridine to **1** employed. In the presence

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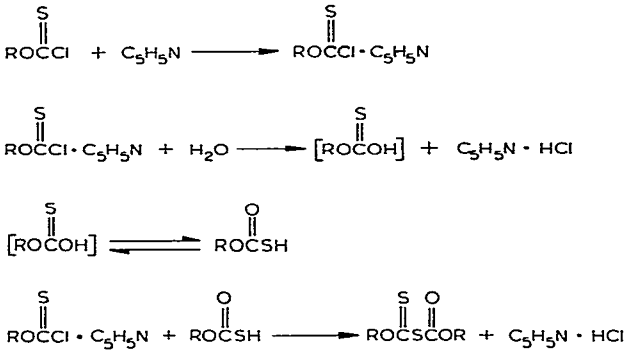
of one molar equivalent of pyridine, a major product was formed (t.l.c.) which was isolated and characterized as 3-*O*-carbonyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose 1,2:5,6-di-*O*-isopropylidene-3′-*O*-thiocarbonyl-α-D-glucofuranose monosulfide (**3**). The structure was formulated on the following basis: elemental analysis gave the correct empirical formula of $C_{26}H_{38}O_{13}S_2$; the i.r. spectrum showed characteristic absorptions at 1025 and 1250 $cm^{-1}$ for —O(C=S)S— and at 1760 $cm^{-1}$ for $\rangle$C=O. On treatment of a dilute solution of **3** with alkali, the u.v. absorption maximum shifted from 278 nm to 304 nm, which is again characteristic for the presence of the —O(C=S)S— group. As expected, on acidification of the alkaline solution of **3** the xanthate group was decomposed and the peak at 304 nm disappeared. Finally, the structure of **3** was proved by its independent synthesis from 1,2:5,6-di-*O*-isopropylidene-3-*O*-(*S*-sodium dithiocarbonyl)-α-D-glucofuranose (**4**) and 3-*O*-(chloroformyl)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**5**).

A possible mechanism for the formation of **3** is as follows:



$$\mathrm{RO\overset{\overset{S}{\|}}{C}Cl} + \mathrm{C_5H_5N} \longrightarrow \mathrm{RO\overset{\overset{S}{\|}}{C}Cl\cdot C_5H_5N}$$

$$\mathrm{RO\overset{\overset{S}{\|}}{C}Cl\cdot C_5H_5N} + \mathrm{H_2O} \longrightarrow [\mathrm{RO\overset{\overset{S}{\|}}{C}OH}] + \mathrm{C_5H_5N\cdot HCl}$$

$$[\mathrm{RO\overset{\overset{S}{\|}}{C}OH}] \rightleftharpoons \mathrm{RO\overset{\overset{O}{\|}}{C}SH}$$

$$\mathrm{RO\overset{\overset{S}{\|}}{C}Cl\cdot C_5H_5N} + \mathrm{RO\overset{\overset{O}{\|}}{C}SH} \longrightarrow \mathrm{RO\overset{\overset{S}{\|}}{C}S\overset{\overset{O}{\|}}{C}OR} + \mathrm{C_5H_5N\cdot HCl}$$

R = 3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose-3-yl

When **1** was treated with excess pyridine, **3** could not be observed by t.l.c. and instead a yellow spot appeared on the plate. The yellow component was characterized as bis(1,2:5,6-di-*O*-isopropylidene-3-*O*-thiocarbonyl-α-D-glucofuranose) monosulfide (**6**), by elemental analysis, i.r. and u.v. spectra, and by its independent synthesis by treatment of **1** with **4**. When pyridine was added to **3**, t.l.c. showed the presence of **6**. Presumably, **3** is an intermediate in the formation of **6**.

*With triethylamine.* — Treatment of an ethereal solution of **1** with triethylamine gave a crystalline compound (**7**) that was soluble in water and insoluble in ether. It gave correct elemental analysis for the triethylamine salt of **1**. N.m.r. analysis [$D_2O$ as a solvent and sodium 4,4-dimethyl-4-silapentane-1-sulfonate as internal standard] showed a multiplet centered at $\tau$ 8.62, which corresponded to 21 protons (nine protons of the triethylamine and 12 protons of two isopropylidene groups), and a quartet centered at $\tau$ 6.11 for six protons.

When a solution of **7** in acetone was heated in the presence of triethylamine or kept at room temperature for a few days, it gave the corresponding 3-diethylthiocarbamate (**8**). The structure of **8** was deduced from elemental analysis and from comparison of **8** (i.r., u.v., and n.m.r. spectra) with an authentic sample[1].

## EXPERIMENTAL

*General.* — N.m.r. spectra were recorded with a Varian A-60* n.m.r. spectrometer. Melting points were determined with a Fisher–Johns apparatus and are uncorrected. Optical rotations were measured at 24° with a Rudolph polarimeter. I.r. spectra were determined with a Perkin–Elmer Model 137 spectrophotometer as Nujol mulls or films cast onto silver chloride plates, and u.v. spectra were recorded with a Perkin–Elmer Model 202 spectrophotometer. Silica Gel G was used as the adsorbent for t.l.c. The eluent was 8:2 (v/v) carbon disulfide–ethyl acetate and the spray reagent, 19:1 (v/v) methanol–sulfuric acid. Microscope slides served for qualitative tests and 10 × 20 cm glass plates, for preparative t.l.c. Compound **1** (ref. 1) and the corresponding 3-chloroformate[3] (**5**) were prepared as described previously. Commercial reagents were used without further purification.

*1,2:5,6-Di-O-isopropylidene-3-O-methoxythiocarbonyl-α-D-glucofuranose* (**2**). — A solution of **1** (100 mg) in methanol (5 ml) was treated by dropwise addition of a solution of methanol (5 ml) containing pyridine (100 mg). After 10 min, t.l.c. showed only one component, having an $R_F$ value the same as that of **2** (0.48). After the solvents had been evaporated, the product was isolated by extraction with ether; yield 88 mg (87%). The i.r. and u.v. spectra were indistinguishable from those of **2** reported earlier[1,2]; $[\alpha]_D$ −44° (*c* 1, chloroform).

*3-O-Carbonyl-1,2:5,6-di-O-isopropylidene-α-D-glucofuranose 1,2:5,6-di-O-isopropylidene-3-O-thiocarbonyl-α-D-glucofuranose monosulfide* (**3**). — (*a*) To a solution of **1** (200 mg) in ether (5 ml), pyridine (47 mg) in ether (5 ml) was added dropwise. After 10 min, glacial acetic acid (3 drops) was added and the mixture was evaporated to a thin syrup, which was extracted with ether. Evaporation of the ether gave 150 mg of residue which, according to t.l.c., contained one major component (**3**) having $R_F$ 0.45. Purification was achieved by preparative t.l.c., $[\alpha]_D$ −44° (*c* 1, acetone).

*Anal.* Calc. for $C_{26}H_{38}O_{13}S_2$: C, 50.2; H, 6.1; S, 10.3. Found: C, 50.4; H, 6.3; S, 10.2.

The i.r. spectrum of compound **3** showed absorptions characteristic of the xanthate group at 1025 and 1250 cm$^{-1}$ and the u.v. spectrum had a maximum at 277 nm (ε 11,200) in ethanol. On treatment of a diluted solution of **3** with alkali the u.v. spectrum showed a maximum at 304 nm (xanthate) which disappeared on acidification.

(*b*) A solution of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (1 g) in methyl sulfoxide (1 ml) was treated with carbon disulfide (1 ml) and sodium hydroxide (5M, 1 ml). The mixture was kept for 10 min, and then neutralized (acetic acid), and

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treated with 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose 3-chloroformate (400 mg) in *p*-dioxane (1 ml). After 10 min, t.l.c. showed two spots having equal intensity. One of the spots $R_F$ having the value of **3** was isolated and characterized as **3** by sulfur analysis, i.r., and u.v. spectra.

*Bis(1,2:5,6-di-*O*-isopropylidene-3-*O*-thiocarbonyl-α-D-glucofuranose) monosulfide* (**6**). — (*a*) A solution of **1** (100 mg) in ether (3 ml) was treated with pyridine (0.2 ml). After 10 min, t.l.c. plates revealed a yellow spot ($R_F$ 0.44), which was isolated by preparative t.l.c. to yield 30 mg of the title compound, $\lambda_{max}^{EtOH}$ 310 (ε 11,500) and 240 nm (8,300).

*Anal.* Calc. for $C_{26}H_{36}O_{12}S_3$: C, 49.0; H, 5.9; S, 15.0. Found: C, 48.9; H, 6.1; S, 14.8.

(*b*) A solution of the sodium salt of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (200 mg) in ether (5 ml) was treated with excess carbon disulfide. The xanthate, which precipitated immediately from ethereal solution, was added to a solution of **1** (76 mg) in ether (2 ml). After 10 min, t.l.c. showed mainly one component which was isolated by preparative t.l.c. and characterized by t.l.c., u.v. and i.r. spectra, and sulfur analysis as **6**; yield 92 mg (64%).

(*c*) A solution of **3** (137 mg) in ether (5 ml) was treated with pyridine (0.2 ml). The color of the solution changed from light yellow to dark yellow and t.l.c. showed two components, which corresponded to **6** and 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose. The ether was evaporated and the residue washed with water. Compound **6** was isolated by preparative t.l.c. to yield 42 mg (30%), characterized as in part (*b*).

*Reaction of* **1** *with triethylamine.* — To a solution of **1** (165 mg) in ether (5 ml), triethylamine (150 mg) was added. Precipitation occurred immediately. The mixture was kept for 15 min and then the precipitate was filtered and washed with ether to give a white solid (205 mg), which was soluble in water and insoluble in ether. It was characterized by sulfur analysis (Found: S, 7.4%; calc. 7.3%) and n.m.r. data (see text) as compound **7**, the triethylamine salt of **1**; m.p. 69–73°, $[\alpha]_D$ $-28°$ (*c* 1.3, 30% acetone), $\lambda_{max}^{H_2O}$ 240 nm (ε 6,550).

A solution of **7** (300 mg) in acetone (5 ml) containing triethylamine (100 mg) was refluxed for 2 min and a gas collected from the reaction flask was identified by mass-spectral data as chloroethane (mass peaks at 64 and 66 for chloroethane, containing chlorine isotopes 35 and 37, respectively). The reaction mixture was concentrated to a syrup and extracted with *n*-hexane (5 ml). The extract was first washed with water and then concetrated to a syrup to yield 238 mg (93%) of product, characterized as the corresponding diethylthiocarbamate (**8**), $[\alpha]_D$ $-38°$ (*c* 2.7, *p*-dioxane), $\lambda_{max}^{ethanol}$ 253 nm (ε 13,200), $\nu_{max}$ ~1500 cm$^{-1}$ (thiocarbamoyl).

*Anal.* Calc. for $C_{17}H_{29}NO_6S$: C, 54.4; H, 7.7; S, 8.5. Found: C, 54.2; H, 7.8; S, 8.6

Compound **8** was also obtained when **7** was kept overnight.

Previously **8** had been prepared by reaction of [3-*O*-(chloromethylsulfenyl chloride)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose] disulfide with triethylamine and by reaction of bis(1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose) 3,3′-[dithiobis-(thioformate)] with diethylamine.

## ACKNOWLEDGMENTS

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## REFERENCES

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